

edited by
Mostafa Nejati
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Annals of Medicine and Healthcare Research

*Proceedings of the 2009 International
Online Medical Conference*



Universal-Publishers

Annals of Medicine & Healthcare Research

Proceedings of the 2009 International Online Medical Conference (IOMC 2009)

Editors
Forouzan Bayat Nejad
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*With forewords by
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Universal Publishers
Boca Raton, Florida • USA
2009

ISBN-10: 1-59942-908-X
ISBN-13: 978-1-59942-908-3
www.universal-publishers.com

Foreword

Wellness & Well-being

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Achieving wellness and hence well-being is the ultimate goal of every human being. On the global scale this is articulated through the Millennium Development Goal (MDG) of the United Nations. Three out the eight MDG provisions directly deal with enhancement and improvisation of health and medical components. At the personal level, it is widely acknowledged that the largest determinant of wellness is health. Holistically, the term health within the context of wellness embraces social, economic, political, physical, spiritual, and mental components. Its hierarchy of societal continuum extends from the person through the community to the nation and global entities. Consequently medical and health issues need to be addressed at each of these levels, on the global scale. Diseases and impairment know no boundary. Understanding, measuring, evaluating, diagnosing, and prognosing are the essential tools of learning and implementing effective and efficacious intervention strategies and tactics. Every domain of knowledge, as explored and articulated in the conference and the ensuing book, is pertinent. New and renewed information are critical in the process of addressing health and wellness issues: including nanotechnology, biology, biochemistry, ecology, medicine, medical practice, traditional health and its practice, physical sciences, cognitive sciences, neurosciences, spiritual enhancers, information communication technology (ICT), and the measuring-analyzing-evaluating tools (diagnostic, mathematic, statistic). As such medical and health

issues are pervasive, of persistent concern, and impact on everyone in every community. The need for community-based social-cultural health action strategy, as predicated primordially on the premises articulated in the Ottawa Health Promotion Strategy of 1986, is evidently implicated here. Moreover the World Health Organization (WHO) 2008 Report stressed the overriding importance of primary health, which dominates community or public health concerns, especially in the rural areas.

Life being a dynamic entity, we are witnessing the evolution of biological characteristics and impactful action of many disease causing organisms. Despite man's impressive progress through science and technology, no disease-causing organism has been subdued forever, let alone being exterminated or driven to extinction. On the contrary, resurgence and reemergence of deadly scourges and plagues, both silent and ostentatious, prevail. Our research explorations need to be in tandem with the pace of evolution and dynamic changes in nature's ecological processes. Biological and ecological changes and changing environment are the very essence of life. As such continually-updated evidence-based-knowledge is most relevant to ensure that medical and health theory and practice stay relevant and current with time. This is a tall order especially for the developing and poor countries. With limited resources these countries need to depend mostly and largely on global open accessed knowledge and information.

Consequently, the role of the International Online Medical Conference (IOMC) and its web entity is timely and pertinent. With the advent of real-time online colloquiums, workshops, newsletter, and impending web-based journal, IOMC is expanding its entity and it is fast emerging as a world-class educational portal and knowledge forum especially for the medical and health domains. Its online 24/365 availability and accessibility are a testimony to its resolve and resilience to becoming a repository and virtual centre of education. As educated men in this era of knowledge society, we deeply know that such endeavour deserves applause and compliments. The

overwhelming success of IOMC second conference (2009) as further evidenced by its ensuing book publication is another major landmark contribution towards developing a global knowledge society. The involvement of every delegate to the global conference is laudable. This second book also simultaneously delineates IOMC's achievement in embedding an online map or ontology of interactive knowledge provision and dissemination involving every committed stakeholder and beholder. After all health and its knowledge and ramifications are everyone's concerns.

A Crucial Role for Health Promotion in the 21st Century

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At a time when healthcare costs are soaring worldwide, the emphasis is placed on prevention to try to contain and hopefully reduce them, particularly in the USA. The cornerstone of prevention is awareness and the gateway to comprehensive population health management is health risk assessment (HRA). The aggregate data gathered from HRAs provide a road map for delivering health promotion and disease management interventions to targeted individuals, which aim at improving clinical and financial outcomes. Science-based information is essential to successful health initiatives. The Stanford Prevention Research Center and the Stanford Health Improvement Program (HIP) have been at the forefront of the preventive field at every step of health promotion: Designing an HRA called the Stanford health and lifestyle assessment and administering it to staff, faculty and their families and disseminating it state-wide, nationally and internationally; Creating motivation assessment tools; Assessing readiness for change; Developing and implementing health promotion programs; Providing primary, secondary and tertiary prevention to the Stanford population and the community-at-large.

Medicine is only at the infancy of adopting really cost-effective prevention as the mainstay of healthcare. Indeed, the most productive and novel approach is to think globally but to operate locally. Although we have nation-wide figures and profiles, they can be misleading and induce erroneous prioritization, design and implementation of health promotion programs resulting in wasted resources. A good example of potential pitfall would be smoking cessation programs. The

average percentage of current adult smokers was 19.8% in the United States population in 2007 whereas it was only 3.7% among the 13,546 benefits-eligible employees at Stanford in 2008. Similarly, smoking prevalence is declining in several developed countries but it is rising in many developing countries. Furthermore, men and women are often unevenly consuming tobacco in different milieus. The mode of consumption may also differ. Therefore, the need for accurate and relevant information is urgent on a whole range of health issues. With the availability of HRAs on the internet as well as intranets, statistics can be collected and analyzed and baselines established on various scales and in a prompt manner. Additionally, HIP can provide proven experience and expertise in health promotion to deciders, policy makers and opinion leaders globally. We hope that the know-how we have accumulated over the last twenty six years will be tapped by those who can benefit from it.

IOMC & Our Vision

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The IOMC organizes an annual online conference (<http://www.iomcworld.com/>) where participants from all over the globe present their papers and research using web conferencing. The 2nd annual conference held on March 14 & 15, 2009 received over 100 abstracts and full papers with topics ranging from infectious disease management in India to health policy in Bosnia. The Scientific Committee of the IOMC was delighted to see this rich exchange of information at the conference and unanimously felt that the IJCRIMPH was an idea whose time had come.

On behalf of the Editorial Board, we are pleased to introduce the first issue of the International Journal of Collaborative Research on Internal Medicine and Public Health (IJCRIMPH). As the official publication of the International Online Medical Council (IOMC), the IJCRIMPH provides a forum for clinicians, researchers and policy advocates in medicine and public health to publish not only their research, but also discussions and commentaries on current topics of general interest.

As the official publication of the IOMC, the journal will review submissions from authors who participated in the online conference. Furthermore, we also want the journal to serve as a resource for trainees and young professionals world-wide, to introduce them to the peer-review process and make medical publication a less onerous undertaking. We have assembled an editorial board of scientific reviews of wide-ranging specialties. The journal has so far been indexed in the EBSCO Academic

Search Premier, IndexCopernicus Journals Master List, Open J-Gate, Medical Journals Index (MJI), SJSU Library Catalog, GFMER, getCITED and the Standard Periodical Directory. It is hoped that the web-based open-access online format of the journal will be particularly helpful for readers where resources may be scarce.

None of this would have been possible without the initiative, drive and resourcefulness of the Executive Editor, Mr. Mostafa Nejati, who conceived the IOMC in 2007 and remains the driving force behind the annual online conference and the journal.

We look forward to this and your contribution to the issues of the IJCRIMPH.

For more information please see <http://iomcworld.com/ijcrimph/>

Table of Contents

Hypercoagulability Due to Protein S Deficiency in HIV-Seropositive Patients	16
Molecular Biology and Genetics in Morphogenesis of Colorectal Adenomas	28
Total Wrist Arthroplasty in Patients with Dysfunctional Wrists	51
The Effects of Supra-Nutritional Dose of Sodium Selenite on Chemically Induced Hepatocarcinogenesis in Male Rats	69
Gastrointestinal parasite infections among school children in displaced areas	87
Renal Dysfunction Following Myocardial Infarction	101
HFE Gene Mutations Among β -Thalassemia Intermediate and β -Thalassemia Minor Individuals in Gaza Strip, Palestine	115
Evaluation of Knowledge and attitude of professional athletes and coaches toward AIDS in Iran	123
Study of Influence Indol-3-Carbinol, Epigallocatechin-3-Gallate and Soy on Proliferation Diseases of the Reproductive System in Women	137
Treatment of Equine Foot in Cerebral Palsy: a study carried out in a Romanian hospital	150

Cytoprotective Effect of <i>Nigella sativa</i> L. on Experimentally Induced Gastric Ulcer in Rats	164
Study of Common Myths and Misconceptions in Management of Animal Bite Cases among Patients Attending Antirabies Vaccination (ARV) Clinic at Indira Gandhi Government Medical College (IGGMC), Nagpur	177
Secretory IgA concentrations in uterine lavages of ewes are influenced by the stage of the oestrous cycle	193
Visceral leishmaniasis and HIV co-infection in patients referred to Ahfad Biomedical Research Laboratory of Ahfad University for Women-Sudan during 2003-2007	200
What is the association between socioeconomic status and total risk of developing cardiovascular disease and death in patients in one rural family medicine clinic?	213
Anti-ulcerogenic Activity of Aqueous Extract of <i>Ficus deltoidea</i> Against Ethanol-induced Gastric Mucosal Injury in Rats	226
A Comparative Study of Efficacy and Tolerability of Ibuprofen vs. Aceclofenac in Osteoarthritis of Knee Joint	236
Transformation in Education of Nurses and Medical Technicians in Past and Today in Federation of Bosnia and Herzegovina	283
Acute Appendicitis: Sensitivity, Specificity and Predictive Values of Ultrasonography	297

Finite Element Model of the Femur Bone	307
A Personal Computer-Based Undergraduate Medical School Curriculum Using SOLE	319
Telemedicine and Medicine Vending Machine for Efficient Health Care, Diagnosis and Treatment	337
Contribution of the Earlier Orthoses in the Obstetrical Brachial Plexus Palsy Management	357
Hearing Aid Implementation through Teeth	373
Wound Healing Activity of Solanum Torvum Aqueous Fruit Extract in Rats	385
Preventing Automobile Accidents in Epilepsy Patients	401
Wound Healing Activity of Aqueous Extract of Allium Sativum L. in Rats	412
Doppler Studies in the Individuals with Injuries around the Hip-Immediately after Injury and after Treatment	423
Cinnamtannin B1: A Small Compound Having Antidiabetes Properties	450
Injury Surveillance System Trial for Medical College Hospital Thiruvananthapuram	466
Application of Conducting Polymer Polyaniline in Biomedical Monitoring	495
Students' Opinion about Training in Primary Health Care	509

Student's Mental Health Literacy and Attitudes toward Depression: findings from a survey conducted at a Malaysian University	521
Sleep Habits and Academic Performance in Medical Students	526
Information Technology Knowledge in Nursing Profession	529
Alpha-lipoic acid and quercetin protect against methotrexate induced-hepatotoxicity in rats	531
Can CA 19-9 and CEA Predict Operability and Survival in Pancreatic Malignancies?	533
Peculiarities of Vascular Component of Communicative Systems in Rectal Adenomas	536
Chronic Infections and management setting in Drug addicts of MMT program in Pinang, Malaysia	541
Postmortem Investigations Following Human Immunodeficiency Virus Infection	543
Emerging Community-Acquired Methicillin-Resistant Staphylococcus Aureus Pneumonia	545
Nitric Oxide and eNOS Gene in Essential Hypertension	548
Tungiasis: A Neglected Health Problem in Rural Cameroon	551
Prevalence of Depression and its Correlates among Unskilled Workers in Al Ain, United Arab Emirates	555

Adverse events following immunization (AEFI) surveillance in Tehran West Health Centre between march 2006 to October 2008	559
Defining Health	566
Attitude and Awareness of Male Attendees of a Tertiary Care Level Hospital in India Regarding Prevention of Parent to Child Transmission of HIV Infection	572
Rethinking the Rules of the Game: Leadership and Strategic Planning Process in Health Development - A Universal Message	574
A Common Surgical Condition with a Devastating Outcome in Rural Australia: a case report on a mis-diagnosed appendicitis	575
Predictors of Mortality and Morbidity in Clostridium Difficile Infection	577
Rural Community Health Carnival: Screening for Chronic Disease Risk Factors in Jeli, Kelantan, Malaysia	579

Hypercoagulability Due to Protein S Deficiency in HIV-Seropositive Patients

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Abstract

Background: Thrombosis due to a hypercoagulable state is a serious clinical problem in HIV-infected individuals that can lead to life-threatening thromboembolic phenomenon. Reported causes of thrombophilia in HIV-infected subjects include antiphospholipid syndrome, increased platelet activation, elevated homocysteinemia, elevated plasma factor VII activity, lupus anticoagulant, activated protein C resistance, protein C deficiency, and acquired protein S deficiency.

Aims & Objectives: To report our experience with 12 HIV-seropositive subjects with laboratory-confirmed evidence of protein S deficiency, with and without venous or arterial thrombosis, and discuss the diagnostic approach to hypercoagulability in HIV infection, and the clinical management of thromboembolic complications in patients with protein S deficiency.

Methods/Study Design: A retrospective review of the medical records of 12 HIV-seropositive patients diagnosed with protein C and S deficiencies at the Lawnwood Regional Medical Center and Heart Institute, Fort Pierce, Florida, from July 2005 through December 2005. All patients were seen by one of the authors (DO), an infectious diseases consultant. Lawnwood Regional Medical Center is a 341-bed, acute care institution and regional referral center for four counties of Treasure Coast, FL, USA.

Results/Findings: Seven subjects had symptomatic thromboembolic manifestations that included deep venous thrombosis (5 subjects), pulmonary embolism (4 subjects), inferior vena cava thrombosis (2 subject), and/or stroke (1 subject). An additional five patients were identified with asymptomatic protein S deficiency. All subjects were African-American. Mean patient age was 44 years (range, 21 to 60 years), and the male:female ratio was 5:7. The mean CD4+ cell count was 102 per mm³ (range 0-343), and the mean HIV RNA level was 71,772 copies/mL (range 1,421-554,237 copies/mL). Only three patients were receiving highly active antiretroviral therapy (HAART) at the time of clinical presentation. All symptomatic subjects received heparin, with or without warfarin, for their thromboembolic event and all but one recovered.

Conclusion: HIV-infected patients should be screened for acquired protein S deficiency, which contributes to hypercoagulability and risk of clinical thromboembolic events. Asymptomatic patients with reduced plasma free protein S levels may benefit from aspirin primary prophylaxis.

Keywords: Protein S deficiency, hypercoagulable, thromboembolic, HIV/AIDS

Introduction

Infection with the human immunodeficiency virus (HIV) is a type of hypercoagulable state that predisposes to the development of serious and potentially life-threatening thromboembolic disorders such as deep venous thrombosis, pulmonary embolism, and arterial thrombosis. Reported causes of thrombophilia in HIV-infected subjects include antiphospholipid syndrome (Shen & Frenkel, 2004), increased platelet activation (Shen & Frenkel, 2004), elevated homocysteinemia (Soentjens et al, 2006), elevated plasma factor VII activity (Soentjens et al, 2006), lupus anticoagulant (Majluf-Cruz et al, 2004), activated protein C resistance (Majluf-Cruz et al, 2004), protein C deficiency (Erbe et al, 2003; Majluf-Cruz et al, 2004), and acquired protein S deficiency (Bissuel et al, 1992; Erbe et al, 2003; Hassell et al, 1994; Pulik & Lebreton-Lerolle D, 1992; Soentjens et al, 2006; Sorice et al, 1994; Stahl et al, 1993; Sugerman et al, 1996). We herein report our experience with 12 HIV-seropositive subjects with laboratory-confirmed evidence of protein S deficiency, with and without venous or arterial thrombosis, and discuss the diagnostic approach to hypercoagulability in HIV infection, and the clinical management of thromboembolic complications in patients with protein S deficiency.

Patients and Methods

We retrospectively reviewed the medical records of 12 HIV-seropositive patients diagnosed with protein C and S deficiencies at the Lawnwood Regional Medical Center and Heart Institute, Fort Pierce, Florida, from July 2005 through December 2005. All patients were seen by one of the authors (DO), an infectious diseases consultant. Lawnwood Regional Medical Center is a 341-bed, acute care institution and regional referral center for four counties of Treasure Coast, FL.

Hypercoagulability testing was performed on all 12 subjects and included protein C and S assays, lupus anticoagulant, factor V Leiden, and antithrombin levels. Protein S and C deficiencies were the only coagulopathies detected. All subjects were

screened for common risk factors for thrombophilia including family history, immobilization, recent surgery, and thrombogenic medications. No patient had concurrent malignancy.

Results

Twelve HIV-seropositive with laboratory-confirmed protein S deficiency were identified, and their clinical features are summarized (Table 1). Isolated protein S deficiency was seen in 9 patients, and combined protein S plus protein C deficiency occurred in 3 subjects. Other primary or secondary risk factors for hypercoagulability were not present. Five patients were asymptomatic, and seven subjects had symptomatic, acute thromboembolic manifestations including: deep venous thrombosis plus pulmonary embolus (4 subjects), inferior vena cava thrombosis (1 subject), deep venous thrombosis plus inferior vena cava thrombosis (1 subject), and stroke (1 subject). Thromboembolic events were diagnosed using venous angiodiagrams and high resolution computed tomography (CT) of the lung or abdomen. No patient had previous thrombosis, family history of thrombosis, or prothrombotic conditions. The mean patient age was 44 years (range, 21 to 60 years), and the male:female ratio was 5:7. All subjects were African-American. The mean CD4+ cell count was 102 per mm³ (range 0-343), and the mean HIV RNA level, determined by polymerase chain reaction (PCR) testing, was 71,772 copies/mL (range 1,421-554,237 copies/mL). Only three patients were receiving highly active antiretroviral therapy (HAART) at the time of clinical presentation. All symptomatic subjects received heparin, with or without warfarin, for their thromboembolic event and all but one recovered.

Discussion

Infection with HIV is an independent risk factor for developing venous thromboembolic events.

But HIV is also associated with a variety of acquired coagulopathies that increase the incidence of venous and

arterial thrombosis, including antiphospholipid-anticardiolipin antibodies, increased platelet activation, elevated serum homocysteine levels, lupus anticoagulant, elevated plasma factor VII activity, activated protein C resistance, protein C deficiency, and protein S deficiency (Bissuel et al, 1992; Erbe et al, 2003; Hassell et al, 1994; Pulik & Lebret-Lerolle D, 1992; Majluf-Cruz et al, 2004; Shen & Frenkel, 2004; Soentjens et al, 2006; Sorice et al, 1994; Stahl et al, 1993; Sugerman et al, 1996). The prevalence of protein S deficiency among persons with HIV infection has been reported in 33% to 94% of patients with HIV infection (Bissuel et al, 1992; Hassell et al, 1994; Pulik & Lebret-Lerolle D, 1992; Sorice et al, 1994; Stahl et al, 1993; Sugerman et al, 1996). A study of protein S deficiency among 25 randomly-selected HIV-seropositive men found 19 subjects (76%) with decreased plasma free protein S levels, and this was a statistically significant difference compared to healthy male controls (Stahl et al, 1993). A decrease in protein S levels did not correlate with CD4+ cell count, CDC class, p24 antigen positivity, zidovudine use, or *Pneumocystis carii* prophylaxis, but a linear correlation was seen with duration of HIV infection. Sugerman and coworkers conducted a prospective laboratory evaluation of 34 HIV-infected children and detected free protein S deficiency in 76.5% of subjects; 55.9% had functional protein S deficiency levels < 2SD below the mean of laboratory controls (Sugerman et al, 1996). These authors found no association between protein S deficiency and CD4+ lymphocyte count, cy (CMV) status, HIV p24 antigen, von Willebrand factor antigen, IgG anti-cardiolipin antibodies, or serum beta-2-microglobulin levels. Similarly, a prospective study of 74 HIV-seropositive men found protein S deficiency in 33% of the cohort, with no significant association seen between protein S deficiency and medication use, opportunistic infection, or CD4+ cell count (Hassell et al, 1994). Bissuel et al. (1992) found plasma free protein S deficiency in 41 of 61 (65%) symptomatic and asymptomatic patients infected with HIV-1, and a significant decrease in plasma free protein S levels was observed in HIV-seropositive subjects compared

with healthy controls ($p = 0.0001$). In contrast to the above authors, however, protein S deficiency was associated with disease severity, namely CD4+ lymphocyte count and CDC class. Sorice and coworkers (1994) also found that protein S levels were significantly lower in patients with < 100 CD4+ cells/ul compared to those with higher counts.

Protein S deficiency may result in venous thromboembolic phenomena including deep venous thrombosis, pulmonary embolus, inferior vena cava thrombosis, renal or hepatic vein thrombosis, and intracranial venous and dural sinus thrombosis (Dillmon et al, 2005; Iranzo et al, 1998; Majluf-Cruz et al, 2004; Soentjens et al, 2006), as well as arterial thrombosis leading to stroke Majluf-Cruz, et al., 2004; Mochan et al, 2005; Mochan et al, 2003; Qureshi et al, 1997; Restrepo & McArthur, 2003; Wu et al, 2005). Still, there is a paucity of data on the incidence of clinical thrombosis in HIV-infected individuals with protein S deficiency. Previous literature studies have reported thrombotic events in 1.52% to 18% of HIV-infected patients with protein S deficiency (Majluf-Cruz, et al., 2004; Hassell et al, 1994), but we found a 58% incidence of clotting complications in our small study cohort. Hassel et al (1994) reported an overall incidence of thrombosis of 18% among 74 HIV-infected men, and thrombosis developed in 6.6% of subjects followed prospectively over a median follow-up of 12 months. Development of thrombosis was not significantly correlated with protein S levels. In a case-control study, Mochan and colleagues (2005) found protein S deficiency to be an epiphenomenon associated with HIV infection, and it occurred significantly more frequently in HIV-seropositive subjects compared to HIV-seronegative patients with ischemic stroke ($p < 0.001$). However, when they included HIV-positive patients without stroke as a control group and compared them with the HIV-seropositive stroke group they found that protein S deficiency was statistically related to HIV infection but not to stroke occurrence. Among 35 black South African heterosexuals with stroke, protein S deficiency was the most

common coagulopathy causing clinical clotting abnormalities (Mochan et al, 2003).

Highly active antiretroviral therapy (HAART) has altered the expected frequency of hematologic complications in HIV/AIDS (Sloand 2005). Today, acquired protein S deficiency is a relative rare complication of HIV in the US among persons taking HAART, but is much more common in developing regions of the world where antiretroviral treatment is not as widely available. Interestingly, however, the use of protease inhibitors (PIs) has been implicated as the cause of a hypercoagulable state in HIV-infected with myocardial infarction (Shen & Frenkel, 2004). Majluf-Cruz et al. (2004) reported a rate of thrombosis of 1.52% (cumulative incidence = 0.30% per year) during the 42-month follow-up period of their study of 28 HIV-positive male homosexuals with venous thrombosis, compared to a rate of 0.33% (cumulative incidence = 0.055% per year; $p < 0.001$) in 600 patients in the pre-PI era (Majluf-Cruz et al, 2004). Protein C and protein S deficiency was detected in nine and two patients, respectively, and lupus anticoagulant in one.

There is almost no literature on the management of HIV-seropositive patients with protein S deficiency and thromboembolism. In subjects with clinical thromboembolic events, we noted a good response to treatment with heparin, with or without warfarin. One previous study noted a high incidence of thrombotic recurrences and hemorrhagic complications using oral anticoagulants, and acetylsalicylic acid secondary prophylaxis was successfully employed (Majluf-Cruz et al, 2004). In view of the 58% risk of thromboembolism in our small series of HIV-seropositive patients, we suggest that screening of asymptomatic individuals may be indicated, and those with documented protein S deficiency may benefit from aspirin primary prophylaxis, at least.

The pathogenesis of this HIV-related protein S deficiency is poorly understood. Sorice and colleagues screened for specific anti-protein S antibodies using immunoblotting and showed an overall positivity of 28.6% in HIV-seropositive patients, with a

higher prevalence in symptomatic than in asymptomatic patients (Sorice et al, 1994). Furthermore, the prevalence of positivity for anti-protein S antibodies was higher in HIV-positive subjects with protein S levels < 50%. Another group evaluated the possible role of autoimmune mechanisms in the pathophysiology of HIV-related acquired protein S deficiency and detected anti-protein S antibodies in 31 (56.36%) of 55 HIV-1-positive patients vs. three (20%) of 15 control subjects ($p = 0.012$) (Lafeuillade et al, 1994). These antibodies were associated with a significantly low protein S activity compared to controls. Hooper and colleagues postulated that tumor necrosis factor (TNF)-downregulation of protein S may be a mechanism for local and procoagulant activity and thrombosis in patients with HIV/AIDS (Hooper et al, 1994).

Conclusion

HIV-infected patients should be screened for acquired protein S deficiency, which contributes to hypercoagulability and risk of clinical thromboembolic events. Asymptomatic patients with reduced plasma free protein S levels may benefit from aspirin primary prophylaxis.

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Table 1: HIV-seropositive patients with protein S deficiency, with and without thromboembolic features

Pt No.	Age (yrs)	Sex	CD4+ count (/mm ³)	Viral load (copies/ml)	HAART*	Thromboembolic features	Anticoagulation	Outcome
1	60	M	69	159,723	Yes	DVT ^a ; PE ^b	Heparin/ warfarin ^c	Recovered
2	51	M	-	1,421	Yes	IVC ^d thrombus	Heparin	Hematuria; hospice care
3	31	M	21	-	No	DVT; PE	Heparin/ warfarin w/ maintenance	Recovered
4	37	F	132	66,761	No	DVT; PE	Heparin/ warfarin	Recovered
5	49	F	40	28,100	No	Stroke	Heparin/ warfarin	Recovered
6	46	F	0	554,237	No	DVT; PE	Heparin	Died
7	35	F	12	33,191	No	DVT; IVC thrombus	Heparin/ warfarin	Recovered
8	44	F	343	231,411	No	None	-	-
9	44	F	24	60,856	No	None	-	-
10	33	F	2	126,767	Yes	None	-	-
11	48	M	170	43,114	No	None	-	-
12	51	M	106	21,721	No	None	-	-

* Highly active antiretroviral therapy

a Deep venous thrombosis

b Pulmonary embolism

c Heparin followed by warfarin

d Inferior vena cava

Molecular Biology and Genetics in Morphogenesis of Colorectal Adenomas

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Abstract

This paper highlights a concept on the main stages of development of colorectal adenomas determined as premalignant conditions, genetic pathways of formation of these neoplasms, and describes the epithelial-stromal interactions during oncogenesis. Special attention is paid to the morphogenesis of colorectal adenomas and preneoplastic conditions. The original scheme of morphogenesis of epithelial colorectal tumour is suggested and the increasing grade of epithelial dysplasia in adenoma is noted to be a leading prognostic factor, determining the dynamics of their development.

Keywords: Colorectal adenoma, genetics, morphogenesis

Etiology

In the appearance and development of colorectal adenomas (CRA) a significant role is played by genetic predisposition, along with exogenous and endogenous environment.

Heredity is the principal factor of familial adenomatous polyposis coli having autosomal dominant type of transmission, which is evidently proved by many investigations. As a result of mutation the oncosuppressor gene APC (adenomatous polyposis coli) on chromosome 5q21 is inactivated. These changes are transfer to the following generations. (Kumar,2004:24)

Endogenous factors are numerous ranging from various components of immune status to the age of a patient. Details of the latest investigations reveal that CRA are present about 20% in the fourth, 40% in the fifth and 50% in the sixth decade in patients living in developed countries. (Villavicencio,2000:45) One of the main constituent of this group is history of chronic ulcerative colitis. (Chen,2005:7) In the recent years it is actively considered that many tumors appear hormone-dependently. It is now known that estrogens have protective effect in the risk of colorectal cancer. (Chlebowski,2004:8)

Exogenous factors or carcinogens are traditionally subdivided into chemical, physical and biological. Amongst chemical carcinogens significantly noted are volatile fatty acids and nitrogen compounds. (Gerok,1999:12) Physical factors include various types of radiations and amongst biological factors, most often are considered papillomavirus, cytomegalovirus and Creutzfeldt-Jakob virus. (Jung,2008:21)

Morphogenesis

From the point of view of a morphologist and a physician, starting point of oncogenesis is considered as the preneoplastic conditions. These are pathological events that morphologically

are not characterized by features of atypism, but in some cases they lead to formation of tumor without transitional stages. Final stage of oncogenesis is progression of a malignant tumor. The number of transitional stages may include various numbers of steps.

The conditions that can be designated as preneoplastic for sporadic CRA are following:

1. Hyperplastic polyps in which the foci of dysplasia appear in about 2–5% of cases, which make it possible to consider them as morphological indicators of tumor growth in colorectal mucosa. (Snover,2005:40)
2. Long term chronic ulcerative colitis is a background for development of dysplastic foci in mucosa. (Schneider,1993:38)
3. Transitional mucosa which is localized between large tumor (adenoma, adenocarcinoma of colon) and unaffected mucosa. Transitional zone does not have signs of dysplasia, but demonstrates morphological characteristics, that are not specific to normal mucosa. Therefore it is considered as an intermediate stage in the development of adenoma. (Mori,1990:30)
4. Microadenoma, is a focus of epithelial dysplasia of mucosa, having one or more crypts, a synonym of aberrant crypt foci. (Nucci,1997:31) Microadenomas are able to grow, increase in size and also fuse with each other. All these processes lead to formation of a polyp, i.e. adenoma. Microadenoma is already a tumor and also a stage of subsequent growth of more manifested neoplasia.

Regions of adenomatosis are revealed in polyps in hereditary syndromes of polyposis of intestine (juvenile polyposis, hamartomous polyposis). (Wu,1997:49)

Another one conception of carcinogenesis is the theory “de novo” which explains development of tumor without any

preexisting lesions. (Hamilton,2000:14)

Progression of preneoplastic processes leads to neoplasia. There are two hypotheses that explain the dynamics of formation of CRA from the position of kinetics of transformed cells. (Wright,2002:48) According to the “top-down” hypothesis genetically altered cells on the surface of mucosa and the upper part of crypts proliferate and spread deeply and laterally. New crypts are formed, that are further capable to fuse with each other. Hypothesis “bottom-up” explains the transformation in the area of localization of stem cells, later to which population of transformed cells spreads from the bottom of the crypt to all its parts and forms monocryptous adenoma which eventually can fissure.

According to WHO histological classification, all CRA are subdivided into tubular (TA), tubulo-villous (TVA) and villous (VA). (Hamilton,2000:14) TA is an adenoma in which branching tubules surrounded by lamina propria comprise at least 80% of the tumor. VA is an adenoma in which finger-like processes of lamina propria covered by dysplastic epithelium comprise at least 80% of the tumor. TVA is an adenoma composed of both tubular and villous structures, each comprising more than 20% of the tumor. Recently, another morphological form was introduced, i.e. serrated adenoma, named according to the characteristic morphology of glands that resembles saw-toothed profile. (Longacre,1990:26) Macroscopic types of adenomas are as follows: exophytic (pedunculated and sessile polyps), flat and depressed. (Levine,2006:25) Polyp is a term for any growth protruding above a mucous membrane. Polyps can be readily seen by macroscopic examination or conventional endoscopy.

Dysplasia of epithelium is a necessary feature of any adenoma, and therefore this factor is certainly taken into account in histological conclusion and diagnosis. Also it tells the doctor about the prognosis of process. Classically three degrees of dysplasia are known: mild (D1), moderate (D2) and severe (D3). Currently, a new term intraepithelial neoplasia is

introduced to replace dysplasia. Intraepithelial neoplasia is a lesion characterized by morphological changes that include altered architecture and abnormalities in cytology and differentiation. Low-grade intraepithelial neoplasia corresponds to D1 and D2, and high-grade intraepithelial neoplasia includes severe dysplasia and carcinoma in situ. (Hamilton,2000:14)

Progression of CRA to colorectal cancer occurs in a period of 10–15 years, risk of formation of the latter depends on the following main prognostic factors: size of adenoma (risk of less than 1% at size less than 1 cm, diameter more than 2 cm promises the adenoma a 10% risk of malignization), histological type of neoplasia (TA in 5% of cases progresses to cancer, TVA in 15% and VA in 50% of cases) and degree of epithelial dysplasia. (Kelloff,2004:22) Such adenomas are called advanced and have not only high risk of malignization, but also are precursors of metachronous adenoma even after polypectomy (Winawer,2006:47)

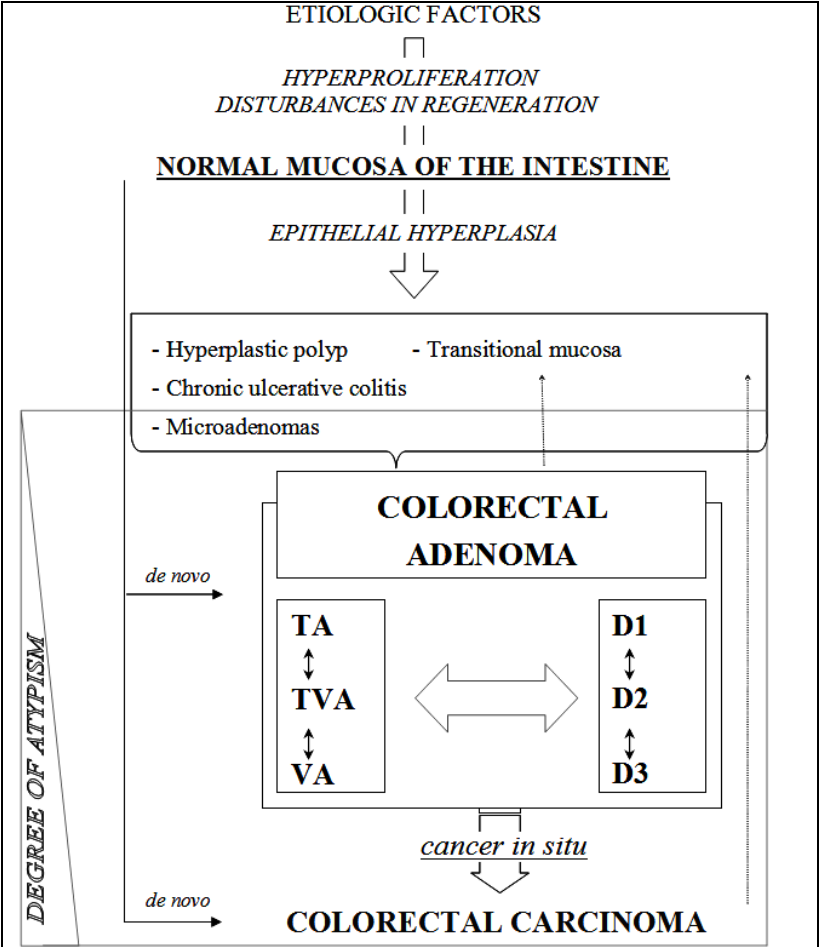
There is a predominance of mild dysplasia in TA, moderate degree is characteristic for TVA and severe in VA. (Rosai,2004:36) Dysplastic changes are dynamic and express the increasing intensity of atypism. And, if reverse transition D2 => D1 is possible, then regression D3 => D2 is sometimes considered to be impossible. (Offerhaus,1984:32) Dysplastic changes in most of the cases are accompanied with macroscopic growth of polyp and predominance of villous elements in its structure, i.e. TA => TVA => VA. In some cases not only VA possesses maximal potential of malignization but also TA and TVA capable of acquiring severe degree of epithelial dysplasia. Result of inevitable progression of such neoplasia will be a transition to invasive cancer after a stage of carcinoma in situ.

Therefore, the main prognostic characteristic of adenoma is considered to be the degree of epithelial dysplasia and not an increase in the size of tumor or transition from one morphological category to other (TA => TVA => VA).

The above mentioned facts are reflected in the following

scheme (Figure 1). These stages of changes are not categorical. On the level of histological types of adenomas and degree of epithelial dysplasia, any combinations are possible, and it is difficult to guess the sequence of oncogenesis. Moreover, tumor growth can stop at a moment, and in some cases even may regress.

Figure-1: Morphogenesis of epithelial colorectal tumors



Genetic basis

General considerations

Despite of a big number of factors that provoke neoplasia, all of them have similar influence on the organism. The transformation of normal cell in to a neoplastic cell due to the action of carcinogenic agents is possible only in the phase of proliferation and it is well known that the mucosa of colon is a self-renovating system. Oncogenesis from a current point of view is considered to be a stepwise process, which includes stages of initiation, promotion and progression. (Kumar,2004:24)

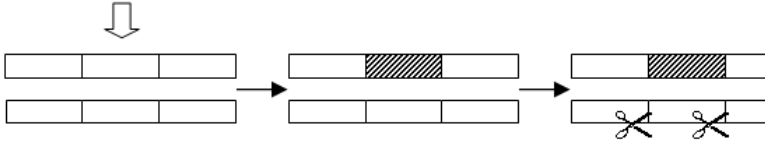
Recently it is accepted, that genesis of CRA and other colorectal tumors occurs due to the mutation in various genes. (Rosai,2004:36) Cause of several genetic defects is a fact that “path” of a colonocyte to histotopographical point of maximal apoptosis is 2–8 times longer than in enterocyte. (Arui,1998:3) It evidently increases the chances of mutation and similarly their subsequent summation.

Molecular rearrangements in the DNA lead to mutation in four main classes of genes: gene-oncosuppressors, genes of reparation, protooncogenes, and genes of molecules of cell adhesions. It is well known that other genes are also exposed to mutations but, these four classes determine the dynamics of the process. Mechanisms of abnormal activity of mutated genes are schematically presented below (Figure 2). Moreover, amplification, hypo- and hyper-methylation of DNA sequences may change the expression of gene without any appearance of mutation. (Henderson,1996:16)

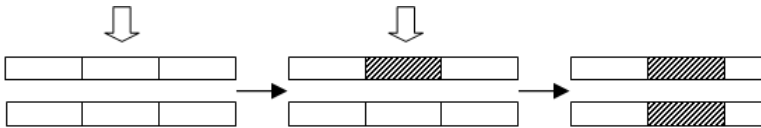
Figure 2: Mechanisms of abnormal activity of mutated genes

1. An allele of gene is exposed to mutation, while the complementary allele is deleted from the chromosome

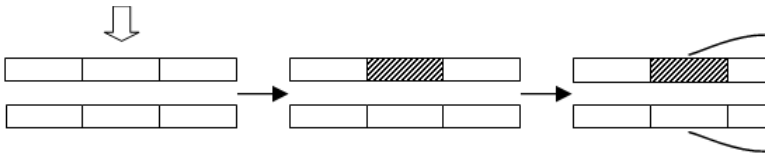
CARCINOGEN



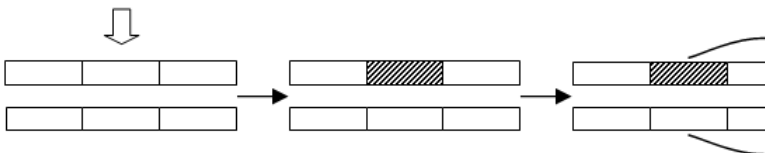
2. Mutation of gene in both the alleles



3. Inactivation of protein product of normal allele by pathological protein encoded by a mutant allele



4. Product of expression of mutated allele does not cause a biological effect, but overall “gene dose” reduces to half, which is insufficient for normal function



Characteristics of genes

Tumor suppressor genes. Gene APC. Location — 5q21. Encodes cytoplasmic protein essential for the activation of apoptosis in colonocytes. Mutation occurs according to the first type of mechanism (deletion). Consequence is cancel of programmed death of aged epithelial cells and further accumulation of mutations. Important property of the product of APC is down-regulation of β -catenine, that acts as regulator of transcription and adhesion, which is lost as a result of mutation and thus further promotes the activation of above mentioned processes. The most striking effects are manifested in patients with familial adenomatous polyposis coli, as the gene is passed vertically and is expressed in earlier periods. It is considered that the mutation of APC is a primary event in the transformation of a colonic cell to a neoplastic cell. (Lynch,2003:27) In that case, deletion of APC is the base for the subsequent stages of oncogenesis. Gene p53. Localization — 17p13.1. Encodes a nuclear protein that regulates the expression of genes that suppress the growth of cells with damaged DNA. Mutation occurs by third mechanism (deletion). As a result, there is an accumulation of constituent mutations that give selective advantage amongst other colonocytes. Mutation of gene p53 is an event that determines the malignant transformation of cells. (Sotamaa,2005:41)

Genes of reparation of DNA (MMR — mismatch repair genes). During colorectal oncogenesis the most often involved genes are MSH2 (2p21), the product of which reveals the damaged locus and MLH1 (3p31.23), which responds to ligation and resynthesis in the damaged strand of DNA. Rarely, mutations in the genes PSH1 and PSH2 are observed that code for proteins that ensures the activity of previous system. Mutation occurs by second mechanism. As a result, there is a high instability of genome, especially in the regions of microsatellite DNA. It is important to note that genes like Bax, APC and gene of receptor of II type TGF- β are localized in these regions that directly participate in the regulation of

proliferation and apoptosis. These changes are the cause of syndrome of hereditary nonpolyposis colorectal cancer. (Lynch,2003:27)

Protooncogenes. K-ras (12p12.1) encoding an oncoprotein that constantly signalizes the nucleus, which stimulates multiplication, is activated by third mechanism. This results into hyperproliferation of epithelial cells. There is significance for progression of adenoma, but not for its malignant transformation. (Glarakis,1998:13)

Genes of molecules of cell adhesions. DCC (18q23.3). Codes for a transmembrane protein of colonocytes that participates in the cell-cell and cell-matrix adhesion. Mutation occurs by fourth type (deletion). As a result there is weakening of contact inhibition and acquiring motility by tumor cell. It is considered as a weak prognostic factor. (Hara,2000:15)

Genetic pathways

It is important to note that a chronological pattern can be traced during the damage to the hereditary apparatus: APC => K-ras => DCC => p53 (first pathway is the pathway of suppressor genes). If the deletion of APC is inherited, the process begins from the birth and leads to a syndrome of familial adenomatous polyposis of colon. In sporadic cases the sequence of mutations starts in older ages when the carcinomas develop in the distal part of large intestine. During the realization of second mechanism (pathway of microsatellite instability) primary damages are in the system of mismatch repair genes. This involves mutations in Bax and APC genes (intersections with the previous cascades are possible here, but without involvement of K-ras). This pathway, similarly as the first is expressed in the hereditary syndrome like hereditary nonpolyposis colorectal cancer, which is characterized by formation of flat carcinomas in the right side of colon. (Marra,1995:28)

Currently, the idea about genetic mechanisms is yet more

detailed that are combined in 5 molecular pathways of colorectal oncogenesis: pathway of chromosomal instability, pathway of microsatellite instability with high and low levels of instability, pathway of hMYH and pathway of CpG islets methylation. (Jass,2007:20)

The pathway of chromosomal instability, which is specific for 80% of cases, is characterized by the presence of chromosomal changes that affect the short arm of fifth chromosome with inactivation of gene APC. Chain of the subsequent events includes loss of multiple allelic insertions and deletions, change in the total amount of DNA in the cell, and point mutations in genes K-ras and p53. (Fodde,2001:11) In that case, the given mechanisms lay a pattern which was denoted earlier for the pathway of suppressor genes.

The pathway of microsatellite instability is characterized by numerous mutations in multiple repeating sequences of DNA (microsatellites), but without aneuploidy and chromosomal changes. During this the microsatellite instability with high levels of instability is a classical type, the type with low level of instability is not well studied yet. (Mori,2003:29)

The pathway of hMYH is characterized by biallelic mutation in the gene of repair hMYH (in which the mutant allele is inherited from both the parents), that accompanies the disturbance in the process of restoration of damaged DNA and initiation of tumor growth. (Al-Tassan,2002:2) However, in these rare cases, the chromosomal and microsatellite instability are insignificant.

The pathway of CpG islets methylation is epigenetic and plays an important role in every third case of colorectal oncogenesis. (Ogino,2006:33) CpG islets in specific regions lead to suppression of gene expression. Therefore, if the gene MLH1 undergoes methylation than the subsequent changes will occur by the pathway of microsatellite instability. In the reverse situation chromosomal instability may develop.

Thus, from the above mentioned facts, molecular biological

parameters, details of cytogenetics and immunohistochemistry will reveal individual prognosis for every patient with colorectal neoplasia in the near future.

Peculiarities of epithelial-stromal complex

Characteristics of epithelial component

Colorectal adenomas are characterized by changes in their epithelial component that are known as atypism.

1. Atypism of cell division and differentiation: shortening of cell cycle, active proliferation (Bychkov,2008:6), increase activity of telomerase (Yoshida,1999:50), “dedifferentiation” of epithelial cells.
2. Antigenic atypism: increase in the levels of carcino-embryonic antigen. (Kelloff,2004:22) Increased expression of antigens such as IPO-38, p53, Ki-67, PCNA, CA-242, SIMA. (Abbaszadegan,2007:1) Such facts clarify role of monoclonal antibodies for diagnostics and differential diagnosis of neoplastic processes in colorectal mucosa.
3. Biochemical atypism: switch role of anaerobic glycolysis in the bioenergetics of a cell, increase synthesis of oncoproteins, decrease in the activity of certain enzymes (lactase, 5-nucleotidase, acidic phosphatase) in the tissues of adenomas. (Borkje,1987:5)
4. Physico-chemical atypism: acidification, hydration, decrease in surface tension, and increase in surface negative charge of cell. (Williams,1999:46)
5. Functional atypism: decrease in the secretion of mucus, change in the syalomucins and sulfomucin proportion. (Hara,2000:15)
6. Morphological atypism (cellular and tissue): Manifestations of cellular atypism: cellular pleomorphism, i.e. decrease in the number of goblet cells; nuclear pleomorphism (increase in size, hyperchromatism); increase in the nucleus-

cytoplasm ratio, displacement in the position of nucleus (Rosai,2004:36), increase in the number of nucleoli (Hennigan,1994:17), increase in the number of mitoses (Polyak,1996:34). Increase in the absolute and relative area of parenchyma, different changes in the stroma of tumor are the manifestations of tissue atypism.

Characteristics of stromal component

Stroma is composed of cell populations (fibroblasts, lymphocytes, plasma cells, macrophages, fibrocytes and others), extracellular matrix (basal membrane and interstitium), vessels and nerve terminals. Neoplastic cells participate in the formation of the stroma by the following mechanisms:

1. Production of cytokines that stimulate the multiplication of cells in the stroma (FGF, TGF).
2. Synthesis of the components of extracellular matrix (laminin, fibronectin) and their receptors. (Ioachim,1999:18)
3. Degradation and modification of components of matrix with metalloproteins, particularly MMP-7. (Boedefeld,2003:4)
4. Production of attractants that promote migration of haematogenous cells in the stroma of tumor, resulting into formation of cellular infiltration by CD4+ and CD8+ lymphocytes (with typical subepithelial localization) and macrophages. (Cui,2007:9; Tanaka,2006:43)

Angiogenesis in adenoma is influenced by stroma as well as by the epithelial component of tumor. It is evident due to the production of factors of angiogenesis (VEGF, bFGF, TGF- β 1, cyclooxygenases). (Boedefeld,2003:4) However, secretion of these products at this stage is not as significant as in the subsequent stages, therefore, it is more important that expression of angiopoetin-1 which prevents neoangiogenesis

decreases. (Shen,2006:39)

Epithelial-stromal interactions

In the epithelial-stromal complex of adenoma, many types of interactions (intercellular, cellular-matrix) are provided by the means of various molecular factors which modulate the morphogenesis of tumor. The basic groups of factors of interactions are oncogenes and antioncogenes, molecules of adhesion, components of extracellular matrix and soluble mediators.

A significant decrease in the levels of integrins VLA-2, VLA-3, VLA-5 is described. (Stallmach,1992:42) Also, there is disturbance in the expression of L-CAM from the family of cadherins, which is considered as early event in the tumor growth. Molecules of L-CAM support the integrity of epithelial monolayer and their levels decreases significantly during growth of adenoma. (van der Wurff,1992:44) APO-1 (CD 95) is the surface cell receptor that transmit apoptotic signal after binding with a specific ligand and it is lost at the progression of adenomas. (Reipert,2005:35) The extracellular matrix undergoes changes such as the proportion of collagen of I and II type and fibronectin are increased and the distribution of laminins vary according to their molecular mass. (Gerok,1999:12)

The intensity of stromal infiltration influence on the expression of mediators produced by immune cells, i.e. the expression of interleukins like IFN- γ , IL-4, IL-5, IL-6, IL-8, IL-12, IL-18, TNF- α is increased. (Rubie,2007:37) In patients with CRA there is also an increase in the serum levels of proinflammatory cytokines TNF- α and IL-6. (Kim,2008:23) These facts reveal the close relation between inflammation and tumor growth and thus explains the use of anti-inflammatory agents for the prophylaxis of colorectal cancer. (Levine,2006:25)

Communicative systems

Years of research in the peculiarities of epithelial-stromal interactions in various neoplastic processes allows introducing a concept of communicative systems, composed of microcirculatory vessels, nerve terminals and their cellular microsurrounding. (Dorosevich, 2002:10) These histophysiological complexes combined as one is often considered individually as parenchymatous and stromal structures. According to this concept, all the elements of parenchyma and stroma are studied as the components of communicative systems where the main reference points are microcirculatory vessels and vegetative nerve terminals. Changes in the stromal component of a tumor are accompanied by the parenchymal rearrangements and sometimes they are the leading ones. On a genetic level, it is revealed that chromosomal and microsatellite instability is characteristic not only for epithelial cells but also for stromal cellular elements of CRA. (Ishiguro,2006:19) A study for past 20 years has shown that the changes in the system “epithelium-stroma” occur synchronously. Peculiarity of each stage of tumor growth was characterized by a specific dynamic of cell population of stroma.

Mathematical analysis of cellular microsurrounding of vascular and nerve component of communicative systems allows revealing on the light-microscopic level of those intercellular correlations, which usually are interpreted on a more deep level of investigation. And thus, micromorphometric indicators further prove to be prognostic factors. Also it is revealed that the changes in the stroma of a tumor may predict its behavior.

Conclusion

Introduction of methods of molecular biology and immunohistochemistry in the pathological practice dictates the necessity of knowledge of a pathologist about molecular genetic peculiarities of pathological processes. It is shown that, it is important to reveal the genetic and molecular biological

rearrangements in the epithelium, which is a base for further tumor growth.

The concept of synchronization of parenchymatous and stromal components of CRA currently received a confirmation at a genetic level. Model of growth of colorectal cancer is considered one of the best studied and assumes the existence of not only precancerous conditions (adenomas) but also earlier stages of oncogenesis, so called preneoplastic conditions (precursors of adenomas).

The value of determination of prognostic factors of CRA on a light microscopic level is possible only at a parallel study of parenchymatous and stromal components of a neoplasia that confirms the study of morphogenesis of the mentioned tumors from a position of communicative system.

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This study was performed by the financial support of Russian Humanitarian Scientific Foundation in frame of scientific research project No. 07-06-58606a/C.

Total Wrist Arthroplasty in Patients with Dysfunctional Wrists

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Abstract

Background: The wrist is essential for augmentation of fine motor control of the hand and fingers. The normal wrist motion involves a complex interaction of multiple articulations from the radius, ulna and carpal bones. Hence, when a disease process disrupts any one of these elements, a painful, deformed and dysfunctional wrist arises. Total wrist arthroplasty is considered an alternative surgical option to wrist fusion for the management of advanced wrist arthritic diseases. Though less commonly performed in comparison to lower-limb arthroplasty, wrist arthroplasty has its role as a salvage procedure to alleviate pain and to preserve function in the wrists.

Method: Four patients were collected from the Centre of Hand Surgery, and medical records of these patients were reviewed. The patients were carefully selected through multiple interviews and medical consultations. The patient's pre- and post-operative functional status was closely followed over an average period of five years to ensure the continuity of progress. A summary table was formulated to provide an

objective survey of both quantitative and qualitative improvement of a patient's wrist function.

Results: The four patients underwent wrist arthroplasty received different types of prostheses. This is an indication of a lack of universal acceptance of wrist anatomy and biomechanics. Regardless, all patients in this study series had improved functional outcomes and satisfactory results from their total wrist arthroplastic procedures. Pain-relief was the most successful aspect of wrist arthroplasty during post-operative follow-ups. The successful outcome of these patients in the case series has proven that total wrist arthroplasty can provide pain relief and an improvement in hand function through appropriate patient selection, careful peri-operatively planning, sound operative technique and well-designed postoperative hand therapy.

Introduction

The wrist is essential for augmentation of fine motor control of the hand and fingers (Volz & Robert, 1977). The normal wrist motion involves a complex interaction of multiple articulations from the radius, ulna and carpal bones (Anderson et al., 2005). Further to the importance of normal functioning of the wrist is the balance that exists between the soft tissues, the wrist flexors and extensors in particular. When a disease process disrupts any one of these elements, a painful, deformed and dysfunctional wrist arises. Rheumatoid arthritis is by far the most common pathology causing wrist joint destruction, followed by degenerative osteoarthritis and less commonly psoriatic arthritis and other autoimmune diseases (Lawler et al., 2006).

Total wrist arthroplasty has been developed as an alternative to arthrodesis to allow pain free function of the wrist while more importantly preserving range of motion. The goals of a total joint arthroplastic procedure are to provide long-term pain relief, to achieve a stable fulcrum and to restore functional range of motion (Huang et al., 2002). Total wrist arthroplasty is no exception. Since the first documented wrist replacement by Gluck in 1890 (Huang et al., 2002), advances in design, material and operative techniques are still based on a fundamental principle of a joint prosthesis: to imitate the anatomical and physiological construct of a normal joint. Such a concept is critical to achieving a successful wrist arthroplastic operation with prosthetic longevity.

This study reviews four patients who underwent total wrist arthroplasty using various types of prostheses. Each individual case is analysed with pre- and post-operative comparative figures and radiography. The study also acknowledges any alternative management options undertaken by the patients pre-operatively, a reminder to the readers that many of the disease progress affecting the wrists also carries significant systemic morbidities and a devastating impact on a individual's quality of life.

Materials and Methods

The four patients in this study all had total wrist arthroplastic procedures and were assessed pre- and post-operatively by Associate Professor W. B. Conolly at the Centre of Hand Surgery. The patients were also reviewed by the hand therapists associated with the Centre of Hand Surgery for pre- and post-operative rehabilitation. An insight into these patients' progress was made possible through medical records and wrist radiographs. Variants, such as documentation bias, were minimised as all of the patients were from one surgical centre and were assessed by the same surgeon.

Studies, which evaluate specific wrist prostheses based on their success and failure rate, (Huang et al., 2002; Lorei et al., 1997; Rossello et al., 1997; Volz & Robert, 1977) were applied as background knowledge to formulate a summary table for the purpose of this study. A number of criteria are employed to help categorise indications, anatomy, operative techniques, types of prosthesis, complications and subsequent revision surgery. Furthermore, the table has a comparative purpose to allow documentation of the pre- and post-operative status of a patient's wrist function (Table 1). The table is designed not only to assess the quantitative advancement of the wrist joint post-operatively, but also to appreciate any qualitative improvement during a patient's recovery (Table 2).

Table 1: Pre- and post-operative status of a patient's wrist function

	Indication	Anatomy	Prosthesis	Operative technique	Other relevant operations
Patient 1	<ol style="list-style-type: none"> Sever rheumatoid arthritis (RA) Pain 	Left radiocarpal joint	Mayo Clinic implant	<ol style="list-style-type: none"> Uncemented Dorsal capsule repaired 	<ol style="list-style-type: none"> Swanson MP implants in 4 fingers Thumb MP ligament repair
Patient 2	<ol style="list-style-type: none"> RA Stiffness Weakness Pain 	Right radiocarpal joint	Swanson's prosthesis with titanium grommets	<ol style="list-style-type: none"> Uncemented Proximal row carpectomy Dorsal capsule repaired 	
Patient 3	<ol style="list-style-type: none"> RA Pain Stiffness Swelling 	Right radiocarpal joint Right radioulnar joint	Biaxial prosthesis	<ol style="list-style-type: none"> Cemented Proximal row carpectomy Dorsal capsule repair 	<ol style="list-style-type: none"> Darach's procedure Extensor synovectomy
Patient 4	<ol style="list-style-type: none"> Osteoarthritis Stiffness Weakness Pain 	Left radiocarpal joint Left radioulnar joint	Biaxial prosthesis	<ol style="list-style-type: none"> Cemented Proximal row carpectomy Dorsal capsule repair 	<ol style="list-style-type: none"> Darach's procedure

Table 2: Qualitative improvement during a patient's recovery

	Post-op pain level	Function	ROM pre-op*	ROM post-op	Complication
Patient 1	None	Improved		Flex/Ext 50/45 45	Superficial wound infection
Patient 2	Mild	Improved	Virtually None	Flex/Ext 15/5 Pro/Sup 25/18	None
Patient 3	None	Improved	Flex/Ext 50/30** Pro/Sup 80/70**	Flex/Ext 30/15 Pro/Sup 80/70	Stiffness MUA***
Patient 4	None	Improved	Flex/Ext 44/30 Pro/Sup 90/10 RD/UD 22/22**	Flex/Ext 44/44 Pro/Sup 78/80 RD/UD 15/20	Ulnar bony spur

* ROM: range of motion

** Flex/Ext: flexion/extension

** Pro/Sup: pronation/supination

** RD/UD: radial deviation/ulnar deviation

*** MUA: manipulation under anaesthesia

Case studies

Patient 1

A 75 year-old female patient underwent total wrist arthroplasty of her left wrist. She had suffered from long-standing severe rheumatoid arthritis with bilateral wrist involvement. Stiff, painful wrists and a loss of grip strength were the main complaints. After having minimal success from non-operative treatments such as physiotherapy and analgesic medication, she sought operative options.

She underwent a number of procedures. A total left wrist arthroplasty with an un-cemented Mayo Clinic implant was performed. A standard dorsal approach was used. In addition, Swanson's metacarpophalangeal (MP) joint implants were used to replace the severely destructed metacarpophalangeal joints in her 2nd, 3rd, 4th and 5th fingers. The MP joint of the thumb was unstable due to severe inflammatory changes and ligament laxity. This was managed by ligament repair. Soft tissue integrity was closely observed and preserved to ensure good coverage of the joints and to achieve better joint stability.

The patient was followed up over a course of 16 months. The operation was complicated by one episode of superficial *Staphylococcus aureus* wound infection at one month post-operation. The infection settled with one course of oral antibiotics. The functional assessment at 12 months post-operatively showed a reasonable pain-free range of motion of 45 degrees wrist extension and 50 degrees flexion. The wrist was stable and showed no signs of prosthetic displacement both clinically and radiographically. The grip strength, however, had minimal improvement at sixteen months. The patient continued to receive hand therapy for strengthening exercises.

Patient 2

A 74 year-old right hand dominant female patient underwent right total wrist arthroplasty using the Swanson prosthesis with titanium grommets via a standard dorsal approach in 1993. Rheumatoid arthritis had caused extensive joint destruction to both of her wrists and upper limbs (Figure 1). Stiff, painful and weak wrists were impairing the quality of life. The patient also revealed great concerns about her diminishing mobility since she could no longer rely on her right hand to use her walking aid.

The patient demonstrated minimal relief of symptoms with physiotherapy and analgesic medication. The right wrist showed virtually no flexion nor extension. The patient then underwent a number of less invasive procedures including steroid injections and one attempt of manipulation under anaesthesia (MUA) in 1987. With short-lasting result, she then proceeded to synovectomy and silicone sheet interposition of the right wrist later that year. As rheumatoid arthritis continued to cause irreversible destruction to multiple joints in the hand including the radio-ulnar and radiocarpal joints, the patient underwent right index and middle finger proximal interphalangeal joint replacements, the resection of distal ulna and silastic sheet interposition arthroplasty of the right radioulnar joint in 1989.

Meanwhile, the patient had left wrist resection implant arthroplasty with silicone interposition sheet and additional distal ulna resection in 1990 to combat the disease progress in the left wrist.

Troubled by persistent pain and a limited range of motion in the right wrist, the patient underwent right total wrist arthroplasty in 1993 as a salvage procedure (Figure 2). The operation went successfully with no complications. The patient was followed-up over a course of 5 years, and already at 8 months post-operatively, she had a pain-free right wrist capable of 15 degrees of flexion, 5 degrees of extension, 25 degrees of pronation and 18 degrees of supination. The wrist

showed marked increase in grip strength and an overall improvement in function. The patient continued to undertake physiotherapy focusing on wrist extension. The joint was stable both clinically and radiologically with no signs of prosthetic loosening or displacement.



Figure 1: A radiograph showing severe rheumatoid arthritis in the right wrist.

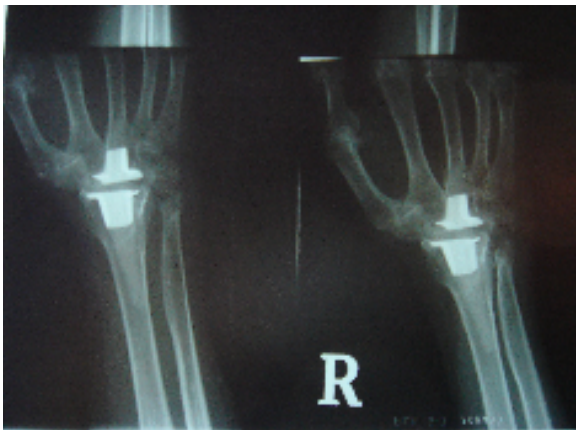


Figure 2: A radiograph showing the Swanson type prosthesis with 2 titanium grommets in the right wrist.

Patient 3

A 69 year-old right hand dominant female patient suffered from rheumatoid arthritis in both upper limbs and lower limbs, especially in hands and feet. She had retired from work, but was still active at home and only required minimal assistance with housework. Though her rheumatoid arthritis was well controlled by weekly methotrexate and daily low dose prednisone, the pre-operative x-ray of both wrists already revealed significant destructive changes in all joints especially in radiocarpal and intercarpal joints. Clinically, both wrists, more so in the left, were unstable with wrist joint subluxation at radiocarpal joints. In addition, the wrists were painful, stiff and markedly swollen.

In 1995, the patient first underwent left wrist arthrodesis via an intramedullary rod, and the thumb metacarpophalangeal jointed was fused. The result was a pain-free stable left wrist.

In 2000, troubled by pain in the right wrist, patient underwent total wrist arthroplasty of her right wrist with a cemented biaxial module along with extensor synovectomy and distal ulnar resection via a standard dorsal approach (Figure 3). Pre-operatively, the right wrist was able to perform 30 degrees of flexion, 30 degrees of extension, 80 degrees of pronation and 70 degrees of supination, and it had a grip power of 6 kilograms. The operation resulted in the resolution of pain; however, the wrist continued to be stiff and was slow to respond to hand therapy. Despite diligent physiotherapy, the right wrist exhibited 15 degrees of flexion and extension and uneasy forearm rotation 4 months post-operation.

The patient later returned to the theatre for MUA of the right wrist in the view to optimise the function of the biaxial prosthesis, and to mobilise the wrist from potential scar tissues as a result of the operation. The outcome was a wrist with 30 degrees of flexion, 15 degrees of extension, 80 degrees of pronation and 70 degrees of supination. The patient was

encouraged to continue wearing a protective splintage and practicing mobilisation and strengthening exercises.

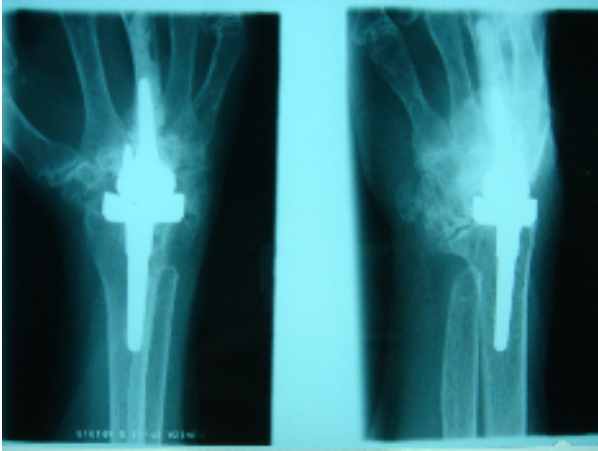


Figure 3: A radiograph showing a cemented biaxial prosthesis and distal ulna resection on the background of a severe rheumatoid arthritic right wrist

Patient 4

A 75 year-old right hand dominant female patient, with debilitating osteoarthritis of both wrists and multiple joints in the fingers, was reviewed at the clinic. The wrists were painful and stiff on examination. In addition, there were early symptoms of carpal tunnel syndrome with positive Tinel's sign over median nerves. At the time of the presentation, the patient was living a low-demanding life style with regular home services.

With no relief from conservative treatments, the patient underwent right wrist arthrodesis with right iliac bone graft at the age of 71. The right wrist remained pain-free post-operatively.

In 2000, the patient returned for an operative option for the

left wrist as osteoarthritis further progressed. The pre-operative x-ray revealed generalised osteoporosis and severe osteoarthritis changes in radiocarpal joint (Figure 4). There were also signs of reactive sclerosis of the scaphoid and distal radius. A subsequent bone scan concurred with the x-ray findings. The patient was offered a total wrist arthroplasty with the use of a cemented biaxial prosthetic module, which included the resection of the proximal third of carpal row and distal ulna (Figure 5). The post-operative recovery was uneventful.

The wrist remained pain-free after 24 months, and the patient was discharged from the hand therapy clinic with a satisfactory 44 degrees of flexion and extension, 78 degrees of pronation, 89 degrees of supination, 15 degrees of radial deviation and 20 degrees of ulnar deviation.

Midway through her 6 year follow up, the patient started to experience pain whilst performing ulnar deviation of the left wrist, alongside with symptoms of carpal tunnel syndrome. The x-ray showed some bony irregularity in the distal radioulnar joint; the wrist was otherwise stable. A reactive bony spur was the likely diagnosis. The carpal tunnel was injected with corticosteroid. The patient later underwent surgery for resection of the ulnar bony spurs.



Figure 4: A radiograph showing severe degenerative osteoarthritic destruction in the left wrist, PIP joints and DIP joints of all fingers

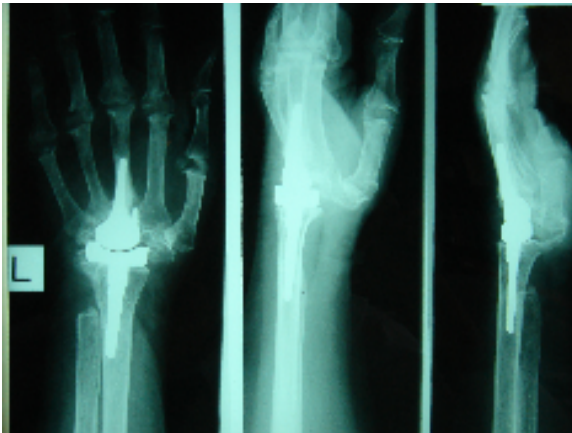


Figure 5: Plain radiograph showing the left wrist post total wrist arthroplasty (TWA) with a cemented biaxial implant. In addition to TWA, the patient also underwent distal ulna osteotomy, and received Swanson metacarpo-phalangeal joint replacement in other fingers

Discussion

All four patients in this study series had improved functional outcomes and satisfactory results from their total wrist arthroplastic procedures. Three patients suffered from long-standing rheumatoid arthritis, while one had degenerative osteoarthritis affecting the wrists. A variety of implants were used. In two cases, cementing techniques were applied in accordance to the type of the prosthesis.

At follow-up, pain relief was the most successful aspect of total wrist arthroplasty. Minimal or no pain was reported in all of the patients. Though one patient developed reactive bony spurs causing pain on ulnar deviation, the pain resolved with a simple resection procedure of the osteophytes. The improvement in stability of the wrist joint was also universally found in these patients. Functional gain, including improved range of motion and grip strength, from the total wrist arthroplasty was augmented with regular hand physiotherapy tailored to the individual patient.

The reason behind these successful total wrist arthroplasty in these patients is three-fold. Firstly, there were strict selection criteria. Patients were carefully selected based on their underlining disease progress and their base-line activity level. Three patients suffered from rheumatoid arthritis, and their disease progress had been closely monitored and well-controlled with medications. Studies show that patients with rheumatoid arthritis are found to be more favourable for total wrist arthroplasty, as in comparison to those with systemic lupus erythematosus induced jointed destruction which predisposes to joint laxity (Carlson & Simmons, 1998).

In addition, high-demand patients or heavy labourers are noted to be contraindicative to wrist arthroplasty (Costi et al., 1998; Murray, 1996). All of the patients in the study were retired or not working. They lived a lifestyle of low-demanding activities; nevertheless, they all had a good level of independence pre-operatively. Two of the patient had undergone wrist arthrodesis of their contralateral wrist prior to having total

wrist arthroplasty, in an attempt to maintain their independence. Many studies have found good outcomes with the concept of patient undergoing arthodesis in one wrist and total arthroplasty in the other (Cooney et al., 1984; Lawler et al., 2006). With this operative combination, patients can have one completely stable wrist joint and one wrist with a wider range of motion to optimise the quality of their lives.

Secondly, the operative technique played a important role in the successful outcome of total wrist arthroplasty in this study. As Huang et al. suggest, functional wrist motion is dependent upon adequate tendon structure and mechanical wrist balance (Huang et al., 2002). Soft tissue balance across the wrist and joint anatomy need to be preserved during a joint replacement operation to minimise the rate of implant failure. All of the four wrist arthroplastic operations in this study followed the conventional dorsal approach to allow exposure of the extensor tendons. The patients were assessed pre-operatively for tendon damages or tension imbalance in the wrists. In some cases, extensor tendons were repaired, and in all cases, dorsal capsules were repaired. The bone quality was also observed during pre-operative planning. As some studies suggest, long lasting fixation of an uncemented prosthesis is dependent solely on bony ongrowth on the implant surface (Cooney et al., 1984; Lorei et al., 1997). One patient with severe osteoporosis went on to have a cemented biaxial prosthesis, and the end result was a long-lasting stable prosthesis.

Finally, careful patient selections and good operative technique were complemented by well-designed hand therapy protocols, which helped patient achieve their maximum level of functioning while protecting healing tissues and joint structures post-operatively. Total wrist arthroplasty is a salvaging operative technique for severely damaged wrists. All the patients in the study not only suffered from joint destruction but also related soft tissue inflammation, and they had all sought non-operative therapies such as hand-therapy prior to

undergoing total wrist arthroplasty. Pre-operatively, hand therapy aimed to provide pain relief and preservation of wrist function. Post-operatively, hand therapy protocols targeted the restoration of wrist moment without overstressing the articular and periarticular tissues (Lockard, 2004). These protocols included initial immobilisation, splinting, and followed by gentle active or active assisted range of motion exercises. Many of the patients continued to practice these exercise protocols for several years after their surgery.

Conclusion

As this study of case series reveals, there are several models with varying designs of total wrist arthroplastic prosthesis available. This indicates a lack of universal acceptance of wrist anatomy and biomechanics (Lawler et al., 2006). Regardless, total wrist arthroplasty is an attractive alternative to wrist arthrodesis for managing severely dysfunctional arthritic wrist joints.

The successful outcome of these patients in the case series has proven that total wrist arthroplasty can provide pain relief and an improvement in hand function through appropriate patient selection, careful peri-operatively planning, sound operative technique and well-designed postoperative hand therapy.

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The Effects of Supra-Nutritional Dose of Sodium Selenite on Chemically Induced Hepatocarcinogenesis in Male Rats

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Abstract

Background: Hepatocellular carcinoma (HCC) is one of the lethal cancers in the world, mainly in the developing countries. Selenium is an essential micronutrient mineral that found mainly in soils. The dose and effects of selenium on HCC are controversial.

Aims: The aim of this study was to investigate the effects of sodium selenite at a supra-nutritional dose (4 mg/L), using preventive and therapeutic approaches, on chemically induced hepatocarcinogenesis in rats.

Methods/ Study Design: Forty four male Sprague – Dawley rats (120 – 190 g) (6 – 8 weeks) were obtained from the Laboratory Animal Resource Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia (UKM), Malaysia, and divided randomly into six groups, six or eight rats in each group: negative control (normal rat chow and drinking water), positive control (Diethyl nitrosamine (DEN) + 2-Acetylaminofluorene (2-AAF)), preventive group (selenium at a dose of 4 mg/L for 4 weeks, then DEN + 2-AAF), preventive control (respective control for preventive group: selenium for four weeks but no DEN or 2-AAF), therapeutic group (selenium after four weeks of DEN injection) and therapeutic control (respective control for therapeutic group: selenium for eight weeks but no DEN or 2-AAF). Using the Solt and Farber model but without surgery, hepatocarcinogenesis was induced by a single intraperitoneal injection of DEN (200 mg/kg body weight) and two weeks later, the carcinogenic effect was promoted by 2-AAF (0.02%), which was incorporated into the rat chow. Hematoxylin and eosin plus Gordon and Sweets methods were used to stain liver tissues. Immunohistochemistry was used to stain Glutathione – S – transferase – placenta (GST-P).

Findings: During the entire period of study, no obvious physical changes or symptoms in hair, nails or skin were seen among all experimental groups. The numbers and sizes of hepatic nodules in preventive and therapeutic selenium treated groups were significantly decreased ($P < 0.05$) when compared with the positive control. Microscopic analysis of these two

groups showed that the majority of nodules were hyper-plastic with preserved liver architecture whereas the positive control was full of neo-plastic nodules with a completely disrupted liver architecture. Immunohistochemistry of GST-P showed that the number and surface area of nodules were significantly decreased ($P < 0.05$) in the therapeutic group only when compared with the positive control.

Conclusion: Selenium at a supra-nutritional level in the preventive and therapeutic groups was able to reduce, but not inhibit, the formation of liver nodules without toxicity.

Keywords: Selenium, HCC, GST-P

Introduction

Hepatocellular carcinoma (HCC) is common in the developing countries such as China, Korea and Africa (Parkin et al. 2005). Although, it is low in the developed countries, however, recent study of But et al. (2008) showed that HCC is increasing in the developed countries such as USA, UK and France. Chronic infection with hepatitis B and C are the major risk factors for HCC worldwide (El-Serag & Mason 2000). Other factors that contribute to the formation of HCC include exposure to aflatoxin, alcohol abuse, hemochromatosis, fatty liver disease and androgenic steroid use (Gurusamy 2007). It is important to mention that risk of any cancer in humans or animals is dependent on environmental, occupational and recreational exposure to carcinogens as well as spontaneous events must reflect species variation in the efficiency of various cancer critical processes (Kinoshita et al. 2006).

Diet and nutrition related factors play an important role in many diseases such as diabetes, cardiovascular diseases and many cancers (Key et al. 2004). One of the ways that thought to reduce the risk of cancer is the dietary intake of foods that is rich in antioxidant agents. It has been reported that diets high

in fruits and vegetables are associated with lower risk of many cancers such as stomach, colon and esophagus (Genkinger et al. 2004). It is important to note that although the protective relationship of fruits and vegetables is well documented, it is still unclear which specific elements within fruits and vegetables responsible for the beneficial effects (Willett 2000). In fact, general health recommendations are focused on the importance of well – balanced nutrition in preventing various diseases, including cancer (Vinceti et al. 2001). It has been suggested that food, which contains various antioxidants, including selenium, helps to protect against oxidative damage in the body (McCarty 2001).

Selenium occurs naturally in soil. It flows through the food chain from soil to plants and then to humans and animals (Whanger 2002). Thus, selenium content of food varies from one region to another, depending on the selenium content of the soil. It was thought that the anticarcinogenic activity of selenium could be associated with the nutritional requirement as certain selenoprotein enzymes are involved in antioxidant defense (Fahey et al. 1997). However, many studies have shown that selenium anticarcinogenic activity requires supra-nutritional concentrations that are much higher than required for the synthesis of selenoprotein enzymes (Kelloff et al. 2000; Ganther 1999; Ip 1998). It has been suggested that the dietary selenium intake (100 – 500 µg per day), above the Dietary Reference Intakes (DRIs), which is 55 µg per day (IOM 2000) is required for selenium chemoprevention (Clement 1998).

To date, the use of selenium in preventing or treating cancers is limited and controversial. Thus, the aim of the present study was to investigate the effects of sodium selenite at a supra-nutritional dose (4 mg/L) using preventive and therapeutic approaches on chemically induced hepatocarcinogenesis in rats.

Materials and methods

Chemicals

Sodium selenite, DEN, and 2-AAF were obtained from Sigma Chemical Co, Germany. Hematoxylin, eosin and silver nitrate from BDH, UK. Paraffin waxes, xylene, denatured ethyl alcohol and formaldehyde from MERCK, Germany. GST-P from MBL, Japan. Envision HRP labelled polymer anti-rabbit and DAB from DakoCytomation, Denmark. Ultra V Block and TBS with Tween 20 (20X) from LABVISION corporation, U.K.

Animals and diet

Male Sprague-Dawley rats (120 – 190 g) (6 – 8 weeks) were obtained from the Laboratory Animal Resource Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia. They were housed in plastic cages (3 – 4 rats per cage) with wood chips for bedding. The animals were acclimatized to standard laboratory conditions (temperature 22 – 25 °C, humidity 55 ± 10% with a 12 hour light-dark cycle) for one week before the commencement of the experiments. During the entire period of study, the rats had free access to food and water. According to the manufacturers of basal diet (Gold Coin Co, Ltd, Malaysia) , Mouse Pellet 702-P contains 0.2 mg/kg of selenium, which is within the recommended reference range. The recommendations of University Kebangsaan Malaysia Animal Ethics Committee (UKMAEC) for the care and use of animals were strictly followed throughout the study (UKMAEC No: FSKB/2006/Jamaludin/22- August/170-December-2006).

Experimental Design

Forty four rats were randomly divided into 6 groups, 6 or 8 rats in each group, as follow: Group 1 (negative control): rats were given normal rat chow and drinking water. Also, a single intraperitoneal (I.P) injection of saline (0.9%) was given. Group 2 (positive control): liver tumors were induced with a single I.P injection of DEN at a dose of 200 mg/kg body weight in saline

(Solt & Farber 1976). Two weeks after DEN administration, the carcinogen effect was promoted by 2-AAF (0.02%). The promoter was incorporated into the rat chow for 10 weeks. Group 3 (Preventive group): 4 weeks before DEN administration, rats were fed with sodium selenite (4 mg/L) through drinking water and stopped at week 4 (the day of commencement of DEN administration). Group 4 (Preventive control): rats in this group served as controls for group 3. Rats were given sodium selenite for 4 weeks only. No DEN or 2-AAF was given. Instead, a single I.P injection of saline (0.9%) was given. Group 5 (therapeutic group): 4 weeks after starting of DEN administration (as in Group 2), the rats were treated with sodium selenite (4 mg/L) through drinking water and this continued until the completion of the experiment (8 weeks). Group 6 (therapeutic control): rats in this group served as controls for group 5. Rats were given sodium selenite for 8 consecutive weeks. No DEN or 2-AAF was given. Instead, a single I.P injection of saline (0.9%) was given. 16 weeks after the initiation of the experiment, all the rats were fasted overnight and then killed by cervical dislocation under ether anesthesia. The amount of food and water intake was measured and the body weights of all rats were recorded once a week. Sodium selenite supplementation in drinking water and normal drinking water was renewed every 2–3 days. Diet with 2-AAF was freshly prepared and wood chips for bedding were changed weekly.

Histological Analysis

Immediately after sacrifice, all livers were taken, weighed and examined macroscopically for gross morphology. Nodules were identified from the reddish – gray background by their grayish–white color spots. The numbers and sizes of all nodules were measured in millimeters of diameter. The nodules were categorized into three groups according to their diameter (>1 mm, 1–3 mm and <3 mm) as described by Moreno et al. (1981). Representative pieces from each lobe of the liver were

cut and fixed in 10 % buffered formalin. Paraffin-embedded blocks were sectioned at a thickness of 4 μm and stained with hematoxylin and eosin and Gordon and Sweet's methods.

GST-P Immunohistochemistry

Paraffin sections of liver were dewaxed in xylene (3 changes), hydrated through graded concentrations of alcohol (100%, 95%, 70% and 50%) and then to water for 5 min. After the sections were washed with TBS and Tween 20 (20X) 3 times, 15 min each, they were incubated with 3% H_2O_2 for 30 min at room temperature to block endogenous peroxidase activities. The sections were washed with TBS and Tween 20 (20X) 3 times, 15 min each and incubated with ultra V Block for 5 min at room temperature to remove non-specific staining. After ultra V Block was drained and removed, but not washed, sections were incubated with GST-P 1:2500 diluted in TBS and Tween 20 (20X) at room temperature for 90 min. After washing with TBS and Tween 20 (20X) 3 times, 15 min each, sections were covered with 100-150 μL of Envision HRP labelled polymer anti-rabbit and incubated at room temperature for 30 min. After washing with TBS and Tween 20 (20X) 3 times, 15 min each, sections were covered with DAB solution for 3 min. After washing in running tap water for 5 min, sections were counterstained with Mayer's haematoxylin for 3 min and blued in running tap water for 5 min. Finally, the sections were dehydrated in alcohol, cleared in xylene and mounted in DPX. The sizes, numbers and areas of GST-P positive foci were measured by the KS-300 program (Zeiss, Germany) connected with an Olympus microscope (Olympus Optical, Japan) using a camera (Stemi, SV6, Japan) attached with a computer. Foci were considered positive for GST-P if there are greater than 0.2 mm in diameter (Ito et al. 1988). The number of GST-P positive foci was expressed as number per cm^2 and the area of GST-P positive foci was expressed as surface area (mm^2/cm^2) (Watanabe et al. 1994).

Statistical Analysis

Data were expressed as means \pm standard deviation (SD). The data were analyzed using Statistical Package for Social Sciences (SPSS) version 13. Shapiro-Wilk test was used to check the normality of the variable (Coakes & Seed 2003). Accordingly, Student's t and Mann – Whitney's U tests were used to analyze data that follow normal or non-normal behavior of distribution pattern, respectively (Mahajan 1997). Differences in statistical analysis of data were considered significant at $P < 0.05$.

Results

No obvious symptoms or changes in hair, nails or skin were seen among all groups of rats. Water intakes for all groups were 10.5 – 12.5 ml per 100 g body weight. However, food intakes differed; positive control, preventive and therapeutic groups had an average of 5.30 – 7.10 g per 100 g body weight whereas negative, preventive and therapeutic controls had an average of 9.20 – 11.0 g per 100 g body weight. For unknown reasons, 3 rats died before the end of the study, one from the preventive group (week 4), preventive control (week 5) and therapeutic control (week 5). The overall death rate was 6.82%.

In the positive control, there was a significant decrease in body weight compared with the negative control, and significant increase in liver and relative liver weights compared with the negative, preventive and therapeutic controls. The preventive and therapeutic groups showed a significant decrease in body weight and significant increase in liver and relative liver weights compared with preventive and therapeutic controls, respectively (Table 1). Treatment with selenium maintained the body, liver and relative liver weights in preventive and therapeutic controls when compared with the negative control. Thus, selenium at 4 mg/L had no side effects on the growth of rats. The total numbers of hepatic nodules were more pronounced in group 2 (422) as compared with group 3 (149)

or group 5 (135). In addition, preventive and therapeutic selenium treated groups largely reduced the numbers and sizes of the hepatic nodules (Table 2). Interestingly, preventive group inhibited the appearance of hepatic nodules, measuring more than 3 mm in diameter, and only 33 hepatic nodules, measuring 1–3 mm in diameter, were found. Also, therapeutic group carried similar effects with a total of only 6 nodules, measuring more than 3 mm in diameter, were found. Untreated with DEN and 2-AAF were free of hepatic nodules.

Macroscopically, rats in the positive control revealed enlarged and irregular livers with varying multiple grayish – white color spots on the liver surface. Cut surfaces of the liver nodules also showed many varying sizes of grayish – white spots. On the other hand, the preventive group (selenium for 4 weeks, then DEN + 2-AAF) and the therapeutic group (selenium after 4 weeks of DEN injection) showed less irregularity and enlargement of liver tissues with less grayish–white color spots on the liver surface. The negative, preventive and therapeutic controls were free of any apparent abnormality.

Histological analysis of the liver sections from the negative control revealed a normal architecture with normal liver parenchyma. The hepatocytes were small, dark and free of nodules. Preventive and therapeutic group controls exhibited similar liver architecture (Figure 1). On the other hand, the liver in the positive control (DEN + 2-AAF) showed a completely disrupted architecture. The liver was displaced with variably-sized neoplastic nodules. The hepatocytes were paler, showed enlarged vesicle nuclei with prominent nucleoli, and showed fine discontinuous reticular fibers (Figure 2). However, the preventive and therapeutic selenium treated groups revealed that the liver was nodular but largely preserved architecture (Figure 3). The majority of varying-sized nodules were hyperplastic with occasional neoplastic nodules. In comparison with the positive control, the number of these nodules was less.

The means, numbers and areas of GST-P positive liver foci are shown in Table 3. Rats in the negative, preventive and therapeutic controls did not develop any GST-P positive foci. Therapeutic group showed that there was a significant decrease in the number of foci per cm^2 (17.7) and surface area of foci ($0.04 \text{ mm}^2/\text{cm}^2$) when compared with the positive control 44.06 and $0.15 \text{ mm}^2/\text{cm}^2$, respectively. Although there was a decrease in means of foci, number of foci per cm^2 and surface areas of GST-P positive foci in the preventive group, but it was not a significant.

Discussion

The major aim of this study was to examine the preventive and the therapeutic effects of selenium on induced hepatocarcinogenesis in male rats. It has been reported that nearly all types of primary liver tumours known to occur in humans can be reproduced by chemicals in laboratory animals, especially in rats (International Conference on Harmonization 1997). In hepatocarcinogenesis, pre-neoplastic foci appear weeks or months before the appearance of HCC, and this led to the development of a number of *in vivo* models for the study of early neoplasia in rat liver (Farber & Sarma 1987).

The findings of the present study show that sodium selenite at a dose of 4 mg/L has reduced, but not inhibited, the development of the liver cancer in male rats. It must be clarified that inhibition in the initiation or prevention in the promotion stage of hepatocarcinogenesis by selenium treatment was not a total inhibition or prevention as the nodules present in both treatments. The gross examination of all the rats in the positive control, preventive and therapeutic groups contained various sizes of nodules, which are easily visible on the surface of livers as well as in cut sections. The positive control showed high numbers of three sizes of nodules. In contrast, the preventive and therapeutic groups showed less numbers of nodules. In addition, microscopic analysis of the preventive and therapeutic groups confirmed

that the majority of these nodules were hyperplastic with maintaining the normal architecture of the liver. Thus it can be said that selenium dose did not inhibit the formation of such nodules but it reduces or delays them significantly. This importance must not be ignored. Indeed, there is an increasing body of various data that indicates selenium plays an important role in cellular protection against cytotoxic agents. In addition, this study shows that selenium at a dose of 4 mg/L did not produce any toxicity or symptoms.

The significant reduction in the body weight observed in the positive, preventive and therapeutic groups following exposure to DEN and 2-AAF could be due to impaired hepatic function. The appetite of these rats was decreased and subsequently less food intake compared with untreated groups. This finding disagrees with other previous studies where it was reported that food intake of treated groups (DEN with Phenobarbital) was statistically similar to untreated groups (Thirunavukkarasu et al. 2000). The formation of nodules in the liver following DEN and 2-AAF exposure could explain the increase in the liver weights in positive, preventive and therapeutic groups.

The experimental protocol employed in this study was based on the prevention and therapeutic effects on selenium in the initiation and promotion stages of hepatocarcinogenesis, respectively. In the present study, an organic form of selenium presented dual effects, both showed to decrease the number and size of nodules. Thus, selenium has shown to have an inhibition effects during initiation and prevention during promotion. Many potential cancer chemopreventive agents can be categorized broadly as blocking agents, which inhibits the initiation of hepatocarcinogenesis, or suppressing agents, which arrest or reverse its promotion or regression (Greenwald 2001). The above findings suggest that selenium could be classified as blocking and suppressing agents.

Solt and Farber (1976) model was chosen to study hepatocarcinogenesis in rats because it is the most widely used method in rodents. DEN and 2-AAF are widely used liver

carcinogens in rodents (Lee & Lee 1999). DEN (initiator) causes liver damage while 2-AAF (promoter) inhibits regeneration of hepatocytes (Gupta et al. 1988). Partial hepatectomy (PH) was not performed for two reasons. First, PH can cause pain and secondly it may increase mortality rate in the treated animals. In addition, it has been reported that PH produces numerous changes in the physiological state of the animals such as mobilization of fat stores (Maza et al 1997), alterations in metabolizing enzymes (Trautwein et al. 1997), and changes in liver protein synthesis (Kimura et al. 1997).

This particular model of resistant hepatocyte has a high rate of nodule formation. Using the same model, some researchers have reported that 99–100 % of the generated hepatocyte nodules are positive for GST-P (Glutathione S – Transferase - Placental) (Camargo et al. 1993; Bitsch et al. 2000). It has been reported that the mean diameter of the foci, the number of foci per cm² and the surface area of foci are adequate to be the basis for interpretation of such experimental results (Moore et al. 1981; Pitot et al. 1980). In the positive group (DEN and 2-AAF), the means, numbers and surface areas of GST-P positive foci were higher than those in selenium treated groups. In particular, treatment with the therapeutic group has shown a significant reduction in both, the number and surface area of GST-P positive foci, indicating that selenium might be attributed to the prevention of nodule formation on chemically induced hepatocarcinogenesis in rats. The findings of this study are in line with other previous studies (Masudai et al. 2001; Hasegawa et al. 1991; Kitano et al. 1998). GST-P, which is not expressed in normal rat-liver, is considered to be a marker for hepatocarcinogenesis in rats (Tatematsu et al. 1985).

This study used an inorganic form of selenium as sodium selenite, it is suggested that natural form of selenium such as Brazil nuts, eggs or fish, with known amount of selenium, should be used for further research. In conclusion, selenium at a supra-nutritional level in the preventive and therapeutic groups was able to reduce, but not inhibit, the formation of

liver nodules without obvious toxicity.

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Gastrointestinal parasite infections among school children in displaced areas

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Abstract

During the past two decades hundred thousands people moved either from Western Kordofan State and Darfour during the flooding and famine in 1988 or from the Southern Sudan as a result of civil war. The present study was designed to determine the prevalence of enteroparasites among school children in two displaced areas namely, Mayo and Abuzied around Khartoum State, together with determining environmental, socio-economic and behavioral factors. Stool samples were collected from 1500 school children (age 4-17 years) from each of the two displaced areas (total of 3000). One sample was obtained for each child. Stool specimens were preserved in 10% formaldehyde solution and examined at the

Biomedical Research Laboratory of Ahfad University for Women by the Sedimentation and Sugar floatation techniques. High prevalence rates were obtained among children enrolled in this study (42%). Significant differences were obtained by gender and by age. High prevalence rate was obtained among the age group 8-<12 (53.4%). Total prevalence rate of children in Mayo was 44.3% and in Abuzeid 39.7%. Significant difference by gender was obtained, M/F ratio was 43.7%/56.3% in both areas. Male to Female ratio for Mayo was 41.8%/58.2% /and Abuzeid.45.7%/54.3 % (P<.001). Significant difference was obtained by age in positive children. High prevalence was among age group 8-<12 in Abuzeid (56%) and (51.1%) in Mayo. Eight parasite species were recovered including, *G.lambliia*, *E.histolytica*, *H.nana*, *E.vermicularis*, *S.mansoni*, *Taenia*, *E.coli* and Hook worm. Single 33.7%. Double 18.8% and triple (4%) infections were reported. *G.lambliia* was the most common in double and triple infections followed by *H.nana*. Different clinical symptoms were reported among positive children including, abdominal pain (46.0%) diarrhea (32.1%) vomiting (27.4%) fever (40.1%) and anal irritation (18.5%). Parent's educational level, defecation site, self cleaning, washing hands after defecation and the source of drinking water were among the most important determinants of these parasitic manifestations among children in both areas.

The paper concluded that the infection rates obtained in this study were alarming and may point out towards high prevalence also among community members. Their presence among young children at this age could have serious impact on their nutritional and health status.

Improvement of community sanitation, provision of clean drinking water and implementation of health education programs may contribute significantly to the control of this health problem.

Introduction

Infections due to intestinal parasites are common throughout the tropics presenting serious public health problems in developing countries (Ramsay *et al.* 1991, Erko & Tedla. 1993, WHO, 1986 and Roma & Worku 1997).

health workers, whose priority lies within acute and fatal infections, may overlook them. However most of these infections are chronic, and have profound effect on nutrition (Stephenson *et al.* 1993), growth (Hadju *et al.* 1996), cognitive function (Simeon *et al.* 1995) and anemia (Dossa *et al.* 2001 and Torlesse & Hodge, 2001) in infants, school age children and adults. These infections also contribute to a lower IQ level and stunted physical and mental well being (Bahader *et al.* 1995).

These infections are rapidly spreading in slums, shantytowns and squatter settlement, a trend that is likely to continue with the increasing and unplanned urbanization (WHO, 1995).

In recent years hundred thousands of people from rural areas in Southern and Western Sudan migrated to Khartoum State as a result of civil war and famine. They settled around the state in camps and temporary dwellings devoid of most of the basic community services. A number of studies has been conducted on gastro-intestinal parasites in Sudan. All these studies reported high prevalence of gastrointestinal parasites (Hakim and Mogga 1983, Homeida 1991 & 1994). However studies done among displaced people in are scarce and most of them were carried out in the South (Marnell *et al.* 1992 & Magabo *et al.* 1998).

The present study was designed to determine the prevalence of gastrointestinal parasites among displaced communities around Khartoum State. Environmental, socio-economic and behavioral factors.

This study was undertaken to investigate the magnitude of this problem among school children in two displaced areas around Khartoum State.

Objectives

1. To investigate the prevalence of gastrointestinal parasites among displaced school children.
2. To identify determinant factors of these parasitic infections.

Material and Methods

Study area

The study was carried out at Abuzeid locality, West Omdurman city and Mayo, Khartoum State. Population in this area consists of different tribes who moved either from Western Kordofan State and Darfour during the flooding and famine in 1988 (Abuzied) or the South and Darfour (Mayo) as a result of civil wars. They were poor people. Most of the families depend on women as source of income as they work as house maids or tea sellers. Men either without or working in marginalized jobs. There are two basic schools in each area, one for boys and the other for girls. The main source of drinking water is a deep-bore well and tanks. Water usually kept in barrels in these schools where children share their cups.

Study subjects

3000 school children aged 6 - > 16 years from girls and boys schools in each area were investigated.

Study design

Cross sectional study in which all school children in both male and female schools in two displaced areas were screened for presence of gastrointestinal parasites. Factors that may contribute to the prevalence of parasites were investigated.

Sample size

3000 displaced school children were enrolled in this study.

Sampling technique

Total coverage of both male and female schools in each area was made.

Data collection

Demographic data

These included administrative information such as name, sex, age and area of residence.

Clinical data

These included presence of abdominal pain, diarrhea, vomiting, fever, and anal irritation.

Epidemiological data

Prevalence rate, types of parasite species other information on parents educational level presence or absence of latrine, water sources as well as behavioral and self-hygiene data were recorded.

Specimen collection

The names and ages of the children were obtained from the school records. The purpose of the study was explained to the children, in presence of teachers, to get their consent for participation in the study. Children were then asked to go to the school toilets and pass a small volume of feces into plastic containers labeled with full name of the child and date of specimen collection.

Specimen preservation

After submission of the stool specimen formaldehyde saline solution (4%v/v) was added and the specimen was well mixed using an applicator to break up lumps. More of preservative was added to cover the whole sample. The containers were tightly screwed and packed carefully in a box and transported to the laboratory where they were stored at room temperature.

Stool examination techniques

Two stool examination techniques were used for recovery of protozoan cyst and trophozoites and for worm's ova.

Sugar Floatation

Sheather floatation (Garcia & Bruckner 1997) was used for stool examination. A fixed stool specimen was properly emulsified and centrifuged to obtain pellet. After decanting the supernatant, pellet was thoroughly mixed in 10 ml saturated (58.6%w/v) sugar solution. The test tube is then filled to the rim with the same media. Avoiding formation of air bubbles, a cover slip was placed on top of the test tube and the later was left to stand in upright position for 45-60 minutes. The cover slip was carefully removed and placed on glass slide and examined under the microscope. A drop of iodine was added when staining was needed.

Sodium Dodecyle Sulfate (SDS) sedimentation

This is a concentration sedimentation method used in our laboratory in which the SDS was used for stool digestion. formaldehyde fixed stool specimen was emulsified in 8ml medium containing Sodium Dodecyle Sulphate (0.05w/v) and sodium chloride (0.9 % w/v). Stool specimen was properly homogenized in the detergent medium, and then passed through nylon gauze of 400 µm mesh size to remove coarse particles. The filtrate is returned to the test tube and left to settle. After one-hour incubation, a large drop of the sediment was transferred to a clean glass slide, covered with a cover slip and examined under the microscope.

Data analysis

Data collected from each areas was entered and analysed using the SPSS. Data for both areas was merged and analysed. Chi-square was used for comparison of data.

Results

The overall prevalence of gastrointestinal parasites among children enrolled in this study was 42%. When data was obtained for eah area 44.3% was recorded in Mayo and 39.3% in Abuzeid (Table1). Eight parasite species were recovered including, *G.lamblia*, *E.histolytica*, *H.nana*, *E.vermicularis*, , *Taenia*, *E.coli* ,*S.mansoni* and Hook worm in Abuzeid areas and same

species were recovered from children in Mayo except *S.mansoni* (Table2). Single (33.7), double (18.8%) and triple (4%) infections were recorded (Fig.1). *G.lambliia* was mostly observed in double and triple infections followed by *H.nana* in each area. Significant difference was found by gender in each area. Male to Female ratio for Mayo was 41.8%/58.2% /and Abuzeid.45.7%/54.3% $P<.001$ (Table 4,5). Significant difference in age prevalence rate was obtained ($p<.001$).The highest prevalence rate (53.4%) was obtained among the age group 8-<12 (Table 6). Different clinical symptoms were reported among positive children (data not presented) including, abdominal pain (46.0%), diarrhea(32.1), vomiting(27.4), fever(40.1) and anal irritation(18.5).

Highest positivity was recorded among children whose fathers and mothers were primary school level, (64.1%&53.3%respectively). Prevalence reported among children without latrines was 66.7%, those who donot wash their hands after defecation was 57.2% and 58.3% among children who drink from barrels in the schools (data not presented).

Table 1: Results of positive children by area

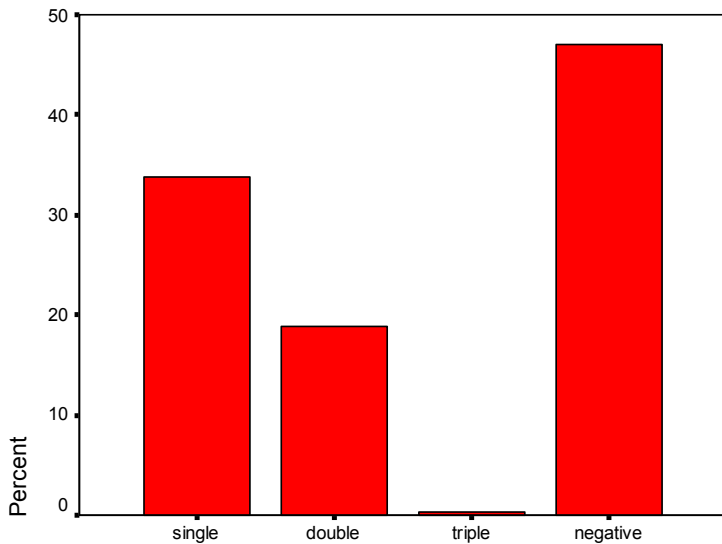
Study Area	Count	Positivity		Total
		negative	*positive	
Mayo	Count	835	665	1500
	% within Area	55.7%	44.3%	100.0%
	% within Positivity	48.0%	52.8%	50.0%
Abuzaid	Count	905	595	1500
	% within Area	60.3%	39.7%	100.0%
	% within Positivity	52.0%	47.2%	50.0%
Total	Count	1740	1260	3000
	% within Area	58.0%	42.0%	100.0%
	% within Positivity	100.0%	100.0%	100.0%

* $P>.001$

Table 2: Type of parasites recovered from children in Abuzeid

Type of parasites	Abuzied	Mayo
H.nana	11.3%	10.8%
G.lambliia	13.6%	15%
E.histolytica	5.2%	9.36%
E.coli	0.9%	0.46
H.nana+E.histolytica+G.lambliia	0.5%	0.3%
H.nana+ E.histolytica	1.1%	2.7%
H.nana+G.lamlblia	3.6%	3.7%
E.histolytica+G.lambliia	1.5%	5%
E.vermicularis	.7%•	0.4%
Evermcularis+H.nana	.1%•	0.1%
E.coli+G.lambliia	0.5%	•
Taenia Species	0.3%	0.06%
Taenia Species&E.histolytica	••j•	0.06%
S.mansoni	0.1%	•
G.lambliia+S.mansoni	0.1%	•
Taenia+G.lambliia+E.histolytica	0.1%	•
Hookworm	0.1%	•
G.lambliia+H.nana+Hookworm	••	0.06%
E.histolytica and E.coli	••	0.06%
Total	39.7	44.3%

Figure 1: Infection styles among children in both areas



Result

Table 4: Results of children examined by gender in Abuzied area

			Type of result		Total
			-Ve	+Ve*	
Sex	Male	Count	478	272	750
		% within Sex	63.7%	36.3%	100.0%
	% within Type of result	52.8%	45.7%	50.0%	
Sex	Female	Count	427	323	750
		% within Sex	56.9%	43.1%	100.0%
	% within Type of result	47.2%	54.3%	50.0%	
Total		Count	905	595	1500
		% within Sex	60.3%	39.7%	100.0%
		% within Type of result	100.0%	100.0%	100.0%

P<0.001*

Table 5: Results of children examined by gender in Mayo

			Type of Result		Total
			-Ve	+Ve	
Sex	Male	Count	472	278	750
		% within Sex	62.9%	37.1%	100.0%
		% within Type of Result	56.5%	41.8%	50.0%
	Female	Count	363	387	750
		% within Sex	48.4%	51.6%	100.0%
		% within Type of Result	43.5%	58.2%	50.0%
Total	Count	835	665	1500	
	% within Sex	55.7%	44.3%	100.0%	
	% within Type of Result	100.0%	100.0%	100.0%	

P<0.001*

Table 6: Gastrointestinal parasites among children in both areas at different age groups

			Positivity		Total
			negative	Positive*	
Age	4 and less than 8 years	Count	350	204	554
		% within Age	63.2%	36.8%	100.0%
		% within Positivity	20.1%	16.2%	18.5%
	8 and less than 12 years	Count	821	673	1494
		% within Age	55.0%	45.0%	100.0%
		% within Positivity	47.2%	53.4%	49.8%
	12 and less than 16 years	Count	518	363	881

	% within Age	58.8%	41.2%	100.0%
	% within Positivity	29.8%	28.8%	29.4%
16 years and above	Count	51	20	71
	% within Age	71.8%	28.2%	100.0%
	% within Positivity	2.9%	1.6%	2.4%
Total	Count	1740	1260	3000
	% within Age	58.0%	42.0%	100.0%
	% within Positivity	100.0%	100.0%	100.0%

*P<.001

Discussion

Intestinal parasite infection is one of the major causes of morbidity in developing countries. Most of these infections are chronic, contributing to malnutrition among children and reducing host resistance to other diseases. Children being the victims serve also as source of infection thus contributing to transmission.

Results obtained in this study revealed high prevalence and wide spectrum of these parasites (42%). Previous studies in Sudan had shown occurrence of the same parasites species in man (Steketee and Muhlland 1982, Reckart *et al.* 1985). No recent studies were carried out to allow for comparison and most of those published were carried out in the South, however same parasites were recorded in these studies. Magambo *et al.* (1998) reported higher prevalence rates among children of 6-10 years age in the South including *E.histolytica* (28.4%), *G.lamblia* (9.8%) hookworm (13.1%) *Strongyloides* (3.3%) *S.mansoni* (2.2%) *T.trichiura* (1.8%). They did not report *A.lumbricoides* or any of the cestode worms. Homeida *et al.* (1991) reported that only 53 out of 724 were found to be infected with geohelminths in Juba. Marenell *et al.* (1992) reported a prevalence rate of 66% among refugees in Juba including *Hookworms* (36%), *S.mansoni* (11%), *Strongyloides*

spp.(20%), *A.lumbricoides* (1.2%), *T.trichiura* (0.8%), and *T.saginata* (0.4%). Similar to our findings Marenell et al(1992) reported hook worm in children stool in lower percentage. In this study the highest prevalence rate obtained among children between 8-12years can be related to age related behaviour which contribute to exposure.

The infection rates obtained in this study were alarming and may point out towards high prevalence also among community members. Since only one sample was examined in this study higher prevalence rate might be obtained if two or three samples were examined.

Presence of helminth parasites and in particular *A.lumbricoides* and *Ancylostoma species* among young children at this age could have serious impact on the nutritional and health status. Previous studies have established a clear relationship between helminth infections and decreased growth rate in unprivileged children (Hagel, *et al.* 1999). Prevalence of iron deficiency anaemia increased steadily with the increase in hookworm infection (Stoltzfus *et al.* 1996). *A.lumbricoides* infections were considered a risk factor for ocular signs of vitamin A deficiency (Curtale *et al.* 1995). The higher prevalence among females can not be justified within the scope of this studies. In those displaced populations, women work as tea sellers in the three towns of the capital or as housemaids and men as workers in different places and therefore can introduce this infection into the capital city. Although different clinical manifestations were recorded including diarrhoea, abdominal pain, vomiting, fever and anal irritation, it is rather difficult to relate these symptoms solely to gastrointestinal parasites recorded in this study. Prevalence rates were higher among children whose parents were less educated, those who have no latrine and not washing hands after defecation and those drink from barrels in the schools. This would clearly indicate that low level of awareness together with low sanitation and self hygiene are important determinants of these infections among children under study.

Conclusion & Recommendations

These data illustrated clearly the significant role of socio-economical, environmental and sanitation as well as other behavioral factors in infection. Improvement of community sanitation, provision of clean drinking water and implementation of health education programs may contribute significantly to the control of this health problem. Further investigations are needed to determine the effect of these parasitic infections on children nutritional and health status.

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Renal Dysfunction Following Myocardial Infarction

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Abstract

Background: Cardiovascular disease is a killer disease with a wide prevalence globally. It is a well known fact that a close relationship exists between cardiovascular disease and renal dysfunction. Patients who develop cardiovascular diseases are more prone to develop renal dysfunction. Mortality in such patients would sometimes result due to impaired renal function rather than the primary event, namely myocardial infarction. Baseline renal function is a potent independent risk factor for adverse events after MI. Recognizing and assessing the renal function is therefore of utmost importance in management of patients with acute myocardial infarction.

Objectives: This study was carried out to ascertain the incidence of renal dysfunction in patients following myocardial infarction (MI). It also sought to establish whether there was a relationship between the severity of MI and renal dysfunction.

Methodology: A retrospective study was carried out using case records of ICU patients of PSG Hospitals, a tertiary care hospital over a period of three months. The plasma troponin T, serum urea and creatinine levels were noted down. A total

of 182 patients with age ranged from 23 to 90 years, who had biochemical evidence of acute myocardial infarction (AMI) with serum troponin T values $> 0.03\text{ng/ml}$ were included in the study. They were classified into two groups based on a cut off value of 1.5 mg/dl for s.creatinine levels: Group I 'AMI with renal dysfunction' had 54 cases while 'AMI without renal dysfunction' had 128 cases.

Results: The incidence of renal dysfunction amongst patients with AMI was 29.67%. The mean values of plasma troponin T levels were $1.35 \pm 2.33\text{ ng/ml}$ in the 'AMI with renal dysfunction' group as against $1.282 \pm 2.48\text{ ng/ml}$ in 'AMI without renal dysfunction' group. Although the mean troponin T values were higher in group I, the difference was not statistically significant ($P > 0.05$). The mean values of serum creatinine and blood urea in group I were significantly higher than group II (2.34 ± 1.86 , $1.1 \pm 0.47\text{ mg/dl}$ and 65.07 ± 12.48 , $28.51 \pm 16.34\text{ mg/dl}$, respectively, $P < 0.001$).

Conclusion: A significant percentage of patients with myocardial infarction show evidence of renal dysfunction. This demonstrates the intimate functional relationship between the cardiac and renal functions. The incidence of ARF following MI is higher in the older age groups.

Implications: There is an intimate functional relationship between cardiac and renal function. Patients with MI should be investigated for evidence of renal dysfunction in the immediate post infarction period. Serum creatinine and urea should be assayed during the follow up period as well to detect deterioration of renal function.

Keywords: Myocardial infarction, troponinT, serum creatinine

Introduction

Cardiovascular disease is a killer disease with a wide prevalence globally. It is a well known fact that a close relationship exists between cardiovascular disease and renal dysfunction. Patients with end stage renal disease have a high incidence of

cardiovascular diseases such as ischemic heart disease, angina, congestive heart failure and stroke. Cardiovascular mortality is 10-20 times higher in patients with end stage renal disease than in the general population (Levin et al., 2002). There are several studies which have documented their relationship (Beattie et al., 2001; Culleton et al., 1999).

The converse is also generally known to be true, that is, patients who develop cardiovascular diseases are more prone to develop renal dysfunction. Mortality in such patients would sometimes result due to impaired renal function rather than the primary event, namely myocardial infarction. Recognizing and assessing the renal function is therefore of utmost importance in management of patients with acute myocardial infarction. Serum urea and creatinine are considered as ideal parameters to evaluate the renal function.

Myocardial Infarction (MI) is the irreversible necrosis of heart muscle due to imbalance of oxygen supply and demand. Cardiovascular diseases cause 12 million deaths throughout the world each year, according to the third monitoring report of the World Health Organization, 1991-93. The Indian subcontinent has the highest rate of cardiovascular diseases globally (Goyal & Yusuf, 2006).

The appearance of cardiac enzymes such as lactate dehydrogenase, Creatine Kinase (CK) and CK MB, in the circulation generally indicates myocardial necrosis, amongst these enzymes CK MB is considered to be the most specific marker of MI (Apple, 1994). Serum myoglobin is also considered to be a marker of MI (Apple, 1994). According to the American College of Cardiology (ACC)/American Heart Association (AHA) consensus statement on MI (William et al., 2004), cardiac troponin T and troponin I are considered the criterion standard in defining and diagnosing MI. Serum levels of troponins increase within 3-12 hours from the onset of chest pain, peak at 24-48 hours, and return to baseline over 5-14 days (Katus, 1991).

Troponin is a complex of 3 proteins that is integral to muscle contraction in skeletal and cardiac muscle. It has 3 subunits-

troponin T (cTnT), troponin C and troponin I. Human myocardium contains 4 isoforms of cTnT, but only one of these is characteristic of normal adult heart. However, fetal forms of cTnT are re-expressed in cardiac muscle injury and regeneration. Thus, the assay used to measure cTnT levels has high cardiac specificity and can provide comparable information about myocardial infarction. The American College of Cardiology and The European Society of Cardiology in 2000, acknowledged that the elevation of cTnI, and cTnT is a cornerstone in the diagnosis of AMI (William et al., 2004).

The research by H.L.Hillege et al concludes that renal function markedly deteriorates after a first MI (Hillege et al., 2003). Furthermore, an impaired baseline renal function adds to prognostic risk of developing CHF in patients after a first MI. According to the study by Sorensen et al, renal dysfunction is an important risk factor after acute MI (Sorensen et al., 2002). Baseline renal function is a potent independent risk factor for adverse events after MI. Worsening renal function has been shown to influence outcomes in the heart failure population, but its impact on cardiovascular risk in the post-MI period has not been well defined. Monitoring serum creatinine in patients during the first few weeks after MI may help to identify those who are at highest risk and guide effective long-term therapeutic choices according to the study by Jose et al (2006). Even mild renal disease, as assessed by the estimated GFR, should be considered a major risk factor for cardiovascular complications after MI as concluded by the study done by Anvekar et al (2008).

Objectives

The objectives of the present study were therefore to determine the prevalence of renal dysfunction following MI and to find out if there is a correlation between degree of MI as reflected by cTnT levels and degree of renal dysfunction as reflected by serum creatinine levels.

Materials and Methods

This retrospective study was carried out by reviewing the records of patients with an established diagnosis of AMI. The following biochemical parameters were noted down from the case records.

(a) Plasma troponin-T (b) Serum creatinine (c) Serum urea.

The records of 182 patients who were diagnosed with acute myocardial infarction (AMI) and admitted into the Intensive Care Unit (ICU) of PSG Hospitals, from December 2007 to February 2008 were scrutinized. Only those cases with plasma troponin-T levels > 0.03 ng/ml were included in the study. The patients were divided into two groups based on serum creatinine levels.

Group 1: AMI with renal dysfunction, with serum creatinine ≥ 1.5 mg/dl

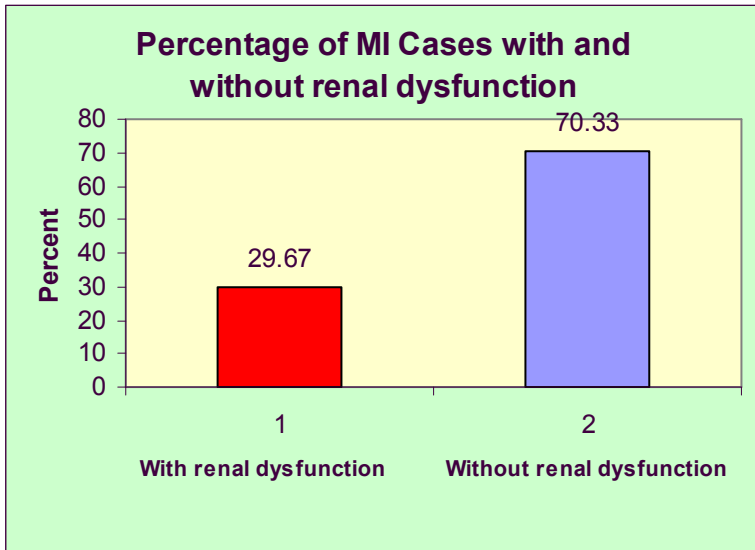
Group 2: AMI without renal dysfunction with serum creatinine < 1.5 mg/dl.

Biochemical parameters

Blood samples were collected from patients on admission. Serum urea and serum creatinine were estimated using fully automated Olympus AU400 clinical chemistry analyzer (Bartels & Bohmer, 1971; Sampson et al., 1980). Cardiac troponin-T was estimated in EDTA plasma using the ELECSYS 1010 system (Roche diagnostics) with Roche diagnostic troponin-T kit, based on electrochemiluminescence immunoassay technique (Grahame et al., 2003). The results were statistically analyzed using chi-square test (Grahame et al., 2003).

Results

Amongst a total number of 182 cases with myocardial infarction, 54 showed biochemical evidence of impaired renal function. The percentage of cases that showed biochemical evidence of renal dysfunction was 29.67. This is representative of the incidence of renal dysfunction in patients who have had MI. (Graph 1)



Graph 1: The percentage of MI cases with and without renal dysfunction

Patients were divided into two groups based on the serum creatinine levels. Group I – Patients with S. Creatinine >1.5 mg/dl. Group II –Patients with S. Creatinine ≤ 1.5 mg/dl. Plasma troponin T, serum creatinine and serum urea levels of the two groups are shown in table 1.

Table 1: Mean values of Plasma troponin T, serum creatinine and urea among studied groups

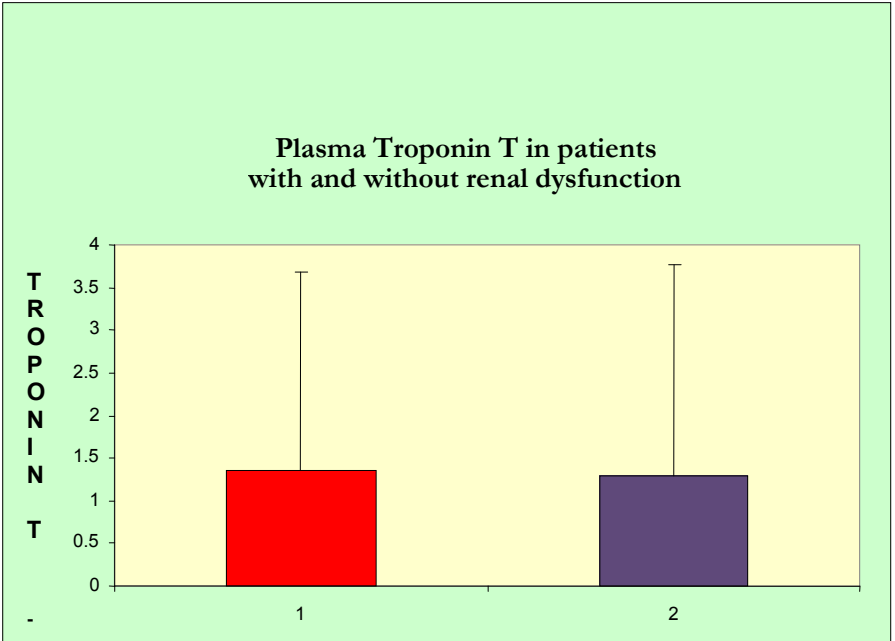
n	Troponin T (ng/ml)	Serum creatinine (mg/dl)	Serum urea (mg/dl)
Group I -54	1.35 ± 2.33	2.34 ± 1.86	65.07 ± 12.48
Group II-128	1.282 ± 2.48	1.10 ± 0.47	28.51 ± 16.34
Statistical significance	NS	p < 0.001	p < 0.001

Values are expressed as mean ± SD

Graph II: Troponin T levels – Group I Vs Group II

Although the mean plasma troponin T levels of group II was slightly higher as compared with group I it was not statistically significant. This could be attributed to the high scatter of values in the two groups.

Graph II



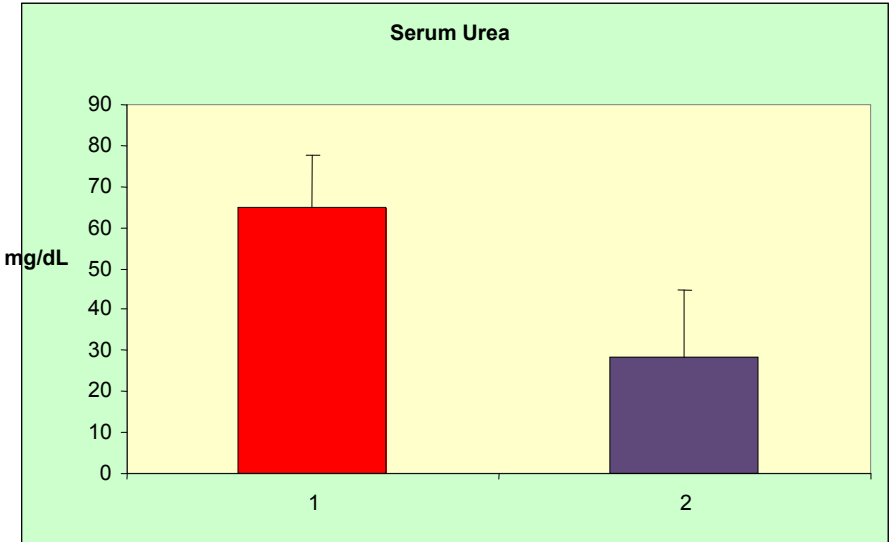
I

1. Group I: AMI with renal dysfunction
2. Group II AMI without renal dysfunction

Serum urea and creatinine –Group I Vs Group II – (Graph III and IV)

Group II had significantly higher levels of serum urea and creatinine as compared with group I. This was expected as the cases for group II were chosen with a cut off value of 1.5 mg/dl for serum creatinine.

Graph III



Graph IV

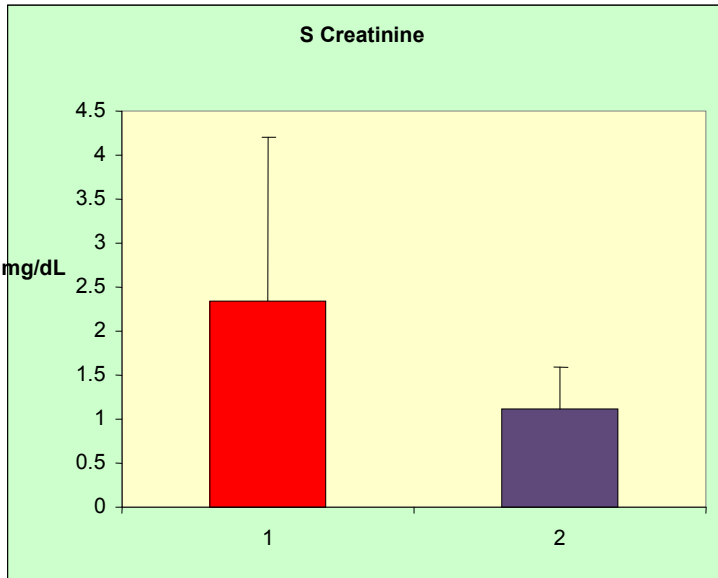
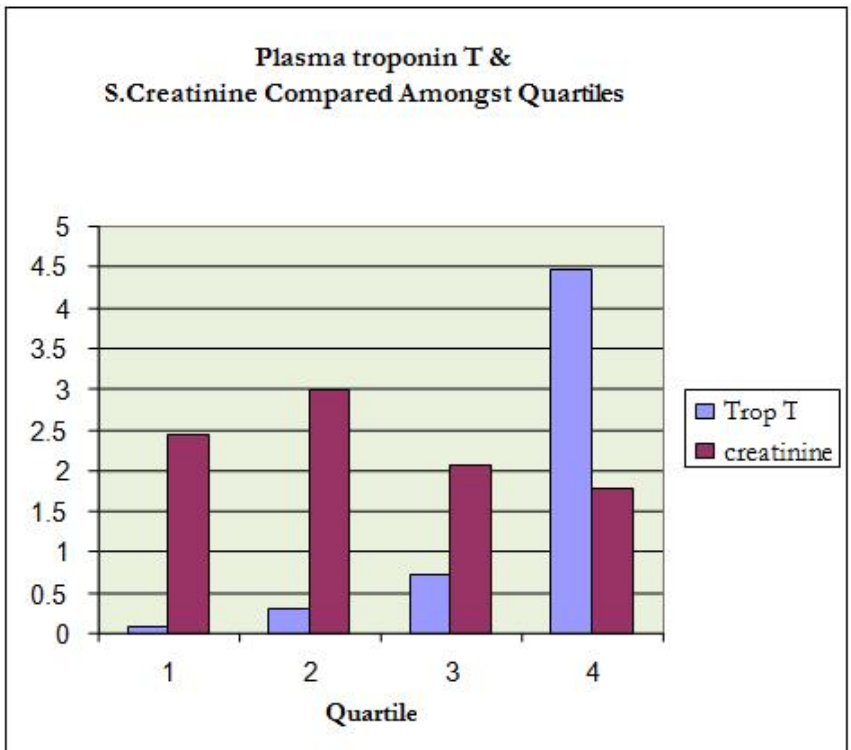


Table 2: mean serum creatinine levels of the four quartiles compared

Quartiles	Trop-T (mean) ng/ml	S. Creatinine (mean) mg/dl
I	0.076	2.43
II	0.302	2.99
III	0.721	2.08
IV	4.458	1.78

Graph V: plasma Troponin T levels compared with S creatinine amongst quartiles



The results revealed that there was no correlation between plasma troponin T levels and s. creatinine ($r = 0.1026$, $P > 0.05$).

Graph VI : The number of patients who develop ARF following MI was higher with advancing age

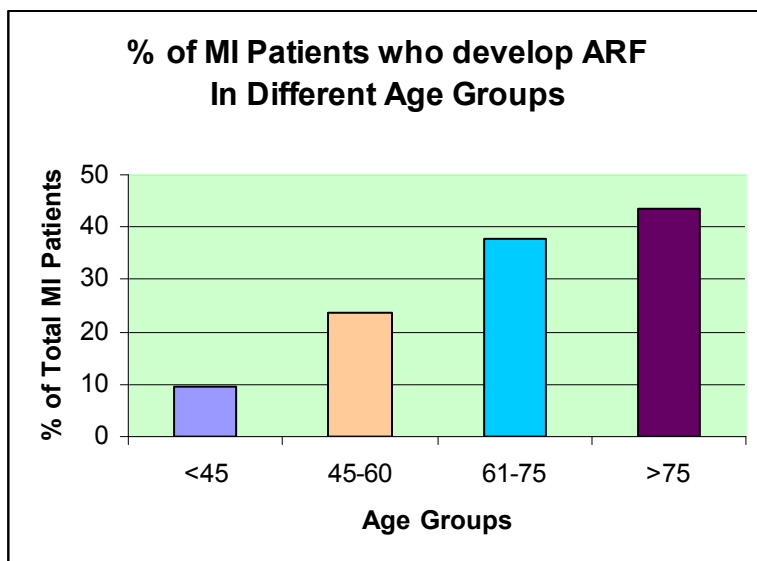


Table 3: Age-wise Distribution of MI patients who develop ARF

Age (Years)	No. of MI patients with ARF	No. of MI patients without ARF	% With ARF
< 45	2	19	9.52
45-60	17	55	23.61
61-75	25	41	37.87
>75	10	13	43.47

The results of table (3) revealed that there is a rise in renal dysfunction with advancing age in the study population. (Chi Square =9.56 , $P < 0.05$).

Discussion

Information regarding the cardio-renal axis in patients after a myocardial infarction is limited. This study therefore, aimed at examining a possible cause and effect relationship between myocardial infarction and renal dysfunction.

The retrospective study has answered the two questions that were posed; namely, the incidence of renal dysfunction after MI and the possibility of renal dysfunction as a sequel to myocardial infarction.

Almost 30% of MI cases had biochemical evidence of renal dysfunction in the form of elevated s.creatinine. The possible explanations for the raised levels of s.urea and s.creatinine are as follows:

(a) Pre-renal: In patients after an MI, a decline in the cardiac output could lead to an impaired renal perfusion, fall in the glomerular filtration rate which is finally reflected as raised levels of urea and creatinine.

(b) Renal: Impaired renal function is a manifestation of end organ damage (Garg et al., 2002). Since the assay of s. creatinine was done in the immediate post-infarction period, it is likely that this percentage would rise if these cases were to be followed up over longer time frames.

(c) Pre- existing renal disease: Another contentious point with regard to raised levels of serum creatinine in group II is the fact that no information was available regarding the renal status of these patients prior to myocardial infarction. It is possible therefore, that some of these patients might have had a compromised renal function prior to the episode.

About 70% of MI cases showed no biochemical evidence of renal dysfunction. The possible explanations could be:

(a) The kinetics of creatinine generation and excretion are well characterized and even an abrupt change in renal function will not result in gross changes in s.creatinine within the acute period following MI (Hallynck et al., 1981).

(b) Although s.creatinine is considered to be the gold standard for detecting renal dysfunction, it is well known that it is still

not sensitive enough to detect loss of nephron function at an early / sub-clinical stage.

Hillege et al (2003) have found that renal function markedly deteriorates after a first MI. Furthermore they state that an impaired baseline renal function adds to the prognostic risk of developing CHF in patients after a first MI (Hillege et al., 2003). The findings of the present study are in agreement with what has been reported by these authors.

An accelerated decline in renal function even in the absence of renal disease has been observed in diabetes, severe hypertension, dyslipidemia and CHF of which MI is the strongest predictor (Hillege et al., 2003).

Effect of Age: An important finding in the present study has been that, when patients with MI are stratified with respect to age, there is a statistically significant rise in the incidence of renal failure with advancing age (Chi Square = 9.56, $P < 0.05$). It is a well established fact that GFR declines at the rate of 1ml/ min/ year beyond the age of 40 even in healthy human adults¹⁷. Between the ages of 40 and 60, the kidney loses approximately 20% of its mass, primarily from the cortex. When superimposed by an acute stressful condition such as MI, which is known to affect renal perfusion and oxygenation, it is not surprising to find that the incidence of ARF is higher in the older age groups.

Conclusion

A significant percentage of patients with myocardial infarction show evidence of renal dysfunction. This demonstrates the intimate functional relationship between the cardiac and renal functions. The incidence of ARF following MI is higher in the older age groups.

Recommendations

- Patients with MI should be investigated for evidence of renal dysfunction. Serum urea and creatinine should be determined in these patients in the post infarction period for early detection of renal dysfunction.

- These parameters have to be assayed even during the follow up period to detect deterioration of renal function.

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HFE Gene Mutations Among β -Thalassemia Intermediate and β -Thalassemia Minor Individuals in Gaza Strip, Palestine

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Abstract

Background: Hereditary hemochromatosis (HH) is an autosomal recessive disorder of iron metabolism caused by mutations in the HFE gene.

Objectives: The aim of this study was to determine the occurrence of C282Y and H63D mutations among β -thalassemia intermediate and β -thalassemia minor subjects residing in Gaza Strip.

Materials and Methods: The study population consisted of 25 thalassemics intermediate who do not depend on regular blood transfusion, 30 thalassemia minors and 30 normal persons as the control group. The presence of mutations was

determined using PCR-RFLP technique on genomic DNA extracted from blood specimens.

Results: The results indicated that none of the control subjects showed HH due to C282Y or H63D mutation. Results of the thalassemia intermediate group showed that 5 (20%) are heterozygous, and that 3 (12%) of them are homozygous for H63D. Thalassemia minor group results showed that 7 (23%) of them are heterozygous, and that 2 (7%) are homozygous for H63D mutation. The C282Y mutation was not recorded in any of the subjects.

Conclusion: This study recommends that all thalassemics "major and intermediate" and thalassemia minor should be screened for HFE gene mutations.

Key World: Hereditary hemochromatosis (HH), β -thalassemia, PCR- RFLP and Gaza Strip

Introduction

Hereditary hemochromatosis is inherited in an autosomal recessive manner. Iron overload in hereditary hemochromatosis is attributable to excessive dietary iron absorption. Increased absorption leads to accretion of toxic levels of iron in multiple organs, which causes organ damage and dysfunction and as a result it leads to hepatomegaly, congestive heart failure, gonadal dysfunction, loss of body hair, arthritis, or any combination of these manifestations (Bulaj et al., 1996; Lyon et al., 2001).

Hereditary hemochromatosis results from mutations in the HFE gene which is located on the short arm of chromosome 6 (6p21.3). The most common mutation described is a G to A transition at nucleotide 845, which substitutes a tyrosine for a cysteine at amino acid position 282, hence the name C282Y mutation. The prevalence of the homozygous C282Y mutation ranges from 1 in 200 for whites to 1 in 4,000 for those of African-American heritage, the allele frequency in the Caucasian population is 0.063. Interestingly, this mutant allele

was not reported so far in the Middle East area (Feder et al., 1996; Mura et al., 1999).

Two other mutations H63D and S65C have been described in some cases of hemochromatosis. The H63D mutation is a C to G transversion at nucleotide position 187, which substitutes an aspartic acid for histidine at amino acid 63 (i.e., H63D). Persons homozygous for the H63D mutation and those who are compound heterozygotes (with the C282Y mutation) have a low rate of phenotypic expression, accounting for approximately 5% and 15% of the cases of hereditary hemochromatosis, respectively. The S65C mutation is an A to T substitution at nucleotide position 193, resulting in cysteine replacing serine at amino acid 65 (Alsmadi et al., 2006; Hasb, 2001).

The Mediterranean anemia “Thalassemia” is one of the chronic inherited diseases characterized by iron overload and prevails in the Mediterranean basin countries. The percentage of thalassemia minors in Palestine ranges between 3.0% to 4.5% (Sirdah et al., 1998).

This study was conducted in order to determine the occurrence of C282Y and H63D mutations among thalassemia intermediate and thalassemia minors in Gaza Strip.

Materials and Methods

Genomic DNA from the three subject groups was extracted from whole blood samples using the Wizard Genomic DNA Purification Kit (Promega, USA). All samples were genotyped for the C282Y and H63D mutations using PCR-RFLP methods, using the primers shown in Table 1.

Table 1: PCR primers used in the study

Primer	Sequence	Expected band size	Reference
Forward: C282Y	5'- CAATGGGGATGGGACCTACC -3'	340bp	(Girouard J. et al, 2001)
Reverse: C282Y	5'- CACTGATGACTCCAATGACT -3'		
Forward: H63D	5'- AAGGCCTGTTGCTCTGTCTC -3'	388bp	The genome database
Reverse: H63D	5'- GCTCCCACAAGACCTCAGAC -3'		

The PCR was carried out in a total volume of 25 µl, using the primers shown in Table 1. The reaction components for C282Y contained 2.5 µl of 10 x PCR buffer, MgCl₂ 25 mM, dNTPs 200 mM, Primers (20 pmol each), Taq DNA polymerase 5 U/uL and template DNA (about 100 ng).

The thermal cycler program was set as follows:

step1: Denaturation for 15 min at 95 ° C, step2: Melting for 45 sec at 95 °C, step3: Annealing for 30 sec at 57 °C, step4: Extension for 20 sec at 72 °C, step5: from Step 2 to Step 4 (30 cycle) and step6: Final elongation for 7 min at 72 °C (Girouard et al., 2001).

The reaction components and conditions for H63D were the same except that the annealing temperature was 58 °C.

The amplification products were then digested with the restriction enzymes SnaB1 (for C282Y) and BspH1 (New England Biolabs, USA) for (H63D) as described by (Girouard J. et al, 2001). Digestion products were resolved on 3% agarose gels stained with ethidium bromide.

Ethical Considerations

The objective of the study was fully explained to all participants and/or their parents and their written consent was taken. Moreover, the study was approved by the Helsinki Committee – Gaza.

Results

The results showed absence of C282Y and H63D mutations in the control group. The C282Y mutation was also absent in the thalassemia minor and thalassemia intermediate groups. The H63D mutation was encountered in thalassemia groups as illustrated in Table 2 and Figure 1.

Table 2: Summary of the genotyping results for the thalassemia groups

Group	Normal + / +	C282Y + / -	C282Y - / -	H63D + / -	H63D - / -
Control	30/30 100%	0/30	0/30	0/30	0/30
β -thala. Minor	21/30	0/30	0/30	7/30 23%	2/30 7%
β -thala. Intermediate	17/25	0/25	0/25	5/25 20%	3/25 12%

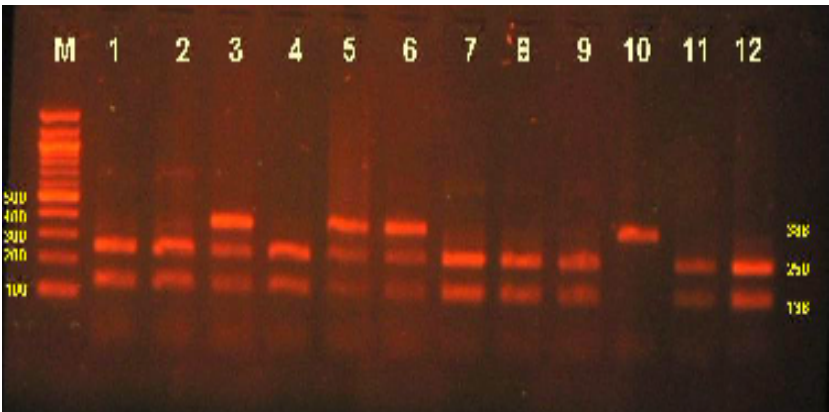


Figure 1: PCR – RFLP products for H63D were run on 3% agarose gel and stained with ethidium bromide. M = 100bp DNA ladder, (1,2,4,7,8,9,11,12) indicate normal genotypes,

while (3,5,6) are illustrative of heterozygous samples, (10) represents a homozygous mutant sample.

Discussion

An interesting outcome of the present study is the absence of C282Y mutation in all the investigated samples. This is in agreement and further confirms that this mutation may not exist in the Middle East region (5,9,10). This result is however, different from that reported by Kaur G. et al, (2004) who studied 81 patients of Asian-African and Middle Eastern origins living in USA and found that 2 patients were positive for C282Y mutation while H63D mutation was not observed (Kaur et al., 2004).

The occurrence of H63D genotypes was highest among β -thalassemia intermediate group. Patients of this group included in the study are not on blood transfusion and consequently iron overload occurs mainly through increased iron absorption. In terms of H63D mutation our results showed that of thalassemia minor 24% were heterozygous and 7% were homozygous, while the respective percentages for the thalassemia intermediate were 20% and 12%. The frequency of H63D mutation in the thalassemia minor is comparable to that reported by Jazayeri et al, 2003 in Iran where they showed that 19.4% of their 56 β -thalassemia minor individuals were heterozygous for H63D, and 3.2% of the same group were homozygous for H63D (Jazayeri et al., 2003). Politou M. et al, (2004) however, showed that none of their 25 Greek thalassemia intermediate patients had mutation in the *HFE* gene (neither C282Y nor H63D mutation) (Politou et al., 2004).

The variations in the prevalence of mutations between studies could be explained by differences pertinent to the study group (e.g., genetic background of the different ethnic groups and founder effect).

This study clearly shows that thalassemia minor and thalassemia intermediate individuals should be genotyped for the *HFE* mutations in order to find out the source of iron

overload in those individuals and find a suitable strategy for their management.

Further studies are needed to examine the occurrence of S65C mutation in Gaza Strip.

Acknowledgement

To all thalassemic patient in Gaza strip, and to my best friend Farid Abu Elamreen.

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Evaluation of Knowledge and attitude of professional athletes and coaches toward AIDS in Iran

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Abstract

Background: On the new data prepared by the World Health Organization (WHO), more than 90% of HIV infected people are in developing countries and there is no drug to cure it. So we have to consider prevention strategies. HIV prevention programs have been implemented for some years in Iran. For example, in high school and university text books. Despite this, preventing programs have not been very successful. Professional athletes and coaches have many journeys to other countries. For this reason, they may be infected. On the other hand, they are in an excellent position to pass information to youth so they can protect themselves from HIV infection. The aim of this study was to evaluate knowledge and attitude of professional athletes and coaches toward AIDS in Iran as such research is lacking.

Methods: This descriptive and analytical study was carried out with 212 coaches, 327 professional athletes and 275 non-athletes people from different backgrounds using a structured questionnaire. Samples were randomly selected, their knowledge and attitude was determined by questionnaire. Level of knowledge and attitude and the relationship between knowledge and attitude were determined by X² and Chi-square test and Pearson correlation coefficients using SPSS.

Results: All study groups have baseline information about AIDS and most of them obtained such information mainly from media, and most frequency of knowledge related to weak level in ordinary people and average level in coaches and very weak knowledge level in professional athletes. 58.7% of coaches and 51.4% of ordinary people and 60.2% of coaches had neutral attitude (Neither agree nor disagree). There was a direct relationship between knowledge level and attitude.

Conclusion: According to these results professional athletes and coaches had little knowledge. Since they are popular among young people and they have important cultural role, they must be given more education.

Keywords: AIDS, Knowledge, attitude, athletes, sport coaches

Introduction

According to global reports, 33 million people in the world are living with HIV in 2007 and approximately 2.7 million people are infected to the virus of HIV (WHO, 2008). 2 million people lost their lives because of this illness in 2007. The major rate of death led by HIV and also the highest rate of new infections to HIV have over 15 years old (WHO, 2008). By all efforts done, this fact exists that AIDS epidemic is growing (Squassi, 2003).

Human immunodeficiency virus is from the retrovirus group (Rezaei, 1999). The viruses in this group stay in the body of host for ever and after serum alteration they have a long non-symptom period before emergence of clinical appearance (Fekri, 2000).

The virus causes dispersal of cellular immunity system and disrupts body defense against diseases by attacking T Helper cells (Rezaei, 1999). Opportunistic infections are common in people with AIDS (Holmes, 2003). HIV affects nearly every organ system. People with AIDS also have an increased risk of developing various cancers. Additionally, people with AIDS often have systemic symptoms of infection like fevers, sweats (particularly at night), swollen glands, chills, weakness and weight loss (Guss 1994, Guss 1994).

Since the infection caused by HIV has become the second infective reason leading to death all over the world (Hatami, 2003) and the major reason of death among the young (Ungan, 2003), considering the rate of athletes' information about AIDS is very important especially they are popular among young people. Also because of multiplicity of their foreign travels, their coaches can be helpful in transmission of information and education of the proper behavioral pattern in reduction of the risk of infection to this disease for the young and adolescents. The current research is done for this reason. Therefore, awareness of their knowledge regarding AIDS can help in reduction and prevention of this illness to great extents.

Methods

The study was carried out in 2007 in Tehran (Iran). It is descriptive-analytic study carried out with 212 coaches, 327 professional athletes and 275 non-athletes people (who had occupations rather than coaches and professional athlete), the samples were selected randomly (according to their identification number), and questionnaire was used to evaluate their state of knowledge and attitude. The questionnaire included of three sections; first section: personal information like age, sex, marital status, level of education, main sources of gaining information about AIDS. The second section: questions concerning state of awareness including questions regarding methods of transmission, non-transmission, essence and general matters of AIDS. The categorization of state of awareness was based on the table of educational marks value.

Great for 18-20, good for 16-17.99, average for 13-15.99, weak for 10-12.99 and very weak for less than 10 were considered (Omidvar, 2002). Third section: questions regarding the attitude. It included questions concerning AIDS patients and their isolation. The categorization of the attitude was considered based on Lickert's criterion, for each response with proper attitude 2 points, non-opinion 1 point and zero for negative attitude. 0-8 was considered negative attitude, 9-16 neutral and 17-24 positive attitudes. In order to compare their state of awareness, the one-way Kruskal and Wallis analysis were used and for investigation of the type of attitude, the χ^2 test was used. The relation between awareness and attitude was determined by Pearson's correlation coefficient and Chi-square test (the boundary of statistic analysis was $p < 0.05$).

Results

The first section of questionnaire shows that among 275 non-athletes people, 152(55.3%) women and 102 (37.1%) men were tested and 21(7.6%) people did not indicate their gender. Among the 212 coaches, 112(52.8%) women and 89(42%) men were tested and 11 (5.2%) people did not indicate their gender. Among the 327 athletes 140 (42.8%) were women, 177 (54.1%) men and 10 people (3.1%) did not indicate their gender (table1).

Table 1: gender of samples

Gender Group	women		No response		men		total	
	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage
non-athletes	152	55.3	7.6	21	102	37.1	275	34.8
Athletes	140	42.8	3.1	10	177	54.1	327	40.2
Coaches	112	52.8	5.2	11	89	42	212	25
Total	404	46.6	5.2	42	368	45.2	814	100

55% of athletes were taking individual sports and 45% group sports (table 2).

Table 2: absolute frequency and the percentage of athletes by the division of sport type

Sport field	frequency	percentage
Individual	170	52.00
Social	157	48.00
Total	327	100

Table 3: distribution of absolute and relative frequency of the awareness state of ordinary people, coaches and sport teachers

Group	Very weak		weak		average		good		total	
	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage	frequency	percentage
non-athletes	74	26.8	97	35.4	95	34.6	9	3.1	275	33.8
coaches	56	26.4	69	32.7	83	39.1	4	1.8	212	26
Professional athletes	130	39.7	98	30	97	29.7	2	0.6	327	40.2
Total	260	31.9	264	32.4	275	33.8	15	1.9	814	100

Average ages were 30.2 non-athletes people, 34.4 in coaches and 22.6 in athletes. Besides, all of them had information about AIDS and their major source of information was media. The athletes compare to non-athletes people had lower level of awareness ($p < 0.01$), the coaches compared to non-athletes people had higher level of awareness ($p < 0.01$) and no group had the awareness of great level. The most frequency among athletes was very weak awareness and weak level among non-athletes people. Concerning the tendency of them regarding achieving information in the field of AIDS, 60.2% of ordinary people, 66.7% of coaches and 56.8% of athletes had a high tendency to gain information in the field of AIDS (table 3).

22.2% of ordinary people, 21.7% of coaches and 65.7% of athletes were aware of transmission of the disease via donation of infected blood. 94.9% of ordinary people, 94.6% of coaches and 91.4% of athletes were aware of transmission of the disease via contaminated needle and syringe. 88.5% of ordinary people, 89.1% of coaches and 80.9% of athletes were aware of transmission of the disease via sexual relationship. 94.9% of ordinary people, 87.7% of coaches and 85.3% of athletes were aware of transmission of the disease via contaminated needle and blade in the barbershop. 93.8% of ordinary people, 84.4%

of coaches and 78.9% of athletes were aware of transmission of the disease via contaminated medical and dentistry devices. Concerning the non-transmission of disease via public pools, 58.2% of ordinary people, 60.8% of coaches and 59.3% of athletes were aware of that. Concerning the non-transmission of disease via insects' stinger, 49.4% of ordinary people, 45.3% of coaches and 43.4% of athletes were aware of that. 64% of ordinary people, 52.8% of coaches and 57.8% of athletes knew that the disease's factor is not transmitted via sneeze and cough. 65.4% of ordinary people, 62.3% of coaches, and 59% of athletes were aware of non-transmission of disease via crowded places. Substantially, awareness of transmission approaches were more than non-transmission approaches. 7.6% of ordinary people, 8% of coaches and 5.5% of athletes knew the meaning of the term "AIDS". 7.3% of ordinary people, 8.5% of coaches and 5.2% of athletes had information on emergence of acute symptoms of disease and 17.8% of ordinary people, 30.2% of coaches and 20.8% of athletes knew about the non-symptom period of disease. Substantially, awareness of disease, symptoms and the period of disease were weaker than transmission approaches (Table4).

Table 4: correct responses of knowledge of non- athletes people, coaches and athletes

Knowledge items	Knowledge level		
	Non-athletes	coaches	athletes
aware of transmission of the disease via donation of infected blood	22.2%	21.7%	65.7%
aware of transmission of the disease via contaminated needle and syringe	94.9%	94.6%	91.4%
aware of transmission of the disease via contaminated medical and dentistry devices	93.8%	84.4%	78.9%
aware of transmission of the disease via sexual relationship	88.5%	89.1%	80.9%
aware of transmission of the disease via contaminated needle and blade in the barbershop	94.9%	87.7%	85.3%
aware of non-transmission of disease via sneeze and cough	64%	52.8%	57.8%
aware of non-transmission of disease via public pools	58.2%	60.8%	59.3%
aware of non-transmission of disease via insects' stinger	49.4%	45.3%	43.4%
aware of non-transmission of disease via crowded places	65.4%	62.3%	59%
knew the meaning of the term "AIDS"	7.6%	8%	5.5%
had information on emergence of acute symptoms of disease	7.3%	8.5%	5.2%
knew about the non-symptom period of disease	17.8%	30.2%	20.8%

Table 5: distribution of absolute and relative frequency of the attitude state of non athletes people, coaches and athletes

		Negative attitude	Neutral attitude	Positive attitude	Total
Non-athletes	Absolute frequency	128	141	6	275
	Relative frequency	46.5%	51.3%	2.2%	100%
coaches	Absolute frequency	64	128	20	212
	Relative frequency	30.1%	60.2%	9.8%	100%
athletes	Absolute frequency	122	192	13	327
	Relative frequency	37.3%	58.7%	4%	100%
Total	Absolute frequency	314	461	39	814
	Relative frequency	38.6%	56.6%	4.8%	100%

Regarding the attitude of them, 38.6% had negative attitude and 56.6% had neutral attitude regarding this disease, while only 4.8% had proper attitude towards AIDS (table5). There was a direct relation between their attitude and awareness.

Discussion

In the current research, the highest state of awareness was weak for ordinary people, very weak for athletes and average for coaches (table 3). The most frequency of attitude in all three groups was neutral (table 5). In a research done on students of obstetrics and nurses of public and Azad University of Babol (Iran), the highest rate of relative frequency was concerning good state of awareness and the highest rate of relative frequency in students of obstetrics was regarding negative attitude and in students of nursery due to neutral attitude (Omidvar, 2002). In a research done in Turkey randomly on 2004 people from different parts of the city, 1048 people had a high awareness of HIV and the ones with higher

education had even a better attitude, but a quarter of them who had lower education believed that this disease is a punishment by God and it can be avoided by good nutrition and sport (DFID, 2006).

According to a research done on students of high school in Yazd (Iran), 35% of them had weak awareness regarding AIDS and 3% had great awareness and the awareness and attitude of students was increasing by their aging and increase of their grade (Shahbazi, 2000).

In survey of awareness and attitude of students of teaching and medical sciences in Iran, 45% of students had low or average awareness in this field and the awareness of teaching students was lower (Parhizgar, 2002).

In a study on the rate of awareness and attitude of students of medical sciences in New jersey and students of Nigeria which was done by Najem (1998), the awareness and attitude of New jersey students were meaningfully higher than students of Nigeria who had different culture and education (Najem, 1998).

In a study of the rate of orphan child nurses' awareness, they had a good awareness of HIV/AIDS and the awareness was higher among women nurses (Onishi, 2008).

In the survey of factory workers in South Africa which was done after an educational program, 62% of them had positive attitude regarding people infected to AIDS (Sloan, 2005).

The research done in Sahara of Africa on 568 people indicated that these people had high awareness of AIDS and its prevention (90%), (Nkya, 2006).

In the only research done on the athletes by Silva (2002), 25 professional players of the youth soccer team were inspected. The subjected athletes had good awareness regarding the approaches of transmission of AIDS, but regarding the chance of their own infection to HIV considering the rate of their vulnerability they didn't have good awareness (Silva, 2002).

In a research in Turkey, the major source of student's information was TV (Ungan, 2003). Also in a research, the students of basic and human sciences preferred TV for gaining

information (Nustas, 2003). In a research on Azad university biology students (Iran) the major sources of information were media (Nasri 2005). In the current research, the major sources of information were media, too.

Considering the current research, the rate of awareness and knowledge of individuals were not in an accepted level which is indicative of the failure of AIDS' public educations. For prevention of AIDS by relying to increasing the state of awareness of society members via public education, we can give proper statistics to the society members in order to make them pay more attention to this illness.

The athletes can have an important role in attracting the society's attention to social matters like HIV/AIDS (Ball, 2003). Besides, the athletes, because of being the pattern for the society, can play important role in guidance of society towards physical health by avoiding risky behaviors and this cannot be gained unless via their higher state of awareness and knowledge. Indeed, because of the close relation of coaches to the young and adolescents (in danger group), for more success of preventive programs in Iran education of this group should be considered. In a research done on Iranian students, the emphasis on education and advertising on the prevention of AIDS in order to increase awareness of students and emphasis of Iranian Ministry of Health, Treatment and Medical sciences on AIDS and preparation of exact statistics are suggested (Shahbazi, 2000). According to the current research, providing professional athletes and their coaches with education not only guarantees their health regarding AIDS, but also because their important role in the society, it can be effective on the prevention of this disease in the whole society.

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Study of Influence Indol-3-Carbinol, Epigallocatechin-3-Gallate and Soy on Proliferation Diseases of the Reproductive System in Women

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Abstract

Background: Recent reports have indicated that indol-3-carbinol (I3C), epigallocatechin-3-gallate (EGCG) and soy may obtain antiproliferation effect.

Aims: To confirm the influence of combination I3C, EGCG and soy on proliferation diseases of reproductive system in women.

Methods: 30 patients ($41,3 \pm 4,28$ age) with diseases of reproductive system with proliferation: benign breast diseases - 6 patients (20%), myoma of body of uterus and adnexitis-4 (13,3%), adenomyosis and polyp of cervix of uterus-5 (16,6%), myoma of body of uterus and adenomyosis-8 (26,6%), myoma of body of uterus and adenomyosis and chronic cystic mastitis-7 (23,3%), were involved in the study. Among them there were 6 postmenopausal women. Nobody from patients took the hormonal treatment before study. Diagnoses were confirmed

by sonographic and mammographic. All the patients took I3C, EGCG and soy per os for 6 months. The women with benign breast diseases estimated their pain according questionnaire for pain, three times: before, in 3 and in 6 months of taking I3C, EGCG and soy. After 3 and 6 months patients were examined by sonographic.

Results: see tables below:

Table A: Changes of scores for pain in mammary glands

Level of pain	Patients (n13), % (before I3C, EGCG and soy)	Patients (n13),% (after 3 month taking)	Patients (n13), % (after 6 month taking)
Severe pain	46,15	0	0
Moderate pain	23,07	23,07	15,3
Mild pain	30,77	15,3*	15,3
None	0	61,63*	69,33

*-p<0,05

The size of cysts in mammary glands changed: when before taking I3C, EGCG and soy it was $1,1 \pm 0,3$ sm then in 3 months it decreased up to $0,60 \pm 0,22$ sm (p=0,0001). Cysts with size 0,5sm and less weren't found in 3 months by sonographic.

Table B: Changes of uterine volume and myoma

Data of ultrasonographic	Before I-3-C, EGCG and soy (n19)	Size after 3 month taking (n19)	Size after 6 month taking (n19)
uterine volume, ml	184,1±4,1	168,3±3,5*	162,2±3,7
myoma, ml	80,1±3,6	72,4 ± 2,4*	70,4 ± 2,1*

*-p<0,05

Conclusion: After 3 month taking I3C, EGCG and soy the decrease in pain, oedema and size of cysts in women with benign breast diseases was confirmed. The decrease in uterine

volume and myoma was statistically significant. No woman showed negative dynamic of proliferation diseases.

Keywords: Reproductive, antiproliferation, indol-3-carbinol, epigallocatechin-3-galate, soy

Introduction

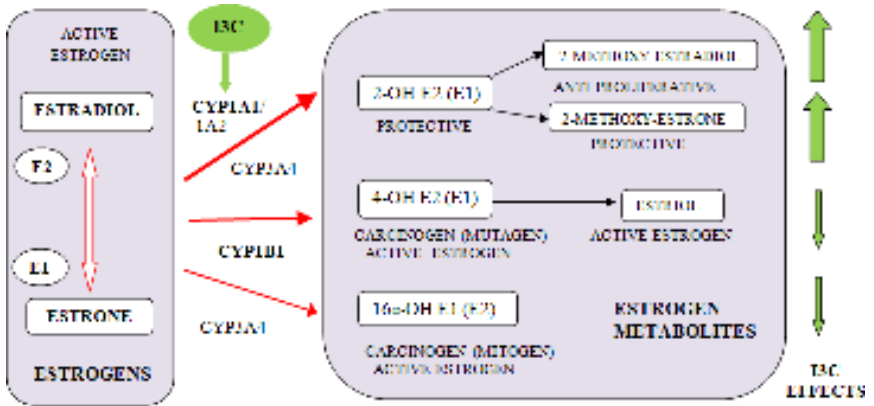
Today early diagnostics and preventive maintenance of proliferative diseases of reproductive system play the important role. The progressing of these diseases makes necessary to take and change hormonal drugs which have plenty of undesirable effects. Women with this diagnosis can be exposed to surgical interventions, but it does not protect them from relapse of disease. Vegetable products with estrogen-like effects are less active than hormonal drugs, but do not possess such quantity of undesirable effects.

Processes which induce proliferative diseases of reproductive system are hormone-dependent. Important role is played by not the very estrogens but their metabolites. The study shows that estron and estradiol only represent 10-15% of all estrogen derivatives and 85-90% is done by metabolites of estrogen: 2-hydroxyestrone (2-OHE1), 4-hydroxyestrone (4-OHE1) or 16 α -hydroxyestrone (16 α -OHE1) (Lord et al., 2002). Isoenzymes of the cytochrom P450 can hydroxylize estron and estradiol at 2-, 4- or 16- positions. Therefore, the metabolites of estrogen are 2-OHE1, 4-OHE1 and 16 α -OHE1. 2-OHE1 synthesizes with participation of enzymes CYP1A1/1A2 and, at a smaller degree, CYP3A4. CYP 1A1 can be induced by cigarette smoking and diet including soy, flax, cruciferous vegetables, indol-3-carbinol (I3C) (Bradlow et al., 1999; Lord et al., 2002; Komori et al., 1993; Bovee et al., 2008; Takashi et al., 1995). 2-OHE1 has no influence on cell proliferation.

16 α -OHE1 is strong agonist of estrogen. It is formed with participation of CYP3A and CYP1B1. CYP1B1 can be induced by xenobiotic carcinogens, pesticide, but not diet. 2-OHE1 binds to a receptor for a short time and 16 α -OHE1 is capable

to bind to a receptor for the period from several hours to several days. Long and strong influence of this metabolite on a cell stimulates its proliferative growth. Mitogen effect of 16 α -OHE1 is twice higher than estradiol. 16 α -OHE1 can influence DNA synthesis and increase cell proliferation. 4-OHE is agonist of estrogen, but its concentration is low, its influence on development of proliferative is non-significant in comparison with 2-OHE1 and 16 α -OHE1. Like 16 α -OHE1, 4-OHE1 possesses estrogen activity and it is capable to damage DNA of cells (Bradlow et al., 1999) (Figure 1). The study shows that CYP1B1 is present in cancer cells, mainly with estrogen-dependent phenotype, in essential quantity.

Figure 1: Metabolism of estrogen and influence of I3C



Receptors of estrogens must be considered. The estrogen is capable to bind to two kinds of receptor - ER α and ER β . Binding of estrogens and estrogen metabolites to ER α leads to more active proliferative response, then to ER β . In a cell, subordinated to cancer transformation or proliferative growth, increases ER α expression in comparison with ER β can be found. On this background the purpose of therapeutic correction should be ER α . A lot of studies have confirmed genetic polymorphisms of ER α (Hamaguchi et al., 2008). In this connection, substances which can change metabolism

of estrogens to antiproliferative 2-OHE1 and reduce 16 α -OHE1 formation are searched actively. I3C makes CYP1A1 more active, forming the basis for antiestrogen protection. Quantity of 16 α -OHE1, which makes the receptors active, decreases and that leads to depression of proliferative growth (Bradlow, 1994; Telang et al., 1997; Chen et al., 1998) (Figure 1). Responses to I3C vary among individuals due to genetic polymorphic variation in the inducibility of CYP1A1. 3,3 – diindolymethane (DIM) is a major product of I3C. Studies in vitro demonstrated depression of endometrial cancer cells by induction of TGF- α expression and secretion (Leong et al., 2001). Cruciferous vegetables (I3C) and less soy isoflavones can induce CYP1A1 which leads to increase in 2-OHE1 level. The activation of CYP1A1 depends on genetic polymorphic variation.

Soy isoflavones are phytoestrogen. Soy can influence on the both estrogen receptors (ERa and ERb) and bind with SHBG. Soy can decrease level of circulating 17 β -estradiol. Study of isoflavones soy demonstrates different results. For example, the study in the animal models (rats) showed suppressing tumorigenesis after taking of genistin and ipriflavon soy (Hooshmad et al., 2008). The study in the ovariectomized rats showed inducing influence of soy on reproductive organs like that of 17beta - estradiol (Rimoldi et al., 2007). Otherwise the study in human breast cancer cells showed inhibition effects of soy (Kim et al., 2008).

Soy is considered to exhibit anticancer effect though the relationship between soy and breast cancer is controversial. Soy also demonstrates estrogen-like effect and can induce proliferative growth of cells. Postmenopausal women especially with high risk of breast cancer are not supposed to need estrogen-like influences and soy did not show any influence on the mammographic density (biomarker for breast cancer risk) in postmenopausal women to the breast cancer risk (Verheus et al., 2008).

Although multiple studies and evidence have not reported the influence of soy on the breast proliferation or mammographic

density and less protective effect, the epidemiologic studies have demonstrated reduction of risk breast cancer among Asian and Japans women taking soyfood. Thus other factors, not soy can be supposed to influence on risk breast cancer (Messina et al., 2008).

Today there is not direct evidence protective effect soy to the breast risk cancer (evidence grade C). However the prospective study showed decrease in risk of colorectal cancer in postmenopausal women taking soy (68 412 respondents) (Yang et al., 2008) and soy may help reduce menopausal symptoms, such as hot flashes (grade evidence B) and cyclical breast pain.

Epigallocatechin-3-gallate (EGCG) of green tea possesses ability of blocking metalloproteinase (MMP) and neoangiogenesis (VEGF) in cancer cells and has antiproliferative effects (Masuda et al.,2002; Roy et al.,2005; Thangapazham et al., 2007). The study shows that in small concentration EGCG pretends as estrogen and stimulate expression and activity ERA, while in greater concentration EGCG, on the contrary, blocks the ERA activity (Kuruto-Niwa et al., 2000; Somers-Edgar et al., 2008). EGCG in vitro is capable to induce of apoptosis and inhibition of cell growth to the breast cancer cells. There is a class of inhibitor of apoptostosis proteins which are included in the cycle of proliferation and resistance to chemotherapy and radiation therapy in breast cancer. EGCG directly and indirectly can block these proteins (Tang et al., 2007). Influence of flavonoids (EGCG, genistin, daidzin and other) on the efflux transporters (P-glycoprotein, multidrug resistance-associated protein 1 (MRP1) and breast cancer resistance protein) has been studied. Flavonoids (genistin, EGCG) demonstrated the inhibitions of P-glicoprotein and another anion transport system (OATP1B1) which can be useful for blocking drug-resistance tumor cells (Wang et al, 2005). A study conducted in healthy postmenopausal women showed that a morning/evening menopausal formula containing green tea was effective in relieving menopausal symptoms including hot flashes and sleep disturbance. Further studies are needed to confirm these results

(grade evidence C).

Aim of the Study

1. To study influence of vegetable products containing I3C, soy and EGCG (biologically active additive (BAA)) in women with proliferative diseases of reproductive system.
2. To confirm efficiency and safety of biologically active additive containing I3C, soy and EGCG in women with proliferative diseases of reproductive system.

Methods

Criteria of inclusion: 1. Patients < 18 from to 45 years, with the confirmed diagnoses: benign breast diseases or chronic cystic mastitis with size of cyst no more than 1,5cm and/or a myoma of uterus of any localization no more than 12 weeks without necessity of operation and/or polyps of cervix of uterus and/or endometriosis. Criteria of exclusion: Pregnancy and lactation; cancer any localization; liver cirrhosis; NYHA III-IV; active hepatitis; renal failure; necessity of emergency operative intervention; myoma is more than 12 weeks, hemorrhagia.

30 patients are included in the open study of influence biologically active additive (BAA) consisted I3C, EGCG and soy on the proliferative diseases of reproductive system in women, aged $41,3 \pm 4,28$. There were 6 postmenopausal women in the study. Nobody of patients took the hormonal treatment before being involved.

Table 1: Distribution of patients with proliferative diseases of reproductive system

The diagnoses	Patients (n =30)	% of patients
Benign breast diseases (chronic cystic mastitis)	6	20 %
Myoma of body of uterus, adnexitis	4	13,3 %
Adenomyosis and polyp of cervix uterus	5	16,6 %
Myoma of body of uterus and adenomyosis	8	26,6 %
Myoma of body of uterus, adenomyosis and benign breast diseases (chronic cystic mastitis)	7	23,3 %

Diagnoses were confirmed by ultrasonographic and mammographic. All patients took I3C per os not less than 300 mg per day, extract of green tea (EGCG) 180 mg per day, soy isoflavones (genistein, dsadzein) 180 mg per day. All the patients took I-3-C, EGCG and soy per os for 6 months. The women with benign breast diseases estimated their pain according questionnaire for pain, three times: before, in 3 and in 6 months of taking I-3-C, EGCG and soy. After 3 and 6 months patients were examined by ultrasonographic. The statistical analysis was realized by Wilcoxon nonparametric method.

Results

Among 30 patients with proliferative diseases of reproductive system included in the study there were 13 patients with benign breast diseases. According to ultrasonographic and mammographic, the most of those with benign breast diseases had cysts (9 patients) and the rest had dominant lumps (4 patients). The patients were not divided into groups because of small quantity of patients. All patients felt pain before taking BAA. The patients estimated the strength of breast pain independently with questionnaire: from absence of pain (none) till as much as possible expressed pain (severe pain). The results were estimated clinically, by questionnaire of pain and by ultrasonography.

Table 2: Changes of strength for pain in mammary glands

Level of pain	Patients (n13), % (before I3C, EGCG and soy)	Patients (n13), % (after 3 month taking)	Patients (n13), % (after 6 month taking)
Severe pain	46,15	0	0
Moderate pain	23,07	23,07	15,3*
Mild pain	30,77	15,3*	15,3
None	0	61,63*	69,33

*-p<0,05

After 3 months the most patients had decrease in pain and oedema in mammary glands. Nobody described severe pain (see table 2).

After 3 months we found decrease of density in mammary glands by ultrasonographic. The size of cysts in mammary glands changed: when before taking I3C, EGCG and soy it was $1,1 \pm 0,3$ sm then in 3 months it decreased up to $0,60 \pm 0,22$ sm ($p=0,0001$). Cysts with size 0,5sm and less (4 patients) weren't found in 3 months by ultrasonographic. After 3 months 5 women who only had benign breast diseases stopped taking BBA because they didn't feel pain any more. Protective effect was kept average $2,3 \pm 0,2$ months.

Among 30 patients with proliferative diseases of reproductive system included in the study there were 21 women with myoma and adenomiosis. The diagnosis was confirmed by ultrasonographic. Our patients didn't need surgical intervention. Among patients with myoma 14 patients had hypermetrorragia and dismenoragia of mild or moderate degree. 5 patients with myoma and adenomyosis didn't have any complains.

Table 3: Changes of uterine volume and myoma

Data of ultrasonographic	Before I-3-C, EGCG and soy (n19)	Size after 3 month taking (n19)	Size after 6 month taking (n19)
uterine volume, ml	184,1±4,1	168,3±3,5*	162,2±3,5
myoma, ml	80,1±3,6	72,4 ± 2,4*	70,4 ± 2,1*

*- $p < 0,05$

After taking BAA we found statistically significant decrease in uterine volume (ml) and size of myoma (ml). The decrease was kept during last 3 months of the study and confirmed by sonographic. After 3 month the number of patients with hypermetrorragia and dismenoragia decreased to 4 (against 14 at the beginning). After $5,3 \pm 0,28$ months of treatment nobody has complains at all.

Conclusion

After 3 month taking I3C, EGCG and soy the decrease in pain, oedema and size of cysts in women with benign breast diseases was confirmed. The decrease in uterine volume and myoma size was statistically significant by sonographic. The number of patients with hypermetrorragia and dismenoragia decreased considerably. At the end of the study there was nobody complaining of these symptoms. No woman showed negative dynamic of proliferation diseases. Our study confirms efficiency and safety of biologically active additive containing I3C, EGCG and soy in the women with proliferative diseases of reproductive system who needn't surgical intervention and/or hormone treatment.

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Treatment of Equine Foot in Cerebral Palsy: a study carried out in a Romanian hospital

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Abstract

Cerebral palsy is expressed by involuntary movement, muscular spasms which can affect a specific part, half or the entire body. The presence of this affection during a certain period, reported to the entire population, illustrates the therapeutic emergency that is cerebral palsy: in Sweden in the 1980's a percentage of 2.4°/oo were affected and in the 1990s approximately 2.5 °/oo [1]. The affections which prevail in Great Britain and which

represent the neurological illness prevalence are represented by: spastic tetraplegia forms, spastic diplegia, extrapyramidal forms, hemiplegia [2]. The present paper shows the advantages and disadvantages of botulinum toxin treatment at young patients suffering from equinovarus foot. We conclude that botulinum toxins can be used as a therapeutic test before any orthopedic intervention on a spastic child. Still, this substance cannot replace posture orthosis, kinetic-therapy, ergo-therapy, electrotherapy, orthopedic surgery.

Keywords: Cerebral palsy, equinovarus, botulinum toxin, physical therapy

Introduction

The present paper discusses a fairly difficult problem in pediatric recovery. Cerebral palsy CP is a central nervous system deficit resulting from a non-progressive lesion in developing brain.

Cerebral palsy is expressed by involuntary movement, muscular spasms which can affect a specific part, half or the entire body (Vigasio et al., 2008).

The lesion can appear during embryonic development, during birth or in the first two years of life, determining motor affections, involuntary movement, persistent tonus and posture affections associated or not with cognitive problems (Hosalkar et al., 2008).

Premature born children have a high risk of cerebral hemorrhage which could lead to the presence of cerebral palsy. The study was carried out in “Nicolae Robanescu Medical Centre Clinic” on 34 patients with equinovarus condition between 1.09.2008 -01.12.2008. The patients were treated using botulinum toxin because all other treatments failed. The present paper tries to validate the hypothesis that the infiltration of botulinum toxin in the treatment of equine foot in cerebral palsy represents one of the more efficient treatment methods today (Grayevet al., 2001). This can allow

improvement of movement and sustained walking for at least 4 to 6 months, as long as the relaxing effect of the toxin lasts.

We will try to validate the hypothesis that botulinum toxin infiltrations to treat equinovarus medical condition as a result of cerebral palsy, as one of the most efficient techniques.

The causes can be structured as follows: before birth, during or around the time of birth and after birth.

Ante-natal causes: appear during the intrauterine development and can be: infections, diabetes (mother's disease), placenta diseases, alcohol consumption, anemia or rHI incompatibility between mother and fetus (Slavek & Klimont, 2003).

Perinatal causes

Appear during birth or right after birth, determining an insufficient oxygenation of the newborn's brain. One of the reason is that, during labor, is necessary to frequently apply the forceps which in some cases may lead to cerebral hemorrhage or cerebral hypoxia. So, a strenuous birth, or a prolonged pregnancy, in which the mother receives sedative medication and anesthetics, can represent a cause for hypoxia or cerebral lesions (Slavek et al., 2005).

The responsible factors that highlight the post-birth causes are those that occur from the moment of birth up until the age of 3-4 years when the brain maturation takes place: encephalitis, meningitis, intoxications and others (Amarenco & Pelvi-perineologie, 2006; Grayevet al., 2001). Although cerebral palsy can have different causes, in the literature there exists a notable similarity of incidence.

The presence of this affection during a certain period, reported to the entire population, illustrates the therapeutic emergency that is cerebral palsy: in Sweden in the 1980s a percentage of 2.4% were affected and in the 1990s approximately 2.5%.

The affections which prevail in Great Britain and which represent the neurological illness prevalence are represented by: spastic tetraplegia forms, spastic diplegia, extrapyramidal forms, hemiplegia.

Spasticity represents one of the characteristic symptoms of cerebral palsy, together with exaggerated tendinous reflexes which result from the hyper-excitability of the extension reflex as a component of the central motor neuron syndrome (Lance), clonus and motor deficit (Ugnow et al., 2007). Spasticity is the most common motor abnormality associated with cerebral palsy and also is an uncomfortable and disabling condition without voluntary muscle movement. The spasticity is considered a resistance to passive movements, impaired active movements, hiperreactivity to exteroceptive stimuli (Edss evaluation scores).

The muscular groups most affected by spasticity are: the great pectoral, posterior deltoid, brachial biceps, round pronator, square pronator, brachioradial, carp radial flexor and ulnar carp flexor.

The purpose of the cerebral palsy patient's treatment is the acquisition of walking and ADL (activities of daily living) autonomy. These can be achieved by a complex scheme of treatment which includes, according to the patient, kinetic-therapy, ergo-therapy, physiotherapy and psychology.

Spasticity is one of the characteristic symptoms of cerebral palsy besides the extreme tendinous reflexes that result from the hyperexcitability of stretch reflex as a component of the central neuron motor syndrome (Lance), clonus and motor deficiency. Spasticity is the most common motor abnormality associated with cerebral palsy and also is an uncomfortable and disabling condition without voluntary muscle movement (Lancioni et al., 2004). The spasticity is considered as a resistance to passive movements, impaired active movements, hiperreactivity to exteroceptive stimuli (Edss evaluation scores).

Muscular groups most affected by spasticity are the following: large pectoral, posterior deltoid, brachial biceps, round pronator, square pronator, and carp's ulnar flexor.

The purpose of treating the patient with cerebral palsy is to achieve walking and autonomy in ADL (activities of daily living). This can be achieved through a complex treatment

composed of physical-therapy, ergo-therapy, physiotherapy and psychotherapy.

The methods utilized in reducing spasticity, in a recovery clinic, are the following: drug methods, orthotic methods, kinetic methods, electrotherapeutic methods, thermotherapy, botulinum toxin and the surgical elongation intervention treatment (Wang et al., 1999).

In the last 10-15 years, alcohol and phenol treatments were replaced with infiltrations with botulinum toxin, this representing one of the methods which proved efficient in cerebral palsy child spasticity treatment.

By using the botulinum toxin the neuro-muscular function has been improved when the muscular retraction hasn't installed yet.

To obtain the reduction of spasticity for the affected muscular groups there were attempted several procedures, including: use of serial plaster apparatus, alcohol infiltrations, but no other method was proven more efficient than the botulinum toxin, argued by concrete facts that represent an important step in neuro-motor evolution.

Botulinum Toxin A is produced by *Clostridium botulinum*, a gram-positive bacterium which causes the flaccid muscular paralysis seen in botulism (Herbaut & Pelv, 2008).

Clostridium botulinum was first recognized and isolated by Emile van Ermengem.

We must first understand the action mechanism of the botulinum toxin on the muscle. Acetylcholine transmits this message from the nerve to the muscle. Sometimes an anomaly of the brain or muscle can lead to a lack of coordination of the muscles. This represents one of the reasons of muscular spasms or apparition of vicious postures, which can cause pain. The botulinum toxin acts against these deficits. In infiltrations, the quantity used is very small and there is a reduced risk of associating or developing another pathology, such as paralysis of body musculature, being known that the toxic dosage is 50 times larger than the therapeutic dosage used in speciality clinics.

This substance is infiltrated in the spastic muscular groups and is divided distinctively to several muscular plaques blocking the discharge of acetylcholine and thus stopping the transmission of nervous signal with the reduction or even elimination of muscular groups spasticity. The botulinum toxin infiltration does not act directly on the main disease and cannot lead to its cure, but by its effects associated with correct recuperatory treatment can prevent the apparitions of vicious positions. Dysport is the drug that contains the botulinum toxin- type A, this being a proteic complex with a molecular weight of 1 140 000.

The drug is used after a decision is made by the recuperatory team, consisting of the physician, kineto-therapist, ergo-therapist, medical nurse. It must be mentioned that any infiltration is performed with the mother or tutor of the child, by showing the toxin bottle beforehand and obtaining a dispersed solution with physiologic serum.

The effect of the injection can be noticed in 24 to 72 hours, while the musculature begins to relax and the movement degree in the affected region begins to improve (i.e: equinovarus foot).

The advantage of botulinum toxin infiltration is the fact that in the relaxation period, the child can learn under the periodic control of the kineto-therapist the scheme of walking and can acquire the ability to perform fine movements with the help of the superior extremities. Even in the cases when the infiltration effect disappears, the patient will be able to establish the best solution in order to correct his own spasticity (it must be mentioned that the relaxing effect of the substance lasts for 4-6 moths). Also, this relaxing effect can increase the patients' life comfort by reintroducing them in the family environment or through the possibility to perform some ergo-therapeutic activities, restoring the daily movement and the usual activities that every person possesses.

It is considered that this procedure is favourable because it is done strictly at a muscular level and not by oral administration

of drugs that can be damaging by spreading to different parts of the body, causing sleepiness, epigastric pain or dizziness.

Another benefit of toxin infiltration, also very important, is the possibility to temporize the surgical intervention, to postpone it to an optimal moment, being known that anaesthesia supplements the stress on the patient's brain.

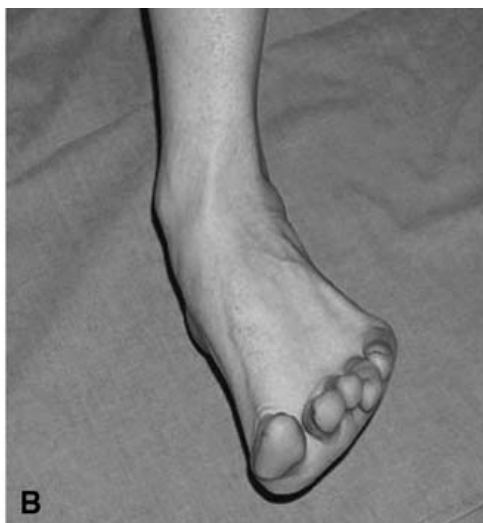
A possible disadvantage of toxin infiltration can be determined by the apparition of flu-like symptoms. Because of this it is necessary to be more prudent in accomplishing the therapeutic protocol in case of infiltration for patients with altered general status or various myopathies.

There can exist, as it does with any type of injection, secondary effects such as pain, slight bleeding or infection risk.

Two of the contraindications of injecting botulinum toxin are: patients whose intellect does not permit an appropriate recovery in the post-injection period, but also the inopportune, exaggerated elongation of the spastic musculature groups. The relaxation of these muscular groups, by blocking the neuromuscular plaque, will not produce any gain of functionality for the locomotive apparatus.

Figure 1 shows the normal foot position (Figure 1 A), and equinovarus foot (Figure 1 B).





Methodology

Although every individual is different regarding the organism's response to the treatment or to certain manoeuvres performed by the recovery team, the objectives are:

Symptomatic

These are represented by improvement of pain, articulation amplitude by increased muscular fibre elasticity and providing the best medical care in order to improve the health status of the spastic patient.

Functional

By these there can be obtained (on a limited period only) the hand's dexterity and its verticalization, creating stability needed to obtain the functional objective represented by orthostatism and walking without support on the external side of the equine foot. For a more efficient supervision of the treatment, the objectives could be divided as follows: reduction of spasticity of muscular groups, pain alleviation, degree of correcting the vicious postures and locomotive apparatus deficits. Due to the

infiltration with botulinum toxine, Kinetic-therapy reveals a valuable role in psychic recovery from neuro-locomotive deficits.

Patients and methods

We studied the evolution of spasticity and disability of equinovarus foot.

The study was done in the “ Dr. Nicolae Robanescu Clinical Neuropsychomotor Medical Recovery Center for Children “ on a group of 34 patients with cerebral palsy, between 1.09.2008 and 1.12.2008 under the guidance of University Lecturer Dr. Liliana Padure and kineto-therapist lecturer Felician Ion.

Patients

The group was composed of patients committed to the Center, which benefited by all forms of treatment (kinetic-therapy, ergo-therapy, psychology, physiotherapy) that the Clinic has to offer.

The patients suffered from equine foot medical condition associated to the clinical form (diparesis, tetraparesis, hemiparesis, paraparesis). Equine foot is a very frequent deformity in cerebral palsy, which includes modifications of shape and direction of the foot, the consequence being an imperfect contact with the floor. It consists of plant flexion and foot adduction and the floor support is done on its external margin. The equine foot is not painful in infants but as the child grows up it causes discomfort and becomes a visible physical deficiency which causes the patient a psychological inferiority. The affected limb that is not treated can become deformed and can lead to an inequality of legs. This is why, the sooner the treatment is initiated the greater the chances are to improve and reduce the deformity which threatens the possibility of maintaining the balance, walking and not only that.

Methods

As far as the imaging methods are concerned after the birth of a child suspected of equine foot, radiography does not usually help a diagnosis because some of the bones of the foot or the ankle articulation are not completely ossified and a certain diagnosis cannot be made.

The spasticity was evaluated on the Ashworth modified scale, all of the patients having a 4 score.

“Ashworth scale” aimed to explore measuring spasticity. An isokinetic dynamometer to quantify resistance to passive stretch and surface EMG was used to verify if a stretch response occurred and if so, at what joint angle”(Cambridge University Press).

The Ashworth scale

- | |
|--|
| <ol style="list-style-type: none">0. No movement1. Palpable contraction ,no visible movement2. Movement but only with gravity eliminated3. Movement against gravity4. Movement against resistance but weaker than normal5. Normal power |
|--|

The frequency of this pathology in medical recovery field is encountered mainly in males (70%) and less in females (30%).

If in the family there is a child with spastic equine foot, the chances that the second child has this affection increase a lot. Neurologic equine foot can indicate other health problems, because it can be associated with other affections such as: spina bifida. This is the reason for investigating other health parameters.

All 34 patients that presented equinovarus foot were infiltrated with botulinum toxin because all the other treatment methods had become insufficient. The patients were recruited from the age of two until 20 years and after all the other methods to relax the spastic musculature were tried.

The infiltration was performed on the adductor muscles of the thigh, sural triceps, lateral peroneal, great pectoral.

Correction of vicious postures of foot by infiltrating triceps sural was: from the group of 34 patients studied, 12 were infiltrated once in the thigh adductors and in sural triceps (5 girls and 7 boys), 14 patients were injected twice in the lateral peroneals (8 girls and 6 boys) and 8 patients were infiltrated three times in the sural triceps.

Table 1: Number of infiltrations, on muscular groups as a function of patients sex and age

Number of patients	Gender	Number of infiltrations	Muscular Group
12	5G/7M	1	Thigh adductors Sural triceps
14	8G/6M	2	Lateral peroneals
8	8G/0M	3	Sural triceps
Total=34	=	=	=

Treatment methods

The injected dosages were chosen according to the weight of the child, the thickness of the muscle which was being infiltrated and the degree of affection of the spastic muscle and also the number of the muscles that needed to be injected.

The evaluation of the results was done for the first time after 8 days since the infiltration, then at 14 days, each time by the whole team that took care of the patient during treatment (physician, kineto-therapist, student) and the time effect will be followed continuously. The side effects were not noticed, except for two girls who presented a slight sensation of muscular fatigability in the muscular groups adjacent to the infiltration, this symptom disappearing after they started walking. The most consistent results were observed at very young patients, using doses of 30 U/kg.

Table 2 Shows the time needed in order to see the results. For each patient we used doses equal to 10-35U/kg of body weight. The injection was a dose of botulinum toxin type A. The difference in doses was determined by finding the right amounts of substance needed to treat each patient. The results were: an increase in the walking distances and the removal of any type of support used while walking (a person, walking stick etc).

Table 2: Time needed for results

Results	24h	48h	72h	168
Number of patients	15	8	7	4

Conclusions

Although the complications of cerebral palsy are various, the equine foot is one of the most frequent pathologies in children. Although there exist various current treatments available, the botulinum toxin is irreplaceable as a therapeutic method, its effects, even temporary, allowing real motor progress.

The botulinum toxins can be used as a therapeutic test before any orthopedic intervention on a spastic child. Still, this substance cannot replace posture orthosis, kinetic-therapy, ergo-therapy, electrotherapy and orthopedic surgery

Results

The results appear in time and represent an association between the reduction of spasticity after toxin infiltration and long time kinetic-therapy.



Before



After

Acknowledgements

The authors would like to acknowledge the staff of “Dr. Nicolae Robanescu Clinical Neuropsychomotor Medical Recovery Center for Children” for their help during the study. We would also acknowledge the patients and their families for accepting to take part in this study.

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Cytoprotective Effect of *Nigella sativa* L. on Experimentally Induced Gastric Ulcer in Rats

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Abstract

Background: *Nigella sativa* seeds are popular in the Middle East and the entire Old world. It is used traditionally as a folk medicine for various remedy.

Aim & Objectives: The present study was done to investigate cytoprotective effect of *N.sativa* seeds in gastric ulcer induced by ethanol in rats.

Methods/Study Design: Four groups of rats were used. First, Control Group or labeled as Group 1 were administered with distilled water; Second, Reference Group or labeled as Group 2, each rat was treated with 50mgml⁻¹ of Cimetidine; Third, test group was labeled as Group 3 was treated with 400mgml⁻¹ of methanol extract of *N.sativa*; and Group fourth which labeled as Group 4 was treated with 400mgml⁻¹ of aqueous extract of *N. sativa*. Each rat received oral pretreatment accordingly. After 30 minutes, all rats were administered absolute ethanol as gastric damaging agent. One hour later, all rats were sacrificed and their stomachs were

observed macroscopically and microscopically (histology examination).

Results/Finding: Grossly, the result showed that rats administered with *N.sativa* seeds extract or cimetidine showed marked antiulcerogenic activity in gastric ulcer. Histologically, rats administered with seeds extract of *N.sativa* have no or mild subcutaneous edema and no leukocytes infiltration compared to control. Aqueous extract of *N.sativa* seeds showed the most significant antiulcerogenic compare to the other groups.

Conclusion: This study demonstrates that aqueous seeds extract significantly prevents gastric ulcer in rats.

Keywords: *Nigella sativa*, cytoprotective, cimetidine, histology

Introduction

Peptic ulcer is a pathological condition whereby ulcers develop around the gastric and duodenal. It occur when there is imbalance between aggressive (acid and pepsin) and defensive factors (mucus, bicarbonate, local prostaglandin synthesis, gastric mucosa blood flow). The ulcers develop when acid and pepsin contained, breach the antrum surface when the protective factor is interrupted. (Grossman, 1981; Katzung, 1995). Stress, ethanol, *H.pylori*, Non-steroidal anti-inflammatory drugs (NSAIDs), smoking cigarettes, large doses and long period of treatment with adenocorticosteroids, coffee and other caffeine containing beverage are ulcerogenic agents that may interrupt the balance of these aggressive and defensive factor thus induce ulcers formation in the stomach (Grossman, 1981).

Nigella sativa Linn (*N. sativa* L.) is a plant belongs to botanical family of Ranunculaceae (D'Antuono *et al.*, 2002).The plant is widely cultivated throughout South Europe, Syria, Egypt, Saudi Arabia, Turkey, Iran, Pakistan, Mediterranean and Northern Morocco and run wild in India (Kirtikar and Basu, 1980; Zaoui *et al.*, 2002). The seeds of *N.sativa* L. or well known as Black

seeds are widely used in the entire Old World including Asia and Africa. Black seeds were used as a spice and condiment or added to bread dough in the Middle East and occasionally used in Europe as both a pepper substitute and a spice (Fararh *et al.*, 2005).

N.sativa had been used for thousands of years as folk medicine as well (El-Dakhakhny *et al.*, 2000). The seeds of *N.sativa* (Black seeds) represent the useful product for medical purpose. Most medical properties are contributed by quinones constituent of which Thymoquinone is the main active constituent of the volatile oil of the black seeds. Thymoquinone possess strong antioxidant properties, anti-inflammatory action with lipid peroxidation (Houghton *et al.*, 1995), anti-histaminergic (Awada and Binderb, 2005). The whole seeds have antidiabetic, antihypertensive, antimicrobial (Fararh *et al.*, 2005), anti-inflammatory (Al-Ghamdi, 2000), antiulcerogenic, antitumor and treatment for asthma as well as (El-Dakhakhny *et al.*, 2000) for treatment of various respiratory and gastrointestinal diseases (Fararh *et al.*, 2005).

The seeds also contain tannins, saponins, quinones, glucosinolates, sterols, and/or triterpenes, arachidonic acid, eicosadienoic acid, linoleic acid and palmitic acid as well as niggellone (Zaman *et al.*, 2004).

In the present study, we have tested the methanol and aqueous extract of the plant against experimental ulcer generated by using absolute ethanol. It may also serve as alternative medicine by using traditional herbal medicine for treatment of disease related to gastric mucosal damage such as peptic ulcer.

Objectives

To evaluate the cytoprotective effect of *Nigella sativa* L. macroscopically and microscopically on experimentally induced gastric ulcer in rats.

Materials and Method

Plant extract

Seeds of *N. sativa* L. (black seeds) were purchased from Egypt. 50 grams of fully ground and dried of black seeds were soaked with hot water and methanol in a 1:10 ratio (in volume) respectively. The crude extracts of the seeds were obtained by using rotary evaporator. Aqueous extract was freeze dried to obtain dried powdered form. Both crude extracts were stored at -20⁰C until time of used. Fresh sample of 5ml/kg of extracts were prepared on the day of oral pretreatment study.

Cimetidine

Cimetidine was used as reference control as its role as antihistamine (H₂) receptor. This drug was obtained from University Malaya Medical centre (UMMC), Kuala Lumpur. Fresh sample of cimetidine of 5ml/kg (50mg/ml) was prepared on the day of oral pretreatment study.

Experimental animals

The *Sprague Dawley* rats were used for the study. The healthy rats that weighted 150-200 grams and ages 6-8 weeks were obtained from the animal house, Faculty of Medicine, University of Malaya. The rats were randomly divided into 4 groups of 6 rats each. They were house separately (one rat per cage) in cages with wide-mesh wire bottom to prevent coprophagy and dominancy. The animals were left for 2 days to acclimatize to the animal room conditions and maintained on standard pellet diet and tap water. The rats were fasted for 48 hours before the oral pretreatment.

Treatment

Water supplement were removed 2 hours before oral pretreatment started. Each rats in group 1 (Control Group) was given 1 ml of distilled water. Meanwhile, each rat in group 2 received 1 ml of Cimetidine (Reference Group). For Group 3 and Group 4 each rat administered 1 ml of methanol extract and aqueous extract respectively. 30 minutes later, 1 ml of

absolute ethanol (100%) was given to the rats to induce ulcer. 15 minutes later, the animals were sacrificed under anesthesia, using diethyl ether vapor. The pyloric and cardiac ends were tied and the stomach were removed and put into 10% buffered formalin to fix the outer layer of the stomach.

Gross Gastric lesion evaluation

The stomach of each of animal was excised and open along the greater curvature and the stomach content was removed. Gastric mucosal lesions were recognized as hemorrhage or linear breaks with damage to mucosal surface. The number of ulcer areas (UA) was calculated under dissecting microscope and ulcer inhibition percentage was calculated according to this formula:

$$\text{Inhibition \%} = [(UA_{\text{control}} - UA_{\text{treated}}) / UA_{\text{control}}] \times 100$$

Histological evaluation of gastric lesions

Then the tissue were trimmed and kept in the cassette and transferred into fresh 10% buffered formalin fixative for overnight. Then the tissue allowed undergoing processing method by using automated machine. Later, the biopsies were embedded in a proper manner in freshly made paraffin to become blocks. The tissues were cut 5 μ m thick in sections using rotary microtome. After the sections were picking up on the slides, they were stained with Haematoxylin and Eosin stain. Sections consisting gastric lesions were examine under light microscope (40X) objective in 0.15mm² area, covering the lesions formed in the experiment.

Statistical analysis

Result are expressed as means + S.E.M. the statistical of the mean ulcer area among the treated group and each of them to both controls were calculated by using Student's T-test, SPSS for Windows Student Version 11.0.

Result

Table 1: Anti-ulcerogenic activity of *N sativa* seeds extract against absolute-ethanol induced gastric ulcer model

Group	Pretreatment	Oral dosage (mlkg ⁻¹)	Ulcer area (Mean ± SEM)	Protection (%)
1	Distilled water	5 mlkg ⁻¹	389.0 ± 55.581 ^a	
2	Cimetidine	5 mlkg ⁻¹	158.00 ± 24.862 ^b	59.38%
3	Methanol extract	5 mlkg ⁻¹	49.50 ± 20.396 ^c	87.28%
4	Aqueous extract	5 mlkg ⁻¹	2.33 ± 0.558 ^c	99.40%

All values are expressed as mean ± S.E.M; means with different superscripts are significantly different ($P < 0.05$).

Both aqueous and methanol extract of black seeds demonstrated markedly cytoprotective effect against ethanol-induced ulcer in rats. The result in table 1 showed administration of absolute ethanol without pretreatment with black seeds extracts or cimetidine caused severe gastric damage with an ulcer area of $389.0 \pm 55.581\text{mm}^2$. Pretreatment with Cimetidine followed by absolute ethanol represent as reference control reduced 59.38% of ulcer area with $158.00 \pm 24.862\text{mm}^2$. Group 4 (aqueous extract) showed the most significant anti-ulcerogenic activity against this model of rats with an ulcer area $2.33 \pm 0.558\text{mm}^2$ and 99.40% inhibition. This followed by Group 3 (methanol extract) with an ulcer area $49.50 \pm 20.396\text{mm}^2$ and 87.28% inhibition of gastric damage. Grossly, the result showed that rats administered with *N.sativa* seeds extract or Cimetidine showed marked antiulcerogenic activity in gastric ulcer. Histologically, rats administered with seeds extract of *N.sativa* have no or mild subcutaneous edema and no leukocytes infiltration compared to control. Aqueous extract of *N.sativa* seeds showed the most significant antiulcerogenic compare to the other groups. These findings indicated that Black seeds extracts possess marked

cytoprotective effect against absolute ethanol induced gastric damage.

Figure 1: Gross appearance of whole stomachs body



Figure 1a - Group 1 (Control Group): Stomach of rat in the ulcer group that pretreated with distilled water. Severe and dark hemorrhagic lineages were visible from outside.



Figure 1b - Group 2: Stomach that pretreated with Cimetidine showing red lineages were shorter, lighter, and less in number compared to Group 1.



Figure 1c - Group 3: The stomach showed no hemorrhagic lineage could be seen from outside.



Figure 1d -Group 4: The stomach show no hemorrhagic lineage could be seen from outside.

Figure 2: Macroscopic appearance for ulcer-induced, pretreatment with Cimetidine, aqueous or methanol extract of *N. sativa* seeds

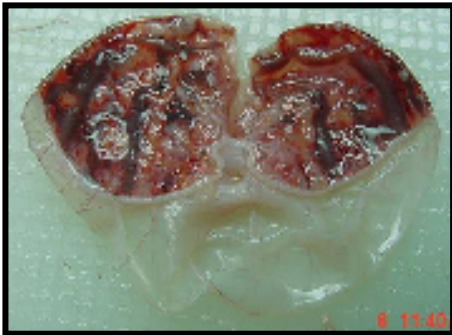


Figure 2a - Group 1 (distilled water pretreated): Markedly presence of severe hemorrhagic lesion could be seen elongated on the glandular part.

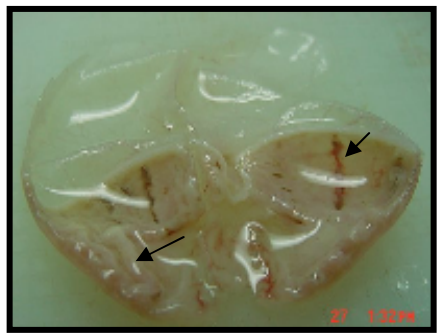


Figure 2b -Group 2 (Cimetidine pretreated): Note that moderate hemorrhagic lesion (right arrowed) developed on the glandular part. The rugae were still intact (left arrowed).

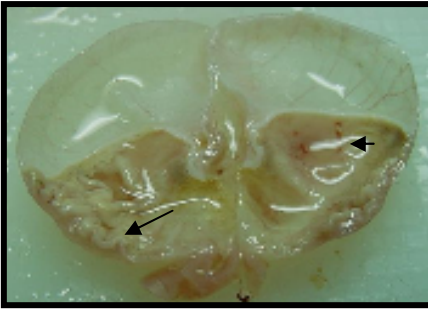


Figure 2c -Group 3 (MeOH extract of Black seeds pretreated): Presence of mild lesion (right arrowed). Markedly reduced the hemorrhagic lesions and rugae was well-preserved (left arrowed).

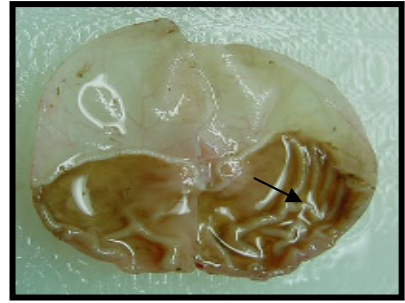


Figure 2d - Group 4 (Aqueous extract of Black seeds pretreated): Note that black seed was very potent inhibit formation of lesion. There were no hemorrhagic lesions whilst the rugae were still intact (arrowed).

Figure 3: Microscopic examination of stomachs on for ulcer-induced, pretreatment with Cimetidine, aqueous or methanol extract of *N. sativa* seeds

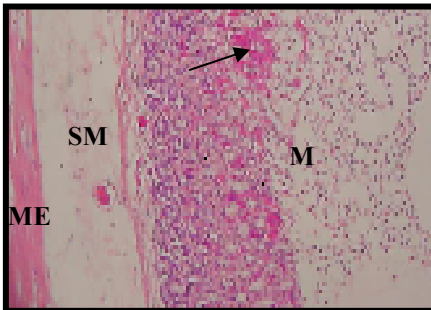


Figure 3a - Group 1 (pretreated with distilled water): Severe damaged of mucosa (M) and deep into submucosa (SM) layer. There were blood clots (upper arrowed) and slough off the epithelial cells (necrotic debris) as well as in the mucosa. There were present of edematous and infiltration of PMN cells in the submucosa layer.

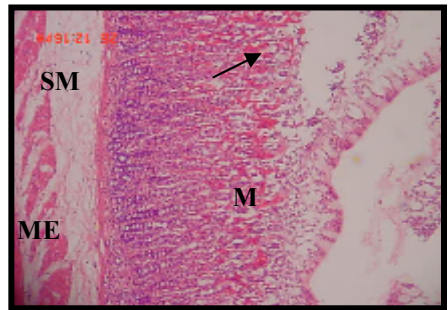


Figure 3b – Group 2 (pretreated with cimetidine): Presence of blood clots (upper arrowed) and moderate disruption of mucosa (M) layer. Some part of the mucosa still intact. Less thicken of edema with moderate infiltration of PMN cells in the submucosa (SM) layer.

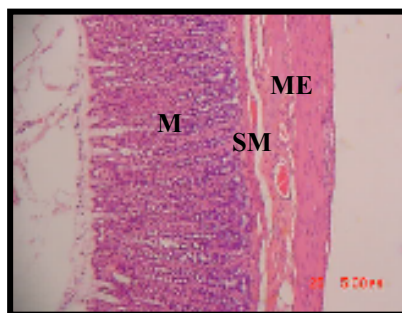
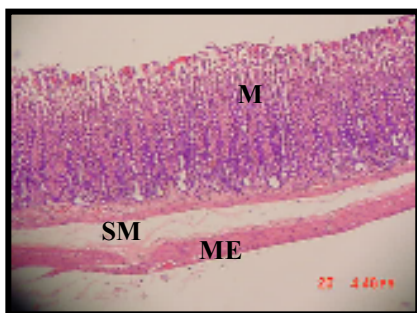


Figure 3c Group 3- pretreated with methanol extract of Black seed: Mild disruption and blood clots present at outer layer of mucosa (M). There is mild edematous formation and less infiltration of PMN cells in the submucosa (SM) layer.

Figure 3d- Group 4 (pretreated with aqueous extract of Black seeds): the mucus layer still intact with no edematous formation in the submucosa layer. It is normal-like appearance.

Discussion and Conclusion

The present study demonstrated that aqueous and methanol extract of Black seeds had cytoprotective effect against ulcerogenic factor such as absolute ethanol. This result is compatible with (El-Dakhkhny et al., 2000) study. Both methanol and aqueous extract showed significantly reduction of gastric lesions compared to group 1 and group 2. Aqueous extract showed the highest inhibition percentage compared to methanol extract. Both plant extract however not significantly different in reducing ulcer formation compared to each other. This may suggest that both solvent may dissolve the main active compound that contained in the Black seeds.

Ulcers are formed due to imbalance between offensive and defensive factors (Salram et al., 2002). Administration of absolute ethanol result in significant increase in plasma concentration of gastric hormone, reduction in mucin, production of free radicals, increase lipid peroxidation as well as histamine concentration in gastric mucosa. Gastric mucus (mucin) is an important protective factor for the gastric mucosa and consists of a viscous, elastic, adherent and

transparent gel formed by 95% glycoproteins that cover the entire gastrointestinal mucosa surface. Mucus is capable of acting as an antioxidant, and thus can reduce mucosal damage mediated by oxygen free radicals (Al-Qarawi et al., 2005). Black seeds showed cytoprotective effect via increased level of mucus and glutathione in the stomach (El-Dakhakhy et al., 2000). From the macroscopic examination, the stomach content of group pretreatment with Black seeds seems stickier compared to ulcer and Cimetidine group thus indicated that *N.sativa* L. enhanced secretion of mucus in the stomach and hence protect the mucosal lining from ethanol-induced ulcer in rats.

Previous studies revealed that Thymoquinone and *N.sativa* oil have anti-inflammatory and may reduce lipid peroxidation as well as lower the oxidative state (El-Saleha et al., 2004). Nigellone, the carbonyl polymer of Thymoquinone, is relatively low concentrations, was effective in inhibiting histamine released from mast cells in vitro (Swamy and Tan, 2000). (Al-Ghamdi, 2001) demonstrated inhibition of eicosanoid generation by fixed oil of *N.sativa* L. was greater than that produced by Thymoquinone. This might explain why *N.sativa* seeds extract in our study showed marked significant inhibition of ulcerogenesis induced by absolute ethanol compared to ulcer and cimetidine group. The study showed aqueous extract is the most significant inhibition of gastric damage. Therefore, the main active constituents of *N.sativa* L. might be more soluble in hot water and thus effective as anti-ulcerogenic against absolute ethanol.

Conclusion

This study revealed that aqueous extract and methanol extract have marked cytoprotective effect against absolute ethanol. Aqueous extract showed the highest percentage compared to methanol extract and cimetidine pretreatment. Further investigations need to be done to identify the main active constituents and the effective concentration that produce cytoprotective effect when induced by ulcer agents.

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Study of Common Myths and Misconceptions in Management of Animal Bite Cases among Patients Attending Antirabies Vaccination (ARV) Clinic at Indira Gandhi Government Medical College (IGGMC), Nagpur

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Abstract

Background/Objective: Rabies is an enzootic and epizootic disease of worldwide importance. Although primary wound care like washing the wound and application of antiseptic is a highly effective measure to reduce chances of developing rabies by 80%, still many myths and misconceptions are present among the people like application of oils, herbs and faith on indigenous medicines of unproven efficacy. This cross-sectional study was undertaken to study these prevalent myths and misconceptions in management of animal bite cases, to study some epidemiological factors in relation to animal bites and to suggest some suitable recommendations based on study findings accordingly.

Material/Methods: This study was designed as a cross-sectional study and included 600 incident cases of animal bite who attended the Antirabies Vaccination (ARV) clinic at Indira Gandhi Government Medical College (IGGMC), Nagpur in May 2005. All cases were interviewed personally and information collected in a pre designed performa. Statistical analysis included calculation of percentages.

Results/Conclusion: It was observed that only 52.83% of cases of animal bite took preliminary wound treatment and were aware of its importance as an effective antirabies measure. 12.5% cases visited quacks initially before reporting to the hospital authorities. Only 44.83% cases opted for antirabies vaccine while 47.50% cases applied topical agents on their wounds with application of oil with salt being the most prevalent practice. 74.83% cases sited “belief” as the sole reason for their visiting quacks and application of these agents. It can be concluded from this study that there are still many myths and misconceptions prevalent in the community inspite of availability of safe and potent vaccines to prevent rabies. There is a need to educate the community about the importance of immediate and adequate post exposure treatment.

Keywords: Rabies, myths and misconceptions, wound care

Introduction

There is no part of the earth providing shelter to man and animals where rabies cannot potentially exist. Even a developed nation like the United States is not free from rabies where about 100 cases occur and thousands take antirabies prophylaxis every year. India belongs to the high incidence category with disease seen all over the country (Park, JE.2001:9). In India every year about 30000 human rabies deaths occur which constitute 60% of the global incidence of 50000 (WHO 1998:17) and 96% of these human rabies deaths are due to bites by dogs (Sehegal S.1996:11). Rabies is 100%

fatal but animal experiments have shown that local wound treatment like cleaning the wound with soap and water and application of antiseptics after cleaning can reduce the chances of developing rabies by about 80%. Still there are many myths and misconceptions associated with wound management in India. These include application of oils, herbs and chillies on wound inflicted by rabid animal, more faith in indigenous medicines which are of unproven efficacy and not wetting the wound because of fear that it would be infected. Analysis of data from Delhi has revealed that more than 99% of hydrophobia cases admitted to the hospital had not washed their wounds with water but had some antiseptic solution, oil or red chillies. Clearly people are not aware of its importance and/or have no confidence in its usefulness as an antirabies measure (C.D. Alert, Oct2000). Since this study is a hospital based study, it may not be representative of the whole population. The study was conducted with an intention to find out the prevalent practices and hence meeting the dire necessity of educating the people lest more cases of rabies would crop up.

Material/Methods

The present study was designed as a cross-sectional study and was carried out during the month of May 2005(1st May-31st May) at the Antirabies Vaccination Clinic at Indira Gandhi Government Medical College, Nagpur. A total of 600 incident cases of animal bite reported at the ARV clinic in the month of May and all were included in the study and hence sampling was not required. Therefore, the sample size was 600 incident cases. Each case of animal bite was interviewed personally regarding demographic characteristics, characteristics related to animal bite and management of wound. The information was collected in a pre designed Proforma. Local examination of wound was done and the cases were classified into different classes of bites as given by the WHO. Each interview took about 20 mins. Statistical analysis included calculation of percentages.

Results

Characteristic qualitative analysis of the respondents was done after the completion of survey and collection of data from the sample. Responses of the interviewees are shown below in the tables. Tables 1-15 present the responses of interviewees.

Table 1: Distribution of subjects according to age and sex

Age (yrs)	Sex		Total
	Male	Female	
0-15	192 (46.27)	83 (44.86)	275 (45.83)
15-30	112 (26.98)	51 (27.56)	163 (127.16)
30-45	65 (15.67)	29 (15.67)	94 (15.66)
45-60	34 (8.19)	15 (8.10)	49 (8.16)
>60	12 (2.89)	7 (3.78)	19 (3.16)
	415 (69.17)	185 (30.83)	600 (100)

Table 1 shows distribution of study subjects according to age and sex. Majority of animal bite cases 275(45.83%) were in the age group of 0-15yrs. A striking feature was that only 152(26.98%) cases were reported in the age group above 30yrs. There was a male preponderance 415(69.16%). The male to female ratio was 2.24:1.

Table 2: Distribution of subjects according to weight

Weight (Kgs.)	No of Subjects		Total
	Male	Female	
< 30 kgs	154 (25.6)	83 (13.83)	237 (39.83)
> 30 kgs	261 (43.5)	102 (17)	363 (60.5)

Table 2 shows distribution of subjects according to weight. 237 (39.83%) cases had weight less than 30kgs which included 154(25.6%) males and 83(13.83%) females. 363 (60.5%) cases had weight more than 30 kgs, which included 261(43.5%) males and 107(17%) females.

Table 3: Distribution of subjects according to area of residence

Area of Residence	No. of Subjects	Percentage
Urban	482	80.33 %
Rural	118	19.66 %
Total	600	100

Majority 482(80.33%) were from urban area.

Table 4: Distribution of subjects according to type of animal bite

Type of Animal	Number	Percentage
Dog	550	91.66
Pet dog	387	64.5
Stray dog	163	27.16
Cat	14	2.33
Monkey	7	1.16
Pig	9	1.5
Horse	1	0.16
Contact with rabid patient	19	3.16
Total	600	100

In 550(91.66%) cases dog was the biting animal. Out of 550 cases of dog bite, 387(64.5%) were by pet dog and 163(27.16%) were by stray dog. There were 19(3.16%) cases of contact with a rabid animal. Cat bite was prevalent in 14(2.33%) cases.

Table 5: Distribution of subjects according to type of exposure

Type of Exposure	No. of Subjects	Percentage
Bite	545	90.83
Licks	4	0.66
Scratching by nails	32	5.33
Contact with saliva of rabid patient	19	3.16
Total	600	100

The predominant type of exposure was by bites 545(90.83%).19(3.16%) cases suffered exposure by saliva of rabid patient. the least type of exposure was by licks 4(0.66%).

Table 6: Distribution of subjects according to nature of bites

Nature of Bites	Number of Subjects	Percentage
Provoked	338	58.17
Unprovoked	243	41.82
Total	581	100

Majority of the bites were provoked 338(58.17%) whereas numbers of unprovoked bites were 243(41.82%).

Table 7: Distribution of subjects according to site of bite

Site of Bites	Number of Subjects	Percentage
Head and neck	187	31.16
Upper extremity	243	41.82
Chest & Trunk	81	13.94
Lower extremity	360	60

An analysis of the site of bite revealed a marked predisposition for lower extremities. 360(60%) bites were on lower extremities followed by 187(31.16%) on head, neck and face.

Table 8. Distribution of subjects according to class of bites

Class of Bites	Number of Subjects	Percentage
Class I	42	7
Class II	315	52.5
Class III	243	40.5
Total	600	100

Of the total 600 subjects, 315(52.5%) had class II bites, 243(40.5%) had class III exposure while only 42(7%) subjects had class I bite. Figure 1 depicts a girl with class III animal bite.



Figure 1: A Girl with Class III Animal Bite

Table 9: Distribution as per immunization status of animal

Immunization Status of Animal	Number of Subjects	Percentage
Fully immunized	135	22.5
Partially immunized	22	3.66
Not immunized	347	57.83
Not known	96	16
Total	581	100

Only 135(22.5%) pet/owned dogs were fully immunized. The number of unimmunised animals was 347(54.83%).

Table 10: Distribution of subjects according to practice of wound cleaning before visiting health services

Wound Cleaned	Number of Subjects	Percentage
Yes	317	52.83
No	283	47.16
Total	600	100

It was appreciable to find that 17(52.83%) cases washed their wounds whereas 283(47.16%) did not take any wound treatment.

Table 11: Distribution of subjects according to agents applied for cleaning of wounds

Agents Applied for Cleaning of Wound	Number of Subjects	Percentage
Water	105	33.12
Soap and water	182	57.41
Dettol or other antiseptic	16	5.04
Water & Dettol	32	10.09
Soap and Water and Dettol	22	6.94

105(33.12%) subjects washed their wound with water only. 204(64.35%) subjects washed their wound with soap and water and 70(22.07%) applied antiseptic on the wound.

Table 12: Distribution of subjects according to type of services visited first

Type of Services Visited First	Number of Subjects	Percentage
Government health authority	395	65.83
Private practitioner	130	21.66
Quacks	75	12.5
Total	600	100

Majority of the cases 395(64.83%) reported to government health authorities, 75(12.5%) cases had visited quacks and

130(21.66%) subjects visited private practitioners before visiting government health authorities.

Table 13: Distribution of subjects according to treatment received

Treatment Received	Number of Subjects	Percentage
Cleaning and dressing of wound	25	4.16
Tetanus immunization	417	78.5
Antirabies vaccination	269	44.83
Any other (mantra)	74	12.33

Majority of patients 417(78.5%) received tetanus immunization. Only 25(4.16%) cases received cleaning of wound. 269(44.83%) received antirabies vaccination. 74(12.33%) cases had resorted to mantras from quacks.

Table 14: Distribution of subjects according to common prevalent practices regarding application on wound

Common Prevalent Practice Regarding Application on Wound	Number of Subjects	Percentage
Oil with salt	212	74.38
Turmeric	110	38.59
Chillies	19	6.66
Salt	16	5.61
Herbs	10	3.5
Lime chalk	6	2.10
Alkali	3	1.05
Kerosene	3	1.05
Ghee	2	0.70
Alum	1	0.35
Alkali	1	0.35
Tea powder	1	0.35
Applied nothing	315	52.5

285(47.50%) cases had applied topical agents on their wounds. The most prevalent practice was application of oil with salt 212(74.38%), turmeric 110(38.59%), chillies 19(6.66%), herbs 10(3.5%), lime chalk 6(2.10%) were the other agents applied.

Figure 2, 3, 4 and 5 shows the various topical agents applied by the people on their wounds.



Figure2: A Case of Animal Bite who Applied Turmeric on the Wound



Figure 3: A Case of Animal Bite who Applied Herbal Paste on the Wound



Figure 4: A Case of Animal Bite who Applied Turmeric and Salt on the Wound



Figure 5: A Case of Animal Bite who Applied Limechalk on the Wound

Table 15: Distribution of subjects according to the reason given for application

Reason for Application	Number of Subjects	Percentage
Belief	161	56.49
Not known	54	18.94
Curative	40	14.03
Stops poison spread	16	5.61
Stops bleeding	13	4.56
Pain relief	1	0.35

161(56.49%) gave the reason as 'belief' for the application of topical agents. 54(18.94%) did not know the significance of their application. 40(14.03%) felt that they are curative and 16(5.61%) believed they stop spread of poison.

Discussion

The present study among 600 incident cases of animal bites revealed that 0-15 years age group is the major age group inflicted by animal. Cases occurred in all age groups but children in age group 0-15yrs because of their inherent fondness to animals fell victims in a significantly greater number (Chhabra M.2004:5). Chhabra et al. (2004)5 observed

that 97% cases of dog bite occurred in children less than 15yrs of age.

The incidence of dog bite cases in this study was about 2 times higher in males as compared to females. There could be a number of reasons for this difference, perhaps the most obvious being that males of all ages are more likely to pet, tease or aggravate an animal than females. Another factor could be that women are more confined to their home environment and are therefore less exposed to dogs particularly stray dogs (Bhalla S.2001:1). Similar age and gender distribution has been reported by other authors in their studies (Banerji SC.1974:2; Chakraborty AK.1972:4; Krishna CK.1976:6; Lakahnpal U.1985:7; Pancharoen C.2001:8; Satapathy DM. 2001:10; Singh J.1998:13; Trivedi CR.1981:16; Wrinkler WG.1979:18; Zaheera 1970:19).In the present study the urban to rural ratio is 4.08, which may not be the true picture as Nagpur is considered as urban. The majority of bite cases were due to dogs, which accounted for 91.66% cases. Dog as the principal biting animal has been reported in many previous studies. (Banerji SC.1974:2; Chakraborty AK.1972:4; Chhabra M.2004:5; (Krishna CK.1976:6; Lakahnpal U.1985:7; Pancharoen C.2001:8; Sekhon AS.2002:12; Singh J.1998:13; Sudarshan MK.2001:14; Wrinkler WG.1979:18; Zaheera 1970:19). 58.17% bites were provoked. It is not unusual to find young children throwing stones at stray animals. This also implies that people have a misplaced sense of fun associated with a certain disrespect for animals.

Although we had anticipated that most of the bite wounds would be on the legs, it was revealing to note that the incidence of bites at this site was as high as 60%. (Trivedi CR.1981:20) in his study reported the incidence to be 72.8%. the most obvious reason for this site seems to be that when standing, walking, running legs are at the same level as the biting animal (Bhalla S.2001:1) Lower extremity as the most common sites of exposure have been reported in many studies (Bhalla S.2001:1; Banerji SC.1974:2; Chhabra M.2004:5; Krishna CK.1976:6; Pancharoen C.2001:8; Sekhon AS.2002:12; Trivedi CR.1981:16)

Of all the animals 57.83% were not immunized. Only 22.5% were fully immunized and 3.66% were partially immunized. The immunization status of 16% animals was not known. This highlights the danger humans are facing amidst such a huge population of unvaccinated animals (Sekhon AS.2002:12)

The main danger is posed by the ignorance about the disease and the common prevalent practices in the management of the wounds. Although 65.83% cases visited Government health authorities for seeking treatment, 12.5% cases still risked their lives by visiting quacks and having faith in mantras. It was appreciable to find that 57% cases had washed their wounds with water but the number of cases who had not taken preliminary wound care was also significant (47.16%). The reason might be that the people are either not aware of its importance or had no confidence in its usefulness as an antirabies measure (Chhabra M.2004:5). This misconception has been reported in other studies too. (Lakahnpal U.1985:7 and Singh J.1998:13).

There are numerous myths associated with animal bite management. The most prevalent myths are application of oil, turmeric, salt, chillies, herbal pastes, lime chalks etc.on the wound exposing the nerve endings further and enhancing the virus entry in the nerves. This also gives a false sense of security that some treatment has been administered (Chhabra M.2004:5) Prevalence of similar myths has been reported in other studies (C.D. Alert, Oct2000; Sekhon AS.2002:12; Sudarshan MK.2001:14).

Majority of the cases did not wash the wound or applied topical agents due to belief (56.49%). The advice was given mostly by relatives or elders. This shows that people still have faith in indigenous medicines of unproven efficacy.

Conclusion

From the study, it can be concluded that though timely institution of post exposure treatment is the only way to prevent human death toll but the initial management of the wound is also of vital importance. Although the practice of

washing wound is quite prevalent, yet a significant number of people are unaware of its significance as an effective antirabies measure. There are also many myths and misconceptions prevalent among people. In spite of availability of safer and potent vaccine free of cost in government hospitals, people still visit quacks and believe in mantras for cure of disease.

Recommendations

- Undoubtedly the timely institution of post exposure treatment or observation of the animal and then treating the patient accordingly with anti rabies vaccine is the only way to prevent death but the initial management of wounds is also of vital importance as it removes the saliva of rabid animal that contains large number of rabies viruses.
- IEC activities should be given impetus to dispel all myths and misconceptions.
- Rabies is primarily of animals and control measures have to be directed towards the natural reservoir of disease. Mass vaccination of commonest reservoir of animals, eg.dog against rabies is the most useful weapon in rabies control. Other methods are sterilization of stray dogs, use of dog collar and dog leash and licensing of dogs from respective corporations.

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Secretory IgA concentrations in uterine lavages of ewes are influenced by the stage of the oestrous cycle

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Abstract

Immunoglobulin A (IgA) act as the first line of defense in the mucosal immune system. The local plasma cells in tissues have the ability to produce IgA, which has a specific polymeric immunoglobulin receptor-mediated transport mechanism for entry into the mucosal secretions. The aim of this study was to quantify the S-IgA in ewes uterine lavage fluids during

follicular and luteal phase. Twelve ewes were used in this study and they were divided into two groups (n=6). All ewes undergo synchronization and slaughtered prior to the experiment. The mucus of the reproductive tract was harvested by flushing using mixture of protease inhibitor cocktail and distilled water. The harvested mucus was kept in the eppendorf tube, centrifuged and stored at -80C. The level of S-IgA of both phases was measured and quantified using ELISA method. From this study, it was concluded that the S-IgA level was significantly higher (P<0.01) in the follicular phase compared to those in the luteal phase.

Keywords: Ewes, follicular and luteal phases, S-IgA levels, uterine lavage.

Introduction

Immunoglobulin A (IgA) act as the first line of defense in the mucosal immune system. The local plasma cells in tissues have the ability to produce IgA, which has a specific polymeric immunoglobulin receptor-mediated transport mechanism for entry into the mucosal secretions (Lamm., 1997). The levels of immunoglobulins (A and G) and antigens-specific antibodies (Abs) in the genital tract of women and rhesus macaque vary with the menstrual cycle. The level of IgA and IgG increase during menses and decrease during the periovulatory period Lu et al.(1999). In sheep, significant increase of the uterine immunity has been observed during follicular phase of oestrous cycle. In contrast, the uterine immunity decreases during luteal phase Ramadan et al. (1997). The aim of this study is quantification of S-IgA in ewes uterine lavage fluids during follicular and luteal phase.

Material and Methods

Animals

Twelve healthy non-pregnant cycling local breed ewes with age between 11 to 13 months and body weight of 16 ± 2.6 kg were

used in this study. All the animals were kept under natural lighting and feeding. The protocol of the study was approved by the Faculty's animal care and use committee, animal utilization protocol number (08R26/Jun 08-May 09). The animals were divided into two groups (follicular and luteal phase; 6 ewes for each) after synchronization of the estrous cycle by insertion of sponges that contained 40mg flugestone acetate for 14 days. Pregnant mare serum gonadotropin (PMSG) (Folligon®) were given (400 I.U) intramuscularly at sponge removal. The animals were allowed to undergo one natural estrous cycle after the removal of the sponge. All the animals were slaughtered and the reproductive tracts were collected. The stage of the oestrous cycle (follicular and luteal phases) was determined by the signs of oestrous exhibited by the ewes. This was further confirmed by morphological and histological evaluation of the ovary and endometrial layers of reproductive tract. If the ovaries exhibited follicles > 5 mm with the absence of any corpus luteum, the ewe was considered to be in the follicular phase of the oestrous cycle. In contrast presence of corpus luteum indicated the luteal phase ewe Perez-Martinez et al (2002). Histologically, straight and narrow tubular glands of the endometrium were observed during follicular phase, but the the presence of the corpus luteum with typical secretory endometrium and the uterine glands begin secretion, dilating and becoming coiled were observed during luteal phase Banks (1993).

Collection of uterine lavage fluids

The uterine lavage fluids were collected by flushing each genital tract with 5 ml of distilled water containing protease inhibitors cocktail (Sigma-Aldrich, USA). Uterine lavage fluids were centrifuged (12000 X g for 5 min at 0 °C) and frozen at -80°C until assayed Lu et al.(1999). S-IgA concentration was measured by enzyme-linked immunosorbent assay (ELISA) Kutteh et al. (1996).

ELISA

S-IgA was assayed by standard direct ELISA system Crowther. (2001). 96-well flat bottom high binding ELISA microplates (Greiner Bio-One, Germany). Plates were coated with replicate optimal concentrations of samples diluted in PBS and incubated overnight at 4 °C. Plates were washed three times in PBS containing 0.05% Tween-20 and blocked with 5% bovine serum albumin (BSA; Merck, Germany) for two hours at 25 °C. Then the plates were washed three times. The plates were incubated with bound rabbit anti-sheep IgA: HRP (Horseradish Peroxidase) (AbD Serotec, UK) 1: 10000 for two hours at 25 °C. Plates were washed again three times, the color developed with ABTS (2, 2', azino-bis (3-ethyl benzathiazoline-6-sulphonic acid)/H₂O₂ substrate (KPL, USA) was measured after 15 min at 414 nm on a Microtiter-Plate ELISA Reader (BIO-TEK, USA).

Statistical Analysis

S-IgA concentrations between the luteal and follicular phases were compared using the Independent T-Test procedure. The statistical procedure was conducted at 95 % confidence level.

Result

The results were analysed by independent sample t-test and presented as mean \pm SEM. This study showed the relationship of the estrous cycle stages to uterine S-IgA concentration in the healthy non-pregnant cycling ewes. The concentration of S-IgA in the follicular phase (0.20 ± 0.01) was highly significant ($P < 0.01$; 95% CI 0.05 to 0.01) as compared with the luteal phase (0.17 ± 0.002).

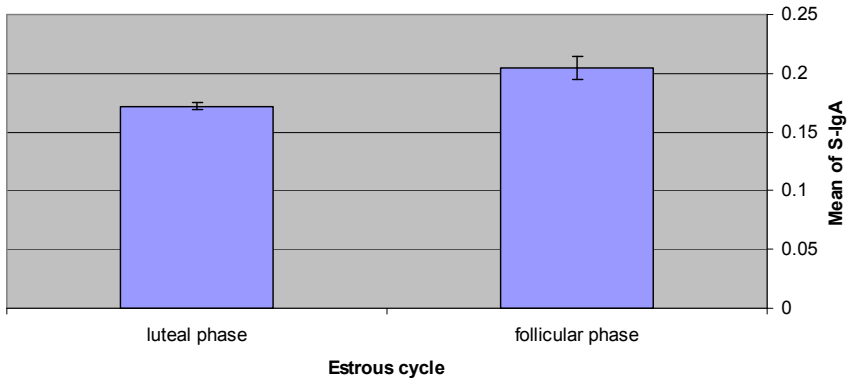


Figure 1: Mean concentration ($\mu\text{g}/\text{ml}$) of uterine S-IgA between follicular and luteal phase of sheep estrous cycle.

Discussion

The results of this study indicated that S-IgA level in sheep uterine secretion varies between the follicular and luteal phase of ewe. The mucosal immunity decreased during luteal phase and increased during follicular phase Lander Chacin et al. (1990). The present result agrees with the previous studies. The difference of immune levels during the stages of estrous cycle, supported by previous studies (as mentioned earlier).

But the main reason for the immunosuppressive during the luteal phase (progesterone hormone) did not fully supported. Hypothesized or supposed to, immunosuppressive effects of progesterone in the uterus are mediated by secretion of a lymphocyte-inhibitory molecule produced by the uterus in response to progesterone Stephenson et al. (1989a), Hansen and Skopets. (1992). A likely candidate for the progesterone-induced immunosuppressive molecule in sheep is Ovine Uterine Serpin, also known as an ovine uterine milk protein Ing and Roberts. (1989).

Conclusion

Current investigation showed that the S-IgA levels in uterine lavage of ewe were influenced by estrous cycle phases. The S-

IgA levels during follicular phase (under estrogen hormone influence) higher than luteal phase (under progesterone hormone influence). The main reason for the immunosuppression during the luteal phase did not fully justified, especially with the presence of potential acquired infection during coitus in the follicular phase and in the same time immune system should decrease accordingly to prevent newly attached fetus rejection by the mother immune system.

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Visceral leishmaniasis and HIV co-infection in patients referred to Ahfad Biomedical Research Laboratory of Ahfad University for Women- Sudan during 2003-2007

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Abstract

Visceral leishmaniasis (VL) is one of the major health problems worldwide. In Sudan, it is one of the most important parasitic tropical diseases. HIV and leishmaniasis are both expanding due to the increasingly overlapping geographical distribution of the two pathogens and the number of cases with co-infection is expected to rise. Laboratory diagnosis of VL is difficult and it mainly depend on demonstration of parasite in organ aspirate but this method lacks the required sensitivity. Due to it is high sensitivity and specificity, the direct agglutination test (DAT) has been recommended as only sero-diagnostic tool to be carried out in Sudan.

The aim of the present study was to assess the incidence of HIV infection among VL patients referred to the Ahfad Biomedical Research Laboratory (ABRL), Ahfad University for Women (AUW) in Sudan during 2003 - 2007 and to investigate utility of DAT for diagnosis of VL in HIV co-infected patients.

A cross sectional study was conducted in which blood specimens and/or lymph node aspirates were collected from all clinically suspected VL patients (n=252) referred to ABRL of AUW during 2003 - 2007. VL was confirmed in 204 patients using direct microscopic examination and/or Direct Agglutination test (DAT). Personal and clinical data was collected through specially designed form. Immunochromatography rapid test was used for HIV screening. HIV reactive sera were confirmed by ELISA. Anti-Leishmania donovani antibody response in VL patients with or without HIV infection was assessed and compared using DAT. Utility of DAT for diagnosis of VL in HIV co-infection patients was investigated.

The results showed co-incidence between VL and HIV (10/204, 5%). Five out of 154 (3.2%) were from Gedaref State and five out of fifty (10%) were from patients referred to our laboratory (ABRL) from Omdurman. A striking finding was that, all VL/HIV co-infected patients were males (100%), their age ranged from 25-46 years. The maximum positively was observed in the age group 32-35 (40%), followed by the age group 40-46 (30%) and 25-27 (20%). Most of them either originally from Gedaref VL-endemic area or they had past history of travelling to Gedaref. Anti-Leishmania antibody response was detected in 98% of the VL patients and in 80% of patient with VL and HIV. P.value was not significant between the two groups (0.29).

This study confirmed co-incidence of VL and HIV in Sudan and that the DAT is a usefulness test for diagnosis of the disease. Further studies are needed to evaluate the sensitivity of DAT in diagnosis of VL cases co-infected with HIV.

Keywords: Visceral leishmaniasis, HIV/AIDS, Sudan

Introduction

Leishmaniasis is a parasitic disease transmitted by the bite of an infected female sandfly whose hosts are animals, such as dogs

or rodents, or human beings (Bryceson, 1996). The parasites can also be transmitted directly from person to person through the sharing of infected needles which is often the case with *Leishmania*/human immunodeficiency virus (HIV) co-infection. The disease has four main forms, depending on the parasite species and the cellular immune system of the patient, cutaneous leishmaniasis, diffuse cutaneous leishmaniasis, mucocutaneous leishmaniasis, visceral leishmaniasis (VL) which are also known as "kala-azar". VL is the most severe form of leishmaniasis; it is usually fatal if left undiagnosed and, then, untreated (Bryceson, 1996).

The geographical distribution of leishmaniasis is restricted to tropical and temperate regions, the living area of the sandfly and it is endemic in 88 countries (16 developed countries and 72 developing countries) on four continents. Ninety percent of the cases are found in Bangladesh, Brazil, India, Nepal and Sudan (WHO, 2000).

Visceral leishmaniasis (VL) or kala-azar is one of the most important parasitic tropical diseases in Sudan, which is one of the most important foci in the world (Osman et al, 2000). In Sudan, the disease was first described by Neave (1904), and the first epidemics in 1936-38 were reported by Stephenson (1984) in the Upper Nile province and Fung area (cited in Osman et al, 2000; Zijlstra & El-Hassan, 2001).

HIV and leishmaniasis are both expanding due to the increasingly overlapping geographical distribution of the two pathogens and the number of cases with co-infection is expected to rise. HIV has caused an increase of Kala-azar cases. HIV patients with Kala-azar have a poor prognosis as Kala-azar stimulates replication of HIV (Davidson, 1997).

HIV patient has deficiency in producing antibodies against new infectious agent. Consequently, serological blood tests for detection of anti-*Leishmania* antibodies may give negative results (MOH, 2003).

In one study from Italy in which level of anti-*Leishmania* antibodies were assessed in series of VL/HIV co-infected patients, up to 13% of the patient did not have antibodies

(Gradoni et al, 1993). This percentage is inversely proportional to CD4 cell depletion. The authors suggested that these patients had acquired leishmaniasis as primary infection because their strong immunologic impairment leads to inability to develop antibodies (Pearson et al, 1983; Murray et al, 1983). Diagnosis of VL/HIV co-infection patients is quite difficult as only 40-50% of VL/HIV co-infection cases have a positive *Leishmania* serology (Gari et al, 1994); therefore, serological blood tests are negative in 20-40% of VL/HIV co-infection patients (cited in MOH, 2003). The authors expected that DAT titres would be lower in such cases, as well. In other study, anti-*Leishmania* antibodies in HIV-positive patients are 50 times less than those in HIV-negative patients (Marry et al, 1992), therefore, there may be many false negative tests. Serological results may show a sensitivity of 70 per cent and specificity of 73 per cent (Stantos-Gomes et al, 2000).

In Southern Europe, bone marrow aspirates that are routinely collected from suspected cases of VL and examined as Giemsa- stained smears. Amastigotes can be detected in 48%-100% of such samples from HIV-positives (Montalban et al, 1990).

Leishmania/HIV co-infection are on increase worldwide, and the situation being alarming in many countries. There is overlap in the distribution of VL and HIV which may contribute to the increasing in co-infection cases (Alvar et al, 1997).

At present, most of the surveillance is carried out in Europe, although the problem of co-infection is widespread (WHO, 2000). Furthermore because the immune system of HIV patients is impaired and due to the presence of other opportunistic diseases, leishmaniasis is difficult to diagnose.

Our present study was aimed to assess the incidence of HIV infection among VL patients referred to the Ahfad Biomedical Research Laboratory (ABRL), Ahfad University for Women (AUW) in Sudan during 2003 - 2007 and to investigate utility of DAT for diagnosis of VL in HIV co-infected patients.

Methods and Study Design

Study design

Cross sectional study. Blood specimens and/or lymph node aspirates were collected from all clinically suspected VL patients (n=252) referred to ABRL of AUW during 2003 - 2007. VL was confirmed using direct microscopic examination and/or Direct Agglutination test (DAT). Personal and clinical data was collected. Immuno-chromatography rapid test and ELISA were used for screening and conformation of HIV, respectively. Anti-Leishmania donovani antibody response in VL patients with or without HIV infection was assessed and compared using DAT. Utility of DAT for diagnosis of VL in HIV co-infection patients was investigated. This study was approved by the Research Ethical Committee of the Federal Ministry of Health to be carried out in Sudan.

Study area and patients

This study was included all suspected kala-azar cases (n=252) attending ABRL, AUW in Omdurman during the period September 2003-October 2007. Cases were referred from Hospital of Tropical Medicine in Omdurman or Gedaref State in Eastern part of Sudan.

Study population and data collection

Clinical data and patient characteristics were collected using standard forms. Data includes sex, age, residence, and clinical complains.

Methods

Samples collection

Lymph node aspirates and/or blood specimens were collected. Serum specimens were separated by centrifugation and were kept at -20° C until used.

Parasitological test for visceral leishmaniasis

Parasitological test with lymph note aspirates were done immediately after collection where aspirates from an enlarged

lymph nodes were smeared, fixed by methanol, stained with Giemsa stain and examined for the presence of *Leishmania* amastigotes (L.D bodies).

Detection of anti-Leishmania antibodies

Serology using DAT was done according to the method described previously (Harith et al, 1988).

In brief, a serum diluent consists of 0.2% gelatin dissolved by heating in physiological saline and 0.8% (v/v) 2-mercaptoethanol was used. All sera were tested at two-fold serial dilution starting with 1:100 up to 1:102400 in V-shape microtiter plate. After addition of antigen (50ul/ well), the plat was carefully shaking by hand on a level surface for half a minute, covered and left for 18 hours at room temperature, the test was read visually against a white background and the end-point reaction was localize as blue spot similar to the control well.

Screening tests for HIV infection

Rapid, simple, qualitative, sandwich immuno assay (Intec Products, INC China, LOT: 2007032005) for detection of antibodies to HIV-1 and HIV-2 was used for qualitative detection of antibodies to human immunodeficiency virus (HIV) in patient's serum. All reactive sera were confirmed using ELISA.

Confirmatory test for HIV

Anti-HIV (1 & 2) ELISA kit (Enzygnost[®], Germany) was used as a confirmatory for the detection of circulating antibodies to Human Immunodeficiency Virus type 1 (HIV-1) and/or Human Immunodeficiency Virus type 2 (HIV-2). Sera were tested according to manufacture instruction using microplate wells coated with synthetic peptides and recombinant antigen corresponding to a highly antigenic segment of HIV-1/HIV-2 envelope and core protein.

Statistical analysis

Mann-Whitney Test was used to analyze and compare anti-*Leishmania* antibody response in HIV positive or negative patients. P-value was calculated.

Results

Co-incidence of VL and HIV

During 5 years and out of 252 VL suspected cases, 204 were founded positive for VL using parasitology and or DAT. Their age ranged from 2-69 years, one hundred- forty three were male (56.7%). Sera were studied for co-incidence with HIV infection. The results showed co-incidence between VL and HIV (10/204, 5%), Fig.1. Five out of 154 (3.2%) were from Gedaref State and five out of fifty (10%) were from patients referred to our laboratory (ABRL) from Omdurman. A striking finding was that, all VL/HIV co-infected patients were males (100%), their age ranged from 25-46 years. The maximum positively was observed in the age group 32-35 (40%), followed by the age group 40-46 (30%) and 25-27 (20%). Most of them either originally from Gedaref VL-endemic area or they had past history of traveling to Gedaref.

Clinical profiles of VL/HIV co-infection patients

The main clinical profile of VL/HIV co-infection patients (n=10) were studied. One patient showed a previous history of VL. All except one patient had fever, appetite loss and weight loss were prevalent in most cases (71%, 100%, respectively). Other clinical manifestation includes epistaxis, diarrhea, cough, emaciation and pale. Except one patient, all patients had lymphadenopathy, either inguinal, epitrochlear or generalized. Splenomegaly and hepatomegaly were among the most common symptoms (88.9%, 71.4%; respectively).

Laboratory findings and indercurrent infections in VL/HIV co-infection patients

The characteristics laboratory findings in patients with VL and HIV were studied. Anemia was reported in all cases (Hb level of 5.5-8.6 g/dl, 38-59%). Pancytopenia (a WBCs count of ≤

2000/cmm) was notice in one patient. Erythrocyte Sedimentation Rate (ESR) was high(≥ 118 mm/hor) in all patients. Co-infection other than HIV, were reported in many cases. VL/TB co-infection was higher (3/10, 30%). VL/malaria co-infection was occurred in two patients (20%) any they were died during treatment. In addition to VL/HIV co-infection, one patient was also infected with malaria and TB.

Antibody response in patients with VL or VL/HIV co-infection

Using DAT, anti-*Leishmania* antibody response was measured in VL patients with or without HIV co-infection (Table1, Fig.2). Out of 204 VL sera tested, 200 were tested positive (DAT titre $\geq 1:3200$) given a sensitivity of 98% comparing to 80% sensitivity for the VL /HIV co-infection patient group (n=10) as two sera were testing negative at a very lower titre (1:100). P.value was not significant between the two groups (0.29).

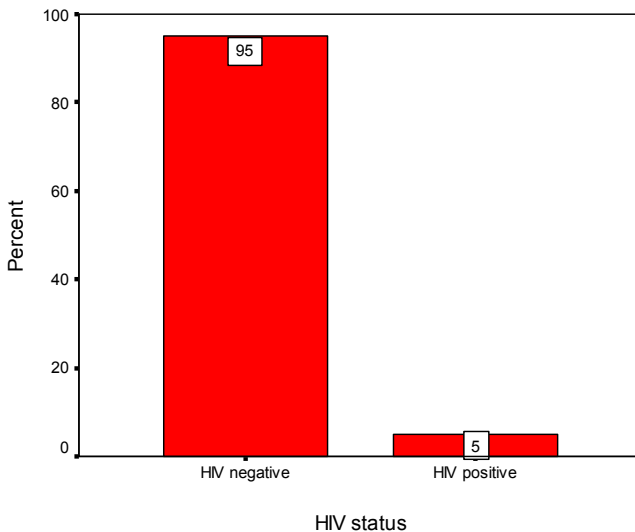


Figure 1: Co-incidence between visceral leishmaniasis and HIV

Table 1: DAT titres in patients with VL or VL/HIV co-infection

	DAT reciprocal titres				
	≤800	1600	3200	6400	12800- ≥102800
VL (n=204)	0 (0%)	4 (2.0%)	23 (11.3%)	18 (8.8%)	159 (77.9%)
VL/HIV co-infection (n=10)	2 (20%)	0 (0%)	1 (10%)	0 (0%)	7 (70%)

Results were frequencies (%).

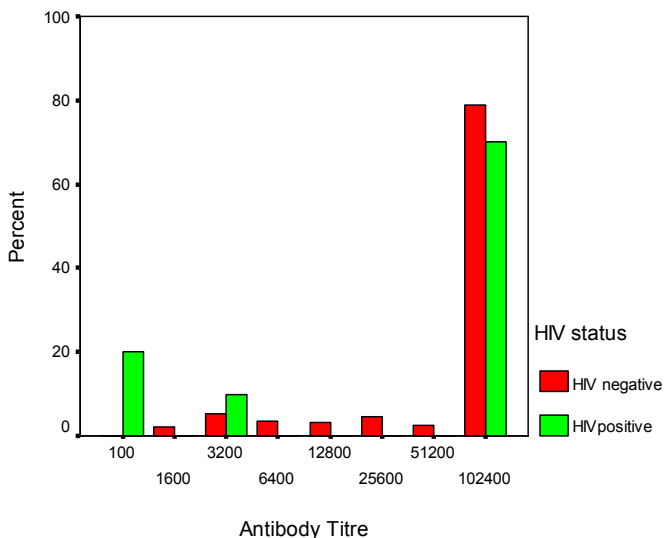


Figure 2: Anti-L.donovani antibody responses in VL and VL/HIV co-infected patient groups

Discussion

Leishmania and HIV co-infection is emerging as a serious new disease and it is on increase worldwide. According to WHO reports (1995, 2000), the areas where *Leishmania* and HIV co-infection is distributed are expanding. So far, thirty- three countries has reported co-infections; in South Europe 25% of 70% of adult VL cases were related to HIV and 1.5 % to 9% of AIDS cases suffer from newly acquired or reactivated VL. In Sudan, the prevalence of VL/HIV co-infection was reported to be 1.6% (MOH, 2003).

In this study, ten (5%) out of 204 VL cases were reported to have co-infection with HIV. All ten patients were male, their age ranged from 25-46 years. The maximum positivity was observed in the age group 32-35 (40%). Most of VL and HIV co-infection cases either originally from Gedaref or they had a past history of traveling to Gedaref. Five out of 154 (3.2%) were from Gedaref and five out of fifty (10%) were from sera collected in Omdourman. No sample detected positive in sera collected in Azzaza Damos-Sinnar State. Although a higher prevalence (5%) was reported in this study, our results were in line with previous studies where it was reported that VL and HIV co-infection is on increase (Alvar et al, 1997) due to the overlapping in the distribution of the two diseases. Comparing to our findings, Desjeux et al (2000) showed that out of 965 cases retrospectively analyzed in the year 2000; 83.2% were males, 85.7% were young adult (20-40 y) and 71.1% were intravenous drug users (Desjeux et al, 2000).

In addition we measured anti-*Leishmania* antibody response in VL patients with or without HIV co-infection, 200 out of 204 VL patients were tested positive (DAT titre \geq 1:3200) given sensitivity of 98% compared to 80% sensitivity for VL and HIV co-infection patient group as two sera were testing negative at a very lower titre (1:100). As previously reported, co-infection by HIV and *Leishmania* enhanced immunologic disturbance, both infections switch the predominant cellular immune response from HIV induced immuno-depression predominates over the cellular response caused by the parasite

(Alvar et al, 1997). In addition, HIV mediated inhibition of proliferative response to *Leishmania species* (Wolday et al, 1994). Therefore, serological tests for *Leishmania* may give negative results. This fact is confirmed by our finding where 2/10 (20%) VL/HIV co-infection cases were DAT negative. In one study from Italy in which level of anti-*Leishmania* antibodies were assessed in series of VL/HIV co-infected patients, up to 13% of the patient did not have antibodies (Gradoni et al, 1993). Other studies reported that only 40-50% of VL/HIV co-infection cases have a positive *Leishmania* serology (cited in MOH, 2003) compared to 80% positivity reported in this study. Therefore, our findings indicate the usefulness of DAT for diagnosis of VL in HIV co-infection cases.

Conclusion and Recommendations

This study demonstrated that there is co-incidence between VL and HIV in Sudan. A higher prevalence (5%) was reported compared to previous studies. Anti-*Leishmania* antibody response was detected in 80% of the VL/HIV co-infection cases demonstrating the usefulness of the DAT in the diagnosis of the disease.

Therefore, we recommend the following:

- Further studies are needed to ascertain the accurate prevalence of VL/HIV co-infection and to study epidemiology of the disease in Sudan.
- The potential of other diagnostic tools, such as rk39 rapid test, for diagnosis of VL in HIV co-infection need to be evaluated.

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What is the association between socioeconomic status and total risk of developing cardiovascular disease and death in patients in one rural family medicine clinic?

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Abstract

Association between socioeconomic status (SES) and total risk of developing cardiovascular disease and death (CVDrisk) has been shown in many studies as clinical significant influence of SES on many risk factors separately and in complex interaction.

Aims: Our aim was to estimate association between SES and CVDrisk in patients in our family medicine clinic by CVD risk factors separately and total CVDrisk.

Methods: SES was estimated by gender and personal monthly income (PMI). According to PMI, all patients (85) were divided in five groups in comparison with average monthly salary and average monthly pension for the region evidenced by Federal Office of Statistics, Federation of Bosnia and Herzegovina. These groups were: 1-patients with salary over the average, 2-

patients with salary under the average, 3-patients with pension over the average, 4-patients with pension under the average and 5-patients without personal income- unemployed or/and with social welfare. CVDrisk was estimated in patients age 40-65(49) and without diabetes mellitus (DM) by HeartScore Web-based program. They were divided in two groups regarding HeartScore result. Those with HeartScore higher than 5% were classified in high risk group and those $\leq 5\%$ in low risk group. Patients with DM (5) and over the age of 65(31) were directly classified in high risk group. Separately, risk factors that were compared by SES groups were: hypertension-HT (systolic > 140 or treated), hypercholesterolemia-H ($H > 5\text{mmol/L}$), smoking cigarettes-SC and DM (diagnosed previously). We used X (Hi)² test for statistical evaluation.

Results: We found statistically significant association between lower economic status (3rd, 4th and 5th group) and high CVDrisk ($p < 0.05$). Regarding the gender, we found close to statistically significance association between low SES (3rd and 4th group) and high CVDrisk in men but not in women. Concerning observed risk factors separately, HT was significant associated with lower SES (from 2nd to 5th group) and SC with higher SES (1st group). H and DM didn't show significant association with SES in our patients.

Conclusion: We have got the fact that mostly of observed patients are in low SES but high CVD risk. HT was present in high percent in all patients but mostly in low SES groups. Results we have got give us very important information about how SES does influence on our patients CVDrisk and what are the groups that we should give special attention

Keywords: Socioeconomic status, cardiovascular risk, risk factors, family medicine

Introduction

Cardiovascular risk assessment

Global risk assessment has become an accepted component of clinical guidelines and recommendations in cardiovascular medicine. The aim is to provide a valid estimate of the probability of a defined cardiovascular event over a period of five or ten years in individuals free of clinical manifestations of cardiovascular disease at the time of examination.

The Framingham Heart Study and the Framingham Offspring Study were the first epidemiological studies that prospectively collected population based data on the association between risk factors and the occurrence of fatal and non-fatal coronary and other cardiovascular events in a systematic and sustained fashion.

The Framingham authors themselves had cautioned about generalizing from their data. And, indeed, an increasing number of reports suggest that this procedure is misleading under various circumstances. When applied to different populations, for example from Southern Europe, or in studies with a more recent onset and follow up period, the observed absolute risk is often substantially lower than predicted by the Framingham algorithms (BMJ, 2003; Buitrago et al., 2006; Menotti et al., 2000)

Several reasons account for this overestimation of absolute risk. Firstly, the Framingham baseline assessment was performed in 1968-75. Declining secular trends in cardiovascular mortality and morbidity, as shown impressively in the MONICA project, account for a widening gap between predictions based on disease rates observed in the past and event rates obtained in more recent study periods. Secondly, populations differ substantially in their absolute cardiovascular risk levels, implicitly limiting the external validity of any prediction algorithm that is based solely on one population. Thirdly, increasing proportions of the population are treated with blood pressure and lipid lowering drugs, so attenuating the predictive power of a given untreated risk factor level at baseline. Finally, population specific levels and trends in

potentially interacting risk factors, such as alcohol consumption, homocysteine, or triglycerides, may further confound absolute risk predictions (BMJ, 2003)

To overcome this problem, Brindle et al in their study used a simple recalibration method by multiplying individual predicted risk with the average ratio of observed over predicted risk (Brindle et al, 2003). Another approach was put forward by the SCORE (Systemic COronary Risk Evaluation) study group (Conroy et al., 2003).

SCORE system

The European Society of Cardiology initiated the development of a risk score system (SCORE) using data from 12 European cohort studies (N=205,178) covering a wide geographic spread of countries at different levels of cardiovascular risks. The SCORE data contains some 3-million person-years of observation and 7,934 fatal cardiovascular events. The SCORE database was born combining results from: 12 European cohort studies and 250,000 patients data collected.

The SCORE risk assessment is derived from a large dataset of prospective European studies and predicts fatal atherosclerotic CVD (cardiovascular diseases) events over a ten year period.

This risk estimation is based on the following risk factors: gender, age, smoking, systolic blood pressure and total cholesterol.

The threshold for high risk based on fatal cardiovascular events is defined as "higher than 5%", instead of the previous "higher than 20%" using a composite coronary endpoint.

This SCORE model has been calibrated according to each European country's mortality statistics. In other words, if used on the entire population aged 40-65, it will predict the exact number of fatal CVD-events that eventually will occur after 10 years.

The relative risk chart may be used to show younger people at low total risk that, relative to others in their age group, their risk may be many times higher than necessary. This may help to motivate decisions about avoidance of smoking, healthy

nutrition and exercise, as well as flagging those who may become candidates for medication. This chart refers to relative risk, not percentage risk.

Benefits of using SCORE are: intuitive, easy to use tool ; takes account of the multifactorial nature of CVD; estimates risk of all atherosclerotic CVD, not just CHD (coronary heart diseases); allows flexibility in management – if an ideal risk factor level cannot be achieved, total risk can still be reduced by reducing other risk factors; allows a more objective assessment of risk over time; establishes common language of risk for clinicians; shows how risk increases with age; the new relative risk chart helps to illustrate how a young person with a low absolute risk may be at a substantially higher and reducible relative risk (Heartscore, 2009; Escardio, 2009; Graham, 2007)

Many studies has shown that SCORE is a powerful tool to estimate the cardiovascular risk for European population in comparing with many algorithms derived from Framingham study that overestimate absolute coronary risk in countries characterized by a lower incidence of coronary events (Buitrago et al., 2006; Menotti et al., 2000).

HeartScore® is the interactive tool for predicting and managing the risk of heart attack and stroke in Europe. HeartScore® is aimed at supporting clinicians in optimizing individual cardiovascular risk reduction. HeartScore® can easily be adapted to different countries and different cultures and thus, make it easier for clinicians to have rapid, interactive access to appropriate local preventive advice.

HeartScore® is available in country-specific (calibrated) versions for Sweden, Germany, Greece, Spain, Poland and Cyprus.

Translated versions are available for Bosnia & Herzegovina & Russia. A roll-out plan of national version is currently under way with the National Cardiac Societies (Escardio, 2009; Heartscore, 2009).

In the European Guidelines on CVD Prevention, it is not recommended to assess risk in patients with diabetes. They have by their lack of glucose control declared themselves at

high risk and should therefore be treated with maximum intensity. HeartScore® uses data from the SCORE study and in this study the definition of diabetes varied between the 12 centres who supplied their data. The SCORE group is actively pursuing ways to incorporate diabetes into the model, but it will take some time until this task is fulfilled (Heartscore, 2008). Patients with known stable CVD, diabetes, or very high single risk factors should be treated similarly to those with high SCORE risks (Graham, 2007).

Socioeconomic status and cardiovascular risk

Socioeconomic status could be assessed by many different parameters as race/ethnicity, economic status, education and gender (Loucks et al, 2007; Salsberry et al., 2007).

In National Health and Nutrition Examination Survey III (NHANES III) economic effects on CVD risk (as group of factors included in metabolic syndrome) were seen for women, but not men. Women in the lowest economic group were more likely to be at risk in four of the five risk categories when compared with women in the highest economic group (Salsberry et al., 2007).

The findings from NHANES III provide biologic mechanistic evidence of previously documented associations between SEP (socioeconomic position) and such clinical disorders as type 2 diabetes and coronary heart disease. These results underscore the clinical significance of SEP, particularly for women (Loucks et al, 2007).

There are some hypothetic models of influence of socioeconomic risk factors on cardiovascular diseases. One of them is that low socioeconomic status could have negative influence on individual emotional reaction concerning bad conditions for use health and social insurance system, bad work conditions, low self-respecting, everyday stress conditions, feelings of hostility, anger and depression. These emotional reactions could be cause of developing bad life habits as smoking cigarettes, bad nutrition, alcohol use, low physical activities, overweight and obesity. These bad life habits

are risk factors by themselves for cardiovascular diseases and together with bad psychosocial and socioeconomic status form complex cause-effect circle (Everson et al., 1997; Oldenburg et al., 1996; Rajevic et al., 2003).

Second possible model is connected with the fact that in people with low socioeconomic status, health culture and health habits are also in low level. Also health culture is part of global culture of one nation and it could have different influence on cardiovascular diseases. Low socioeconomic status has bad influence on both, men and women but concerning the continuing stress situation related to this status, men are a little bit more in risk than women (Everson et al., 1997; Oldenburg et al., 1996; Rajevic et al., 2003).

Aims

Our aims were to estimate association between socioeconomic status and cardiovascular diseases risk in patients in our family medicine clinic in Central Bosnia&Herzegovina by CVD risk factors separately and total CVD risk and to give some suggestions concerning the prevention and treatment of found situation and results in these patients.

Methods and Materials

We observed 85 patients in one rural family medicine clinic in city of Kakanj, Central Bosnia.

CVD risk was estimated in patients age 40-65(49) and without diabetes mellitus (DM) by HeartScore® Web-based program.4 They were divided in two groups regarding HeartScore® result. Those with HeartScore® higher than 5% were classified in high risk group and those with HeartScore® \leq 5% in low risk group. Patients with DM (5) and over the age of 65(31) were directly classified in high risk group. Risk factors that were observed and separately compared to socioeconomic status were: hypertension-HTA (systolic $>$ 140 or treated), hypercholesterolemia-H (H $>$ 5mmol/L), smoking cigarettes-SC and DM (diagnosed previously).

Socioeconomic status (SES) was estimated by gender and personal monthly income (PMI). According to PMI, all patients were divided in five groups in comparison with average monthly salary and average monthly pension for the region evidenced by Federal Office of Statistics, Federation of Bosnia and Herzegovina (Statistical Yearbook, 2008; Zenicko-dobojski, 2008). These groups were: 1-patients with salary over the average, 2-patients with salary under the average, 3-patients with pension over the average, 4-patients with pension under the average and 5-patients without personal income-unemployed or/and with social welfare. We used X^2 (The Chi-square test) test for statistical evaluation.

Results

We observed 85 patients, 60 (70.6%) females and 25 (29.4%) males. Mean age were 60.18 with min.40 and max.78. We found according to previously mentioned criteria that 49.4% of patients were in high risk group to develop CV disease or CV death. Regarding gender, 56% of males were in high risk group and 46.7% of females. ($p>0.05$)

Comparing CVD risk among socioeconomic groups, we found statistically significant association between lower economic status (3rd, 4th and 5th group) and high CVD risk ($p<0.05$). (Figure-1)

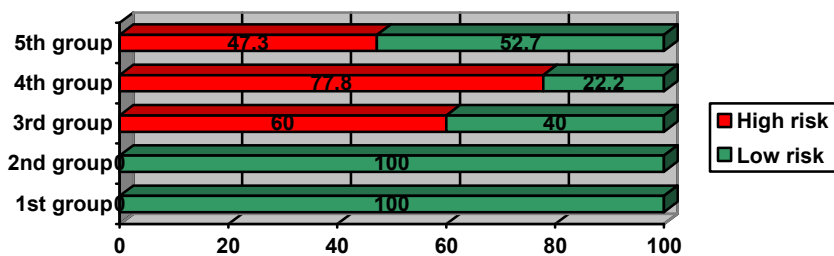


Figure 1: Cardiovascular risk according to socioeconomic groups

Regarding observed risk factors separately, we found that hypertension was significant associated with lower socioeconomic status (from 2nd to 5th group)($p < 0.05$) and smoking cigarettes with higher socioeconomic status (1st group)($p < 0.05$). Hypercholesterolemia and DM didn't show significant association with SES in our patients. (Figure-2)

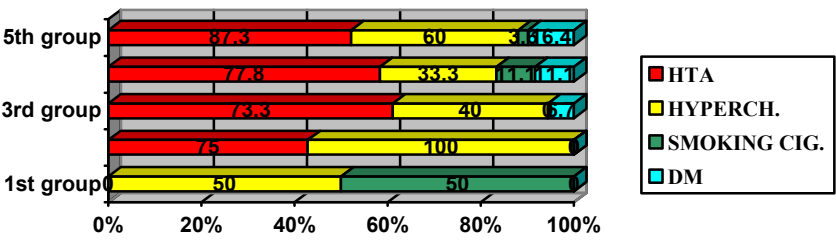


Figure 2: Distribution of hypertension (HTA), hypercholesterolemia (HYPERCH.), smoking cigarettes (SMOKING CIG.) and diabetes mellitus (DM) according to socioeconomic groups

Regarding the gender, we found close to statistically significant association between low socioeconomic status (3rd and 4th group) and high CVD risk in men (Figure-3) but not in women (Figure-4).

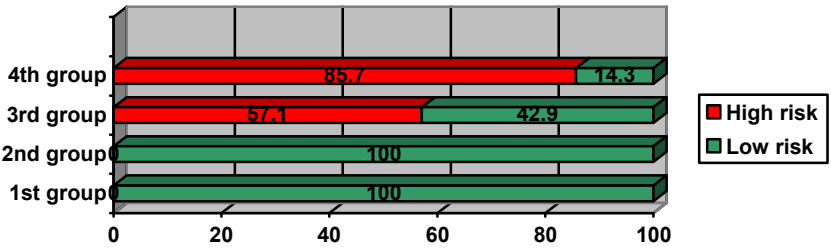


Figure 3: Association between CVD risk and socioeconomic status in men

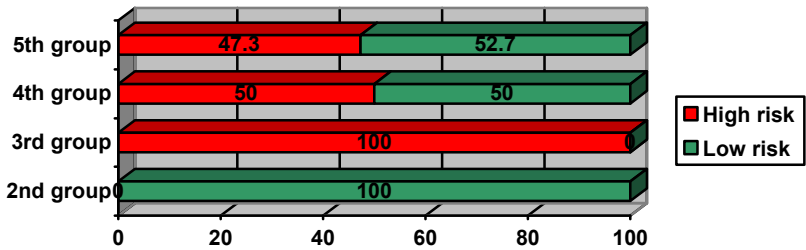


Figure 4: Association between CVD risk and socioeconomic status in women

Conclusion

According to our results we have got high percent of high risk patients in observed sample, little more in men than women. We found the fact that mostly of observed patients are in low socioeconomic status but in high cardiovascular disease and death risk. This fact was found more in men than in women. Hypertension and hypercholesterolemia were present in high percent in all patients but hypertension mostly in low socioeconomic groups. Results we have got give us very important information about how socioeconomic status does influence on CVD risk in our patients and what are the groups

that we should give special attention as men and low income individuals. Also, we saw that some of risk factors as hypertension and hypercholesterolemia have high prevalence and mostly connected to high total CVD risk, so those should be the target for health promotion and politics. What we can do in our family medicine clinic is to point to importance of all risk factors, specially the most prevalent, to educate patients, to point to importance of changing health culture and health habits and completely life style for the purpose to decrease cardiovascular diseases and death risk and events.

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Anti-ulcerogenic Activity of Aqueous Extract of *Ficus deltoidea* Against Ethanol-induced Gastric Mucosal Injury in Rats

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Abstract

Background: *Ficus deltoidea* is a native epiphytic shrub widely distributed in several countries of the Southeast Asia and commonly known as *Mas cotek* in Malaysia. Different parts of

the plant are used traditionally for decades to treat various kinds of ailments. Very few studies on *F.deltoidea* have been reported; only on its fruit extract which demonstrate inhibitory effects against Angiotensin-I Converting Enzyme (ACE), suggesting to posses anti-hypertensive properties (Abdullah *et al.*, 2008) and from the study done by Sulaiman *et al.*, (2002) stated that an aqueous extract of *F.deltoidea* leaves possess antinociceptive activity in laboratory animals, which gives a supportive fact towards the traditional use of this plant to overcome painful sensation.

Aim: This current study was undertaken to evaluate the anti-ulcer activity of this plant extract against ethanol-induced gastric ulcers in rats.

Method: The ulcer healing activity of whole-plant extract of *Ficus deltoidea* was studied in gastric ulcer induced by ethanol in rats. Four groups consist of six adult male *Sprague Dawley* rats per group (body weight ranges between 180-200 g) were orally pre-treated respectively with: distilled water (negative control), 250 mg kg⁻¹, and 500 mg kg⁻¹ *F.deltoidea* extract (experimental), and 20 mg kg⁻¹ omeprazole (positive control) thirty minutes before oral administration with absolute ethanol 5 ml kg⁻¹ to generate gastric mucosal injury. After one hour later, the rats were sacrificed and the ulcer areas and histological sections of gastric walls were determined.

Result: The statistical significance of differences between groups was assessed using one-way ANOVA which value of $p < 0.05$ was considered as significant. Grossly, the negative control rats exhibited severe mucosal injury whereas pre-treatment with *F.deltoidea* and omeprazole rats resulted in significantly less ($p < 0.001$) gastric mucosal lesions production. The gastric protection was more prominent in 500 mg kg⁻¹ *F.deltoidea* extract than 250 mg kg⁻¹. Histological studies confirmed the results when compared to the pre-treated groups of rats, where negative control rats showed very severe and deep gastric mucosal necrotic damage, along with edema and leucocytes infiltration of the submucosal layer.

Conclusion: In conclusion, the present finding suggests that *F.deltoidea* extract have potency in promoting ulcer protection as ascertained by the comparative significant decreases in ulcer areas and inhibition of submucosal edema and leucocytes infiltration of submucosal layer under histological supervision.

Keywords: Ficus deltoidea, plant extract, peptic ulcer, gastric ulcer healing, gross lesion, histology

Introduction

In current clinical practice, peptic ulcer has become one of the most common gastrointestinal disorders to occur among developed countries which caused by the disruptions of the gastric mucosal defence and repair systems (Grossman, 1981). Previous studies has discovered a large number of medicinal plants and dietary nutrients which posses gastro-protective activity (Kath and Gupta, 2006; Malairajan *et al.*, 2007). *Ficus deltoidea* is a native ephyphytic shrub widely distributed in several countries of the Southeast Asia. In Malaysia, it is commonly known as *Mas cotek*, *serapat angin*, *telinga beruk* and other few names. Different parts of the plant are used traditionally to treat various kinds of ailments. The fruits are chewed to relieve headache, toothache and cold; powdered root and leaves of the plant has been applied externally to wounds and sores, and around the joints for relief of rheumatism and traditionally consume as herbal drink for women after childbirth to help in strengthen up the uterus (Sulaiman *et al.*, 2002) Besides being one of the popular herbs used in Malay traditional medicine, its pharmacological properties have not yet been studied. Very less publications indicating scientific findings of this plant has been published; only two studies on *F.deltoidea* have been reported; fruit extract of *F.deltoidea* demonstrate inhibitory effects against Angiotensin-I Converting Enzyme (ACE) enzyme, suggesting it posses anti-hypertensive properties (Abdullah *et al.*, 2008) and report by Sulaiman *et al.*, (2002) stated that an aqueous

extract of *F.deltoidea* leaves contains pharmacologically active constituents which possess antinociceptive activity in laboratory animals, and this might give a supportive fact towards the traditional use of this plant in overcome painful condition. There is no scientific documentation yet about the anti-ulcerogenic activity of *F.deltoidea* whole-plant extract in rats, therefore, the current study was undertaken to evaluate the anti-ulcer activity of this plant extract against ethanol-induced gastric ulcers in rats.

Materials and Methods

Omeprazole

Omeprazole is in a class of drugs called proton pump inhibitors used for the treatment of conditions such as peptic ulcers. Omeprazole blocks the enzymes in the wall of the stomach from producing acid. By blocking the enzyme, the production of stomach acid is decreased, thus allowing the stomach to heal. In this study, omeprazole was used as the reference anti-ulcer drug, and was obtained from the University Malaya Medical Centre (UMMC) Pharmacy. The drug was administered orally to the rats in concentrations of 20 mg kg⁻¹ suspended in distilled water (5 ml kg⁻¹) (Pedernera *et al.*, 2006).

***Ficus deltoidea* whole-plant extract**

Whole-plant of *Ficus deltoidea* was purchased from Chemical Engineering Pilot Plant (CEPP), University of Malaysia Technology (UTM), Skudai. The dried sample was then ground into powder using Wiley mill (40-60 mesh). The dried powdered plants were successively extracted with water. The extract was then dissolved in distilled water and administered orally to two groups of rats in concentrations of 250 mg kg⁻¹, and 500 mg kg⁻¹, body weight (5 ml kg⁻¹), respectively.

Experimental animals

Adult male *Sprague-Dawley* rats were obtained from the Animal House, Faculty of Medicine, University of Malaya, Kuala Lumpur (Ethics No. PM 28/9/2006 MAA (R)). The rats

weighed between 180 – 200 g. They were fasted for 48 hours before the experiment (Garg *et al.*, 1993), but were allowed free access to tap water up till 2 hours before the experiment. During the fasting period, the rats were placed individually in separate cages with wide-mesh wire bottoms to prevent coprophagy. On the day of experiment, the rats were randomly divided into 4 groups of 6 rats each. The groups were numbered 1 to 4.

Group 1 rats were negative controls and each received distilled water only orally (5 ml kg⁻¹); Groups 2 and 3 received 250 mg kg⁻¹ and 500 mg kg⁻¹ *F.deltoidea* whole-plant extract by the same route respectively; Group 4 rats received 20 mg kg⁻¹ omeprazole as positive control. Thirty minutes after pre-treatment, all rats were administered orally with absolute ethanol 5 ml kg⁻¹. After one hour later, all animals were sacrificed by overdoses of diethyl ether and their stomachs were rapidly removed (Paiva *et al.*, 1998).

Gross evaluation of gastric lesions

Any ulcers would be found in the gastric mucosa, appearing as elongated bands of hemorrhagic lesions parallel to the long axis of the stomach. Each gastric mucosa was examined for damage. The length (mm) and width (mm) of the ulcer on the gastric mucosa was measured by a planimeter (10 x 10 mm² = ulcer area) to assess the ulcer areas under dissecting microscope (x1.8). The area of each ulcer lesion was measured by counting the number of small squares, 2 mm x 2 mm, covering the length and width of each ulcer band. The sum of the areas of all lesions for each stomach was applied in the calculation of the ulcer are (UA) wherein the sum of small squares x 4 x 1.8 = UA mm² (Kauffman and Grossman, 1987). The inhibition percentage (I %) was calculated by the following formula:

$$(I\%) = [(UA_{\text{control}} - UA_{\text{treated}}) \div UA_{\text{control}}] \times 100\%.$$

Histological evaluation of gastric lesions

Specimens of the gastric walls of each rat were fixed in 10% buffered formalin and processed in a paraffin tissue processing machine. Sections of the stomach were made at a thickness of 5 μm , stained with hematoxylin and eosin and analyzed microscopically.

Statistical analysis

All values were reported as mean \pm S.E.M. The statistical significance of differences between groups was assessed using one-way ANOVA. A value of $p < 0.05$ was considered significant.

Results

Gross evaluation of gastric lesions

Rats orally administered with omeprazole or *F.deltoidea* whole-plant extracts 30 minutes before administration of absolute alcohol showed significantly ($p < 0.001$) reduction of the mean gastric ulcer area compared to rats pre-treated with only distilled water (Table 1, Figures 1 and 2). Also rats pre-treated with omeprazole or 500 mg kg⁻¹ *F.deltoidea* extracts significantly ($p < 0.001$) reduced the formation of gastric ulcers area induced by ethanol compared to rats pre-treated with 250 mg kg⁻¹ *F.deltoidea* extracts (Table 1). The *F.deltoidea* whole-plant extract exerted the cytoprotective effects in a dose-dependent manner (Table 1).

Histological evaluation of gastric lesions

The rats pre-treated with only distilled water before administration of ulcer-inducing absolute ethanol showed markedly extensive damage to gastric mucosa, the lesions extend deeply to mucosal layer, oedema and leucocytes infiltration of submucosal layer. Rats pre-treated with omeprazole or *F.deltoidea* extracts had comparatively better protection of the gastric mucosa as seen by marked reduction in ulcer area, and absence of oedema and leukocyte infiltration of submucosa (Figures 3 and 4).

Discussion

Results from this study showed that oral administration of rats with *F.deltoidea* extracts significantly protect the gastric mucosa from ulcer induction by absolute ethanol compared to negative control rats which were treated with distilled water. The cytoprotective effect was confirmed through histological examinations of the gastric tissues of the animals that shows marked prevention of mucosal lesions and inhibition of edema and leucocytes infiltration of submucosa. Using absolute to induce formation of gastric lesions is a well-known rapid and convenient method of screening plant extracts for anti-ulcer potency and cytoprotection in terms of the absence or reduction in macroscopically and microscopically visible lesions. Ethanol induced necrotic lesions in the gastric mucosa by its direct toxic effect, reducing the secretion of bicarbonates and production of mucus (Marhuenda *et al.*, 1991), stasis in gastric blood flow, which contributes to the development of the hemorrhagic lesions of gastric mucosa (Holzer *et al.*, 1991). Bicarbonate ion is produced and trapped by mucus, creating a gradient of pH from 1-2 in the lumen to 6-7 at the mucosal surface, thus preventing gastric acid and pepsin from digesting the mucosa. The pathogenic effects of ethanol could be due to disturbances in gastric secretion, alterations in permeability, gastric mucus depletion and free-radical production (Salim, 1990). Lipid peroxidation is one of the important factor involves in ulcerogenesis which results in the production and release of chemical substance that recruits and activates polymorphnuclear leucocytes (Salram *et al.*, 2002). Previous study done by Kobayashi *et al.*, (2001) showed that teprenone exerts a protective effect against mucosal lesions through preservation of gastric mucous synthesis and secretion, and inhibition of neutrophil infiltration and enhanced lipid peroxidation in the ulcerated gastric tissue. Increase in neutrophil infiltration into ulcerated gastric tissue delays the healing of gastric ulcers in rats as reported by Fujita *et al.*, (1998) and Shimizu *et al.*, (2000) whereby neutrophils mediate

lipid peroxidation through the production of superoxide anions (Zimmerman *et al.*, 1997). Oxygen free radicals derived from infiltrated neutrophils in ulcerated gastric tissues have inhibitory effect on gastric ulcers in rats (Suzuki *et al.*, 1998). As a conclusion, our study indicate that pretreatment of *F.deltoidea* extract had significantly reduced ulcer area against absolute ethanol-lesion induction and this mechanism probably be due to stimulation of gastric mucous secretion and inhibition of edema and leucocytes infiltration in submucosal gastric tissue.

Acknowledgments

The authors express gratitude to the staff of the Animal House, Faculty of Medicine for the care and supply of rats, and to the University of Malaya for the financial support (e-Science fund grant 12-02-03-2051).

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A Comparative Study of Efficacy and Tolerability of Ibuprofen vs. Aceclofenac in Osteoarthritis of Knee Joint

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Introduction

Osteoarthritis

Osteoarthritis (OA) is a chronic progressive degenerative disease of unknown etiology which affects mainly the weight bearing joints. Osteoarthritis may be classified into 2 types:

1. Primary osteoarthritis is of unknown origin, occurring in previously intact joints, with no apparent initiating factor and occurs in older individuals.
2. Secondary osteoarthritis which occurs secondary to some recognizable local or systemic factor i.e. mechanical derangement, pyogenic infection, epiphysial separation and intra-articular fractures.

The prognosis of primary type is better than that of secondary type. The end stage of both types may be the same, but the progression of the primary type is usually slower and relentless. Some of the predisposing factors are:

1. Age: Although osteoarthritis is more common after the 4th decade, but expanded research has shown that many young people also suffer from the earlier manifestations of the disease.

2. Sex: More common in menopausal females. Points to the protective role of estrogen before menopause. Mainly knee joint is involved.
3. Obesity: Predisposes weight bearing surfaces of the joint to abnormally increased pressure. It is a risk factor for OA of knees and the hands in early life (Handy, 2000).

Pathologically, in osteoarthritis the cartilage shows changes of degeneration and subsequent formation of new subchondral bone. The main protein is collagen protein and giant proteoglycans. With age, the cells (chondrocytes) do not form proper collagen to withstand the normal stresses of life. There is focal chondromucoid softening with a loss of chondroitin sulfate from cartilage matrix causing unmasking of collagen fibers (Bennet et al, 1942). There are areas of repair seen as disordered proliferation of chondrocytes in destroyed cartilage (Collins, 1939). When the pressure load is beyond the tolerance of the tissue, there is concomitant reduction in viscoelasticity and stiffness of articular cartilage results. This leads to fibrillation with clefts penetrating deeper and deeper into the articular cartilage with loss of cells (Collins, 1949). The collagen framework is more vulnerable to stress and thus disruption of the collagen framework and fibrillation results leading to osteoarthritis.

Signs and Symptoms of OA (Hochberg, 1997)

Symptoms	<ul style="list-style-type: none"> • Pain at rest or at night (less common) • Pain or aching with use of joint. • Joint stiffness lasting less than 30 minutes after inactivity • Reduced movement • Feeling of instability or buckling of the knee.
Signs	<ul style="list-style-type: none"> • Localization of tenderness at joint margins • Firm swelling at joint margin • Restricted range of motility • Crepitus (crackling) on joint movement • Mild inflammation (small effusion) • Mal-alignment, deformity (late stage)

The radiological features of OA of knee (Fergusson, 2001).

1. Narrowing of joint space
2. Patellofemoral OA
3. Altered bone contour
4. Bone sclerosis (sub-chondral sclerosis)
5. Bone cysts (Sub-chondral cysts)
6. Periarticular calcification
7. Soft tissue swelling

Classification of osteoarthritis with Functional Capacity

Depending upon functional capacity the Steinbroker's classification divides osteoarthritis into 4 classes (Sharma et al, 1999).

Class 1 Ability to carry on usual activities.

Class 2 Normal activity despite handicap or discomfort or Limited mobility of one or more joints.

Class 3 Perform only little or none of the activities of usual occupation or of self-care.

Class 4 Incapacitated, bedridden or confined to wheel chair permitting little or no self care.

Treatment of osteoarthritis by and large is conservative. Surgical treatment (Knee replacement surgery and arthroplasty) is reserved for patients not responding to conservative treatment (Jordan et al, 2003).

Conservative treatment includes rest, weight reduction, physiotherapy, skin traction, analgesics and NSIADs.

Aim of Treatment (Doomra and Sharma, 2000):

- To relieve pain.
- To increase muscle strength.
- To maintain joint mobility.
- To minimize disability and to limit functional impairment.
- To repair cartilage and its regeneration.

Osteoarthritis of Knee Joint being common, so this comparative study of clinical efficacy and tolerability of ibuprofen and aceclofenac in patients of osteoarthritis of knee joint is planned to evaluate the claim about efficacy and tolerability of ibuprofen in comparison to aceclofenac.

Ibuprofen

It was the first of the propionic acid derivative orally administered non-steroid anti-inflammatory drugs to be used in most countries. It has prominent anti-inflammatory effects in addition to having analgesic and antipyretic actions. It is a potent inhibitor of the cyclo-oxygenase which thus results in a marked reduction in prostaglandin synthesis. Inhibition of prostaglandin biosynthesis prevents their hyperalgesic effect upon sensory nerves. Inhibition of vasodilator prostanoid formation (PGE-2) diminishes the vascularity and transudation of fluid which are two of the principle manifestations of inflammation (Dollery, 1991).

Aceclofenac

It is an orally administered phenylacetic acid derivative with effects on a variety of inflammatory mediators. Through its analgesic and anti-inflammatory properties, aceclofenac provides symptomatic relief in a variety of painful conditions. The drug inhibits synthesis of the inflammatory cytokines (IL)-1 beta and tumour necrosis factor (TNF), and inhibits prostaglandin E2 (PGE2) production. It also has inhibitory effects on synovial level effusions.

Aceclofenac stimulates the synthesis of IL-1 receptor antagonist in human articular chondrocytes subjected to inflammatory stimuli and that 4²-hydroxy-aceclofenac has chondroprotective properties attributable to suppression of IL-1 beta-mediated promatrix metalloproteinase production and proteoglycan release (Dooley et al, 2001).

It is to be noted that only symptomatic relief is achieved. No effect on cartilage destruction and underlying disease process

has been found. Osteoarthritis of Knee Joint being common, so this comparative study of clinical efficacy and tolerability of ibuprofen and aceclofenac in patients of osteoarthritis of knee joint is planned to evaluate the efficacy and tolerability of ibuprofen in comparison to aceclofenac.

Aims and Objectives

To study in patients of Osteoarthritis of knee:

- Comparison of efficacy of Aceclofenac and Ibuprofen in Osteoarthritis of knee
- Comparison of tolerability of Aceclofenac and Ibuprofen in Osteoarthritis of knee

Materials and Methods

This study included a total number of 50 patients of osteoarthritis of knee joint (unilateral or bilateral) coming to the OPD of the Orthopaedic Department of Government Medical College and Rajindra Hospital, Patiala.

A detailed history and physical examination was carried out in these patients by the doctor concerned. Patients of either sex (30-75 years) with confirmed diagnosis of osteoarthritis of knee joint were considered. Informed consent (English/ Punjabi) was obtained from all patients after fully explaining them the details of the study. The total duration of study was 6 weeks.

Inclusion Criteria

1. Age between 30-75 years.
2. Both the genders are eligible for study.
3. Patients with confirmed osteoarthritis of knee joint.

Exclusion Criteria

1. Patients with renal disease or cardiac disorders before the study.
2. Patients with active gastrointestinal ulceration before the study.
3. Patients with hepatic or coagulation disorders as we will have confusion identifying risk factors.

4. Patients receiving antineoplastic agents, corticosteroids, gold salts, pencillamine, colchicines, anticoagulants, antimalarials within one month prior to the study at the time of inclusion in the study.
5. Patients with other types of inflammatory arthritis (rheumatoid arthritis), gout or post traumatic OA of the knee.
6. Patients belonging to Class IV of Steinbrocker functional capacity classification.
7. Patients who did not show a flare up of the disease within 15 days of discontinuing NSAIDs or other analgesics prior to inclusion in the study.
8. Patients with previous hypersensitivity to NSAIDs.
9. Patients scheduled for hospitalization or bed rest.
10. Patients scheduled for joint replacement surgery due to arthritis.
11. Pregnant women and nursing mothers.
12. Female patients taking contraceptives.

Study Protocol

A simple randomized, double blind, parallel group study of 50 patients of osteoarthritis of knee joint was conducted.

The patients were divided into two groups of 25 each. 25 patients were given Aceclofenac 100mg bid and 25 patients were given Ibuprofen 400mg tds for 6 weeks.

No other drug commonly used for treatment of osteoarthritis was given during the test. The study was conducted in accordance with the principles of good clinical practice and Helsinki declaration of 1975 (Spiker, 1997). The study protocol was approved by Research and Ethics Committee of the Government Medical College, Patiala.

Eligibility of the Patients

All the newly diagnosed patients with confirmed diagnosis of symptomatic OA of unilateral/bilateral knee in flare for at least 3 months or longer before the study and belonging to Steinbrocker functional capacity of Class I, Class II and III were

included in the study (Sharma et al, 1999). Flare is defined as worsening of sign and symptoms of the disease after stopping analgesic and anti-inflammatory drugs or other criteria if the patient is not taking any symptomatic treatment. Patients already taking other analgesic drugs were included in the study after workout period of 15 days and flare was confirmed as a base line visit according to predefined criteria.

Treatment Groups

Eligible patients fulfilling the mentioned criteria were divided equally and randomly into 2 treatment groups with similar study design and procedure at each clinical visit.

Group A – Aceclofenac Group

Eligible 25 patients (9 males and 16 females) were given Aceclofenac 100mg bid.

Group B – Ibuprofen Group

Eligible 25 patients (8 males and 17 females) were given Ibuprofen 400mg tds.

Follow-ups for Clinic of Assessment

All the patients were directed to report in the outpatient department for clinical assessment after 3 weeks and 6 weeks.

Parameters of Study

Data was collected on patients demographic characteristics functional status involving different parameters like pain intensity, joint tenderness, swelling, erythema, pain on movements, functional capacity and overall assessment.

Demographic Characteristics

1. Age of the patient.
2. Sex of the patient.
3. Diagnosis (unilateral/bilateral OA of knee).
4. Duration of the disease.
5. Steinbroker functional capacity classification.

Functional Status

Functional status of the patients with OA of the knee joint was evaluated by:

- Using Likert version of 5 point scale (Bolognese et al, 2003) where '0' represent "none", '1' is "mild", '2' is 'moderate', '3' is "severe" and '4' is "extreme".
- The pain was also measured by Visual Analogue Scale (VAS). VAS (Kelly, 2001) is a standardized vertical scale from 0 to 100 and the least pain is 'zero' and the maximum pain being marked 100.

Safety Treatment

All the adverse events in each treatment group were noted.

Compliance

Compliance to the treatment by the patient was assessed by counting the number of tablets consumed from the foil.

Observations and Tabulations

The results of above observations of individual patients were pooled for each group. Data was statistically analysed using student's 't' test. The results were finally analysed in tables and graphs. The Statistical methods used for analysis of data were as described by Crossland (1982) and Ghosh (1984).

Various statistical methods used were:

- Mean Values
- Standard Deviation
- Standard Error
- Student's 't' test (Paired 't' test)
- Unpaired t-test
- Chi-square Test
- Fishers exact test
- 'p' Value- A difference between the treated and control group which would have arisen by chance is 'p' value. If it is less than 0.05, it is considered significant (S), 'p' value less than 0.001 is

considered highly significant (HS). If it is equal or more than 0.05, it is considered non-significant (NS).

Observations and Results

This study comprised of 50 patients of osteoarthritis coming to the out patient department (OPD) of Orthopaedic department of Government Medical College and Rajindra Hospital, Patiala which is divided into two groups. A detailed history and physical examination was carried out in these patients. Patients of either sex (age 30-75 years) with confirmed diagnosis of osteoarthritis of knee joint of more than 3 months duration and fulfilling exclusion criteria were considered. Eligible patients were divided equally and randomly into two treatment groups. Group A patients were given Aceclofenac and Group B patients were given Ibuprofen as random.

Table 1: Patients demographic profile

Characteristics		Aceclofenac Group A	Ibuprofen Group B
Gender	Male	9 (36%)	8 (32%)
	Female	16 (64%)	17 (68%)
Age	Mean \pm SD	52.84 \pm 9.91	52.74 \pm 5.08
	30-45 years	7 (28%)	6 (24%)
	46-60 years	15 (60%)	16 (64%)
	61-75 years	3 (12%)	3 (12%)
Diagnosis	Left knee	8 (32%)	10 (40%)
	Right knee	7 (28%)	9 (36%)
	Both knee	10 (40%)	6 (24%)
Functional Capacity Classification	I	1 (4%)	2 (8%)
	II	11 (44%)	11 (44%)
	III	13 (52%)	12 (48%)
Disease Duration (months)	Mean \pm SD	10.40 \pm 8.22	8.93 \pm 6.80
	1 year	17 (68%)	18 (72%)
	1-2 year	6 (24%)	5 (20%)
	2-3 year	2 (8%)	2 (8%)

Table 1 shows demographic profile of the patients in both the groups.

Group A- Aceclofenac (n=25)- In this group 9 (36%) male and 16 (64%) female patients enrolled.

In the age group 30-45 years there were 7 (28%) patients; in the age group 46-60 years there were 15 (60%) patients and in the age group 61-75 years there were 3 (12%) patients with mean age of this group being 52.84 ± 9.91 years.

The patients having diagnosed with OA in left knee were 8 (32%); with OA of right knee were 7 (28%) and OA of both knees were 10 (40%).

This group consisted of 1 (4%) patient from Class I, 11 (44%) from Class II and 13 (52%) patients from Class III of the Steinbroker Functional Capacity Classification.

In this group 17 (68%) were diagnosed OA of <1 year duration, 6 (24%) patients with OA of knee in between 1-2 years duration and 2 (8%) patients with OA of knee in between 2-3 years duration with mean duration of the disease of this group being 10.40 ± 8.22 months.

Group B- Ibuprofen (n=25)- In this group 8 (32%) male and 17 (68%) female patients enrolled.

In the age group 30-45 years there were 6 (24%) patients; in the age group 46-60 years there were 16 (64%) patients and in the age group 61-75 years there were 3 (12%) patients with mean age of this group being 52.74 ± 5.08 years.

The patients having diagnosed with OA in left knee were 10 (40%); with OA of right knee were 9 (36%) and OA of both knees were 6 (24%).

This group consisted of 2 (8%) patients from Class I, 11 (44%) from Class II and 12 (48%) patients from Class III of the Steinbroker Functional Capacity Classification.

In this group 18 (72%) were diagnosed OA of <1 year duration, 5 (20%) patients with OA of knee in between 1-2 years duration and 2 (8%) patients with OA of knee in between 2-3 years duration with mean duration of the disease of this group being 8.93 ± 6.80 months.

Pain Intensity

Table 2: Change in pain intensity in both groups at the end of treatment

Change in Pain Intensity	Aceclofenac		Ibuprofen		X ²	'p' Value
	No.	%age	No.	%age		
Improvement	19	76	16	64	0.86	0.35
No change	5	20	8	32	NA	NA
Deteriorated	1	4	1	4	NA	NA

($p \geq 0.05$, NS)

Table 2 represents the change in pain intensity in number of patients in both the groups.

In patients taking aceclofenac, 19 (76%) showed improvement, 5 (20%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 16 (64%) patients showed improvement, 8 (32%) showed no change and 1 (4%) showed deterioration.

The difference in number of patients showing improvement in pain intensity between groups was statistically not significant ($p = 0.35$).

Table 3: Mean \pm SD, intergroup and intertime comparison of pain intensity within the both groups

Duration	Acceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	2.84 \pm 0.37	2.6 \pm 0.51	0.061
3 week	1.96 \pm 0.54	2.08 \pm 0.57	0.449
6 week	1.60 \pm 0.71	1.72 \pm 0.61	0.525
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.001**	
3 vs 6 weeks	0.004**	0.009**	
0 vs 6 weeks	0.001**	0.001**	

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 3 represents change in pain intensity at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean pain intensity was 2.84 \pm 0.37 at 0 week, 1.96 \pm 0.54 at 3 weeks and 1.60 \pm 0.71 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 2.6 \pm 0.51 at 0 week, 2.08 \pm 0.57 at 3 weeks and 1.72 \pm 0.61 at 6 weeks. By taking inter group comparison, p= 0.061 at 0 week, p= 0.449 at 3 weeks and p= 0.525 at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that p= 0.001 at 0 vs 3 weeks, p= 0.004 at 3 vs 6 weeks and p= 0.001 at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that p= 0.001 at 0 vs 3 weeks, p= 0.009 at 3 vs 6 weeks and p= 0.001 at 0 vs 6 weeks.

Table 4: Mean %age change of pain intensity in both groups

Duration	Acceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	30.67 \pm 21.37	17.33 \pm 27.84	0.032*
3-6 weeks	17.33 \pm 27.84	14.67 \pm 26.92	0.732
0-6 weeks	42.67 \pm 30.07	26.67 \pm 22.53	0.039*

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 4 represents mean percentage (%) change in pain intensity in both groups.

In patients taking aceclofenac, the mean %age change in pain intensity was 30.67 \pm 21.37 at 0-3 weeks, 17.33 \pm 27.84 at 3-6 weeks, 42.67 \pm 30.07 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 17.33 \pm 27.84 at 0-3 weeks, 14.67 \pm 26.92 at 3-6 weeks and 26.67 \pm 22.53 at 0-6 weeks. By comparing the mean %age change in pain intensity between both the groups it was observed that p=0.032 at 0-3 weeks, p=0.732 at 3-6 weeks and p=0.039 at 0-6 weeks.

PAIN (VAS)

Table 5: Mean \pm SD, intergroup and intertime comparison of PAIN(VAS) within the both groups

Duration	Acceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	70.20 \pm 10.45	61.20 \pm 12.56	0.008**
3 week	46.20 \pm 12.60	48.40 \pm 14.50	0.563
6 week	33.60 \pm 17.05	41.00 \pm 13.23	0.093
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.001**	
3 vs 6 weeks	0.001**	0.001**	
0 vs 6 weeks	0.001**	0.003**	

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 5 represents change in pain (VAS) at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean change in pain (VAS) was 70.20 ± 10.45 at 0 week, 46.20 ± 12.60 at 3 weeks and 33.60 ± 17.05 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 61.20 ± 12.56 at 0 week, 48.40 ± 14.50 at 3 weeks and 41.00 ± 13.23 at 6 weeks. By taking inter group comparison, $p=0.008$ at 0 week, $p= 0,563$ at 3 weeks and $p= 0.093$ at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that $p= 0.001$ at 0 vs 3 weeks, $p= 0.001$ at 3 vs 6 weeks and $p= 0.001$ at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that $p= 0.001$ at 0 vs 3 weeks, $p= 0.001$ at 3 vs 6 weeks and $p= 0.003$ at 0 vs 6 weeks.

Table 6: Mean %age change of PAIN(VAS) in both groups

Duration	Aceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	32.23 ± 21.64	19.80 ± 20.82	0.04*
3-6 weeks	28.93 ± 28.04	13.29 ± 20.40	0.027*
0-6 weeks	47.27 ± 38.07	28.12 ± 27.39	0.020*

* $p < 0.05$ significant at 5% significant level

** $p < 0.01$ significant at 1 % significant level

*** $p < 0.001$ highly significant at 0.1% significant level

Table 4 represents mean percentage (%) change in pain (VAS) in both groups.

In patients taking aceclofenac, the mean %age change in pain (VAS) was 32.23 ± 21.64 at 0-3 weeks, 28.93 ± 28.04 at 3-6 weeks, 47.27 ± 38.07 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 19.80 ± 20.82 at 0-3 weeks, 13.29 ± 20.40 at 3-6 weeks and 28.12 ± 27.39 at 0-6 weeks.

By comparing the mean %age change in pain (VAS) between both the groups it was observed that $p=0.032$ at 0-3 weeks, $p=0.732$ at 3-6 weeks and $p=0.039$ at 0-6 weeks.

Joint Tenderness

Table 7: Change in joint tenderness in both groups at the end of treatment

Change in Joint Tenderness	Aceclofenac		Ibuprofen		X ²	'p' Value
	No.	%age	No.	%age		
Improvement	18	72	15	60	0.80	0.37
No change	6	24	8	32	NA	NA
Deteriorated	1	4	2	8	NA	NA

($p \geq 0.05$, NS)

Table 7 represents the change in joint tenderness in number of patients in both the groups.

In patients taking aceclofenac, 18 (72%) showed improvement, 6 (24%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 15 (60%) patients showed improvement, 8 (32%) showed no change and 2 (8%) showed deterioration.

The difference in number of patients showing improvement in joint tenderness between groups was statistically not significant ($p=0.37$).

Table 8: Mean \pm SD, intergroup and intertime comparison of joint tenderness within the both groups

Duration	Aceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	2.12 \pm .833	2.6 \pm 0.63	0.346
3 week	1.36 \pm 0.49	2.00 \pm 0.58	0.001**
6 week	1.08 \pm .49	1.76 \pm .44	0.001**
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.001**	
3 vs 6 weeks	0.032**	0.031**	
0 vs 6 weeks	0.001**	0.001**	

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 8 represents change in joint tenderness at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean joint tenderness was 2.12 \pm .833 at 0 week, 1.36 \pm 0.49 at 3 weeks and 1.08 \pm .49 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 2.6 \pm 0.63 at 0 week, 2.00 \pm 0.58 at 3 weeks and 1.76 \pm .44 at 6 weeks. By taking inter group comparison, p= 0.346 at 0 week, p= 0.001 at 3 weeks and p= 0.001 at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that p= 0.001 at 0 vs 3 weeks, p= 0.032 at 3 vs 6 weeks and p= 0.001 at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that p= 0.001 at 0 vs 3 weeks, p= 0.031 at 3 vs 6 weeks and p= 0.001 at 0 vs 6 weeks.

Table 9: Mean %age change of joint tenderness in both groups

Duration	Aceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	29.23 \pm 23.64	14.80 \pm 20.82	0.02*
3-6 weeks	23.90 \pm 38.05	7.29 \pm 34.40	0.057
0-6 weeks	41.27 \pm 38.07	18.12 \pm 27.39	0.028*

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 9 represents mean percentage (%) change in joint tenderness in both groups.

In patients taking aceclofenac, the mean %age change in joint tenderness was 29.23 \pm 23.64 at 0-3 weeks, 23.90 \pm 38.05 at 3-6 weeks, 41.27 \pm 38.07 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 14.80 \pm 20.82 at 0-3 weeks, 7.29 \pm 34.40 at 3-6 weeks and 18.12 \pm 27.39 at 0-6 weeks.

By comparing the mean %age change in joint tenderness between both the groups it was observed that p=0.02 at 0-3 weeks, p=0.057 at 3-6 weeks and p=0.028 at 0-6 weeks.

Swelling

Table 10: Change in swelling in both groups at the end of treatment

Change in Swelling	Aceclofenac		Ibuprofen		X ²	'p' value
	No.	%age	No.	%age		
Improvement	15	60	11	44	1.28	0.26
No change	9	36	13	52	NA	NA
Deteriorated	1	4	1	4	NA	NA

(p \geq 0.05, NS)

Table 10 represents the change in swelling in number of patients in both the groups.

In patients taking aceclofenac, 15 (60%) showed improvement, 9 (36%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 11 (44%) patients showed improvement, 13 (52%) showed no change and 1 (4%) showed deterioration.

The difference in number of patients showing improvement in swelling between groups was statistically not significant ($p=0.26$).

Table 11: Mean \pm SD, intergroup and intertime comparison of swelling within the both groups

Duration	Aceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	1.72 \pm 0.73	1.86 \pm 0.62	0.537
3 week	1.12 \pm 0.33	1.56 \pm 0.51	0.001**
6 week	0.92 \pm 0.57	1.36 \pm 0.49	0.005**
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.001**	
3 vs 6 weeks	0.05*	0.057	
0 vs 6 weeks	0.001**	0.001**	

* $p<0.05$ significant at 5% significant level

** $p<0.01$ significant at 1 % significant level

*** $p<0.001$ highly significant at 0.1% significant level

Table 11 represents change in swelling at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean swelling was 1.72 \pm 0.73 at 0 week, 1.12 \pm 0.33 at 3 weeks and 0.92 \pm 0.57 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 1.86 \pm 0.62 at 0 week, 1.56 \pm 0.51 at 3 weeks and 1.36 \pm 0.49 at 6 weeks. By taking inter group comparison, $p=0.537$ at 0 week, $p=0.001$ at 3 weeks and $p=0.005$ at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that $p=0.001$ at 0 vs 3 weeks, $p=0.05$ at 3 vs 6 weeks and $p=0.001$ at 0 vs 6

weeks, while in patients taking ibuprofen it was observed that $p= 0.001$ at 0 vs 3 weeks, $p= 0.057$ at 3 vs 6 weeks and $p= 0.001$ at 0 vs 6 weeks.

Table 12: Mean %age change of swelling in both groups

Duration	Aceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	31.23 \pm 23.64	11.80 \pm 20.82	0.045*
3-6 weeks	14.00 \pm 53.05	8.29 \pm 31.40	0.628
0-6 weeks	41.27 \pm 38.07	18.12 \pm 27.39	0.028*

* $p < 0.05$ significant at 5% significant level

** $p < 0.01$ significant at 1 % significant level

*** $p < 0.001$ highly significant at 0.1% significant level

Table 12 represents mean percentage (%) change in swelling in both groups.

In patients taking aceclofenac, the mean %age change in swelling was 31.23 \pm 23.64 at 0-3 weeks, 14.00 \pm 53.05 at 3-6 weeks, 41.27 \pm 38.07 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 11.80 \pm 20.82 at 0-3 weeks, 8.29 \pm 31.40 at 3-6 weeks and 18.12 \pm 27.39 at 0-6 weeks.

By comparing the mean %age change in swelling between both the groups it was observed that $p=0.045$ at 0-3 weeks, $p=0.628$ at 3-6 weeks and $p=0.028$ at 0-6 weeks.

Erythema

Table 13: Change in erythema in both groups
At the end of treatment

Change in Erythema	Aceclofenac		Ibuprofen		X ²	'p' value
	No.	%age	No.	%age		
Improvement	6	24	3	12	1.22	0.269
No change	18	72	21	84	NA	NA
Deteriorated	1	4	1	4	NA	NA

($p \geq 0.05$, NS)

Table 13 represents the change in erythema in number of patients in both the groups.

In patients taking aceclofenac, 6 (24%) showed improvement, 18 (72%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 3 (12%) patients showed improvement, 21 (84%) showed no change and 1 (4%) showed deterioration.

The difference in number of patients showing improvement in erythema between groups was statistically not significant ($p=0.269$).

Table 14: Mean \pm SD, intergroup and intertime comparison of erythema within the both groups

Duration	Aceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	1.57 \pm 0.626	1.400 \pm 0.563	0.28
3 week	1.30 \pm 0.466	1.333 \pm 0.547	0.81
6 week	1.17 \pm 0.648	1.333 \pm 0.479	0.26
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.043*	0.161	
3 vs 6 weeks	0.255	0.998	
0 vs 6 weeks	0.016*	0.326	

* $p<0.05$ significant at 5% significant level

** $p<0.01$ significant at 1 % significant level

*** $p<0.001$ highly significant at 0.1% significant level

Table 14 represents change in erythema at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean erythema was 1.57 \pm 0.626 at 0 week, 1.30 \pm 0.466 at 3 weeks and 1.17 \pm 0.648 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 1.400 \pm 0.563 at 0 week, 1.333 \pm 0.547 at 3 weeks and 1.333 \pm 0.479 at 6 weeks. By taking inter group comparison, $p=0.28$ at 0 week, $p=0.81$ at 3 weeks and $p=0.26$ at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that $p= 0.043$ at 0 vs 3 weeks, $p= 0.255$ at 3 vs 6 weeks and $p= 0.016$ at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that $p= 0.161$ at 0 vs 3 weeks, $p= 0.998$ at 3 vs 6 weeks and $p= 0.326$ at 0 vs 6 weeks.

Table 15: Mean %age change of erythema in both groups

Duration	Acceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p'value
0-3 weeks	6.667 \pm 43.240	3.333 \pm 20.405	0.687
3-6 weeks	6.667 \pm 55.294	-1.667 \pm 20.692	0.443
0-6 weeks	16.111 \pm 42.992	1.667 \pm 24.507	0.115

* $p < 0.05$ significant at 5% significant level

** $p < 0.01$ significant at 1 % significant level

*** $p < 0.001$ highly significant at 0.1% significant level

Table 15 represents mean percentage (%) change in erythema in both groups.

In patients taking aceclofenac, the mean %age change in erythema was 6.667 \pm 43.240 at 0-3 weeks, 6.667 \pm 55.294 at 3-6 weeks, 16.111 \pm 42.992 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 3.333 \pm 20.405 at 0-3 weeks, -1.667 \pm 20.692 at 3-6 weeks and 1.667 \pm 24.507 at 0-6 weeks.

By comparing the mean %age change in erythema between both the groups it was observed that $p=0.687$ at 0-3 weeks, $p=0.443$ at 3-6 weeks and $p=0.115$ at 0-6 weeks.

Pain on Movement

Table 16: Change in pain on movement in both groups at the end of treatment

Change in Pain on Movement	Aceclofenac		Ibuprofen		X ²	'p' value
	No.	%age	No.	%age		
Improvement	18	72	15	60	0.80	0.370
No change	6	24	9	36	NA	NA
Deteriorated	1	4	1	4	NA	NA

($p \geq 0.05$, NS)

Table 16 represents the change in pain on movement in number of patients in both the groups.

In patients taking aceclofenac, 18 (72%) showed improvement, 6 (24%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 15 (60%) patients showed improvement, 9 (36%) showed no change and 1 (4%) showed deterioration.

The difference in number of patients showing improvement in pain on movement between groups was statistically not significant ($p = 0.37$).

Table 17: Mean \pm SD, intergroup and intertime comparison of pain on movement within the both groups

Duration	Aceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	2.700 \pm 0.535	2.200 \pm 0.664	0.002
3 week	1.700 \pm 0.651	1.867 \pm 0.571	0.295
6 week	1.300 \pm 0.794	1.567 \pm 0.504	0.125
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.001**	
3 vs 6 weeks	0.001**	0.005**	
0 vs 6 weeks	0.001**	0.001**	

* $p < 0.05$ significant at 5% significant level

** $p < 0.01$ significant at 1 % significant level

*** $p < 0.001$ highly significant at 0.1% significant level

Table 17 represents change in pain on movement at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean pain on movement was 2.700 ± 0.535 at 0 week, 1.700 ± 0.651 at 3 weeks and 1.300 ± 0.794 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 2.200 ± 0.664 at 0 week, 1.867 ± 0.571 at 3 weeks and 1.567 ± 0.504 at 6 weeks. By taking inter group comparison, $p = 0.002$ at 0 week, $p = 0.295$ at 3 weeks and $p = 0.125$ at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that $p = 0.001$ at 0 vs 3 weeks, $p = 0.001$ at 3 vs 6 weeks and $p = 0.001$ at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that $p = 0.001$ at 0 vs 3 weeks, $p = 0.005$ at 3 vs 6 weeks and $p = 0.001$ at 0 vs 6 weeks.

Table 18: Mean %age change of pain on movement in both groups

Duration	Aceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	35.03 ± 23.27	12.80 ± 18.82	0.0005**
3-6 weeks	23.00 ± 33.85	11.69 ± 31.40	0.188
0-6 weeks	51.27 ± 32.144	23.12 ± 32.99	0.002**

* $p < 0.05$ significant at 5% significant level

** $p < 0.01$ significant at 1 % significant level

*** $p < 0.001$ highly significant at 0.1% significant level

Table 18 represents mean percentage (%) change in pain on movement in both groups.

In patients taking aceclofenac, the mean %age change in pain on movement was 35.03 ± 23.27 at 0-3 weeks, 23.00 ± 33.85 at 3-6 weeks, 51.27 ± 32.144 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 12.80 ± 18.82 at 0-3

weeks, 11.69 ± 31.40 at 3-6 weeks and 23.12 ± 32.99 at 0-6 weeks.

By comparing the mean %age change in pain on movement between both the groups it was observed that $p=0.0005$ at 0-3 weeks, $p=0.188$ at 3-6 weeks and $p=0.002$ at 0-6 weeks.

Functional Capacity

Table 19: Change in functional capacity in both groups at the end of treatment

Change in Functional Capacity	Aceclofenac		Ibuprofen		X ²	'p' value
	No.	%age	No.	%age		
Improvement	18	72	15	60	0.80	0.370
No change	6	24	9	36	NA	NA
Deteriorated	1	4	1	4	NA	NA

($p \geq 0.05$, NS)

Table 19 represents the change in functional capacity in number of patients in both the groups.

In patients taking aceclofenac, 18 (72%) showed improvement, 6 (24%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 15 (60%) patients showed improvement, 9 (36%) showed no change and 1 (4%) showed deterioration.

The difference in number of patients showing improvement in functional capacity between groups was statistically not significant ($p= 0.37$).

Table 20: Mean \pm SD, intergroup and intertime comparison of functional capacity within the both groups

Duration	Aceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	2.53 ± 0.55	2.36 ± 0.56	0.281
3 week	1.86 ± 0.45	1.92 ± 0.38	0.156
6 week	1.34 ± 0.58	1.78 ± 0.54	0.008

Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.001**	
3 vs 6 weeks	0.001**	0.02**	
0 vs 6 weeks	0.001**	0.001**	

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 20 represents change in functional capacity at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean functional capacity was 2.53 ± 0.55 at 0 week, 1.86 ± 0.45 at 3 weeks and 1.34 ± 0.58 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 2.36 ± 0.56 at 0 week, 1.92 ± 0.38 at 3 weeks and 1.78 ± 0.54 at 6 weeks. By taking inter group comparison, $p = 0,281$ at 0 week, $p = 0.156$ at 3 weeks and $p = 0.008$ at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that $p = 0.001$ at 0 vs 3 weeks, $p = 0.001$ at 3 vs 6 weeks and $p = 0.001$ at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that $p = 0.001$ at 0 vs 3 weeks, $p = 0.02$ at 3 vs 6 weeks and $p = 0.001$ at 0 vs 6 weeks.

Table 21: Mean %age change of functional capacity in both groups

Duration	Aceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	25.03 ± 23.09	13.80 ± 18.10	0.03*
3-6 weeks	20.00 ± 43.85	11.09 ± 31.40	0.365
0-6 weeks	38.88 ± 52.144	23.12 ± 32.99	0.160

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 21 represents mean percentage (%) change in functional capacity in both groups.

In patients taking aceclofenac, the mean %age change in functional capacity was 25.03 ± 23.09 at 0-3 weeks, 20.00 ± 43.85 at 3-6 weeks, 38.88 ± 52.144 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 13.80 ± 18.10 at 0-3 weeks, 11.09 ± 31.40 at 3-6 weeks and 23.12 ± 32.99 at 0-6 weeks.

By comparing the mean %age change in functional capacity between both the groups it was observed that $p=0.03$ at 0-3 weeks, $p=0.365$ at 3-6 weeks and $p=0.160$ at 0-6 weeks.

Overall Assessment

Table 22: Change in overall assessment in both groups at the end of treatment

Change in Overall Assessment	Aceclofenac		Ibuprofen		X ²	'p' value
	No.	%age	No.	%age		
Improvement	18	72	15	60	0.80	0.370
No change	6	24	9	36	NA	NA
Deteriorated	1	4	1	4	NA	NA

($p \geq 0.05$, NS)

Table 22 represents the change in overall assessment in number of patients in both the groups.

In patients taking aceclofenac, 18 (72%) showed improvement, 6 (24%) showed no change and 1 (4%) showed deterioration, while in patients taking ibuprofen 15 (60%) patients showed improvement, 9 (36%) showed no change and 1 (4%) showed deterioration.

The difference in number of patients showing improvement in overall assessment between groups was statistically not significant ($p= 0.37$).

Table 23: Mean \pm SD, intergroup and intertime comparison of overall assessment within the both groups

Duration	Aceclofenac Mean \pm SD	Ibuprofen Mean \pm SD	Inter group Comparison 'p' value
0 week	2.64 \pm 0.56	2.2 \pm 0.48	0.003**
3 week	1.76 \pm 0.50	1.96 \pm 0.41	0.097
6 week	1.44 \pm 0.62	1.567 \pm 0.62	0.304
Inter Time Comparison within Group (p value)			
0 vs 3 weeks	0.001**	0.006**	
3 vs 6 weeks	0.006**	0.001**	
0 vs 6 weeks	0.001**	0.001**	

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 23 represents change in overall assessment at different time intervals within groups, inter group comparison and inter time comparison within group.

In patients taking aceclofenac, the mean overall assessment was 2.64 \pm 0.56 at 0 week, 1.76 \pm 0.50 at 3 weeks and 1.44 \pm 0.62 at 6 weeks, while in patients taking ibuprofen the mean pain intensity was 2.2 \pm 0.48 at 0 week, 1.96 \pm 0.41 at 3 weeks and 1.567 \pm 0.62 at 6 weeks. By taking inter group comparison, p= 0.003 at 0 week, p= 0.097 at 3 weeks and p= 0.304 at 6 weeks.

Further by taking inter time comparison within group, in the patients taking aceclofenac it was observed that p= 0.001 at 0 vs 3 weeks, p= 0.006 at 3 vs 6 weeks and p= 0.001 at 0 vs 6 weeks, while in patients taking ibuprofen it was observed that p= 0.006 at 0 vs 3 weeks, p= 0.001 at 3 vs 6 weeks and p= 0.001 at 0 vs 6 weeks.

Table 24: Mean %age change of overall assessment in both groups

Duration	Acceclofenc Mean \pm SD	Ibuprofen Mean \pm SD	'p' value
0-3 weeks	28.83 \pm 23.09	8.82 \pm 18.05	0.0001***
3-6 weeks	16.00 \pm 43.95	18.09 \pm 31.90	0.708
0-6 weeks	38.01 \pm 52.18	26.12 \pm 33.99	0.308

*p<0.05 significant at 5% significant level

**p<0.01 significant at 1 % significant level

***p<0.001 highly significant at 0.1% significant level

Table 24 represents mean percentage (%) change in overall assessment in both groups.

In patients taking aceclofenac, the mean %age change in overall assessment was 28.83 \pm 23.09 at 0-3 weeks, 16.00 \pm 43.95 at 3-6 weeks, 38.01 \pm 52.18 at 0-6 weeks; while in patients taking ibuprofen the mean %age change was 8.82 \pm 18.05 at 0-3 weeks, 18.09 \pm 31.90 at 3-6 weeks and 26.12 \pm 33.99 at 0-6 weeks.

By comparing the mean %age change in overall assessment between both the groups it was observed that p=0.0001 at 0-3 weeks, p=0.708 at 3-6 weeks and p=0.308 at 0-6 weeks.

Tolerability

Tolerability and Safety Treatment was assessed by adverse effects

Table 25: Adverse effects

Adverse Effects	Acceclofenac		Ibuprofen		X ²	'p' Value
	No.	%age	No.	%age		
Abdominal Pain	5	20	7	28	0.44	>0.05
Constipation	1	4	1	4	0.00	>0.05
Diarrhea	1	4	2	8	0.00	>0.05
Dyspepsia	4	16	5	20	0.00	>0.05
Epigastric Pain	6	24	13	52	4.16	<0.05*
Flatulence	1	4	1	4	0.00	>0.05

Heart Burn	12	48	14	56	0.57	>0.05
Indigestion	5	20	7	28	0.44	>0.05
Nausea	4	16	6	24	0.50	>0.05
Vomiting	4	16	6	24	0.50	>0.05
Headache	4	16	4	16	0.16	>0.05
Tiredness	1	4	4	16	0.89	>0.05

$p \geq 0.05$ Not Significant

$p < 0.05$ Significant

Table 25 shows that in patients taking aceclofenac the incidence of heartburn was 12(48%), epigastric pain 6(24%), indigestion 5(20%), abdominal pain 5(20%), dyspepsia 4(16%), nausea 4(16%), vomiting 4(16%), flatulence 1(4%), constipation 1(4%), diarrhea 1(4%), headache 4(16%) and tiredness 1(4%).

In patients taking ibuprofen the incidence of heartburn was 14(56%), epigastric pain 13(52%), indigestion 7(28%), abdominal pain 7(28%), dyspepsia 5(20%), nausea 6(24%), vomiting 6(24%), flatulence 1(4%), constipation 1(4%), diarrhea 2(8%), headache 4(16%) and tiredness 4(16%).

The difference in side effects were statistically not significant except of gastric pain which was found to be statistically significant.

Compliance in Aceclofenac (Group A) and Ibuprofen (Group B)

Compliance was ensured by counting the number of tablets consumed from the foils. All the patients in Group A (patients taking aceclofenac) and Group B (patients taking ibuprofen) complied 100% with the treatment during the study period of 6 weeks.

Discussion

The problems related to osteoarthritis (OA) knee and its management are expected to increase with rise in the proportion of elderly population. Therefore, it was important to study the effect of treatment on patients suffering from a

chronic condition such as OA of knee. Although NSAIDS provide effective symptomatic treatment for OA, yet the use of NSAIDS is limited due to their potential life threatening gastrointestinal tract (GIT) adverse effects especially in elderly patients. COX-2 specific inhibitors (Coxibs) have the potential for causing fewer GIT adverse affects and have comparable efficacy to the conventional NSAIDS and have been used for treatment of acute as well as chronic painful conditions such as dysmenorrhoea and OA.

A randomized, double blind parallel group study of OA of knee joint was conducted out for 6 weeks in orthopaedic out patient department (OPD) of Government Medical College and Rajindra Hospital, Patiala. Total 50 patients were enrolled and randomly divided into 2 groups: Group A (Aceclofenac 100mg bid, n=25) and Group B (Ibuprofen 400 mg tds, n=25). In Group A (patients with Aceclofenac) male and female patients were included in the study with mean age of years and with mean duration of months. In this group patients belonged to class II and patients to class III of the Steinbrokers Functional Capacity classification.

In Group B (patients with Ibuprofen) male and female patients were included in the study with mean age of years and with mean duration of months. In this group patients belonged to class I, class II and patients to class III of the Steinbrokers Functional Capacity classification.

Functional Status

In this study, functional status was assessed by using VAS (Visual Analogue Scale) on pain intensity and by using Likert 5 point scale on different parameters like pain intensity, joint tenderness, swelling, erythema, pain on movement, functional capacity and overall assessment.

At '0' week most of the patients enrolled in the study could conduct their normal activities but with discomfort or limited mobility.

Aceclofenac- Group A

The percentage (%) of patients showing improvement in pain intensity was 76%. The mean pain intensity at 0 week was 2.84 ± 0.37 and 1.60 ± 0.71 at 6 weeks ($p=0.001$).

Ward et al (1995) conducted a multicentre randomized double blind parallel group study to investigate efficacy and safety of aceclofenac (200 patients) in OA of knee with diclofenac (197 patients) at rest and observed that 74.5% patients taking aceclofenac showed improvement at rest ($p<0.001$).

Kornasoff et al (1997) conducted a multicentre, 12 week, randomized, double blind, parallel group clinical trial to compare the efficacy and safety of aceclofenac (190 patients) with naproxen (184 patients) in OA of knee and found that 76.2% patients taking aceclofenac showed improvement in pain at rest.

The baseline mean pain score by VAS was 70.20 ± 10.45 and showed improvement at 6 weeks to 33.60 ± 17.05 ($p=0.003$).

Busquier et al (1997) conducted a multicentre, randomized double blind parallel group study to compare the efficacy and safety of aceclofenac (123 patients) with piroxicam (117 patients) and found pain intensity to change in patients taking aceclofenac by mm ($p<0.001$).

Torri et al (1994) conducted a double blind controlled study to compare aceclofenac with piroxicam and found pain intensity by VAS in patients taking aceclofenac to change by mm ($p<0.01$).

Diaz et al (1996) compared the efficacy and tolerability of aceclofenac versus diclofenac in OA of knee and found that pain intensity by VAS in patients taking aceclofenac to change by mm ($p<0.001$).

In present study the percentage of patients showing improvement in joint tenderness was 72%. The mean joint tenderness at 0 week was 2.12 ± 0.833 and 1.08 ± 0.49 at 6 week ($p=0.001$).

Ward et al (1995) conducted a multicentre randomized double blind study between aceclofenac and diclofenac in OA of knee and found that 72.4% of patient's showed improvement with aceclofenac.

Kornasoff et al (1997) conducted a multicentre 12 weeks randomized double blind parallel group study between aceclofenac and naproxen in OA of knee and found 82% patient showed improvement in joint tenderness with aceclofenac.

In this study the percentage of patients showing improvement in swelling was 60% and the mean swelling at 0 week was 1.72 ± 0.73 and 0.92 ± 0.57 at 6 week ($p=0.001$).

Ward et al (1995) conducted a randomized double blind study between aceclofenac and diclofenac in OA of knee and found that 58.3% patients ($p<0.05$) showed improvement with aceclofenac.

Kornasoff et al (1997) conducted a multicentre 12 weeks randomized double blind clinical trial between aceclofenac and naproxen in OA of knee and found 82% patient showed improvement in swelling with aceclofenac.

In the present study the percentage of patients showing improvement in erythema was 24% and the mean erythema was 1.57 ± 0.626 at 0 week and 1.17 ± 0.648 at 6 week ($p=0.326$).

Ward et al (1995) conducted a randomized double blind study between aceclofenac and diclofenac in OA of knee and found that 23.4% patients ($p<0.05$) showed improvement in erythema with aceclofenac.

Kornasoff et al (1997) conducted a multicentre 12 weeks randomized double blind clinical trial between aceclofenac and naproxen in OA of knee and found 43.4% patient showed improvement in erythema.

In this study the percentage of patients showing improvement in pain on movement was 72% and the mean pain on movement was 2.700 ± 0.535 at 0 week and 1.300 ± 0.794 at 6 week ($p=0.001$).

Ward et al (1995) conducted a randomized double blind study between aceclofenac and diclofenac in OA of knee and found that 70.2% patients ($p<0.05$) showed improvement in pain on movement with aceclofenac.

Busquier et al (1997) conducted a multicentre, randomized double blind parallel group study to compare the efficacy and

safety of aceclofenac with piroxicam and found that there was significant change in pain on movement ($p < 0.001$) in patients with aceclofenac.

Diaz et al (1996) compared the efficacy and tolerability of aceclofenac versus diclofenac in OA of knee and found that was significant change in pain on movement ($p < 0.01$) in patients with aceclofenac.

Ward et al (1995) conducted a randomized double blind study to investigate the efficacy and safety of aceclofenac with diclofenac in OA of knee and found that there was statistically significant change in pain on movement in patients with aceclofenac (10° increase) ($p < 0.005$).

Kornasoff et al (1997) conducted a multicentre 12 weeks randomized double blind clinical trial to investigate the efficacy and safety of aceclofenac with naproxen in OA of knee and found that there was statistically significant change in pain on movement in patients with aceclofenac.

In this study the percentage of patients showing improvement in functional capacity was 72% and the mean functional capacity was 2.53 ± 0.55 at 0 week and 1.34 ± 0.58 at 6 week ($p = 0.001$).

Ward et al (1995) conducted a randomized double blind study between aceclofenac and diclofenac in OA of knee and found that 74% patients on aceclofenac showed improvement in functional capacity ($p < 0.05$).

Busquier et al (1997) conducted a multicentre, randomized double blind parallel group study to compare the efficacy and safety of aceclofenac with piroxicam and found that there was significant change in functional capacity (both knee flexion and extension) in patients on aceclofenac.

In this study the percentage of patients showing improvement in overall assessment was 72% and the mean overall assessment was 2.64 ± 0.56 at 0 week and 1.44 ± 0.62 at 6 week ($p = 0.001$).

Ward et al (1995) conducted a randomized double blind study between aceclofenac and diclofenac in OA of knee and found

that 74.5% patients on aceclofenac showed improvement in functional capacity ($p < 0.05$).

Gualda et al (2007) compared aceclofenac with acetaminophen in OA of knee and observed that there was significant improvement in pain and functional capacity with aceclofenac.

Ibuprofen- Group B

The patient showing improvement in pain intensity was 64%. The mean pain intensity at 0 week was 2.6 ± 0.51 , at 3 weeks and further decreased to 1.72 ± 0.61 at 6 weeks ($p = 0.001$).

Singh and Singla (1997) conducted a comparative evaluation of ibuprofen + paracetamol combination in patients suffering from OA of knee and observed that there was improvement in 48% of patients having pain at rest with ibuprofen.

The mean pain (VAS) in group B (Ibuprofen) was 61.20 ± 12.56 at 0 week, 48.40 ± 14.50 at 3 week which decreased to 41.00 ± 13.23 at 6 weeks ($p = 0.003$).

Baumgartner et al (1996) compared the efficacy and tolerability of ibuprofen and diclofenac sodium and observed that there was relief of pain with Ibuprofen ($p = 0.006$).

In the present study 60% patients showed improvement in joint tenderness. The mean joint tenderness was 2.6 ± 0.63 at 0 week, 2.00 ± 0.58 at 3 weeks and further decreased to 1.76 ± 0.44 at 6 weeks ($p = 0.001$).

Singh and Singla (1997) conducted a comparative evaluation of ibuprofen + paracetamol combination for 4 weeks in patients suffering from OA of knee and observed that there was improvement in 43.5% of patients having joint tenderness with ibuprofen

In the present study 44% patients showed improvement in swelling. The mean swelling was 1.86 ± 0.62 at 0 week, 1.56 ± 0.51 at 3 weeks and 1.36 ± 0.49 at 6 weeks ($p = 0.001$).

Singh and Singla (1997) conducted a comparative evaluation of ibuprofen + paracetamol combination for 4 weeks in patients suffering from OA of knee and observed that there was improvement in 42% of patients having swelling with Ibuprofen.

In the present study 12% patients showed improvement in erythema. The mean score of erythema was 1.400 ± 0.563 at 0 week, 1.333 ± 0.547 at 3 weeks and further decreased to 1.333 ± 0.479 at 6 weeks ($p=0.326$).

In the present study 60% patients showed improvement in pain on movement. The mean pain on movement was 2.200 ± 0.664 at 0 week, 1.867 ± 0.571 at 3 weeks and further decreased to 1.567 ± 0.504 at 6 weeks ($p=0.001$).

Singh and Singla (1997) conducted a comparative evaluation of ibuprofen + paracetamol combination for 4 weeks in patients suffering from OA of knee and observed that there was improvement in 50% of patients having pain on movement with Ibuprofen.

In the present study 60% patients showed improvement in functional capacity. The mean functional capacity was 2.36 ± 0.56 at 0 week, 1.92 ± 0.38 at 3 weeks and further decreased to 1.78 ± 0.54 at 6 weeks ($p=0.001$).

Lewandowshi et al (1992) observed in 1156 patients of OA that there was significant pain relief in symptoms of pain at rest, pain on movement, swelling and morning stiffness with ibuprofen.

Mukherjee (1996) concluded after prospective open non comparative study in 12 patients of OA and 12 patients for rheumatoid arthritis for 4 weeks that severity of pain, Tenderness and swelling, duration of morning stiffness, limitation of movement of effected parts, global assessment of change in clinical condition improved considerably with ibuprofen.

Comparitive improvement in Functional Status between Aceclofenac (Group A) and Ibuprofen (Group B)

The improvement in pain intensity was shown by 76% patients taking aceclofenac. The mean score was 2.84 ± 0.37 at 0 week, 1.96 ± 0.54 at 3 weeks and 1.60 ± 0.71 at 6 weeks ($p=0.001$). The mean percentage change was 30.67 ± 21.37 at 0 week, 17.33 ± 27.84 at 3 weeks and 42.67 ± 30.07 at 6 weeks with aceclofenac.

The improvement in pain intensity was shown by 64% patients taking ibuprofen. The mean score was 2.6 ± 0.51 at 0 week, 2.08 ± 0.57 at 3 weeks and 1.72 ± 0.61 at 6 weeks ($p=0.001$). The mean percentage change was 17.33 ± 27.84 at 0 week, 14.67 ± 26.92 at 3 weeks and 26.67 ± 22.53 at 6 weeks with ibuprofen.

By comparing the pain intensity in both the groups the difference in percentage of patients showing improvement was statistically not significant ($p=0.35$) at 6 weeks. The difference in mean pain score was not statistically significant ($p=0.525$) at 6 weeks. The difference in mean percentage change in pain intensity was statistically significant ($p=0.039$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing pain intensity in osteoarthritis of knee.

Pain (VAS)

The mean pain score (VAS) of patients taking aceclofenac was 70.20 ± 10.45 at 0 week, 46.20 ± 12.60 at 3 week and 33.60 ± 17.05 at 6 week ($p=0.001$). The mean percentage change in pain (VAS) was 32.23 ± 21.64 at 0 week, 28.93 ± 28.04 at 3 weeks and 47.27 ± 38.07 at 6 weeks with aceclofenac.

The mean pain score (VAS) of patients taking ibuprofen was 61.20 ± 12.56 at 0 week, 48.40 ± 14.50 at 3 weeks and 41.00 ± 13.23 at 6 weeks ($p=0.003$). The mean percentage change in pain (VAS) was 19.80 ± 20.82 at 0 week, 13.29 ± 20.40 at 3 weeks and 28.12 ± 27.39 at 6 weeks with ibuprofen.

By comparing the pain (VAS) in both the groups the difference in the mean pain score was statistically not significant ($p=0.093$) at 6 weeks. The difference in mean percentage change was statistically significant ($p=0.020$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing pain (VAS).

Joint Tenderness

The improvement in joint tenderness was shown by 72% patients taking aceclofenac. The mean joint tenderness was 2.12 ± 0.833 at 0 week, 1.36 ± 0.49 at 3 weeks and 1.08 ± 0.49 at

6 weeks ($p=0.001$). The mean percentage change was 29.23 ± 23.64 at 0 week, 23.90 ± 38.05 at 3 weeks and 41.27 ± 38.07 at 6 weeks with aceclofenac.

The improvement in joint tenderness was shown by 60% patients taking ibuprofen. The mean joint tenderness was 2.6 ± 0.63 at 0 week, 2.00 ± 0.58 at 3 weeks and 1.76 ± 0.44 at 6 weeks ($p=0.001$). The mean percentage change was 14.80 ± 20.82 at 0 week, 7.29 ± 34.40 at 3 weeks and 18.12 ± 27.39 at 6 weeks with ibuprofen.

By comparing the joint tenderness between the two drugs, difference in percentage of patients showing improvement was statistically not significant ($p=0.37$) at 6 weeks. The difference in mean joint tenderness was not statistically significant ($p=0.001$) at 6 weeks. The difference in mean percentage change is statistically significant ($p=0.28$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing joint tenderness in OA of knee.

Swelling

The improvement in swelling was shown by 60% patients taking aceclofenac. The mean swelling was 1.72 ± 0.73 at 0 week, 1.12 ± 0.33 at 3 weeks and 0.92 ± 0.57 at 6 weeks ($p=0.001$). The mean percentage change was 31.23 ± 23.64 at 0 week, 14.00 ± 53.05 at 3 weeks and 41.27 ± 38.07 at 6 weeks with aceclofenac.

The improvement in swelling was shown by 44% patients taking ibuprofen. The mean swelling was 1.86 ± 0.62 at 0 week, 1.56 ± 0.51 at 3 weeks and 1.36 ± 0.49 at 6 weeks ($p=0.001$). The mean percentage change was 11.80 ± 20.82 at 0 week, 8.29 ± 31.40 at 3 weeks and 18.12 ± 27.39 at 6 weeks with ibuprofen.

By comparing the swelling between the two drugs, difference in percentage of patients showing improvement was statistically not significant ($p=0.26$) at 6 weeks. The difference in mean swelling score was not statistically significant ($p=0.005$) at 6 weeks. The difference in mean percentage change in swelling was statistically significant ($p=0.028$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing swelling in OA of knee.

Erythema

The improvement in erythema was shown by 24% patients taking aceclofenac. The mean erythema was 1.57 ± 0.626 at 0 week, 1.300 ± 0.466 at 3 weeks and 1.17 ± 0.648 at 6 weeks ($p=0.016$). The mean percentage change was 6.667 ± 43.240 at 0 week, 6.667 ± 55.294 at 3 weeks and 16.111 ± 42.992 at 6 weeks with aceclofenac.

The improvement in erythema was shown by 12% patients taking ibuprofen. The mean erythema was 1.400 ± 0.563 at 0 week, 1.333 ± 0.547 at 3 weeks and 1.333 ± 0.479 at 6 weeks ($p=0.326$). The mean percentage change was 3.333 ± 20.405 at 0 week, -1.667 ± 20.692 at 3 weeks and 1.667 ± 24.507 at 6 weeks with ibuprofen.

By comparing the erythema between the two drugs, difference in percentage of patients showing improvement was statistically not significant ($p=0.269$) at 6 weeks. The difference in mean erythema score was not statistically significant ($p=0.26$) at 6 weeks. The difference in mean percentage change in erythema was statistically significant ($p=0.115$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing erythema in OA of knee.

Pain on Movement

The improvement in pain on movement was shown by 72% patients taking aceclofenac. The mean score of pain on movement was 2.700 ± 0.535 at 0 week, 1.700 ± 0.651 at 3 weeks and 1.300 ± 0.794 at 6 weeks ($p=0.001$). The mean percentage change was 35.03 ± 23.27 at 0 week, 23.00 ± 33.85 at 3 weeks and 51.27 ± 32.144 at 6 weeks with aceclofenac.

The improvement in pain on movement was shown by 60% patients taking ibuprofen. The mean score in pain on movement was 2.200 ± 0.664 at 0 week, 1.867 ± 0.571 at 3 weeks and 1.567 ± 0.504 at 6 weeks ($p=0.001$). The mean percentage

change was 12.80 ± 18.82 at 0 week, 11.69 ± 31.40 at 3 weeks and 23.12 ± 32.99 at 6 weeks with ibuprofen.

By comparing the pain on movement between the two drugs, difference in percentage of patients showing improvement was statistically not significant ($p=0.370$) at 6 weeks. The difference in mean pain on movement was not statistically significant ($p=0.125$) at 6 weeks. The difference in mean percentage change was statistically significant ($p=0.002$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing pain on movement in OA of knee.

Functional Capacity

The improvement in functional capacity was shown by 72% patients taking aceclofenac. The mean functional capacity was 2.53 ± 0.55 at 0 week, 1.86 ± 0.45 at 3 weeks and 1.34 ± 0.58 at 6 weeks ($p=0.001$). The mean percentage change was 25.03 ± 23.09 at 0 week, 20.00 ± 43.85 at 3 weeks and 38.88 ± 52.144 at 6 weeks with aceclofenac.

The improvement in functional capacity was shown by 60% patients taking ibuprofen. The mean functional capacity was 2.36 ± 0.56 at 0 week, 1.92 ± 0.38 at 3 weeks and 1.78 ± 0.54 at 6 weeks ($p=0.001$). The mean percentage change was 13.80 ± 18.10 at 0 week, 11.09 ± 31.40 at 3 weeks and 23.12 ± 32.99 at 6 weeks with ibuprofen.

By comparing the functional capacity between the two drugs, difference in percentage of patients showing improvement was statistically not significant ($p=0.370$) at 6 weeks. The difference in mean functional capacity score was not statistically significant ($p=0.008$) at 6 weeks. The difference in mean percentage change in functional capacity was statistically not significant ($p=0.160$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing functional capacity in OA of knee.

Overall Assessment

The improvement in overall assessment was shown by 72% patients taking aceclofenac. The mean overall assessment score

was 2.64 ± 0.56 at 0 week, 1.76 ± 0.50 at 3 weeks and 1.44 ± 0.62 at 6 weeks ($p=0.001$). The mean percentage change was 28.83 ± 23.09 at 0 week, 16.00 ± 43.95 at 3 weeks and 38.01 ± 52.18 at 6 weeks with aceclofenac.

The improvement in overall assessment was shown by 60% patients taking ibuprofen. The mean overall assessment score was 2.2 ± 0.48 at 0 week, 1.96 ± 0.41 at 3 weeks and 1.567 ± 0.62 at 6 weeks ($p=0.001$). The mean percentage change was 8.82 ± 18.05 at 0 week, 18.09 ± 31.90 at 3 weeks and 18.09 ± 31.90 at 6 weeks with ibuprofen.

By comparing the overall assessment between the two drugs, difference in percentage of patients showing improvement was statistically not significant ($p=0.370$) at 6 weeks. The difference in mean overall assessment score was not statistically significant ($p=0.304$) at 6 weeks. The difference in mean percentage change in overall assessment was statistically not significant ($p=0.308$) at 6 weeks.

Thus, the result shows that aceclofenac is better than ibuprofen in decreasing overall assessment in OA of knee.

Busquier et al (1997) compared aceclofenac (100mg bid) with piroxicam (20 mg od) and observed that there was 33.8 mm change in pain intensity score by VAS ($p<0.001$) as compared to patients given piroxicam in which there was 34.8 mm ($p<0.001$) change in pain intensity score by VAS.

Torri et al (1994) compared aceclofenac (100mg bid) with piroxicam (20 mg od) and observed that there was 35.7 mm change ($p<0.001$) in pain intensity score by VAS in patients given aceclofenac as compared to patients given piroxicam in which there was 38.5 mm ($p<0.001$) change in pain intensity score by VAS.

Diaz et al (1996) compared aceclofenac (100mg bid) with piroxicam (50 mg bid) and observed that there was 29.7 mm ($p<0.001$) change in pain intensity score in patients given aceclofenac as compared to 27.1 mm ($p<0.001$) in VAS in patients given diclofenac.

Busquier et al (1997) compared functional capacity of aceclofenac (100 mg bid) with piroxicam (20 mg od) and

observed that there was 12.4 degree change ($p < 0.001$) in knee flexion, 2.5 degree change in knee extension ($p < 0.001$) in patients given aceclofenac and 8.1 degree change in knee flexion ($p < 0.001$) and 1.7 degree change in knee extension ($p < 0.01$) in patients given piroxicam.

Torri et al (1994) compared functional capacity of aceclofenac (100 mg bid) with piroxicam (20 mg od) and observed that there was 10 degree change ($p < 0.001$) in knee flexion, 2.6 degree change in knee extension ($p < 0.01$) in patients given aceclofenac and 9.1 degree change in knee flexion ($p < 0.01$) and 2.3 degree change in knee extension ($p < 0.01$) in patients given piroxicam.

Diaz et al (1996) compared functional capacity of aceclofenac (100 mg bid) with piroxicam (20 mg od) and observed that there was 6 degree change ($p < 0.01$) in knee flexion, 0.5 degree change in knee extension ($p < 0.01$) in patients given aceclofenac and 5 degree change in knee flexion ($p < 0.01$) and 0.3 degree change in knee extension ($p < 0.01$) in patients given piroxicam.

Busquier et al (1997) compared aceclofenac (100 mg bid) with piroxicam (20 mg od) and observed that there was 3.7 (knee function score) change ($p < 0.001$) in overall assessment in patients taking aceclofenac while there was 2.8 (knee function score) change ($p < 0.001$) in overall assessment in patients taking piroxicam.

Diaz et al (1996) compared aceclofenac (100 mg bid) with diclofenac (50 mg bid) and observed that there was 3.4 (knee function score) change ($p < 0.01$) in overall assessment in patients taking aceclofenac while there was 3 (knee function score) change ($p < 0.01$) in overall assessment in patients taking diclofenac.

Gualda et al (2007) compared aceclofenac with acetaminophen in OA of knee in a double blind 6 weeks randomized trial and observed that aceclofenac is superior to acetaminophen in relieving pain and in improving functional capacity.

Dionne (2003) compared ibuprofen with selective COX-2 inhibitor celecoxib and observed that time of onset of

meaningful pain relief was shorter with ibuprofen than celecoxib, and the peak analgesic effect and total analgesia is substantially greater with ibuprofen than celecoxib.

Singh and Singla (1997) conducted a comparative evaluation of ibuprofen + paracetamol combination in randomized parallel group, multidose study in OA of knee and observed that the difference in improvement of pain intensity, stiffness, tenderness restriction in physical activity, swelling of knee joint, overall assessment in patients taking ibuprofen to be significantly better than combination of ibuprofen and paracetamol. Also the difference in number of patients showing improvement in pain on movement, pain at rest, tenderness, swelling and functional capacity was significantly better in ibuprofen than in combination of ibuprofen and paracetamol.

Leon and Juan (1981) compared the 50 patients of ibuprofen and diclofenac in OA in a single blind study for 6 weeks and observed that the analgesic and tolerance of ibuprofen is superior to diclofenac.

Bradley et al (2001) conducted a comparative study between ibuprofen and acetaminophen and observed that ibuprofen and acetaminophen are comparably effective in treating pain in OA of knee.

Baumgartner et al (1996) conducted a comparative study of ibuprofen and diclofenac in OA of knee and observed that ibuprofen was significantly superior to diclofenac in treating resting pain, pain on movement and carrying out other physical activities.

Boureau (2004) compared the efficacy of ibuprofen with paracetamol in OA of knee and concluded that the difference in stiffness, pain and physical function was significantly in favour of ibuprofen.

Adverse Effects

In this study in patients taking aceclofenac the incidence of heartburn was 12(48%), epigastric pain 6(24%), indigestion 5(20%), abdominal pain 5(20%), dyspepsia 4(16%), nausea

4(16%), vomiting 4(16%), flatulence 1(4%), constipation 1(4%), diarrhea 1(4%), headache 4(16%) and tiredness 1(4%).

In patients taking ibuprofen the incidence of heartburn was 14(56%), epigastric pain 13(52%), indigestion 7(28%), abdominal pain 7(28%), dyspepsia 5(20%), nausea 6(24%), vomiting 6(24%), flatulence 1(4%), constipation 1(4%), diarrhea 2(8%), headache 4(16%) and tiredness 4(16%).

The difference in side effects were statistically not significant except of gastric pain which was found to be statistically significant, Thus considering the results it is seen that both drugs are well tolerated but tolerability of aceclofenac is better than ibuprofen.

Ward et al (1995) compared the efficacy and tolerability of aceclofenac with diclofenac and observed that adverse effects like dyspepsia, epigastric pain, heartburn, indigestion are less common in patients taking aceclofenac than diclofenac.

Bjordal et al (2004) concluded that the potential of aceclofenac to cause gastroduodenal damage is less than that of diclofenac in a study of Non Steroidal Anti-inflammatory Drugs including COX-2 inhibitors in osteoarthritic pain.

Baringartter et al (1996) conducted a study between ibuprofen and diclofenac and conducted there were fewer gastrointestinal side effects in ibuprofen than diclofenac.

Muller-Fassbender et al (1994) compared glucosamine sulphate with ibuprofen in OA of knee and concluded that 35% of patients on ibuprofen reported adverse events mainly of gastrointestinal origin vs 6% adverse events with glucosamine.

Compliance

Compliance was ensured by counting the number of tablets consumed from the foils with the patient of subsequent follow up visit after 3 weeks and 6 weeks. In this study, all the patients taking aceclofenac (group A) and ibuprofen (group B) complied (100%) with the therapy throughout the study period of 6 weeks.

Conclusion

From the results of present study it is concluded that:

- Both Aceclofenac and Ibuprofen were effective in treating Osteoarthritis of knee joint with each drug showing significant changes in different parameters.
- Aceclofenac is superior to Ibuprofen as it produced improvement in greater number of patients, and produced greater change in parameters as shown by difference between the two drugs in mean percentage change in different parameters.
- Adverse effects like epigastric pain, dyspepsia, heartburn, abdominal pain were less with Aceclofenac than Ibuprofen.

Summary

This randomized Double blind parallel group study of comparison of efficacy and tolerability of Aceclofenac and Ibuprofen in osteoarthritis of knee joint was carried out in orthopedic out patient department (OPD) of Rajindra Hospital, Government Medical College, Patiala for 6 weeks. Total 50 patients were enrolled and randomly divided into tds, n=25). All the particulars of the patients were noted and detailed history with baseline demographic characteristics, and duration and severity of disease were noted. The results of observations of individual patients were compiled in each group and statistically analysed.

Considering the efficacy; the number of patients showing improvement in different parameters like pain intensity, pain (VAS), joint tenderness, swelling, erythema, pain on movement, functional capacity and overall assessment were significant in both Aceclofenac and Ibuprofen. The number of patients showing improvement in different parameters were more in Aceclofenac than Ibuprofen, though the difference in number of patients showing improvement was statistically not significant.

Improvement in functional status of both drugs was observed by calculating their respective mean scores at different time intervals in different parameters like pain intensity, pain (VAS),

joint tenderness, swelling, erythema, pain on movement, functional capacity and overall assessment and were found to be significant in both groups.

The efficacy of Aceclofenac and Ibuprofen was compared by difference in mean percentage change. Since the mean percentage score was more in Aceclofenac than Ibuprofen in parameters like pain intensity, pain (VAS), joint tenderness, swelling, pain on movement the difference was statistically significant.

The mean percentage score was also more in Aceclofenac than Ibuprofen in parameters like erythema, functional capacity and overall assessment, however, the difference was statistically not significant.

Comparing the tolerability of Aceclofenac and Ibuprofen it was observed that both the drugs were tolerated well and no serious side effects were observed with any of the drug. Adverse effects like epigastric pain, dyspepsia, heartburn, abdominal pain, was more common in Ibuprofen than Aceclofenac but the difference in GIT adverse effects was statistically not significant, However, it was observed that the difference in epigastric pain was statistically significant.

In this study, all the patients taking Ibuprofen and Aceclofenac complied (100%) with treatment throughout the study period of 6 weeks.

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Transformation in Education of Nurses and Medical Technicians in Past and Today in Federation of Bosnia and Herzegovina

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Abstract

Background: Nurses and medical technicians in Bosnia and Herzegovina (B&H) have past through four phases on their way to transformation of their educational process. Those phases are: a period of mediaeval Bosnia, a period of auxiliary nursing, a period of high school nursing and now a period of university education in nursing.

Aims: The aims of this paper are to make review of educational process in nursing through history in B&H and to find factors that should be eliminated for the purpose of having better and high quality nursing care professionals.

Methods: Following methods were used in doing this work: a method of theory analysis, a method of observation and a descriptive method.

Conclusion: This process of transformation of education in nursing in B&H is long-lasting process. In each one of these periods, medical care had high quality no matter of level of education in that period. Nurses and medical technicians became privileged with getting opportunity for continual medical and professional education. That will surely affect improvement in medical care also. Possibility of doing scientific and research work in nursing education give additional contribution to improvement of medical care.

Young people who study nursing should be affected with more professionalism and empathy toward the patients. Presence of national, international and world nurses associations is necessary for the reason to implement improvement in professional and social status of nursing care professionals.

Suggestions: Concerning temporarily situation in B&H, it is necessarily to do professional pedagogic screening in primary school; to choose professional and qualitative people for leading and taking responsibility for material and staff resources in medical institutions; to disable completing nursing education that is not under supervision of the government; to improve communication among the staff themselves or eventually by involving psychologists or specialist for communication; nurses and medical technicians should be taught only by higher-educated professionals who have experience in theory and practice of taking care of patients; to organize professional associations from small to bigger ones in order to protect the profession itself from internal and external problems; multidisciplinary approach in making curriculums for nursing education; young, inexperienced students should meet all advantages and disadvantages of the profession during the secondary school so that they can be ready for doing their job well; to introduce practical duties to young colleagues gradually going from easier to more difficult jobs.

Keywords: Nurse, medical technician, nursing, education, high quality medical care

Introduction

There are many obstacles, for medical nurses/technicians on their way of education, needed to be solved so that they can be real professionals.

Firstly, it is important to say that curriculums in our schools are too wide or do not observe actual events at all. In spite of the most contemporary precaution in every-day medical practice, the mortality rate is on the increase.(Konjhodzic, 1996:8)

Unfortunately, it often happens in it's the most virile period of life. Of course medical nurses/technicians are not responsible for this, but their education should be improved in order to get them ready for all problems that can occur.

Secondly, it should be noticed that modern medical idea is going to be with more quality and easily understood. Therefore, a tendency of abolition of a lot of methods and contents in medical textbooks is on the increase.(Konjhodzic, 1996:8) The educational way of medical nurses/technicians in B&H has followed social and political events in the country on its way of evolution. It is better to point out that the events have had a great influence on education of all health professionals.

Thirdly, the way of getting knowledge and competence throughout the educational system is found on basic medical researches and sciences. Because of that, a medical nurse/technician should know the essentials of fundamental scientific fields.

Finally, it could be said that the peak of medical nurses/technicians education is reached through the symbiosis of medical theoretical knowledge and practice (experience) and then, they are prepared to give quality and full medical attention to patients.

It can be said that there are four pillars of educational system of medical nurses/technicians. They are: studying of theory of medical disciplines, practicing medical treatments, learning how to manage with material and personnel resources and finally, having opportunity to go forward in academic career.

In nowadays, in overflow of information technology, also in medical science, information is always a few steps forward in comparing with our education. That's why there are „gaps“in our educational system and in our knowledge. We can see this, for example, in subject of Medical Communication. It is well known, it is the base of high-quality and two way communication with patients in every day practice, but it is not given deserved place and attention to this subject in our educational system. When there is not quality and knowledge in

communication with patients, there is always chance to make big mistakes with catastrophic outcomes.

Nurses and medical technicians in Federation of Bosnia and Herzegovina (FB&H), the part of Bosnia and Herzegovina (B&H) together with Republic of Srpska and District Brcko, have past through four phases on their way to transformation of their educational process. The same process includes all mentioned parts of today B&H. Those phases are: a period of mediaeval Bosnia, a period of auxiliary nursing, a period of high school nursing and now a period of university education in nursing. These period were very dynamic evolutionary but also limited with many factors. The most imported was, surely, lack of academic education in field of nursing that should make experts in theoretical and empiric aspects of profession, which will educate new generations in the same field.

Aims

Aims of this paper were: to make review of educational process in nursing through history in B&H and to find factors that should be eliminated for the purpose of having better and high quality nursing care professionals.

Methods

Following methods were used in doing this work: a method of theory analysis, a method of observation and a descriptive method.

Discussion

All four phases of educational transformation will be described separately in this section.

A period of mediaeval Bosnia

Although, the care of sick and injured people is as old as mankind is, there were not difference between doctors and other medical staff in past because one man did all, diagnosis, treatment and care. That was the case in Mediaeval Bosnia too.

Not only were Bosnian Kings well-built and handsome-looking but all people in Mediaeval Bosnia.(Group of authors, 1996:27) What this means is that they were healthy because sick people cannot look like they were. Therefore it is clear that taking care about health was very important in that time. There was no real medical education, but there were people whose medical treatment was based on some spiritual and herbal methods of nursing. Their medical knowledge was inherited repeatedly during their Bogomilian way of life.

It is known that the Middle Ages was a period of obscurantism.(Konjhodzic, 1996:36) and Roman Catholic inquisition, therefore there was no a big success in medicine. Unfortunately Mediaeval Bosnia was attacked by Chancery and crusaders because of living Bogomils there, who did not want to convert into Christianity. Because of a lot pressure from the Roman Catholic Church, the coming of Turkish army in Mediaeval Bosnia was a salvation. The Ottoman Empire was known to be the most organized state and the force of arms in those times. As a result of this, every part of the state was highly coordinated, especially an institution of the Principal Doctor (Turkish: Hekimbaşı), who inspected and controlled working of Muslim and non-Muslim doctors. (İhsanoglu, 2004:331)

Arabic medicine is known to have been very developed in the period. Consequently, many hospitals were established in the world. (Konjhodzic, 1996:37) By the year 1110 there were over 60 hospitals and other social institutions in Baghdad and in Cordoba over 50 of them. Because of that there were a lot of medical workers, beside doctors, who took care of the sick.

All medical care was done by Turkish army-doctors (Konjhodzic, 1996:39) in the second part of the Middle Ages in Bosnia. It lasted till 1866, when the first hospital was established in Sarajevo. It was a foundation-hospital in Sarajevo (Bosnian: Vakufska Bolnica-Sarajevo), beside four hospitals that had been established during the Ottoman Empire.(Masic, 2004:5) After this period Bosnians went to schools either in Istanbul or in Vienna. (Konjhodzic, 1996:39) It depended on

their religion. Despite of this there was no professional trainings of medical workers in Bosnia.

After the arrival of Austria-Hungary in the territory of Bosnia, doctors from Austria and Czech Republic headed up in the Terrestrial Hospital Sarajevo, where domestic workers did all nursing in spite of the fact that they were not certified nurses.

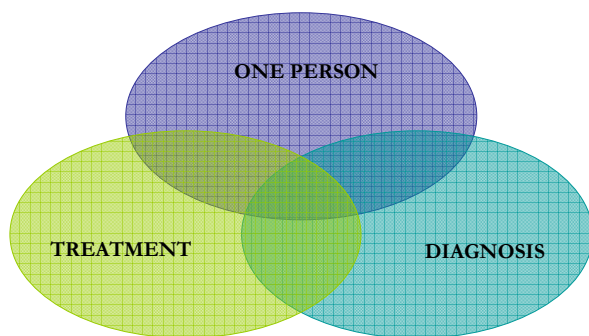


Figure 1: Schematic illustration of medical approach toward the patient in period of mediaeval Bosnia

A period of auxiliary nursing

After the arrival of Austria-Hungary in the territory of Bosnia some changes happened in medical services. It should be mentioned that Austrians were interested in reputation of themselves in every segment of human's life. Furthermore, there was a wish for investing money in an idea of importance of medical services (Masic, 2004:5) and general health. In that period many country hospitals were built (Masic, 2004:5) where a lot of certified medical workers were employed mostly from Austria and Czech Republic, but also from other European countries. The most important project was establishing of Terrestrial Hospital in Sarajevo where many medical professionals were educated in the following period. This hospital, without doubt, made European fundament of Health system in future Bosnia and Herzegovina. At the beginning, Sarajevo Terrestrial Hospital intended to be a plagiarism of

University Hospital in Vienna. Eventually it was achieved, because it was established on European standards in that time. That's why it is said, it was the best hospital in Balkan, (Masic, 2004:6) where many medical professionals from Vienna Medical School came to work.

The number of medical workers in this institution increased many times. In addition, this hospital was the center where all medical personnel educated (Masic, 2004:6) for the whole country, B&H. This is also the place from where, after the Second World War, University professors for Medical Faculty in Sarajevo came.

The period after the arrival of Austria-Hungary in the territory of Bosnia was full of different events in the world. Firstly, there were two World Wars, which were reasons that a lot of medical workers attended medical trainings in military units. As a result of this they continued to work in hospitals as medical nurses/technician. Their way of education mostly based on practical knowledge. Although there were pharmacies that were very organized (Masic, 2004:5) in order to help people in Bosnia, they used different medical and technical actions patterned on their military instructors or traditional medical treatments.

This period could not be separated from the period when the first medical secondary school established and medical workers became certified in educational institutions under the sponsorship of the government. Despite of this fact, auxiliary nurses from this period were employed in country wide health institutions until the last war/aggression in Bosnia 1992-1995.

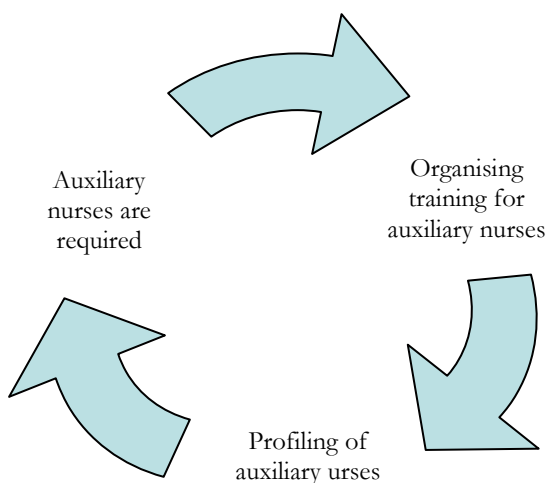


Figure 2: Schematic illustration of profiling of auxiliary nurses

A period of high school nursing

This period is said to be a bit discriminative for male nurses because there is no an appropriate term for male nurses in the Bosnian language. A *nurse* is a name used for a female nurse, where a *medical technician* is used for a male nurse. The same case is when women finished secondary school and become a laboratory technician; there is no a name for female one. These are, not only, two examples which point out that something should be done so that genders can be equal. Fortunately, there are a lot of associations that intend to improve the situation. It is high time that linguists offered a better solution. Up to that moment we will use official title- nurse/ medical technician.

This period was started by establishing first medical secondary schools after the World War II. Not only do medical nurses/technicians go to medical secondary schools in B&H, but they do it in other Republics in ex Yugoslavia. Medical secondary schools were established in the towns where there were hospitals (Jolic, Vicovac, Dordevic, 1988:20) so that students can get practical knowledge. Before the war in B&H there were more medical schools in the territory of B&H such

as medical school in Sarajevo, Zenica, Tuzla, Travnik etc. They were connected (Jolic, Vicovac, Dordevic, 1988:20) with hospitals where students get their practice. In these schools the curriculum of medical practice (Jolic, Vicovac, Dordevic, 1988:20) was made in order to do have practices in nearby hospitals without disturbing other activities in them.

In the textbook 'The care of patients', it is said, 'Not only should nursing pupils be taught about medical matter but they should be taught to be responsible, conscientious, devoted, sympathetic towards the sick, accurate, sincere, friendly etc. For all, medical workers by their attitude and behavior should be good examples to nursing pupils.' Despite of this good advice of the quotation from the textbook, it is not taken seriously in real life throughout the period. However all these components and many also important ones should be included in the curriculums and taken seriously in real life. Moreover older professions should help young ones to choose the right profession. In this period many medical post-secondary schools were established which later became institutions of higher education.

Finally, I can say that in this period nursing pupils were taught to be more professionals than human beings with empathy toward the patients. Of course, many other causes may contribute to situation like this. However, we must not forget that God in The Holy Qur'an says: 'One who saves a human being, as if he saves all human beings.' It is also important to point out that a medical worker can become a patient. What then? Then one can realize that being a medical worker is not easy but it is more difficult to be a patient and be depended on one's help.

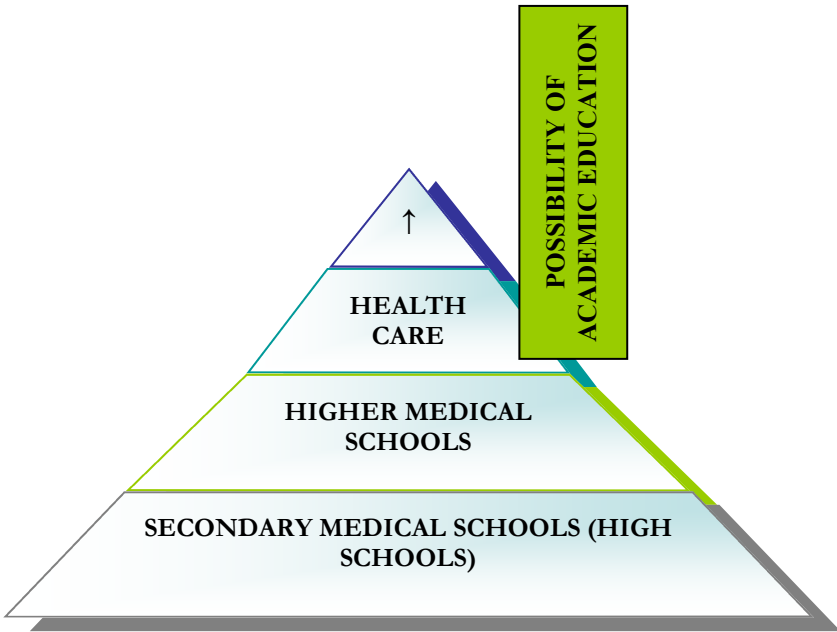


Figure 3: Schematic illustration of transformation of medical (nursing) educational institutions

A period of university education in nursing

It is extraordinary that medical nurses/technicians have opportunity for higher education. That is a great improvement in medical care. Getting university educated medical workers is an advantage, not only for patients but for the country too.

However, there are some problems such as a lack of appropriate titles of professionals on certificates they get after graduating. Moreover, an exact work place for medical workers is not regulated by the statutes of work. And managers can choose cheaper workers by law. As a result of this, suitable workers are employed, but not efficient ones. All these problems should be resolved so that young people can have better future in Federation B&H and in the whole country B&H. It is important to say that in this period of transition all medical nurses/technician, who have been working for decades, must not be betrayed by the government or the

people who decide their destiny. They are people who have been taking care about patients and helping them in every situation. The process of education of medical nurses/technicians is not completed in the moment when they graduate. Furthermore, their education should be a long-lasting process. Therefore, they should attend congresses, workshops, meetings, etc. At the moment when they finish the school, then they, again, go to real school-the school of life where patients wait for their help.

All things considered, a job of medical nurses/technicians is not autonomous but a team work of all medical workers and also non-medical workers.

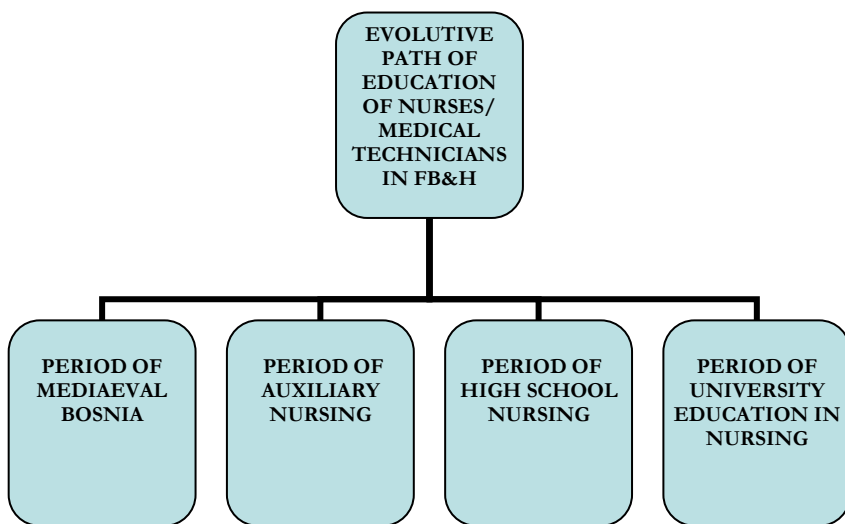


Figure 4: Schematic summary of evolutive path of education of nurses/ medical technicians in Federation of B&H (FB&H)

Conclusions

- This process of transformation of education in nursing in B&H is long-lasting process.
- In each one of these periods, medical care had high quality no matter of level of education in that period.

- Nurses and medical technicians became privileged with getting opportunity for continual medical and professional education.
- That will surely affect improvement in medical care also.
- Possibility of doing scientific and research work in nursing education give additional contribution to improvement of medical care.
- Young people who study nursing should be affected with more professionalism and empathy toward the patients.
- Presence of national, international and world nurses associations is necessary for the reason to implement improvement in professional and social status of nursing care professionals.

Suggestions

Concerning temporarily situation in B&H, it is necessarily to do:

- professional pedagogic screening in primary school;
- to choose professional and qualitative people for leading and taking responsibility for material and staff resources in medical institutions;
- to disable completing nursing education that is not under supervision of the government;
- to improve communication among the staff themselves (Stankovic, 1978:534) or eventually by involving psychologists or specialist for communication;
- nurses and medical technicians should be taught only by higher-educated professionals who have experience in theory and practice of taking care of patients;
- to organize professional associations from small to bigger ones in order to protect the profession itself from internal and external problems;
- multidisciplinary approach in making curriculums for nursing education;

- young, inexperienced students should meet all advantages and disadvantages of the profession during the secondary school so that they can be ready for doing their job well;
- to introduce practical duties to young colleagues gradually going from easier to more difficult jobs.

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Acute Appendicitis: Sensitivity, Specificity and Predictive Values of Ultrasonography

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Abstract

Background: Acute appendicitis (AA) is a common clinical problem. Accurate and prompt diagnosis is essential to minimize morbidity otherwise delay in treatment increases the risk of perforation and complicates the clinical course. Although diagnosis of AA is traditionally made on the basis of medical history and clinical findings supported by laboratory results, the relatively recent introduction of new imaging technology; ultrasound, potentially has changed the management plan.

Objective: The aim of this study was to evaluate ultrasonography (US) as an imaging study for diagnosis in acute appendicitis.

Methods & Materials: This prospective study included 191 patients, presented to the emergency department of Sina hospital (Tehran, Iran), with acute appendicitis feature during 2005-2006. The impact of radiologic imaging tool; US in the management of suspected appendicitis was assessed in 95 patients. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR⁺), negative likelihood ratio (LR⁻) and accuracy of US and negative appendectomy rate (NAR) were calculated. Statistical analysis

was done using SPSS-13 software. P value of < 0.05 was considered as level of significance.

Results: All 191 patients underwent appendectomy. They were 134 (70.2%) male and 57 (29.8%) female patients, with a median age of 23y. US performed on 95 (49.7%) patients. The sensitivity, specificity, PPV, NPV, LR^+ and LR^- of US in diagnosis of acute appendicitis were as follow: 85%, 75%, 90%, 64%, 3.4 and 0.2. Total accuracy of US was 82%. Overall NAR was 13.1%. NAR in males and females were 9.7% and 21%, respectively ($P=0.03$). In our study NAR in females of childbearing age was 26.9%. In those with preoperative US, NAR was 9.5%.

Conclusion: Preoperative right lower quadrant assessment by US was found to provide valuable guidance in the management of a patient with suspected appendicitis. Following this guidance led to beneficial changes; as improved diagnosis and reduced the NAR. US was sensitive and relatively specific for the diagnosis of AA and had a significant association with positive appendectomy.

Keywords: Ultrasonography, appendicitis, appendectomy, accuracy

Introduction

AA is one of the most common causes of acute abdominal pain (Bursaly et al, 2005). Rapid diagnosis of AA is essential to minimize morbidity, which remains substantial if perforation occurs. While prompt diagnosis of acute appendicitis is desirable, complication rate in negative laparotomy is not negligible.

Diagnostic accuracy varies by sex, with a range of 78%–92% in male and 58%–85% in female patients. These differences reflect the fact that appendicitis may be extremely difficult to diagnose in women of childbearing age, because symptoms of acute gynecologic conditions such as pelvic inflammatory

disease may manifest similarly (Bongard et al, 1985, Nakhgevany and Clarke, 1986)

Negative appendectomies ranges between 8-12% and 25-45% in males and females, respectively (Raman et al, 2002, Gwynn, 2001 and Wong et al, 2002).

Although history and physical examination remain paramount, often times the clinical diagnosis may be difficult (Applegate et al, 2001).

Antibiotics and effective surgical management have substantially reduced appendicitis-related mortality; however, deaths from appendicitis still occur, particularly in the elderly (Birnbaum and Wilson, 2000).

The goal of modern surgical management essentially is to provide a balance between the rate of false-negative laparotomy and the rate of perforation at the time of surgical exploration (Velanovich and Satava, 1992, Memon and Fitzgibbons, 1997). Traditionally the diagnosis of AA is made on the basis of medical history and clinical findings supported by laboratory results, but the advent of relatively new imaging study; ultrasound (US) potentially has changed "the rules of the game".

US first described for appendicitis in 1981, as a result of its rapid, safe (lack of ionizing radiation), inexpensive and relatively accurate diagnosis, remained the diagnostic imaging procedure of choice in many centers for the next years (Applegate et al, 2001, Sivit, 2004, Kaiser et al, 2002 a, 2004 b).

US has been widely and accurately used for the diagnosis of AA. High diagnostic accuracy has been reported in numerous studies for US, thereby decreasing the rate of negative appendectomy without perforation rate on the increase (Guillerman et al, 2002, Eldar et al, 1997, Pieper et al, 1982). This study aimed to evaluate US as a medical imaging study for diagnosis of AA.

Methods & Materials

A total of 191 consecutive patients highly suspected of having appendicitis, prospectively studied during the years of 2005 and 2006.

Eligible patients for this study were patients presented with clinical feature suggested of AA to the emergency department of Sina hospital (Tehran University of Medical Science, Iran), and underwent operation. All patients underwent routine work-up consisting of medical history, physical examination, WBC counts and urinalysis.

Ultrasonographic evaluation was studied in 95(49.7%) patients with equivocal presentation. Ultrasonographic examinations were performed by expert radiologists using a 7-MHz linear-array transducer (sequoia; Acuson, Mountain View, CA). Sonographic criterion for diagnosis of AA was visualization of a blind ending, non-compressible intestinal segment with no peristaltic activity arising from cecum that measured more than 6 mm in diameter, with or without appendicolith. The pre-operative findings were compared with surgical and pathologic results when laparotomy was performed.

Sensitivity, specificity, positive and negative predictive value (PPV, NPV), positive and negative likelihood ratios (LR⁺, LR⁻) and accuracy of sonography were calculated. NAR was calculated. Statistical analysis was done by using SPSS-13 software. For comparison of categorical variable, we used two-tailed Pearson's χ^2 test or Fisher's exact test. A P value < 0.05 was considered significant.

Results

All 191 patients included in this study, underwent appendectomy. They were 134 (70.2%) male and 57 (29.8%) female patients, with a median age of 23 (range 9-73 years). Most patients were between 20-29 years old. The frequency of symptoms and signs associated with acute appendicitis are listed "see Table 1".

Table 1: Frequency of symptoms and signs associated with acute appendicitis

Sign & Symptom	Positive Appendectomy	Negative Appendectomy	P value
*RLQ Pain	42(25.3%)	2(8%)	0.07
*RLQ tenderness	84(50.6%)	13(52%)	0.83
Rebound tenderness	120(72.3%)	17(68%)	0.64
Local guarding	122(73.5%)	10(40%)	§0.002
Voluntary guarding	120(72.3%)	15(60%)	0.24
Involuntary guarding	17(10.2%)	6(24%)	0.09
Generalized guarding	158(95.2%)	21(84%)	0.18
McBurney tenderness	95(57.2%)	15(60%)	0.83
Rovsing` sign	143(86.1%)	13(52%)	§0.000
Psoas sign	97(58.4%)	10(40%)	0.09
Obturator sign	147(88.6%)	21(84%)	0.51
Cough sign	29(17.5%)	2(8%)	0.38
Temperature $\geq 38^{\circ}\text{C}$	128(77.1%)	15(60%)	0.08
‡TLC raised	42(25.3%)	2(8%)	0.07

*RLQ= Right lower quadrant

‡TLC= Total leukocyte count

§=P value<0.05

Right lower quadrant assessment with US performed on 95(49.7%) patients. They were 44(46.3%) males and 51(53.7%) females.

Overall, ultrasonographic assessment was done for 32.8% and 89.5% of male and female patients, respectively.

Twenty-five patients (13.1%) had negative appendectomy (13 males and 12 females). Rate of negative appendectomy in males and females was 9.7% and 21% respectively (P value>0.05).

Females of childbearing age (15-35y) were 52 patients with NAR of 26.9%.

Overall in patients with pre-operative US, NAR was 9.5%. Total accuracy, sensitivity, specificity, PPV, NPV, LR⁺ and LR⁻ of US in diagnosis of acute appendicitis were shown "see Table 2".

Table 2: Diagnostic accuracy of Sonography

	Sensitivity	Specificity	*PPV	[†] NPV	# LR ⁺	** LR ⁻	Total accuracy
Sonography	85%	75%	90%	64%	3.4	0.2	82%

*PPV=Positive predictive value
likelihood ratio

LR⁺ = Positive

[†]NPV=Negative predictive value
likelihood ratio

**LR⁻ = Negative

Discussion

The clinical diagnosis of AA is based primarily on patient history and on physical examination results. Patients with clinical signs and symptoms typical of AA undergo immediate surgery without radiologic evaluation. While the clinical diagnosis may be straightforward in patients who present with classic signs and symptoms, atypical presentations may result in diagnostic confusion and delay in treatment (Birnbaum and Wilson, 2000). Patients with the disease may present with a wide variety of clinical manifestations, and the diagnosis may elude even the most experienced clinicians (Williams, 1983).

The results of this study indicate that clinical assessment on its own is inaccurate in evaluating the likelihood of a positive appendectomy in patients presenting to emergency department with suspected acute appendicitis. Paulson et al, showed that history taking and physical examination remains the diagnostic cornerstone in patients presenting with RLQ pain, not all patients will have a classical presentation and further diagnostic investigations are indicated (Paulson et al, 2003).

Imaging studies, including ultrasonography (US), have an increasingly important role in cases of equivocal presentation. Radiologic imaging usually is requested in patients with atypical or confusing clinical findings.

US has been widely and accurately used for the diagnosis of AA. High diagnostic accuracy has been reported in numerous studies for US, thereby decreasing the NAR without

perforation rate on the increase (Velanovich and Satava, 1992, Deutsch and Leopold, 1998). In our study US had sensitivity of 85% and specificity of 75%.

US is rapid, noninvasive, inexpensive, and requires no patient preparation or contrast material administration. Because US involves no ionizing radiation and excels in the depiction of acute gynecologic conditions, it is recommended as the initial imaging study in children, in young women, and during pregnancy (Birnbaum and Wilson, 2000).

AA may be extremely difficult to diagnose in women of childbearing age and they have the highest NAR of 35-45% because symptoms of acute gynecological conditions may manifest similarly (Paulson et al, 2003, Yakoe and Jeffrey, 1994). In our study NAR in women aged 15-35 years was 26.9% and in all females was 21%. Wilcox and Traverso reported this diagnostic problem has led to false NAR as high as 47% in female patients aged 10–39 years (Wilcox and Traverso, 1997).

In our study false negative imaging results were infrequent but still occurred and therefore, a close clinical re-examination and communication with the radiologist was of utmost importance for the appropriate final decision. US was sensitive and relatively specific for the diagnosis of AA and had a significant association with positive appendectomy. Further reduction in the NAR can be achieved if US is performed by highly trained and experienced sonologists with a close rapport between the surgeons and sonologists.

Unnecessary delay in surgery should be prevented by prompt preparation and performance of pre-operative US so as to further reduce the perforation rate (Adetiloye and Al'Damegh, 2004).

Preadmission imaging in the patients may lead to earlier diagnosis, lower in-hospital perforation rates, and reduced hospital stays.

Conclusion

The goal of imaging is to maximize diagnostic efficacy while minimizing cost and risk to the patient. Preoperative right lower quadrant assessment by US was found to provide valuable guidance in the management of a patient with equivocal presentation, as improved diagnosis and reduced the incidence of negative appendectomy. US was sensitive for diagnosis of AA and had a significant association with positive appendectomy.

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Finite Element Model of the Femur Bone

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Abstract

Bone density and modulus of elasticity are influencing factors on load transfer mechanism and, if not entered correctly in finite element models, may produce unreliable results. For this reason, anatomically accurate finite element models of bones with accurate geometry and material properties retrieved from CT-scan data are being widely used to make realistic investigations on the mechanical behaviour of bone structures and implant fixation. Mechanical property of bone is inhomogeneous and its variation depends on individual. It influences on the total stiffness and stress condition of the bone. Therefore, mechanical analysis considering inhomogeneous property is necessary for patient oriented evaluation of bone in clinic. If the finite element method is used, the inhomogeneous analysis is possible by giving a material property to an element one by one. For this, extreme fine meshing is required. Here in this paper, we will see how a 3D Model can be generated for finite element analysis incorporating inhomogeneous properties. The study is applied to FEA modelling of femur based on CT images.

Keywords: Biomechanics, Finite Element Method, Image Processing, Computational Mechanics, Bone, Individual Modeling, Inhomogeneous, X-Ray CT

Introduction

In clinical application of computational biomechanics, mechanical analysis considering only standard or normal patient models is not sufficient to discuss clinical problems. Analysis based on individual or patient specific modeling considering characteristics of organ shape and tissue construction is indispensable. The specific method to make patient oriented computational models noninvasively based on cross-section images obtained from X-ray CT or MRI making element models directly obtained from voxel data of three dimensional image processing.

The mechanical property of bone (especially Young's modulus) is essentially inhomogeneous related to variation of bone density distribution. Range of mechanical property variation of a bone depends on individual, and it influences on the total stiffness and stress condition of the bone. Therefore, mechanical analysis considering inhomogeneous property of bone is necessary for patient oriented evaluation in clinic. In this study, we used "MIMICS 12.01" and "ANSYS 11.0" to create FEA model that is inhomogeneous in nature, giving material property to each element.

Methodology

Calibrated CT datasets of the femur bone are downloaded in DICOM image format and exported to Mimics 12.01 software, an interface between CT-scan and finite element software.

The outer contours of the femur bone were created in Mimics, saved as an IGES file, and read into ANSYS finite element software where an anatomically correct three-dimensional geometry of the femur bone is created from the contours and meshed into tetrahedral elements. Bone mat program was used to identify the voxels belonging to each element by interposing the FEA model and the DICOM image. The Hounsfield Unit of the voxels corresponding to each element are averaged and converted to gray values, then to bone mineral density and modulus of elasticity. In this way, each element of the femur model will be assigned to a unique material property, depending on the bone mineral density at that location. CT images are a pixel map of the linear X-ray attenuation coefficient of tissue. The pixel values are scaled so that the linear X-ray attenuation coefficient of air equals -1024 and that of water equals 0. This scale is called the Hounsfield scale. Using this scale, fat is around -110, muscle is around 40, trabecular bone is in the range of 100 to 300 and cortical bone extends above trabecular bone to about 2000. For a display setting of true color (32-bit) mimics displays a CT image, using upto 256 gray values.

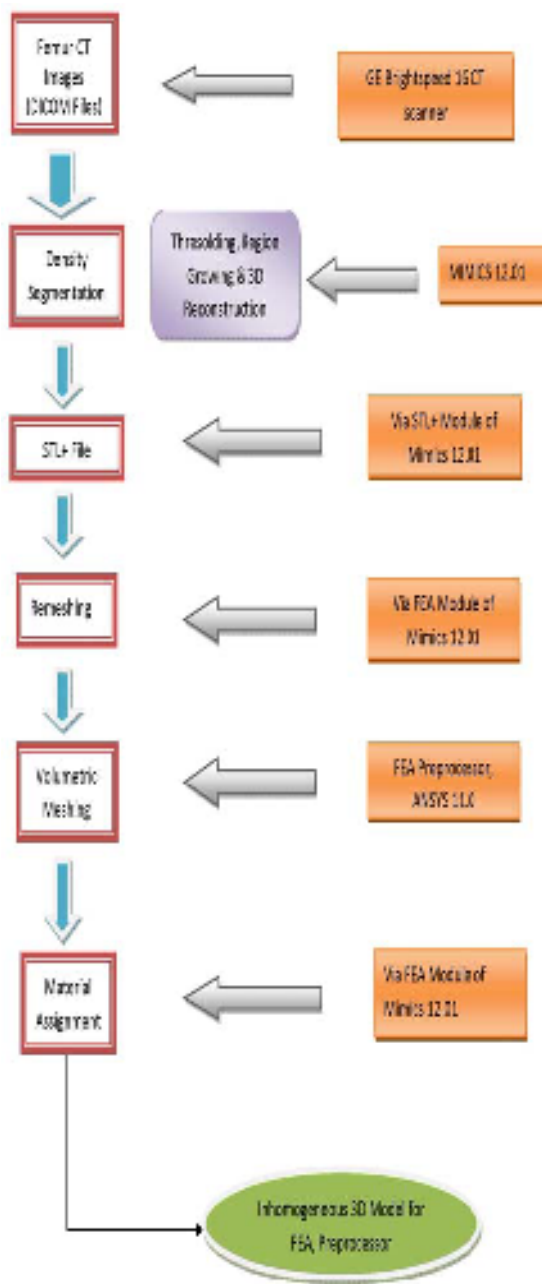


Figure 1: Modelling methodology

The mapping of pixel values into gray levels is specified by a level and a width. A gray scale is centered about its level. The extent of the gray scale is specified by its width.

Density Segmentation (3D Reconstruction)

CT data was obtained from scanner, consisted of two dimensional gray scaled images of a normal human male. The images were converted into three-dimensional models using an interpolation algorithm embedded in medical imaging software called Mimics 12.01, by Materialize. The gray-scaled values of the images represent the density of the material scanned.

By setting threshold values it was possible to separate the cortical and cancellous bone.

MIMICS imports CT and MRI data in a wide variety of formats and allows extended visualization and segmentation functions based on image density thresholding. 3D objects are automatically created in the form of masks by growing a threshold region on the entire stack of scans.

The various steps involved are:

1. Importing the medical data (DICOM images)

The MIMICS software allows the automatic importation of the 482 slice images generated in the CT scan. A pixel size of 0.338 mm was automatically calculated accounting the present image resolution (1024 x 1024 pixels) and the acquisition FOV. The slice distance was correctly determined corresponding to 0.4 mm. The pixel size and the slice distance guarantees the coherent dimensional reproducibility of the models generated during the segmentation process.

The CT images obtained were then processed to filter the required data and detect the femur shape.

2. Thresholding

Thresholding base on Hounsfield units was done to ensure that segmentation object will contain only those pixels of the image with a value defined. In order to include all the cortical and

trabecular bone at the foot bone structure and exclude the cartilage regions, a lower limit of 226 HU and an upper limit of 2000 HU were defined.

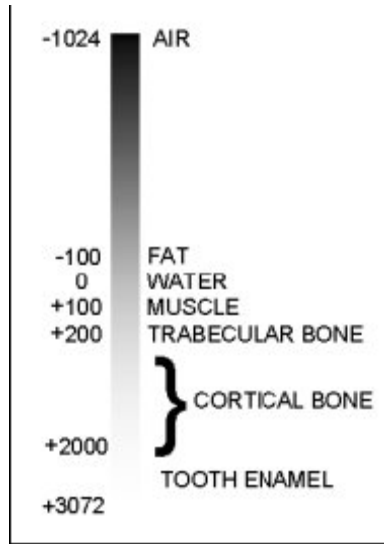


Figure 2: HU scale

3. Region growing

The region growing process allows splitting the segmentation in different and separated part.

4. 3D reconstruction

The generated region mask was used to develop 3D model for the bone. The 3D reconstruction is based on 3D interpolation techniques that transform the 2D images (slices) in a 3D model. For this reconstruction case, gray values interpolation was used associated with the accuracy algorithm for achieving a more accurate dimensional representation of the femur.

Remeshing

Using MIMICS STL+ module, femur was converted into stereolithography files (STL, bilinear and interplane interpolation algorithm). Native STLs are improper for use in

FE Analysis because of the aspect ratio and connectivity of the triangles in these files. The REMESH module attached to MIMICS was therefore used to automatically reduce the amount of triangles and simultaneously improve the quality of the triangles while maintaining the geometry. During remesh, the tolerance variation from the original data can be specified (quality of triangles does not mean tolerance variation from the original data). The quality is defined as a measure of triangle height / base ratio so that the file can be imported in the FEA software package without generating any problem.

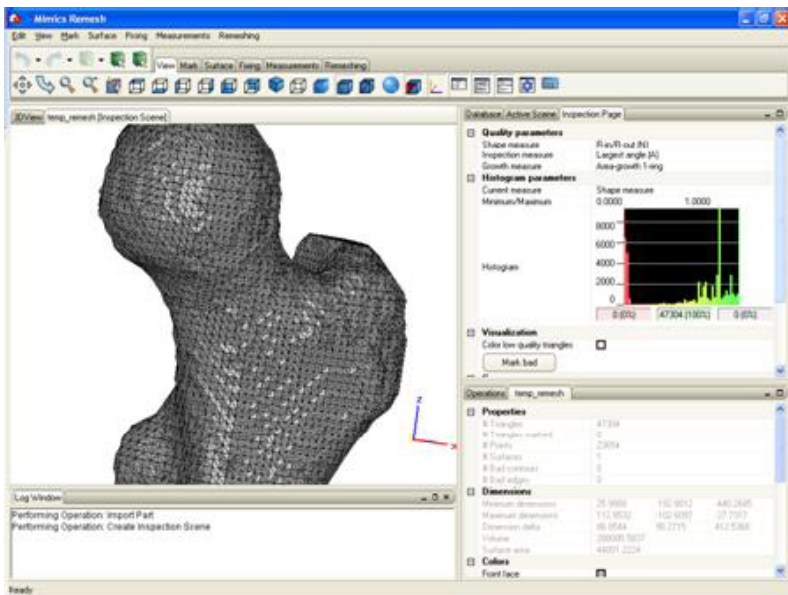


Figure 3: Remeshing of surface mesh

After remeshing:

- Amount of details are reduced
- Amount of triangles of the model is reduced
- Qualities of the triangles are improved
- The amount of triangles while preserving the quality is reduced
- Extra shells are removed
- Intersecting triangles are eliminated completely

Volumetric Meshing

After the surface mesh was calculated for the femur and was remeshed to make it suitable for FEA purpose. The remeshed file was exported to an ANSYS file for volumetric meshing to assign volume mesh to the femur in IGES format. It was exported to ANSYS 11.0 as an ELEMENT BASED file i.e, the part was exported as a mesh, having triangles as element, so that the quality of remeshed femur model is preserved while importing. Default surface element type imported by remeshed femur model from Mimics was SHELL93. To perform volumetric meshing in Ansys, a new solid element type SOLID92 was added to the model in Ansys preprocessor. Volume mesh was obtained using FVMESH command.

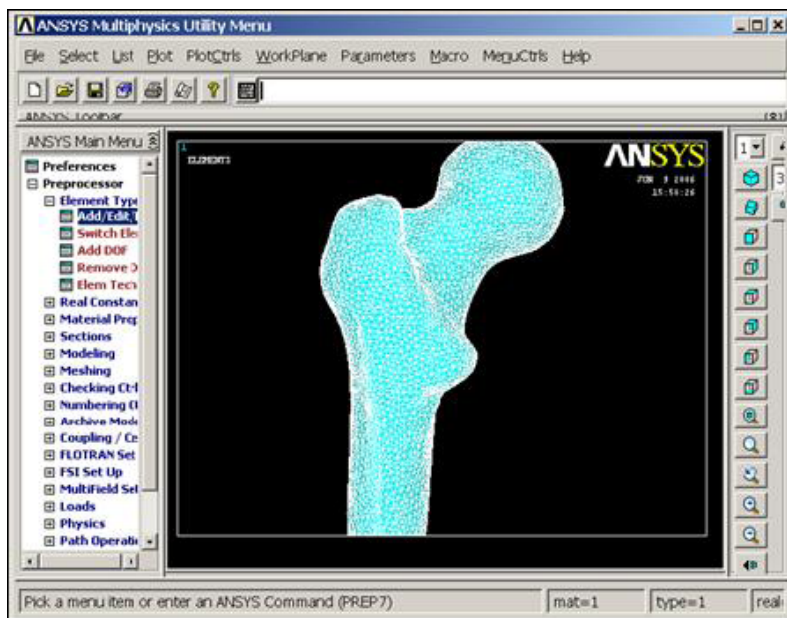


Figure 4: Volumetric meshing of remeshed femur in Ansys

Material Assignment

For assigning material property to the femur model (volume mesh), the gray values for each element was automatically calculated and exactly assigned to each element by calculating intersection between the voxels by Mimics. By discretization the range of all gray values was subdivided into equal intervals. An empirical expression of the form $A + B \cdot X^C + D \cdot X^E$ was used to convert the gray value into a density and E-Modulus value.

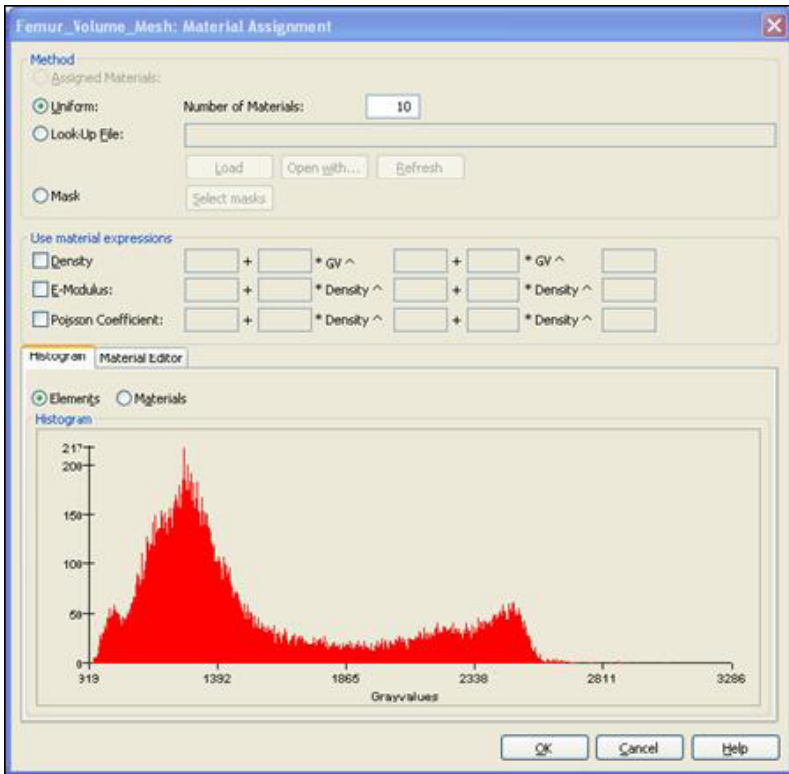


Figure 5: Graph showing the amount of element that was assigned to particular gray value

Volumetric mesh of the femur was imported from Ansys in IGES format in form of node and element file in Mimics FEA module for material assignment. Gray values are then

converted into material property. For this uniform method was used. The range of gray values in volumetric mesh was divided into 10 divisions, i.e. the number of materials taken is 10 and each division represents a material.

The following expressions were used to convert gray values of each material to density and EModulus respectively.

$$\text{Density} = -13.4 + 1017 * \text{gray values}$$

$$\text{E-Modulus} = -388.8 + 5925 * \text{density}$$

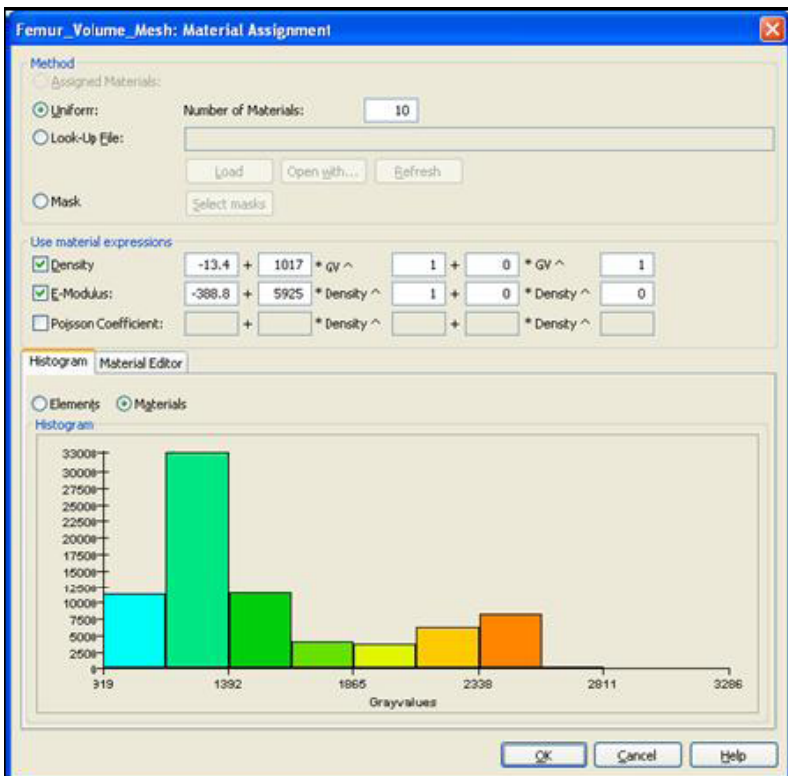


Figure 6: Histograms showing the elements of the FEA mesh colored according to their materials

The volumetric mesh, together with the material assignment is exported to Ansys, Patran Neutral and Abaqus files and can then be used to do FEA analysis on the mesh.

Results

3D inhomogeneous anatomical model of femur bone is generated with material property, which can further be analyzed in any FEA software.

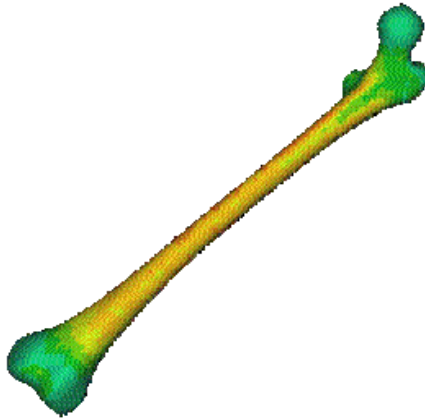


Figure 7: Inhomogeneous 3d model OF femur bone with material assignment

Discussions

This model shows that the mechanical properties vary across the femur bone, which is in accordance with other studies and is another step closer to physiological conditions because each individual element is assigned to a specific value of Young's Modulus. This femur model is accurate in terms of geometry and material properties and could be used in investigations for more realistic predictions of different methods of fixation, different prosthesis designs and different loading conditions.

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A Personal Computer-Based Undergraduate Medical School Curriculum Using SOLE

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Abstract

We describe our experience with a personal computer (PC)- and web-based undergraduate curriculum for pre-clinical medical students using the SOLE (Secure Online Environment) education and information system. To test the potential effectiveness of SOLE as a learning tool, we analyzed the patterns of SOLE usage, and usage intensity and consistency among medical students in two pre-clinical courses (4th-year Human Function and 5th-year Pathology) and attempted to link these indicators to academic performance. Categories of SOLE usage included number of website log-ins and number of pages viewed per course. We found that A-B grade 4th-year students accessed course materials more frequently than did C-failing grade students, and both median and mean number of SOLE log-ins declined as student performance decreased. Higher-graded students were also more consistent in their usage of SOLE than were lower-graded students. The range of log-in numbers (variability in frequency of usage) was greater for C-failing grade students than for A-B grade students. Compared to their 4th-year counterparts, 5th-year students increased their intensity of SOLE usage (indicated by the number of pages viewed)

dramatically and numbers were comparable for A-B grade and C-failing grade students. Consistency of usage, however, still remained higher for better-performing students. Furthermore, students preferred SOLE to a traditional paper-based curriculum and felt it improved teaching effectiveness. Based upon usage data and student preferences and perceptions we found web-based SOLE to be an effective and well-accepted educational tool for pre-clinical medical students. This integrative, online educational and information system offers numerous opportunities and advantages for self-assisted instruction that can serve as a foundation for clinical training and professional lifelong learning.

Introduction

More than three decades ago, researchers wrote of computerized instruction as a novel educational tool (Brittin, 1972). Recent trends in medical education include a shift from the traditional, didactic, lecture-oriented approach to a more student-driven, problem-based approach to learning (Simonsohn & Fischer, 2004). Advancements in text management and relational databases allow new levels of integration and interactivity using computer-based educational programs. Today, although individual computerized modules have been used to teach various kinds of basic science and clinical knowledge and skills sets (Almy et al, 1992; Gotlib et al, 1984; Hulsman et al, 2006; Lamperti & Sodicoff, 1997; Lozanoff et al, 2003; Simonsohn & Fischer, 2004), few schools utilize computerization of their entire undergraduate medical student curriculum. In this paper, we describe our evolving experience at the Oman Medical College with an integrative, online educational and information system for pre-clinical medical students.

Methods

Oman is one of the Arabian Gulf countries, sharing borders with Saudi Arabia, the United Arab Emirates, and Yemen. Oman Medical College (OMC) is a community-based medical

school with formal academic relationships with the Robert C. Byrd Health Sciences Center of West Virginia University (WVU) in the United States, and with the Ministries of Health and Education in Oman. Founded in 2001, the College offers a 7-year program of study leading to the M.D. (Doctor of Medicine) degree, as well as a 4½-year program of study conferring the B.Pharm (Bachelor of Pharmacy) degree. The first three years of pre-medical studies are conducted on the Bowsher Campus in the capital city of Muscat, and four years of medical training take place on the Sohar Campus located 200 kilometers from the capital.

Description of SOLE

As a part of its replication of WVU's curriculum for medical undergraduates, OMC has fully adopted SOLE (Secure OnLine Environment) as its web-based education and information system for all undergraduate courses. All courses have didactic lectures which also provide opportunities for questions and clarification, but there are no handouts or printed materials of any kind, and all faculty lecture notes are available on SOLE. Students are required to purchase (self-paying students), or are provided with (Ministry of Health scholarship students), a laptop computer and almost every aspect of academic study at OMC is computerized, from scheduling to test-taking. SOLE is a personal computer (PC)-based resource that allows students to access courses and for instructors to build and maintain those courses. Developed by Academic Technologies (Lexington, KY, USA) as an open-ended system for online course development and management, SOLE harnesses the communication power of the internet within a single sign-on, user-friendly environment. SOLE began as a course delivery system, but has grown to become an environment for many other applications and resources. The system uses Hypertext Markup Language (HTML) as structural markup rather than as display markup, automated linking by the use of relational databases and the Unified Medical Language System (UMLS), and integration of text, images, and multimedia along with

interface designs which promote multiple contexts and collaborative study (Figure 1) (Mattern et al, 1991; Zucker et al, 1996). Text management and relational software features of SOLE include:

Content Delivery [Classroom, Resources, Schedule, Syllabus]

- “Course Home” provides an overview of an entire course, summarizing any changes made the in the last 7 days (Figure 2);
- Various types of file formats supported: Flash™, streaming media, video, PDF, PowerPoint™, etc.;
- Selected parts of SOLE, such as courses, forum, news, announcements, weather, and links to various mobile-formatted websites can be accessed with PDAs or handheld PCs;
- Virtually paper-free format (the College provides almost no paper handouts, although students sometimes print materials from SOLE);
- Single point of access for all educational materials (Figure 3);
- Integrated links to external website resources (one username/password after setup);
- SOLE Web Editor makes it easy to edit a course’s pages from anywhere;
- File Manager allows for easy organization of online files;

Course interactivity [Announcements, Chat, Email, Forum, Journal, Survey, Faculty Lounge]

- Built-in communication tools (Figure 2);
- Synchronous and asynchronous communication tools facilitate student collaboration and a sense of community in the e-learning environment;
- Assessment tools can provide feedback and self-study;

SOLE tools [Calendar, Class Photo Gradebook, and other custom applications]

- Integrated email, calendar, weather, and news;
- Ability to customize portal home page with themes and panel arrangement;
- Online examinations and access to grades recorded in Gradebook;
- Recording and tracking of community service hours/donations;
- Homework repository
- Online trouble ticket system makes it easy to get help with problems;

All OMC instructors have limited (e.g., specific course faculty) or unrestricted (e.g., the dean, associate deans, and department heads) access to WVU's SOLE system. Instructors and students have differential access to certain OMC SOLE functions for purposes of scheduling and confidentiality (especially testing and grading; course lecture materials release, etc.).

Evaluation of SOLE

To test the potential effectiveness of SOLE as a learning resource, we analyzed the patterns of SOLE usage among medical students in OMC's 4th-year Human Function CCMD 730 course, an 18-credit hour integrated course combining the study of physiology, biochemistry, and genetics, and among 5th-year students in the Mechanisms of Disease (i.e., Pathology) course, and attempted to link these indicators to academic performance. Categories of SOLE usage were defined as follows: usage = number of website log-ins per course; usage intensity = number of pages viewed per course; usage consistency = the range of log-in numbers (variability in frequency of usage). Each course is taught as a block (18 contact hours per week for 16 weeks), and all learning materials are on SOLE (PowerPoint™ lectures, reading assignments, sample questions, etc., plus links to sites with supplemental learning materials). Thirty-eight students

completed the Human Function course during the spring of 2006, and 34 students completed the Pathology course in the fall of 2006. Overall, Human Function and Pathology course grades ranged from 60 to 94 and 66 to 92, respectively, with 70 as the passing mark. Seven students scored less than 70 and failed the Human Function course, while four students failed Pathology.

Statistical analysis

Statistical analysis of data was performed using SPSS for Windows™, version 15.0. Data from the 4-item questionnaire for perceived educational effectiveness of SOLE usage were reported as raw frequencies with independently measured variables, and a non-parametric chi square test was utilized to compare questionnaire data. A *one-way* or *one-factor* analysis of variance (ANOVA) was used to determine the association between SOLE usage and academic performance. Data was further analyzed for multiple comparisons in which group means were ranked from smallest to largest, and the number of steps that two means were apart in this ranking was used to compute a range statistic for each comparison (Duncan test). A coefficient of variation value was calculated as a marker of consistency of SOLE usage. We used p value to decide whether to accept or reject the null hypothesis, and a p value < 0.05 was considered statistically significant.

Results

SOLE usage and course performance

In analyzing SOLE usage and course performance, students were grouped as follows: A and B students (i.e., grades of 80-100), high C students (grades of 75-79), low C students (grades of 70-74), failing (F) students (grades less than 70). C-grade students were split into two groups in order to obtain sufficient variability for analysis. The relationship between SOLE usage and course grades is shown in Tables 1 and 2. The highest number of log-ins to the 4th-year Human Function course material on SOLE was 275 (over the 16-week course duration), equivalent to 2.5 log-ins per day while the course was ongoing.

The student with the highest number of log-ins failed the course (overall grade, 66). The lowest number of log-ins was 58, equivalent to 0.5 log-ins per day, and this student also failed the course (overall grade, 60). Overall, better-performing students had a higher number of SOLE log-ins and number of pages viewed. For 5th-year students, compared to their 4th-year counterparts SOLE pages viewed increased for all students, and were comparable between better- and poorer-performing students (Table 2). However, consistency of website usage, as indicated by the coefficient of variation, was significantly higher for better students. Table 3 shows the results of a 4-item questionnaire of preferences for and perceived educational effectiveness of SOLE by 4th- and 5th-year medical students ($n = 66$).

Discussion

We found the use of SOLE by pre-clinical medical students significantly correlated with academic performance. A-B grade 4th-year students accessed course materials more frequently and with more intensity than did C-failing grade students, and both median and mean number of SOLE log-ins declined as student performance decreased. Higher-graded students were also more consistent in their usage of SOLE than were lower-graded students. The range of log-in numbers (variability in frequency of usage) was greater for lowest-graded students than for the A-B grade students. Grade A and B students accessed the material in SOLE on one or two occasions per day. In contrast, some failing students accessed SOLE as infrequently as 0.5 log-ins per day while other failing students accessed SOLE as frequently as 2.5 log-ins per day. Compared to their 4th-year counterparts, 5th-year students increased their SOLE intensity (indicated by the number of pages viewed on SOLE) dramatically although figures were comparable for higher- and lower-graded students. However, when the main outlier was removed from the C students' dataset, there was a statistically significant difference ($p < 0.04$) between C students

and F students. In addition, consistency of usage still remained higher for better students.

Although A-B grade students made more frequent use of materials available on SOLE, it is not clear that the simple act of accessing the material contributed to student performance. Students had to understand the accessed material to do well. Is the material on SOLE easier to access and understand than material from other sources? It is certainly more convenient to get to, accessible 24 hours a day/7 days a week from anywhere on and off campus. Our survey data support the premise that students find it easier to learn material if it is on SOLE, compared to traditional lecture or printed sources. However, the data cannot be used to establish a cause-and-effect relationship, and it remains uncertain if better-performing (A-B grade) students scored higher because they accessed SOLE more frequently, or whether these students access SOLE more frequently because they are better students.

SOLE encourages integration of self-directed and collaborative learning components of virtual group, classroom, and library, and provides a problem-based e-learning environment. As described previously (Hashiba et al, 2000), SOLE allows our instructors and medical students to browse the contents of lecture slides and handouts with synchronous audio using the Internet. They can easily review the most interesting parts of lectures, and listen to complete medical lectures from campus and off-campus venues with narration and slide depiction, whenever convenient.

At some institutions, information skills components may be taught by library faculty and are included in the freshman orientation program and sophomore curriculum courses (Burrows et al, 1989; Schilling et al, 1995). Over a decade, the Virginia Commonwealth University School of Medicine conducted computer literacy surveys of students' levels of knowledge, skill, and experience with computer technology to

guide instructional services and facilities (Seago, et al, 2002). Our students receive only five credit hours of instruction in information technology over their first two years, yet easily adapt to SOLE when it is introduced in their fourth year.

Courses at OMC for 1st- and 2nd-year pre-clinical students use problem-based learning and clinical learning groups extensively in their curriculum. Clinical undergraduate medical education can be supplemented by computerized case presentations that encourage and stimulate problem-solving abilities and differential diagnostic reasoning, thus preparing students for the management of actual clinical situations with real patients. Another interesting example of computer-based clinical learning is the Virtual Medical School at National Taiwan University which utilizes a Hospital Information System (HIS) database that connects electronic medical record (EMR) systems in the hospital to capture and store valuable clinical cases that students use in their early clinical e-learning environment (Shyu, 2004). The system automatically converts real clinical case information from the HIS database into virtual patients by online authoring tools. The Minnesota Virtual Clinic is a web-based educational tool that uses a simulated EMR to expose students to critical basic science and clinical concepts in the context of patient care (Speedie & Niewoehner, 2003). The clinic enrolls a group of simulated patients representing a variety of conditions and cultural backgrounds and follows them over time. Students "attend" the clinic weekly to review the latest developments for its patients. A variety of educational links provide additional access to items of information from simple popup windows for definitions to illustrative images and interactive student exercises. The clinic also provides an introduction to certain informatics areas including basic security and use of an EMR. Other authors have developed a local area network which communicates between the medical school and the teaching hospital, and with access to the National Research Network (RENATER in

France) connected to the Internet network ((Denier et al, 1997).

Computer-based examination is another educational feature of SOLE. Presently, about one-half of our course examinations are given as traditional paper tests and one-half are taken by students using SOLE. Computerized testing offers several advantages for test administration, and there is evidence that some medical students like the use of computer-administered examinations (although ours did not; Table 3) and that the examinations may actually enhance the learning experience (Olgivie, 1999; Stammer 2000). Olgivie and coworkers (1999) found that students readily accepted computer exams and that their study habits were influenced in a positive manner by the computer administered extra-credit examinations.

Conclusions

In conclusion, OMC has successfully substituted a complete, full-featured, online curriculum for a traditional paper-based curriculum, using SOLE as an integrative software that supports the pedagogic goals of the curriculum and addresses the issues of acquisition and updating of materials, robust content-based linking, and integration of online materials into other methods of learning. Depending on the function selected (e.g., exploring the curriculum, searching through course outlines, retrieving PowerPoint™ presentations or handouts, identifying teaching faculty, searching for specific topics), text management or relational database management routines are activated in a manner which are transparent to the user. The program provides dynamic updating of both content and structure and is an easy, user-friendly pathway from the instructor's notes to the finished online product.

At medical schools and hospitals, modern medicine requires rapid access to information including clinical data from nomenclature and knowledge bases, bibliographic databases, and medical records. A PC-based undergraduate medical curriculum using the SOLE system offers numerous

opportunities and advantages for self-assisted instruction that can serve as a foundation for clinical training and professional lifelong learning (Barnett, 1995).

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Table 1: Association between SOLE usage and medical school Year 4 Human Function course performance

Course grade	No. of students	No. of logging range	No. of logging median	No. of logging mean (\pm SD)	<i>P</i> Value	No. of page views range	No. of page views median	No. of page views mean (\pm SD)	<i>P</i> Value
A or B	8	100-220	130	140 \pm 14	-	15-67	50	44.1 \pm 5.5	-
High B	12	109-187	123	130 \pm 7	NS*	7-52	18.5	21.3 \pm 4.7	< 0.01 ⁺
Low C	11	62-204	103	116 \pm 14	NS	5-50	50	32.7 \pm 6.1	< 0.02 ⁺
Failing	7	58-275	87	113 \pm 33	< 0.05	7-50	21	15.1 \pm 2.9	< 0.01 ⁺

* Not significant.

+ Statically significant differences between A + B students vs. C and F students, but no difference between C and F students.

Table 2: Association between SOLE usage and medical school Year 4 Human Function course performance

Course grade	No. of students	No. of logging range	No. of logging median	No. of logging mean (\pm SD)	<i>P</i> Value	No. of page views range	No. of page views median	No. of page views mean (\pm SD)	<i>P</i> Value
A or B	18	53-107	80	80.4 \pm 4.5	-	1105-1756	1407.5	1418 \pm 49.5	-
High B	4	42-79	59.5	60 \pm 8.8	NS* ⁺	939-1303	1163.0	1420 \pm 75.7	NS ⁺
Low C	8	55-158	84.5	79.9 \pm 15.6	NS ⁺	1096-1744	1447.0	1442 \pm 76.1	NS ⁺ ^o
Failing	4	55-156	86	95.8 \pm 21.9	NS	1380-1843	1555.5	1584 \pm 105.1	NS ^o

* Not significant.

+ A or B students vs. all C students.

o When the main outlier was removed from the C students dataset, there was a statistically significant differences ($p < 0.04$) between A or B and F students, and C students and F students.

Table 3: Results of a 4-item questionnaire of preferences for and perceived teaching effectiveness of SOLE by 4th - and 5th-year medical students ($n = 66$).

1. I prefer OMC's personal computer-based curriculum to a traditional paper-based curriculum. (YES – 53; NO – 13)
 2. I feel that the educational effectiveness of OMC's personal computer-based curriculum is (MORE - 61; LESS – 5) than that of a traditional paper-based curriculum.
 3. I prefer online examinations to paper-based examinations. (YES – 40; NO – 26)
 4. I find the single point of access for all educational materials to be a valuable feature of SOLE. (YES – 58; NO – 8)
-



Figure 1: SOLE login page

The image shows a screenshot of a SOLE (Student Online Learning Environment) course page for 'DEMO 101'. The page is annotated with blue lines and text boxes explaining various features.

Left Sidebar Annotations:

- Contains lectures and course materials (points to the 'Content' link)
- For announcements, chat, forum, mail etc (points to the 'Communication Tools' link)
- To post course schedule & Syllabus (points to the 'Schedule' link)
- For Exams & Assignments on Sole (points to the 'Exams' link)
- For students to share & upload files (points to the 'Shared Storage' link)
- To conduct surveys & post textbook details (points to the 'Surveys' and 'Textbook' links)
- Option created as per demand (points to the 'Credits' link)
- Takes to home page where ever you are (points to the 'SOLE Home' link)

Top Navigation Bar Annotations:

- Home: DEMO 101 Home (points to the 'Home' link)
- User Options: Problems? Sign Out (points to the 'User Options' link)
- Calendar (points to the 'Calendar' link)
- Print (points to the 'Print' link)
- Help (points to the 'Help' link)

Main Content Area:

- FORUM POSTS:** New | Last 7 Days | All. No new forum topics available.
- ANNOUNCEMENTS:** New | Last 7 Days | All. No new announcements available.
- EXAMS:** Current. No new exams available.
- SURVEYS:** Current | All. No new surveys available.
- CONTENT:** New | Last 7 Days | All. No new lectures available.

Right Side Annotations:

- Sole Navigation Tool Bar:- Always available at the top of every page in SOLE. Please use this navigation when in SOLE and avoid browser buttons (points to the top navigation bar).
- Home- Links to home page (points to the 'Home' link)
- User Options- For customization of the portal (points to the 'User Options' link)
- Sign out-Ends your session (points to the 'Sign Out' link)
- Calender-Links to your calender (points to the 'Calendar' link)
- E-mail-links yous to your e-mail account configured in SOLE (points to the 'Email' link)
- Help-Provides help for using SOLE (points to the 'Help' link)
- Print-Prints user friendly pinouts (points to the 'Print' link)
- Exam & Assignments details if at all posted (points to the 'Exams' section)
- Home page when a course is selected with latest details of Contents, Sunveys exams/assignments, etc (points to the 'Content' section)

Page Footer:

Page was rendered in: 0.078 sec. | Browser: IE 8 on WinXP | Server: OMC1 | Last Update: 1/17/2006 2:15:25 PM (EST)
seconds ago | Path: /portal/body.asp

Figure 2: Example of a SOLE course page

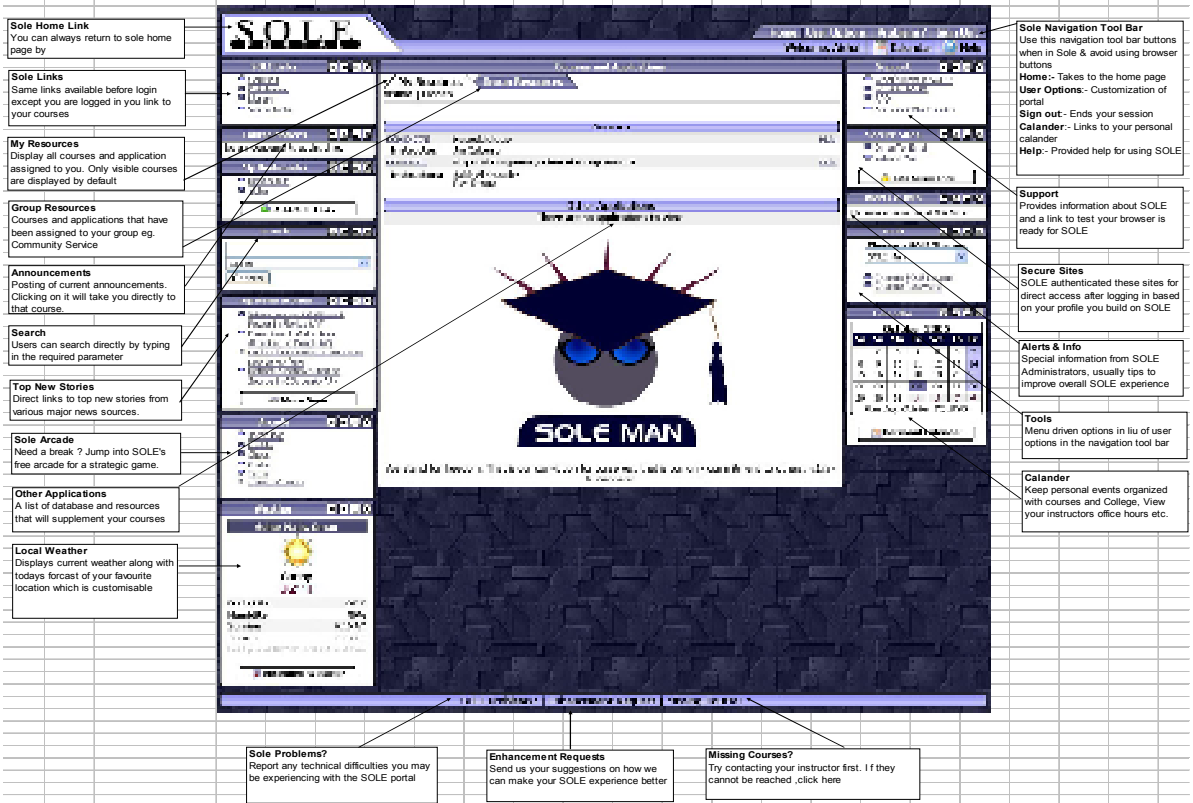


Figure 3: SOLE home page (<http://sole.omc.edu.om>)

Telemedicine and Medicine Vending Machine for Efficient Health Care, Diagnosis and Treatment

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Abstract

Aims: To ensure the high quality health care is feasible to all class of people in nations like India, Africa, and other nations where high quality health care is not accessible. It's practically possible with the technology of Telemedicine and medicine vending machine.

Method: Telemedicine is blooming in the medical sector at present scenario. By constructing a Telemedicine Information Center (TIC) affiliated to high tech multi- specialty hospitals in the state for departments especially for cardiology, diabetes and neurology. Now consider the department of "TIC for cardiology", The dean and senior doctors in the hospital can recruit the passed out students from medical universities, students pursuing higher studies in cardiology and even junior doctors and train them to work and assist in Telemedicine Info Center and clear the cardiology related queries from public with the aid of phone calls. Patient shall be issued with

ID cards entitled with pass- code and bank account code so that the consultation fee via credit or debit system could be charged online with the provided ID card. And designing a hybrid medicine vending machine which follows the same principle as such in the condom vending machine and ticket vending machine, system consists of a keyboard, card swiping track (for crediting the amount) as such in bank atm machines. then placing the tablets and capsules in various compartments provided inside the machine, enabled with suitable refrigeration for medicines and each tablet shall be provided with the specific code number for accessing and vending purpose. For example, consider tablet aspirin, code entitled is ASXO12_TAB, when code is entered; tablet is accessed and vended to the patients from medicine vending machine which is affiliated to the respective health centre.

Conclusion: Telemedicine could offer a high quality health care to patients with low fee cost, time consumption, 99% assured quality consultation and prescriptions from well trained medical professionals. Placing these medicine vending machines in villages, districts, cities which are far from multispeciality care, patients could access the prescribed medicines from it. And also it ensures the job opportunity for doctors and medical professional.

Result: If this technology is achieved, it will be a monument in the field of diagnosis and treatment.

Keywords: Telemedicine, Telemedicine Information Center (TIC), quality health care

Introduction

Tele-Medicine

Telemedicine is a rapidly developing application of clinical procedures, where medical information is transferred via telephone, the Internet or other networks for the purpose of

consulting and sometimes remote medical procedures or examinations.

In order to ensure the high quality health care is feasible to all class of people in nations like India, Africa, and other low economic nations. It's practically possible with the technology of Telemedicine & medicine vending machine and then by establishing a New Health Sector knows as “Tele-Medicine Information Center (TIC)”.

Concept of “TIC”

Establishing “Tele-Medicine Information Center” just like the renowned BPO’S , call centers and other such information centers, and affiliated to and directly controlled by best multi-specialty hospital and research institute in the state.



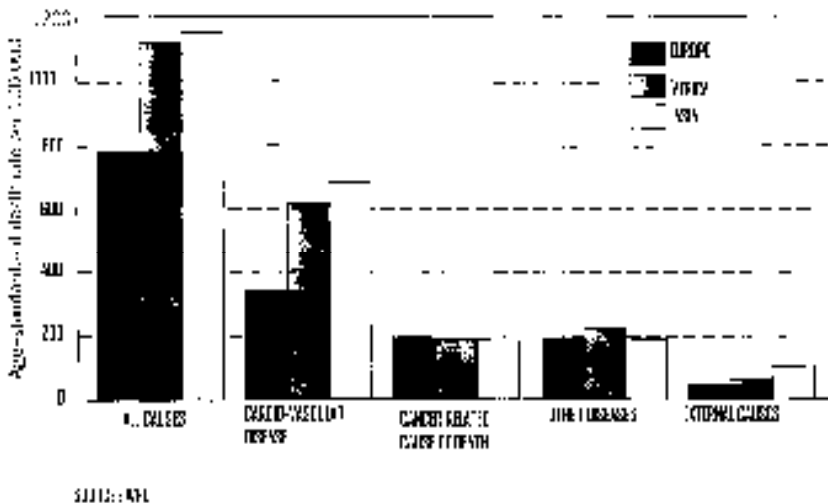
An imaginary model of an “TIC” center

Infra-Structure and Department's

- As infra-structure is concerned, an individual boxed cabin for every Doctors on-duty and personal computer's installed with all the patient profile database software, medical assist software's, image processing software's and communication devices such as web cam, head-phones etc. will be provided.

- As department is considered, various departments could be established such as cardiology, neurology, diabetes, renal, oncology etc...depending on the disease and disorder statistics in the state.

As per the latest survey made by WHO in continents like EUROPE, AFRICA, ASIA the sensex revealed that the increased death rate is due to **CARDIO-VASCULAR DISORDER'S** and **ASIAN NATIONS** tops the chart as well. So first we can establish the "TIC for CARDIOLOGY" as a major stream of department in this sector and depending on the success we can introduce the other departments as well.



Disease & Death-Rate Graphical Statistics in Asia, Africa, Europe

Affiliation & Governing Head of TIC Cardiology Department in South India

As I mentioned before, it as to be affiliated to and directly controlled by renowned medical institute. In south India, the best multi-specialty hospital for Cardio-vascular disease is “MADRAS MEDICAL MISSION” (MMM), Chennai, Tamil Nadu. So as for as the cardio-vascular department is concerned “TIC for CARDIO” can be affiliated and governed by this institute in state Tamilnadu, South India.

Qualification Requirements to Work under “TIC”

As a minimum qualification the candidate must be certified as a doctorate in medicine.

Other Qualification Requirement

- Minimum of 5 years experience as a medical practitioner specifically in cardiology department.
- As in India, certified with MBBS, MD (General medicine), or DM (Cardiology).
- Specialization in the cardiology department is acknowledgeable

Patient Registration & Treatment Procedure

Patient's can register online by downloading & filling the application form and other necessary details and post it through mail or postal service to the governing head.

Authorized Medical smart card will be sent to the residence address through postal service containing all the patient details, patient code, account verification through which they can access the prescribed medicines from medicine vending machine and to pay the consultation fee.

NEW PATIENT FORM

Practice name _____

PATIENT'S DETAILS

Title _____ Surname _____ Given names _____
Date of birth ____/____/____ Male Female
Marital status Single Married De facto Separated Divorced Widowed
Medicare No _____ Private health fund Yes No
Pension, Health Care Card, or Veterans Affairs No (if applicable) _____
Occupation _____
Home address _____
Postal address _____
Phone (home) _____ (work) _____ (mobile) _____
Email _____

EMERGENCY CONTACT (Next of kin)

Name _____ Relationship to patient _____
Phone (home) _____ (work) _____ (mobile) _____

Are you of Aboriginal or Torres Strait Islander origin? No
 Aboriginal Torres Strait Islander Aboriginal and Torres Strait Islander

List allergies and intolerances to medications _____

List regular medications and doses _____

Our practice undertakes research, professional development, and quality assurance/improvement activities to improve patient care. All people accessing personal health information for this purpose have signed a written confidentiality agreement.

I consent to my health record being reviewed as a part of the quality improvement activities at this practice. Yes No

Our practice uses a reminder system to improve the quality of your health care. The practice sends reminders by mail or telephone for procedures such as vaccinations, Pap tests and other health reviews.

I consent to being contacted with reminders as a part of the quality improvement activities at this practice. Yes No

Signature of patient or guardian _____ Date _____

Please advise us if your contact information or Medicare details change.

TRANSFER OF HEALTH INFORMATION

You may have consistently consulted with a GP at another practice. The health information held by that GP may assist us with your future health care needs. You may wish to have a copy or a summary of your health records transferred to this practice. Please ask the receptionist for information about how this can take place.

CDPF 34 (15/06)

➤ Online Treatment: [Educated Patient Profile]

This Session Is For Patients who are all capable to handle the computer and internet procedures. Followings are provided to the applicant's,

- 1) Patient login ID.
- 2) Patient individual profile.
- 3) Health status report.
- 4) Medical insurance and policy.

5) Authorized medical smart card (debit/credit) for fee payment.

6) Emergency help line number PH:22 33 44

➤ **Treatment for Un-Educated and Poor People**

Student community can help the illiterate and uneducated people to become a member by helping them by organizing seminar, effectively by counseling, by helping them to fill the application form and other procedure and guiding them. This kind of service is highly acknowledged in countries like India, Bangladesh, Pakistan and other nations where ill-literacy rate is higher. As soon as the application form reaches the management authority, they shall provide the patient with the following items, [ON THE BASIS OF SPECIAL SCHEME OF POOR AND ILLITERATE]

- 1) Patient ID card.
- 2) Special code account[as for poor and illiterate people]
- 3) Low cost in consultation & treatment fee.
- 4) Patient report from doctor's are sent directly to patient residence address.
- 5) Emergency help line number 11 00.

And “24 hours phone ECG facility” and providing the prescription as early as possible.

New Approach for Health Solution through Tele-Cardiology & Phone “ECG”

It is often difficult for the patient to tell the difference between angina symptoms and heart attack symptoms, therefore it is very Important to recognize the signs of a heart a tack and immediately seek For medical attention. This paper presents a mo bile solution, which Makes use of a wearable wireless

ECG miniature sensor in combination with a mobile phone to collect, store and forward ECG data to a Cardiologist

for analysis. A practical case of remote co siltation is also described.

Introduction

Coronary heart disease is by far the most common n cause of death in many Countries .Every few seconds, someone in Europe is us offering of chest Pain caused by an insufficient supply o f blood to the heart. While a short-term oxygen scarcity usually origins angina pectoris, a Long-term severe lack of oxygen causes a myocardial infarction. A large Damage may generate abs normal ectopic contractions of ventricle, which may eventually lead to a cardiac arrest. Therefore it is very important to identify a heart attack and immediately seek for medical attention. Instead heart attack victims, wait on average two hours or more after the beginning of symptoms, before they seek medical help.

The electrocardiograph is certainly the most effective tool to identify anomalies in the cardiac activity. Since the earliest interpretation o f a human electrocardiogram (ECG) given b y British physiologist Augustus D. Waller 120 years ago ,the analysis methods have been dramatically improved. However today diagnosis is still made by analyzing fractions of wave patterns and irregular rah myths recorded for several minutes.

Portable cardiograph practically exist since 1949 when physician Norman Jeff Halter developed a system used to record ambulatory ECGs over a long-term recording. But it was only less than 10 years ago that researchers from Texas demonstrated the feasibility of transferring ECG data via wireless technology to hand-held computers where it can be reliably interpreted by cardiologist. The emit Health Gateway mobile electrocardiograph offers a simple yet efficient way to be in contact with health professionals anytime and almost anywhere. The system co insists of a wearable wireless 3-lead ECG miniature sensor, which continuously measures the heart

activity and wirelessly transfers the data directly to the mobile phone of the patient. The information is then automatically transferred in real time to the health care provider by using a secure wireless connection such as GPRS, GSM, CDMA, or 3G.

The received information is stored into the Health Gateway server where it is available to the health care professionals for immediate analysis.

Authorized personnel of the health care provider can examine the received data and send an immediate feedback directly to the mobile phone of the patient. The mobile phone also keeps a record of the registered events, which will be available for future reference.

Handling of security and privacy issues

The transmission of binary data is often seen as a possible security threat. Because of its nature, a binary transmission can contain any sort of data including for example viruses or other malware. Therefore it is extremely

important to positively authenticate the sender when exchanging binary data. The system proposed exchanges binary data by using unique session keys and secure protocols.

The first step is the authentication of the sender (mobile phone), which is performed by using a secure HTTPS connection. After authentication, the sender requests a session key from the Health Gateway server.

The unique session key is then used to open a binary connection to a secure socket on the server. The socket communicates by using a Transport Layer Security protocol ensuring that third party cannot eavesdrop or tamper with the content of the message. The session key is then used to open the data transmission session and the transmission of binary data can begin. In case the connection is lost during data transferring, the sender can resume the

transmission by using the same session key. When all of the data is transferred, the sender closes the current session and the key is invalidated. A new session, can only be initiated by starting a new authentication procedure and by requesting a new key. A similar procedure is followed when downloading the information from the Health Gateway server to the remote workstation in use at the cardiologist. Additionally, the unique session key is also used in all the transactions to ensure the correct association between binary data and the initial context i.e. patient data.

The ECG sensor:

The ECG sensor used by the proposed system can be equipped either with integrated or external electrodes. It has a resolution of 12 bits and an adjustable sampling rate, which can reach the exceptional value of 5000 Hz. The adjustable sampling rate makes possible the optimization of the data load for the precision required by the application. For instance a sampling rate of 1000Hz or higher can be utilized when accurately measuring heart rate variability, while sampling rates of 500Hz or less may in some cases be adequate to define the R wave.

The microprocessor onboard the sensor is capable of elaborating the received data on line and can for instance calculate Heart Rate Variability (HRV) and other parameters such as the depression of ST segment and QRS interval. The calculated values can be immediately transferred to the mobile Phone or stored in a local memory for later downloading. The electronic sensor is also equipped with a parametric digital filter, which is capable of cleaning the signal from possible noise. This is particularly significant in substantially reducing noises generated by muscle activities (EMG signals).

A practical use of the proposed system

The system proposed is in use in a study, where ECG data are

recorded over several hours without disturbing the routine daily life of the subjects. The collected data are then Remo tell analyzed by specialists, and correlated to a database of anonymous data.

The study focuses on the fine fluctuations of the R-R intervals, which are analyzed and processed by using a particular algorithm specially created for this purpose. The result is a single parameter called index μ , which expresses the variability of the heartbeats. Although a large number of Studies have been made on HRV, the μ index is calculated in a completely new method, which allows sensitive detection o f HRV in an innovative Way. For each measurement session the algorithm also generates an image in Colors representing the individual characteristics of the heart. These Computer-generated pictures greatly different from one us abject to another And vary with the age of the patient and possible abnormal conditions of the Heart.

Conclusion:

A comp late examination of the heart status should always be carried out with a full (12 lead) ECG, however the system p reposed can quickly Provide important information that would otherwise be missed. In fact this Solution offers the subjects the capability of recording and simultaneously transmitting the ECG signal whenever they feel pain in the chest or heart irregularities. Additionally, the feeling of b eking in virtual contact with the health care Professionals provide as a sense of safety to the subjects, without the hassles of permanent monitoring. According to the preliminary results of the case study described, several Measurements sessions taken in different situations are imp octant to assess the condition of the heart. This wireless ECG miniature sensor combined with the Health Gateway platform offers a valuable tool for easy measurement of ECG without interfering with everyday's life.



Seminar Given by Medical Officials in Khamma Village



Devaki a heart patient unable to get treated for cardiac bypass surgery due to financial crisis and now supported by a social-service organization

- ❖ Many more people around India live unaware about the threat due to cardiology disease.
- ❖ And the worst to the core is that adult's are ignorant about their cardiac arrest and they don't even proceed for a general checkup as it cost's a huge fee's for diagnosis and treatment.
- ❖ Not only adult population but also infants and younger generation have also been a victim of cardiac diseases and disorders.

This is because of unable to access the basic medical care and the factor entirely responsible for this is “LACK OF FINANCIAL AID”. People are unable to offer even for a general diagnostic purpose.

The only solution to terminate this condition is possible by

Tele-Medicine&Technology and Medicine Vending Machine

“Which offers a less expensive health care yet an high quality treatment from highly qualified medical professional's”

Medicine Vending Machine

Introduction for the Vending Machine

After paying, a product may become available by:

- The machine releasing it, so that it falls in an open compartment at the bottom, or into a cup, either released first, or put in by the customer
- The unlocking of a door, drawer, turning of a knob, etc.

Sometimes the product is not just released, but prepared; this

may be the case e.g. in the case of coffee or a ticket that is printed after paying.

The main example of a vending machine giving access to all merchandise after paying for one item is a newspaper vending machine (also called vending box). It contains a pile of identical newspapers. After a sale the door automatically returns to a locked position. A customer could open the box and take all of the newspapers or, for the benefit of other customers, leave all of the newspapers outside of the box, slowly return the door to an unlatched position, or block the door from fully closing, each of which are frequently discouraged, sometimes by a security clamp. The success of such machines is predicated on the assumption that the customer will be honest (hence the nickname "honor box"), which is helped by the fact that having more than one newspaper is not often useful.

Raw Materials for Designing the Vending Machine

Vending machines are constructed primarily from four major raw materials: 1)galvanized steel, 2)Lexan or other plastic, 3)acrylic powder coatings, and 4)polyurethane insulation.

The bulk of the machine is constructed from galvanized steel ranging from 10 gauge to 22 gauge in thickness. The thicker gauges are used for the outside cabinet, external doors, and internal tank. Thinner gauges are used for internal doors and plates, can stacks, and mechanisms such as coin validators and product trays.

➤ **Advantage of Lexan in Medicine Vending Machine**

Lexan, a tough polycarbonate plastic, is used in the front panels of the vending machine. Sheets of Lexan in vending machines usually range from 0.13 in (3.18 mm) to 0.25 in (6.35 mm) in thickness. Lexan is very difficult to break, flame retardant, relatively easy to shape and can be treated to restrict UV rays, light, and heat transmission. Product logos, names, and

illustrations are silk-screened on Lexan sheets, which are installed in channels in the doors of the vending machines.

➤ **Importance of Polyurethane Insulation:**

Polyurethane foam provides the insulation for the inside of the vending machine. The foam is blown between the outer cabinet and internal tank of the machine, where it cures into a very tough, rigid material. In addition to thermal insulation, the stiff foam adds structural stability to both the cabinet and tank of the machine, where the medicines are going to be stored.

Internal & External Design

The basic design of a vending machine begins with the cabinet, the steel outer shell that holds all internal components and which determines the machine's overall size and shape. Inside the cabinet is a steel inner lining called the tank. The tank and the cabinet fit closely together, leaving enough room in-between for a layer of polyurethane foam insulation. In combination, the tank and the foam insulation help keep internal temperatures stable and protect products against temperature extremes outside the cabinet. Although all products and dispensing mechanisms are contained in the cabinet, in the strictest sense, they are actually installed within the tank.

The outer surfaces of the cabinet are coated with an acrylic powder finish that is baked into place. Powder coatings enable the machine to withstand extreme temperatures, salt or sand, abuse by customers, and other conditions requiring high surface durability.

Internal Design of the Unique Vending Machine and Procedure for Accessing the Medicines from it:

Generally if we consider the cardiology disorders there will be maximum of 40 – 50 prescribed capsules for the treatment. So it is highly necessary to place all these capsules into the vending machine for the patient's to access it.

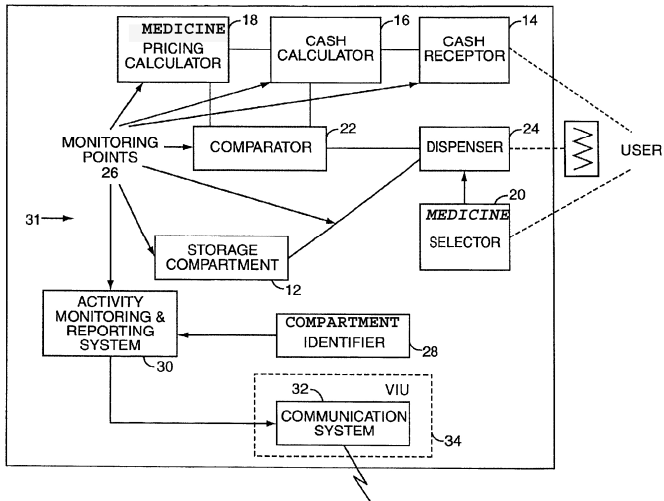
Internal Circuit Diagram of the Medicine Vending Machine

For an example, consider we are placing 5 different capsules in the vending machine & here are the basic procedures for accessing the medicines from the machine.

- ***Providing 5 different compartments for placing those 5 tablets and accessing code for it.***

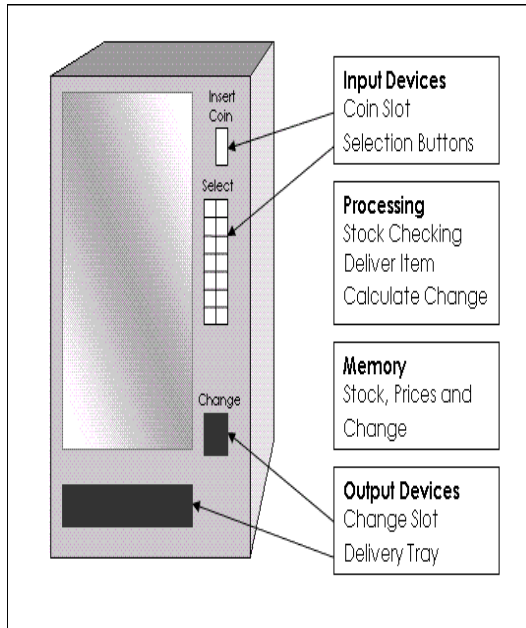
Name Of The Tablet	Access Code	Required No. Of Capsules
1.ASPIRIN	CAS 01	5
2.DISPIRIN	CDS 02	4
3.MONOPRATE	CMP 03	4
4.VASOTRATE	CVT 04	5
5.PALVITRATE	CPT 05	3

MEDICINE VENDING MACHINE



Procedure to Withdraw the Capsules from the Machine

- Swiping the medical smart card in the magnetic strip reader to access our individual account and also to pay the consultant fee.
- Entering the pass code to login to our medical profile.
- Entering the capsule code and required no. of capsules prescribed by the doctor.
- Collect the capsules from the delivery tray.



Schematic View of the Medical Vending Machine



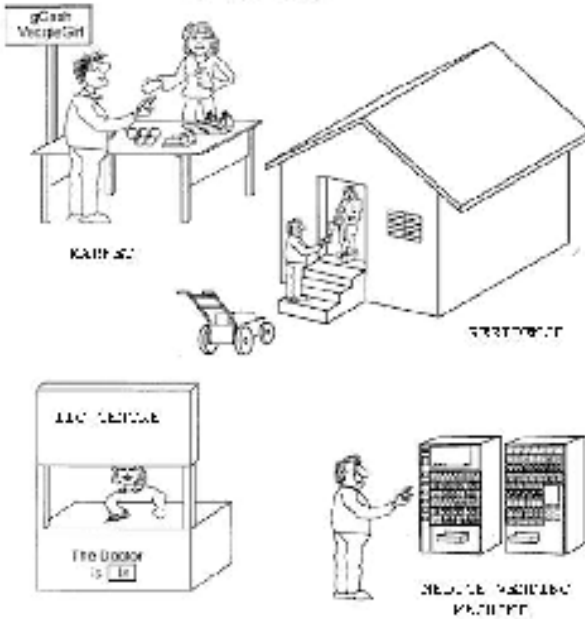
Medicine Vending Machine

Like all other places such as hospital, shopping malls, restaurants, etc., TELE-MEDICINE INFO CENTER should be a major component in our present scenario.

Advantages of TIC

- It's a patient friendly organization.
- It can provide high quality health care from highly qualified medical professionals.
- It can render the best diagnosis & treatment with ultimately low cost.
- It can provide good job opportunities for the doctors & also for the students proceeding for higher studies in their respective departments.
- Medicine vending machine can provide the quality medicines as prescribed by the doctors.

IMAGINARY VIEW OF A TIC CENTRE
IN THE TOWN



Conclusion

Hence the tale-medicine technology along with tale-medicine information center & medicine vending machine can render the high quality health care in the society and to be a major component in the future world.

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Contribution of the Earlier Ortheses in the Obstetrical Brachial Plexus Palsy Management

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Abstract

Obstetrical birth plexus palsy medical condition has been reported to be 1-2% worldwide according to the World Health Organization data with an increased occurrence in under developing countries. The study aims to build an efficient recovery process for children affected by this medical condition and also to support the parents whose children are affected. The sample size was done on 60 children with obstetrical brachial plexus palsy. Confidence level: $P= 95\%$, maximum sampling error: $\pm 6.4\%$. As methods and data collections we used :document analyses and individual semi-structured interview with children's parents.

Of the 60 children we made 2 groups of patients aged between 0 and more than 2 years (maximum age was 5) sample showing the following characteristics: affection, age, sex.

Results: A small amount of patients (treated using plaster cast) from the first group had a favorable evolution (< 5%) as compared to 55% of patients (treated with plaster orthoses) included in group number

To support our study we used Man Whitney U test. 2. The study clearly confirmed the superiority of plaster orthoses treatments over plaster cast treatments in obstetrical brachial plexus palsy on the affected patients from our centre. The study also showed that the recovery periods are a function of the treatment type and patient's age and time until beginning of treatment.

Keywords: Obstetrical brachial plexus, orthoses

Introduction

According to the J Mallet, obstetrical birth plexus palsy (OBPP) hides under their simplicity a syndrome of a particular complexity and gravity.

OBPP refers to injury of the brachial plexus (complete or partial) at the time of delivery. It is described as Erb palsy when referring to the paralysis of the upper plexus C5-C6 or C7, Klumpke palsy when C8-T1 root are affected and Duchenne palsy when there is a complete damage of the plexus. Clinical representation of OBPP was first described in 1764 by Smellie. In 1872 Duchenne described 4 types of complete paralysis of the brachial plexus, identifying an obstetrical paralysis and not a congenital one. In 1874 Erb defines the lesion which involves the upper roots and trunks of the brachial plexus (C5- C6), and in 1885, Klumpke illustrates paralysis of the lower branches of the plexus. The last author he also recognised the importance of the Horner syndrome which is rarely seen in OBPP (Gilbert 1995). Starting from

clinic description concerning OBPP performed by Smellie in 1974, most authors classify and illustrate them as:

1. Upper plexus palsy (Erb- Duchenne/ upper plexopathy) characterized by abduction, lateral rotation of the arm, L-bow flexion, paralysis of supinators muscles which are innervated by the C5-C6 roots.
2. Lower plexus palsy (Klumpke): in which the paralysis affects the muscles of the forearm and hand
3. Total palsy: this is the most severe and presents complete atonia of the arm, with the children often ignoring the arm.

According to A.Nehme et al. (2002/ p. 9-12) it was concluded that damaging the upper roots (C5- C6) is present in 50% of the cases, 25% when it associates the C7 root. The total brachial plexus obstetrical palsy was identified in 25% of the cases.

The same idea is supported by Bjørn Backe et al. (2008, p.1027-1032), considering that OBPP is “the most frequent injury to the newborns, and one of the most compensation claim”.

The most common form of palsy in National Children' Neuro-psycho- motorial rehabilitation medical Centre "Dr. Nicolae Robanescu" for children committed between 2006- 2008 was Erb – Duchenne palsy.

Different study reported that the functional outcome and the duration of spontaneous recovery depended on the type of nerve damaged and the number of injured nerve roots.

Seddon (1943) classified the type of injuries according to the damage of the nerve fibres:

A first degree injury is an oedema (neurapraxia) in the peripheral nerve. The function of the nerves fibres is temporary blocked but returns within a couple of weeks. A second degree injury is axonotmesis which results from a severe trauma or compression of the nerve. In this form of injury some nerves are disrupted (the axon) but the myelin remain intact, in this case the functions returns in few months. In a severe case there is a total disruption of the nerve fibres or root are pulled out of the spinal cord (avulsion). In this case

the recovery process is more complex and it may request surgical reconstruction (involving neurectomy, nerve grafting and/or nerve transfer), a physical programme being also dependent on the type and number of nerves affected.

Considering the patients involved in the study the most frequent paralysis is Duchenne-Erb palsy, 98% of the children who were hospitalised at the National Children' Neuropsychomotorial rehabilitation medical Centre "Dr. Nicolae Robanescu" were identified being affected by it. Factors associated with OBPP are: macrosomia, shoulder dystocia, breech delivery. (Perlow et al. 1996, p. 754-760; Cristofferson et al. 2002, 42-47; Ecker et al. 1997, 643-647). Other associated factors can be: weight gain during pregnancy, maternal disease among mothers, mode of delivery and multiparous mothers who previously had large babies.

Throughout this study we will try to validate the hypothesis that the positioning of the paralyzed upper limb with orthoses is not just necessary but more efficiently than plaster cast treatment and an increasing number of patients is using in the last period, ensuring a proper environment for recovering process.

Methods

We analyzed a sample of 60 children of the 150 children diagnosed with upper obstetrical brachial plexus injuries (Erb's Duchenne, roots C5-C6) committed at the National Children' Neuropsychomotorial rehabilitation medical Centre "Dr. Nicolae Robanescu" in the period of August 2006-August 2008.

Of the 60 children we made 2 groups of patients aged between 0 and more than 2 years (maximum age was 5) sample showing the following characteristics: affection, age, sex (Table 1, 2, and 3).

Table 1: the repartition of the patients

	Gender	Age <1	Age 1-2	Age >2(2-5 years)	Treatment
Group I	M	5			Plaster cast
	F	8			
Group II	M	20	3	3	Ortheses
	F	13	6	2	

The recovering programs were performed on all patients (40 boys and 20 girls) diagnosed with OBPP.

Most of the patients were not able to move their upper limb away from the body, it being inert, flask, with the arm in an adduction position and medial rotated, pronated forearm, fist in flexion, fingers 2 to 5 flexed in the palm, covering the thumb. The supinators motility was impossible to notice. The osteotendinous reflexes dependant on the C5-C6 neuromeres (bicipital), C6 (stilo radial) were abolished. The startle reflex observed in normal infants from birth through the first few months, consisting of abduction and extension of all extremities, followed by flexion and abduction of the extremities was asymmetric, minimized, or even lacking. Other patients presented different attitudes determined by articular rigidity and muscular retraction, or by the long time immobilization in plaster cast.

The patients' age at the moment of the first evaluation was between 1-3 months (13 patients), 1 year (14 patients), 1-2 years (15 patients) and over 2 years (18 patients). Some of them also needed to work for deviations of the vertebral column. The majority of the mothers mentioned that the children were overweight at birth (all patients weighted over 4 kilograms at birth), 5 of them needed forceps extraction and 2 needed brutal manoeuvres from the medical staff that oversaw the birth. In order to evaluate the motor dysfunction the clinical examination was used, which included muscular testing, muscular tonus evaluation and, in older children, a radiology exam of the shoulder and upper extremity. X-ray was performed to the shoulder and upper extremity in order to

exclude bone affections (fractures, sprains, humeral epiphysis detachment) which create the clinical aspect of pseudo paralysis.

The treatment and prognostic for the recovery took into consideration the type and number of the affected nerves.

The 1st group was composed of 13 patients who had plaster cast on upper limb for six weeks in which they didn't have any rehabilitation program. The 2nd group was formed of 47 patients treated using plaster orthoses made in the recovery centre by the prosthesis- orthoses department. All patients were treated in the hospital for periods of 2 weeks. After the treatment period would lapse patients were released for 2-3 weeks, followed by another 2 weeks of treatment in the hospital. The treatment consisted of 2 kineto- therapy sessions (one in the morning and another one in the afternoon), electro-therapy, ergot- therapy, and massage (only for patients older than 1).

The medical team considered essential to respect the following objectives in performing the kineto-therapy program:

1. Preventing articular rigidity and dysfunctional positions.
2. Stimulating the tonus of the paralyzed musculature.
3. Maintaining the tonus of the normal musculature.
4. Preventing and treating vasculotropic forms.
5. Re-education of re-innervated musculature
6. Gaining functionality and ability for the upper limb

Table 2: Patients included in group 1

No. of patients	Gender	Initial outcome (Mallet scale units)	Final outcome Mallet scale units)
8	B	2	2(6 children)
			3(2 children)
4	F	2	2 children
1	F	3	3 children

Table 3: Patients included in group number 2

No. of patients	Gender	Initial outcome (Mallet Scale units)	Final outcome (Mallet Scale units)
23	B	2	2(1children)
			3(13 children)
			4(9 children)
14	F	2	2 (1 child)
			3 (10 children)
			4 (3 children)
9	B	3	4 children
1	F	3	4 children

1. In order to prevent articular ailment and dysfunctional position the medical team used passive analytical movements of the affected joints and also focused on the parents' education regarding the positioning of the paralyzed upper limb in the ortheses and the rules that have to be respected (correct, rhythmic mobilizations).



Figure 1: Types of ortheses

A very important aspect of the recovery program was adapting the ortheses at the moment of recovery and to the anatomic situation of the paralyzed limb.

Four types of ortheses were manufactured at the Recovering Centre (presented in figure 1) which were used and adapted according to patients' needs. In older patients, who presented relatively structured sequelae, the treatment was completed by

corrective methods and even a corset was used in order to correct secondary scoliosis.

2. To stimulate the muscular tonus we used mild tractions, passive mobilization of all the affected upper limb's segments. This objective wants to improve the function of the paralyzed deltoid, biceps, brachial, brahioradial, brachial triceps, external rotators and supinators.

A major feature during the rehabilitation process was determined by active mobilization of the ipsiolateral upper limb, knowing the positive effect that this has in activating the symmetric musculature.

3. To maintain the tonus of the normal musculature, when necessary, we used analytic resistance exercises as spontaneous games, mentioning that they are difficult to perform, depending especially on the child's age, its ability to understand and its disposition at that particular moment.

4. The prevention of vasculotropic phenomena was obtained by passive mobilisations and outside the Kinetotherapy sessions, by maintained antideclive postures with the help of the parents that were previously instructed.

5. The re-education of the re- innervated muscles continues to stimulate the paralysed musculature's tonus, which was one of our previous goals. We consider that is one of the most significant targets because it objectifies a positive evolution.

6. To gain functionality and ability of the upper limb, besides the recovery programs we performed, an important role is played by ergo therapists, who can focus mainly on hand re-education. In order to objectify the evolution the J. Mallet scale was used, which has three degrees, as it can be seen in the addendum.

The methods used were:

- Passive mobilisations
- Passive-active mobilisations
- Kabath method
- Active exercises
- Active movements with opposition

All these treatment options were performed in an analytic and progressive way, after we noticed the first active movements


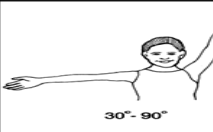













	II	III	IV
Active Abduction	 Less than 30°	 30°- 90°	 More than 90°
External rotation	 0°	 Less than 20°	 More than 20°
Hand to head	 Impossible	 Difficult	 Easy
Hand to back	 Impossible	 Difficult	 Easy
Hand to mouth	 Impossible	 Difficult	 Easy

Figure 2: Mallet Scale

The medical team applies the Mallet Scale (figure 2) based on voluntary upper extremity movements including active abduction, external rotation, hand to the back of neck, hand to back and hand to mouth.

Results

There were a total number of 60 patients during the period of August 2006 to August 2008 in the National Children' Neuro-psycho- motorial rehabilitation medical Centre "Dr. Nicolae Robanescu" the prevalence being of 40% of the committed cases during that period. A part of these children benefited of 2 commitments, others continued the treatment for a period of two years. Of the patients that abandoned the treatment after 2 commitments (9 patients) only 2 of them reached a global motor value higher with one level (on the Mallet Scale) than the global motor value they were diagnostified. The patients that continued the recovery programme longer than two commitments on the final evaluation we noticed the progressive evolution in some of them, as follows: 21 children reached level 4, 22 reached level 3, 8 children stagnated. Children from the first group had a favourable evolution in about 3% of the cases, as compared with the 2nd group where the values were higher by one degree in 55% of the cases; 2 degrees respectively in 18% of the cases, 5% patients stagnated. Both groups had a favourable evolution but by comparing the result of the two groups we saw a better progression in the last group (figure 3).

Of the committed children, 67% were boys and the rest were girls, noticing a higher incidence of obstetrical brachial plexus palsy in boy's births. Considering the age, we noticed that younger patients condition improved more compared to those that came to the doctor at ages older than 2.

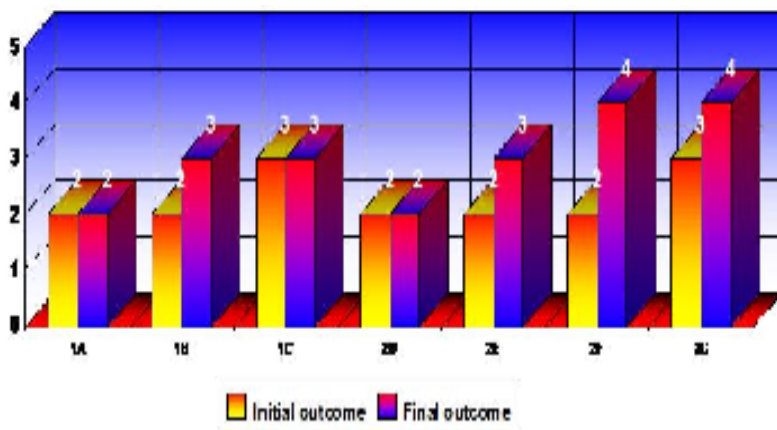


Figure3. Comparative study between patients included in group number 1 versus patients included in group 2

Group No. 1:

(Io= initial outcome; Fo = final outcome)

1A=10 patient with Io=2, Fo=2

1B=1 patient with Io =2, Fo =3

1C=2 patients with Io=3, Fo =3

Group No. 2:

(Io= initial outcome; Fo = final outcome)

2D=3 patients with Io=2, Fo =2

2E=23 patients with Io=2, Fo=3

2F=11 patients with Io=2, Fo =4

2G=10 patients with Io=3, Fo =4

To support the research hypothesis we applied a statistical test. Non-parametric Test: to test the hypothesis that positioning the paralyzed upper limb with orthoses is more efficient than using the plaster cast treatment, we used Mann-Whitney U test. The data used for comparison were the final outcome for which we made null and alternative hypotheses.

For comparison we used the final outcome.

Null hypothesis: among the two groups there was no difference between recovery of the paralyzed superior limb through the use of or theses and plaster cast.

Alternative hypothesis: there is a significant difference between the two groups of subjects investigated.

In the table below (Table 4) values of interest are the Z's and the level of trust p.

We noticed that the final global differ significantly between the two groups.

This value of interest was higher in those who used or theses on their paralysed upper limb (table 5), so we rejected the null hypothesis and accept the alternative hypothesis that there is a statistically significant difference between the two groups.

Table 4: Test Statistics (a)

	Final value
Mann-Whitney U	58,500
Wilcoxon W	149,500
Z	-4,763
Asymp. Sig. (2-tailed)	,000

a: Grouping Variable: group

Table 5: Ranks

		N	Mean Rank	Sum of Ranks
Final value	Group 1	13	11,50	149,50
	Group 2	47	35,76	1680,50
	Total	60		

The study is a explorative, we can not speak of a representative sample from a statistical viewpoint, which does not allow to generalize the data to the whole community.

Results are relevant from the perspective of a case study on recovery methods of children with obstetrical brachial plexus palsy.

Discussion

During the study we acknowledged the importance of motivating the patient and transferring a positive attitude towards using the orthotic device as part of the treatment. The

discussions with parents were mandatory in order to make them understand the importance of the orthoses in the recovering process. We thought it was indispensable that the medical attitude of the staff must take into consideration the following parameters as: the clinical form of the paralysis, the moment of presentation to the doctor, the education and socio-material conditions. With this in mind we must work closely with the patient and we must ensure that he will accept the orthoses and will use it accordingly. This is due to the fact that some devices need a training period to teach the patient how to use them correctly and to avoid the discomfort sensations that may appear.

Certain studies showed that the recovery in OBPP had positive results; with 34 recoveries out of the 35 cases. Very good results were noticed at patients suffering from Erb-Duchenne OBPP. Also we noticed that patients whose biceps did not recover until the age of 6 months had had also a good prognostic without the need for surgical intervention. This finding is backed up by literature (A. Nehme et al. , 2002).

In this sense the initiation of a correct treatment is essential to help in the nervous recovery and preventing vicious attitudes, leaving the surgical treatment to resolve small sequelae.

Some authors as Y. Gerard, P. Petit recommend the importance of using unmovable splinters between mobilizations.

If around the 1950s the English recommended surgical exploration of the brachial plexus and suture of broken elements, Tassin (1983) also suggested surgical intervention when biceps contraction is not reached by the age of 3 months, today the majority of specialists recommends physio-kineto-therapeutic treatment in the initial period when the sequelae did not appear.

Conclusions

Following our study, the immobilization of the upper limb in a plaster cast of abduction-rotation led to unsatisfactory results that were difficult to correct in time, patients having rigidity,

vascular irregularities and in certain situations articulation destruction. Patients that used plaster cast were unhappy with the results (84%), and stopped using it. I would like to mention that patients in Group 1 were children from the early stage of the study. Starting kinetic treatment and corresponding positions for children under 1.5 years led to favorable results.

Acknowledgement

The authors would like to thank the medical staff at the National Children' Neuro- psycho- motorial rehabilitation medical Centre "Dr. Nicolae Robanescu", for all the help during this study and all the parents and patients for accepting to participate in the study.

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Hearing Aid Implementation through Teeth

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Abstract

The idea of this paper is to “use teeth for transmitting sound waves to brain” as teeth have special property of transmitting signals to brain. At present commercially available hearing aids merely amplify the voice signals and propagate them through the auditory canal functioning as a tympanum. Even though this relative functioning might be an alter for tympanum, the temporarily implanted devices are vulnerable to lose coherence with the auditory canal henceforth causing loss of information or even blind signals which disproves its worth. Else while going for permanent implant techniques, it involves surgical operations in organs that are delicate but performing vital functions would be put into risk. The main purpose of a hearing aid is to make a deaf person hear. But the device should also ensure safety for the biological parts of the body.

This paper aims to overcome the above problems by using a hearing aid which will be placed in the deaf person’s tooth. It uses nerve edge (synapses) for sending information from the device to brain using nerve impulses. We use two devices for this purpose i.e. micro speaker as the output device that sends

the signals to the brain and input device is a Microphone which captures the voice signal.

Microphone will be placed as a collar mike to the patient. The transmission between the input and the output is through radio waves. The output circuit is a normal radio receiver circuit along with a vibrator which will be prepared in a micro scale so as to be placed on the tooth. The output of the device is normal voice signal and is converted into nerve impulses by the process of synapses. The person experiences a virtual voice of the speaker and responds to the virtual voice signals. Even in the presence of the noises in the environment the hearing aid would transmit the same to the brain and the deaf person would hear it the same way as a normal person would hear.

Keywords: Tympanum, hearing aid, teeth

Some disadvantages of the existing hearing aids are as follows:

- limited hearing assistance in high frequency range
- ear-molds and acoustic feedback may be annoying and aggravating
- loud noises may be bothersome
- hearing aids for those with severe loss need to be fitted carefully and well monitored, due to noise problems in certain locations
- hearing aids will not restore hearing loss, sometimes only providing limited amount of hearing amplification
- can't swim, shower, or sleep with hearing aids in, because the aid can get damaged or break
- Hearing aids for those with severe loss need to be fitted carefully, assertively, and well-monitored; securing the appropriate audiologist to accomplish aided thresholds that provide ease in "access to conversational sound" may be difficult in some locations

These are the disadvantages to cochlear implants:

- surgical issues, such as vertigo, staph infection, tinnitus
- if have inadequate insurance, surgery can be very expensive
- have to wear body processor in which implant is attached
- long term effects are unknown because it is a relatively new surgery
- if implant is rejected by body or doesn't work for individual, the cochlear is permanently damaged and all hearing capabilities are lost
- programming issues
- low frequency consonant discrimination for placement cues may be more difficult

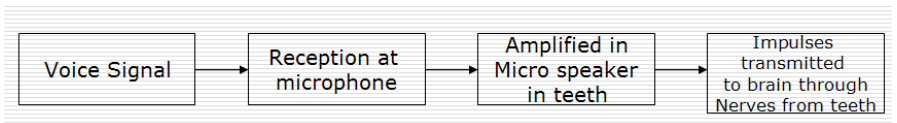
These disadvantages are hard to be rectified and also irreparable. It makes a need to invent a better solution for solving the problems faced by deaf persons. Hence is this paper formulated to drive away the difficulties of people.

Introduction

The idea is to bring a simple, safe and efficient way of amplifying and transmitting sound waves to the brain from a micro speaker implanted in the patient's teeth. It operates as a radio frequency transmitter-receiver device. The voice signal received is modulated as a radio frequency wave and transmitted to the brain as nerve impulses.

This is carried out in various stages. It follows the sequence as shown below...

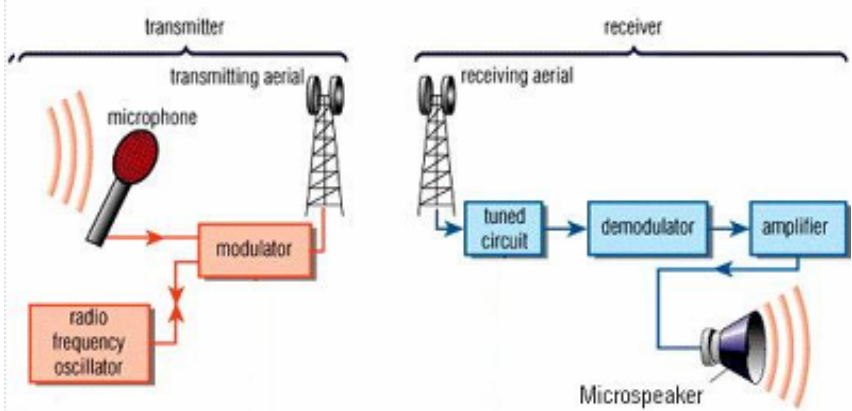
Sequence



- A microphone is used to receive the voice signals.

- The received signals will be transmitted at the same intensity level or the pitch of the voice.
- It is amplified and transmitted to the micro speaker which is attached to the teeth.
- The transmission between the microphone and the speaker is through radio waves.
- The sound waves are coupled with the nerves connecting the teeth and brain.
- This coupling sends the voice signals to the brain directly so that the person experiences a virtual voice of the speaker.
- The receiver responds to the virtual voice signals.

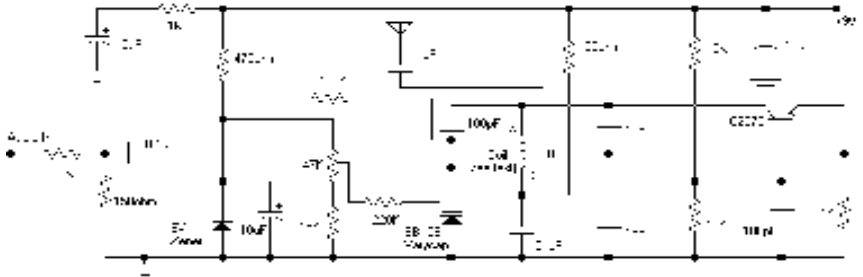
Reception of Signals



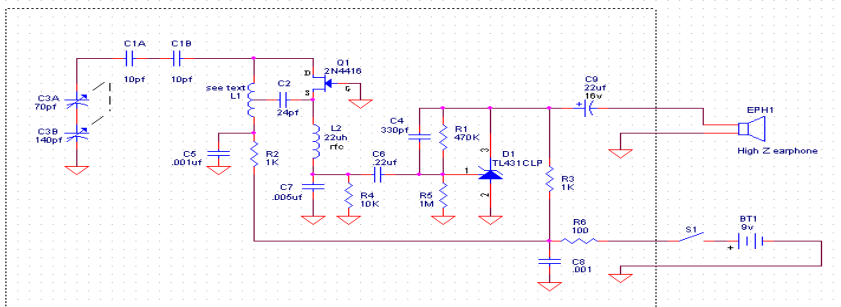
The voice signal from the speaker is received by micro phone and this signal is converted into radio waves and with the help of transmitting aerial the radio waves is transmitted. The micro phone is installed as a collar mike to the patient. This arrangement is made to enable the person receive signals clearly. The received signal is converted in radio frequency in the modulating circuit. These radio frequency waves are transmitted to the receiver circuit which is placed in teeth. This radio signal is then converted into impulses and the output of speaker is voice signal. This voice signal is coupled with the

nerves and hence transmitted to the brain. As radio waves pass through the skin easily and not harmful, the method is **safe**. Ordinary RF circuitry is cheaper when compared to other modulating transmitters hence the method is **simple**. The operational losses in this small circuit is negligible hence an **efficient** method.

FM Transmitter Circuit



FM Receiver Circuit



As the circuit shown, the transmitter circuit is prepared on normal scale which will be placed outside the deaf person. But the receiver circuit will be prepared in micro scale which will be placed in teeth portion which is described below.

Implanting Microspeaker



Micro speaker is placed on the tooth like a clip.

Here the possible question that can arise is that, can it can resist the pressure that occurs during chewing and with water. This is overcome by coating the micro speaker with a ceramic membrane.

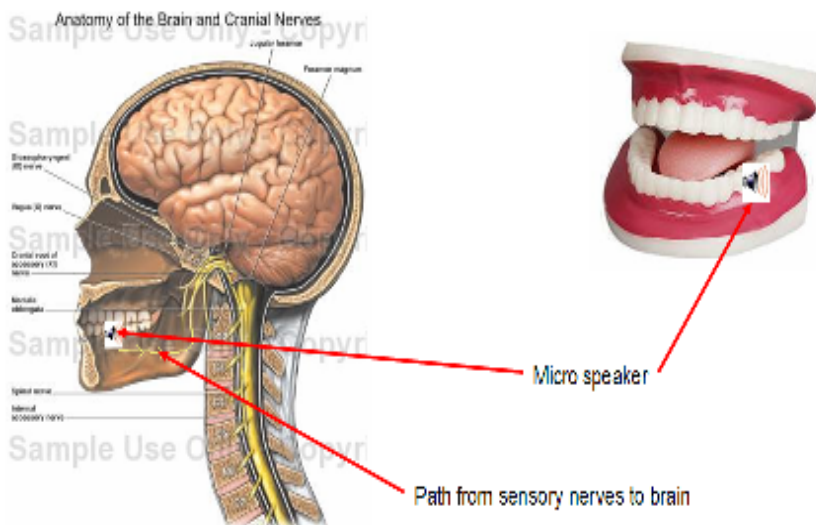
Ceramic membranes are made from inorganic materials (such as alumina, titania, zirconia oxides or some glassy materials) and they are used in membrane operations. They also have excellent thermal stability which makes them usable in high temperature membrane operations.

Along with the micro speaker a **Vibrator** is fixed to the tooth. The vibrator is a piezoelectric crystal which gives mechanical vibrations when electric impulses are applied to it. The intensity of the vibration varies with the electric signal applied which in turn depends on the intensity of the speech signal. It is an essential part of the synapses process.

Micro speaker's circuit is highly compact as it is made in a micro scale i.e. preparing the receiver circuit in a micro scale so as to increase component density and reduce area of implantation. So it is very small compared to tooth and is a highly sensitive receiver.

The voice signal coming out of the speaker is proportional to the input to microphone. This gives the difference in loudness of speaker to the receiving person.

Transmission from Teeth to Brain



The output of speaker is virtual voice signal. This signal is then converted into nerve impulses by edge nerves. This conversion is due to the process called synapses and the impulses produced is transmitted to brain through nervous system. Neurons conduction takes place due the presence of Potassium and Sodium. As the signal reaches brain the receiver responds to the virtual voice signal. It takes only micro seconds to reach brain.

As normal hearing aid has direct affect on human brain it does not do so because it does not have direct contact with brain and only the nerve impulse reaches brain.

Nerves

The nerves act like telephone lines. They receive messages for the brain and transmit the messages from the brain, through the nerve lines, to the correct destination. Minerals play an important role in the transmission of impulses between the nerves and the muscles. They act in nerve responses, muscle contractions, regulating electrolyte balance, and the making of hormones.

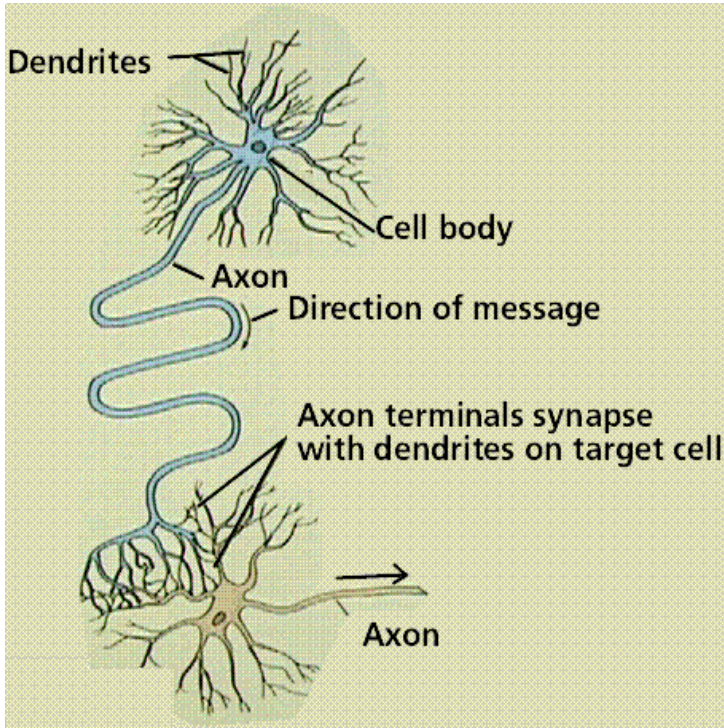
Edge Nerves is a very specific formula composed of calcium and magnesium.

How do neurons conduct impulses?

Neurons maintain different concentrations of certain ions across their cell membranes. Imagine a boat with a small leak below the water line. In order to keep the boat afloat, the small amount of water entering through the leak has to be pumped out, which maintains a lower water level relative to the open sea.

Likewise neurons pump out positively charged sodium ions and pump in positively charged potassium ions. A high concentration of sodium ions is present outside the neuron and potassium ions inside. The neuronal membrane contains specialised proteins called channels, which form pores in the membrane that are selectively permeable. Sodium channels allow sodium ions through the membrane while potassium channels allow potassium ions.

Nerve structure



Neuron communication with each other

It is achieved through synaptic transmission. Neurons communicate at structures called synapses in a process called synaptic transmission. The synapse consists of the two neurons, one of which is sending information to the other. The sending neuron is known as the pre-synaptic neuron (i.e. before the synapse) while the receiving neuron is known as the post-synaptic neuron (i.e. after the synapse).

Neuron communication with each other very fast as we know in micro seconds.

Due to the continuous synapses process a human can act accordingly.

Design specifications used

The design used here is a normal FM transmitting and receiving circuit having the specifications as shown in circuit. This is prepared in micro scale so as to be implemented in teeth.

Resistors

R1 - 22K R2 - 100K R3, R7, R9 - 1K R4, R8 - 100E R5 - 390E R6 - 330E R10 - 15E R11 - 10K

Capacitors

C1, C3, C10 - 1n C2 - 100n C4, C8, C9 - 47pF C5, C11 - 10pF C6 - 100uF/25V Electrolytic C7 - 100pF C12 - 3pF

Transistors

Q1, Q2, Q3 - BC548

Q4 - PN2369 (Plastic casing) or 2N2369 (Metal casing)

MISC.

L3 - 7 turns, 22SWG wire, 3mm ID, Close wound, Air core.

Two hole binocular BALUN core, BALUN wire, 300 ohms

TV feeder wire, JP1 to JP5 - All jumper wires.

SUMMARY

Here as explained above the voice signal is received by micro phone and the micro phone converts voice signal into radio wave. This signal is then transmitted through transmitting aerial.

Signal is received by micro speaker which is placed in teeth and converts radio waves to voice signal and the output of speaker will be voice signal.

This signal is then converted into nerve impulses by edge nerves.

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- Sound waves directly coupled with nerves hence less disturbances
- Radio waves have little effect on human compared to normal hearing aid effect.
- High hearing assistance in high frequency range
- loud noises does not affect much
- This will be giving high efficiency
- Greater ease in high frequency consonant perception
- Distance hearing is likely better than with normal hearing aids
- Greater flexibility & accessibility for repairs

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Wound Healing Activity of *Solanum Torvum* Aqueous Fruit Extract in Rats

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Abstract

The effects of topical application of *S. torvum* fruit extract on the rate of excision wound healing and histology of healed wound were assessed. All four groups of six adult male Sprague Dawley rats each were experimentally wounded in the posterior neck area. A thin layer of blank placebo was applied topically to wounds of Group 1 rats. The wounds of Group 2 and 3 were dressed with placebo containing 5% and 10% *S. torvum* extract, respectively. A thin layer of Intrasite gel was applied topically to wounds of Group 4 animals as reference. Macroscopically, wound dressed with placebo containing 5% and 10% *S. torvum* extract each or Intrasite gel significantly accelerate the rate of wound healing compared to wounds dressed with blank placebo. Histological analysis of healed

wounds confirmed the results. Wounds dresses with placebo containing 5%, 10% *S. torvum* or Intrasite gel showed markedly less scar width at wound enclosure and granulating tissue contained markedly more collagen, proliferating fibroblast with angiogenesis, and no inflammatory cells compared to wounds dressed with blank placebo. In conclusion, placebo containing 5% or 10% *S. torvum* extract-dressed wounds significantly accelerates the rate of wound healing in rats.

Keywords: *S. torvum*, wound healing, histology

Introduction

S. torvum is a small shrub of the Solanaceae family, distributed widely in India, Malaysia, China, Philippines and tropical America. In Malaysia, the seedful fruit is rarely used as a vegetable. The fruits are used for cough ailment, liver and spleen enlargement (Siemonsma and Piluek, 1994). The ripened fruits also useful in the preparation of tonic, haemopoietic agents and treatment of pain (Kala, 2005:11). Phytochemical screening of methanolic extract of sundried *S. torvum* fruits give positive test for alkaloids, flavonoids, saponins, tannins and glycosides (Chah, 2000:2). Antiviral isoflavonoid sulfate and steroidal glycosides were also isolated from the fruits of *S. torvum* (Arthan, 2002:4). Others finding found that the fruit consists of saponin, steroid, chlorogenin, steroidal alkaloids, tannins, saponins, chlorogenone, neochlorogenone and beta-glucosidase (torvosidase) (Mahmood, 1985:24, Carabot Cuervo, 1991:30, Badola, 1993:12, Arthan, 2002:4), which have shown interesting biological activities such as antimicrobial activity (Chah, 2000;2, Wiart, 2004:75) and significantly enhance secretory immunity in the intestine (Israf, 2004:4). Others reported that the extract are useful in the treatment of hyperactivity (Null, 2001), colds and cough (CPR Environmental Education Centre 2001), pimples, skin diseases, and leprosy (Liogier 1990). There is no data available regarding wound healing activity of *S. torvum* fruit extracts. The present

study was undertaken to evaluate the rate of wound healing properties of *S. torvum* extract experimental rats macroscopically and microscopically.

Materials and Methods

Vaseline (100% pure petroleum jelly)

Vaseline is a brand of petroleum jelly originally produced by Chesebrough-Pond's, USA, and currently by Unilever. Vaseline is obtained from the local pharmacy.

Intrasite gel

Intrasite gel was purchased from University Malaya Medical Center Pharmacy. Intrasite gel, is an amorphous hydrogel which gently re-hydrates necrotic tissue, facilitate autolytic debridement, while being able to loosen and absorb slough and exudates, cleaning the way for effective wound healing. It is also designed for wounds that are granulating and epithelialising. It can also be used to provide the optimum moist wound management environment during the later stages of wound closure. It is non-adherent and does not harm viable tissue or the skin surrounding the wound. (Intrasite gel is a trademark for Smith and Nephew Ltd) (Williams, 1994 : 3).

Lignocaine HCl (2%, 100 mg/5 ml)

The local anesthesia drug was obtained from Experimental Animal House, Faculty of Medicine, University Malaya. 1 ml of Lignocaine was injected via subcutaneous (Delta Veterinary Laboratory PTY LTD, NSW 2011).

Plant specimen and preparation of extraction

Fresh *S. torvum* fruit were collected from Kelantan state and identified by comparison with the voucher specimen deposited at the Herbarium of Rimba Ilmu, Institute of Science Biology, University of Malaya, Kuala Lumpur. The fruits were washed with distilled water, sliced and then dried in incubator at 50°C for 5-7 days .The dried samples were grounded into powder using a Wiley mill (40-60 mesh) and then successively extracted

with water by adding 400 g of crude extract to 8,000 ml of sterile distilled water (1:20) in a conical flask which was heated on a hotplate (80°C) for 3 hours with constant stirring. The residue was subsequently removed by filtration using a filter funnel and filter paper. The extract was freeze-dried and the extract was mixed homogeneously with Blank Vaseline in a concentration of 5% and 10% (w/w) each.

Experimental animals

Sprague Dawley adult male rats were obtained from the Animal House, Faculty of Medicine, University of Malaya (Ethic No. PM 28/09/2006 MAA (R)). The rats were divided randomly into four groups of six rats each. Each rat that weighted between 180 - 200 g was housed separately (one rat per cage). The animals were maintained on standard pellet diet and tap water.

Experimentally induced wounds

The animals were anesthetized by diethyl ether. The rats' fur shaved by electrical shaver, disinfected with 70% alcohol and injected with 1 ml of Lignocaine HCl (2%, 100 mg/5 ml). An area of uniform wound 1.8 cm in diameter was excised from the nape of the dorsal neck of all rats with the aid of round seal as described by Morton & Melone (1972) with few modifications (Figure 1). The incision of the muscle layer was avoided and tension of skin was kept constant during the procedure.

Topical application of vehicles

Wounds of Group 1 rats were treated topically with a thin layer of blank Vaseline twice daily. A thin layer of 5% and 10% *S. torvum* extracts in placebo were applied topically twice daily to the wound of Groups 2 and 3 respectively. The wounds of Group 4 rats were dressed with thin layer of Intrasite gel twice daily. The wound was observed daily until complete wound-healing enclosure occurs.

Histological evaluation of healed wounds

The skin specimen from wounds healed areas were fixed in 10% buffered formalin and processed by paraffin tissue processing machine. The healed skin was assessed by taking a 5 μm section, stained with hematoxylin and eosin.

Statistical analysis

All values are reported as mean \pm S.E.M. and the statistical significance of differences among groups were assessed using one-way ANOVA. A value of $p < 0.05$ was considered significant.

Results

Wound healing activity

Grossly, wounds dressed with 5% and 10% *S. torvum* extracts each or with Intrasite gel showed considerable signs of dermal healing and significantly ($p < 0.05$) healed earlier compared to wounds dressed with blank placebo (Table 1; Figures 2 and 3). There were no significant differences between wounds dressed with 5%, 10% *S. torvum* extract or Intrasite gel in the term of rate of wound healing (Table 1). Histologically, wound dressed with *S. torvum* extracts or Intrasite gel showed markedly less scar at wound enclosure (Figures 4 and 5) and granulation tissue contained more collagen fibers, fibroblast and proliferating blood capillaries, and absence of inflammatory cells compared to wounds dressed with blank placebo which contained less collagen fiber, fibroblast and blood capillaries, and more inflammatory cells (Figures 6 and 7).

Table- 1: Time required for wound healing by *S. torvum* in rats.

Animal groups	No of animals	Type of dressings	Healing time (days) (Mean \pm S.E.M)
Group 1	6	Blank Vaseline	19.83 \pm 0.48 ^a
Group 2	6	Vaseline containing 5% <i>S. torvum</i>	14.50 \pm 0.43 ^b
Group 3	6	Vaseline containing 10% <i>S.torvum</i>	13.83 \pm 0.31 ^b
Group 4	6	Intrasite gel	13.33 \pm 0.42 ^b

All values were expressed as mean and \pm standard error mean. Mean with different superscripts were significantly different ($P<0.05$)

Figure 1: 1.8 cm diameter excision wound on day 0 before application of vehicle

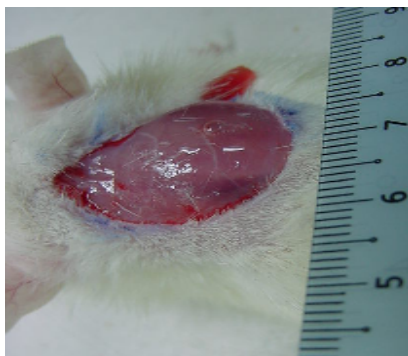


Figure 2: Wound healing dressed with Vaseline containing 10% *S. torvum* extract on day 13.



Figure 3: Wound healing dressed with blank Vaseline on day 19.



Figure 4: Histological section of healed wound dressed with Vaseline containing 10% *S. torvum* showing narrow scar at the wound closure (H & E stain x20).

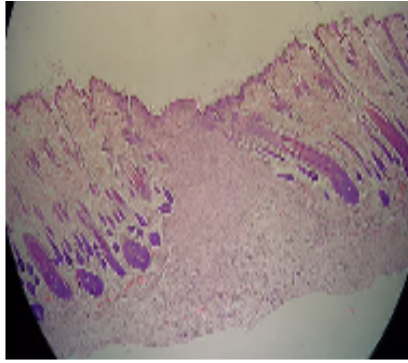


Figure 5: Histological section of wound healing dressed with blank Vaseline, showing wide scar at the wound closure (H & E stain x20).

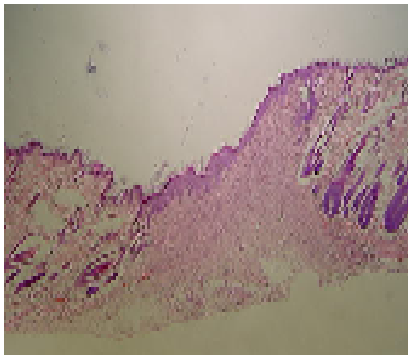


Figure 6: Histological section of healed wound dressed with Vaseline containing 10% *S. torvum* extract. Granulation tissue contains more collagen, fibroblast and blood capillaries, and absence of inflammatory cells (H & E stain x80).

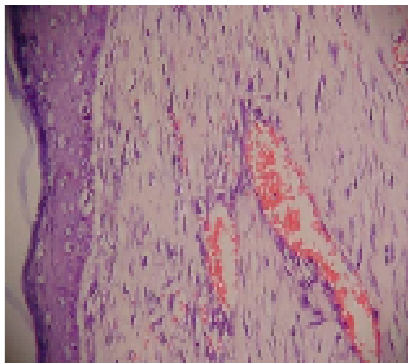
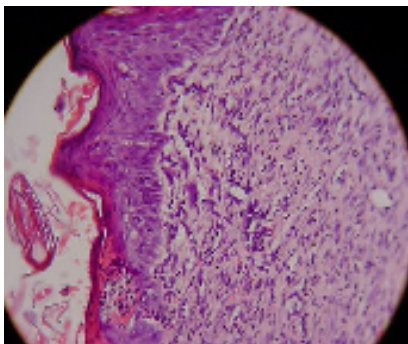


Figure 7: Histological section of healed wound dressed with blank Vaseline. Granulation tissue contains less collagen, fibroblast and blood capillaries, and more inflammatory cells (H & E stain x80).



Discussion

In the present study, topical application of *S. torvum* extract significantly enhanced the rate of wound healing, and granulation contain more collagen, fibroblast and blood capillaries, and no inflammatory cells. Wound healing effects may be due to up-regulation of human collagen I expression

(Bonte, 1993 : 60) and an increase in tensile strength of the wounds (Suguna, 1996 :34). Enhanced healing activity has been attributed to increased collagen formation and angiogenesis (Trabucchi, 1986 :8 and Shukla, 2007 :109). Collagen played a central role in the healing of wounds and it is a principal component of connective tissue and provides a structural framework for the regenerating tissue (Cohen, 1992). Angiogenesis in granulation tissues improves circulation to the wound site thus providing oxygen and nutrients essential for the healing process (Szabo, 1995 : 210) that include-re-epithelization. Stimulation of epithelial cell proliferation and angiogenesis are important for wound healing process (Buntrock, 1982 :21). Similarly, Habibipour (2003) showed that histological analysis of the treated healed wound group contained a large amount of fibroblast proliferation, collagen synthesis, and neovascularization, which resulted in an increased wound tensile strength and accelerated wound healing.

Topical applications of compounds contain antioxidant properties had been proven to significantly improve wound healing and protect tissues from oxidative damage (Martin, 1996: 22). Antioxidants play a vital role in inhibition of lipid peroxidation or by protecting against cellular damage by free radicals. Dietary antioxidants such as ascorbate, α -tocopherol and carotenoids from fruit and vegetables could help to protect cells from damage caused by oxidative stress and fortify the body's defense systems against degenerative diseases (Frei, 1991). The crude *S.torvum* seeds was found to be rich in protein, significant amounts of ascorbic acid, α -tocopherol and total sugars (Sivapriya, 2007:104). Vitamin A, C, E, zinc and amino acids (protein) are good nutrition for wound healing (Jan, 2002:1).Vitamin C is necessary for collagen synthesis (Alison, 2003).Two constituent of collagen; hydroproline and hydroxylysine formed when proline and lysine are hydroxylated by vitamin C (Philips,2000;6).Vitamin C also needed to form a bond between the strands in collagen fibers (Casey, 1998;3).Vitamin C also acts as antioxidant (Alison, 2003;6).

S. torvum fruit extracts have been shown to contain antioxidants (Sivapriya, 2007:104), alkaloids, flavonoids, saponins, tannins and glycosides (Chah, 2000:2) which may thereby mediate wound healing. The flavonoids are known to possess antioxidant activity. It could be conceivable that the *S. torvum* extract exert their wound healing activity through the flavonoids since flavonoids are reported to improve wound healing and protect tissues from oxidative damage (Saurez *et al.* 1996). Additionally, the fruit extract contains antiviral isoflavonoid sulfate and steroidal glycosides (Arthan, 2002:4), alkaloids, tannins and steroids, which exhibit pharmacological activities such as enhancement of the immune system, as well as antimicrobial activity (Ajaiyeoba, 1999:2 and Chah, 2000:2). The observed antimicrobial properties provide support to some of the traditional uses of *S. torvum* juice in ethnomedicine.

Conclusion

In conclusion, the current study revealed that wounds dressed with *S. torvum* extracts, as topical application of wounds significantly accelerate wound healing process and histologically, granulation tissue contained more collagen fiber, fibroblast with proliferating blood capillaries and absence of inflammatory cells.

Acknowledgement

This study was financially supported by the University of Malaya through a grant: 12-02-03-2051 Science Fund RMK-9 Cycle 1/2007.

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Preventing Automobile Accidents in Epilepsy Patients

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Abstract

Our Idea is based on the adults, who have sufferings from Epilepsy (a neurological disorder). Persons with epilepsy are not allowed to use either 2-wheelers or 4-wheelers because epileptic seizures may occur at any time. Patients get seizures due to many factors like tension, Pressure, flash lights, etc. Patients experience many things while driving in traffic. Patients are advised not to use 2 wheelers or 4wheelers to avoid accidents. Patients having 4wheelers are suggested to appoint drivers. These solutions won't be practical enough. A patient sometimes will be forced to use his vehicle. To prevent such problems, the patient is connected to an ambulatory EEG, which continuously records and transmits the EEG wave to the receiver via transmitter. When there is an occurrence of abnormal wave due to the epileptic seizure, the receiver which is connected to the Buzzer and the Mechanical Break system of the vehicle, senses it and automatically stops the vehicle, thus indicating the occurrence of seizures and prevention of accidents on main roads. Buzzer warns the travelers who are behind the patient.

Keywords: Epilepsy, Ambulatory EEG, RFSignal, Receiver

Introduction

Patients with epilepsy are not allowed to drive vehicles due to the untimely seizures that occur even without an indication. This has been a real challenge in the field of medicine. Epilepsy can be easily diagnosed through an EEG, which is recorded for 24 hours. EEG is said to be the best for Epilepsy diagnosis. Each state has individual driving regulations. Those with epilepsy are required to report their condition to the Department of Motor Vehicles (DMV). However, states differ regarding the identity of the person required to do the reporting. Some states require the physician to contact the DMV. Other states require the patient to sign a simple form at the time of application for a license or at the time of license renewal, declaring that they will notify the DMV of changes in their health status or driving ability. When a person with epilepsy wishes to drive for the first time, an application will need to be filled out. When someone who already holds a driver's license is newly diagnosed with epilepsy, that person is responsible to notify the proper authority. Individuals with uncontrolled seizures have a higher risk of an accident if they drive. That is why doctors advise patients with seizures that they should not drive until their seizures are under reasonable control. If a well-controlled patient has a seizure after the doctor changes the medication, the patient may or may not be able to continue driving. Seizures are unpredictable and even a small seizure at the wrong time can lead to an injury or death. The best solution, if possible, is to get the seizures under control. To do this, work together with your doctor to get on the right treatment and to honestly discuss your seizures with him or her.

Epilepsy

Epilepsy is a common chronic neurological disorder characterized by recurrent unprovoked seizures. These seizures are transient signs and/or symptoms of abnormal, excessive or

synchronous neuronal activity in the brain. About 50 million people worldwide have epilepsy at any one time. Epilepsy is usually controlled, but not cured, with medication, although surgery may be considered in difficult cases. However, over 30% of people with epilepsy do not have seizure control even with the best available medications. Not all epilepsy syndromes are lifelong – some forms are confined to particular stages of childhood. Epilepsy should not be understood as a single disorder, but rather as a group of syndromes with vastly divergent symptoms but all involving episodic abnormal electrical activity in the brain.

The human brain emits electrical signals whose detection gives knowledge about the proper functioning of the brain and the detection of abnormalities. This is done with the aid of the ELECTROENCEPHALOGRAM (EEG). The brain consists of a large number of nerve cells called neurons. Each neuron has a series of dendrites which receive signals from other neurons at what are known as synapses. The Nerve cells are interlinked via a large number of branching networks through which they communicate with each other. The cell 'processes' these incoming signals like a kind of biological microprocessor and transmits them via a special projection, called the axon, to the dendrites of other neurons. Generally the brain waves are the summation of neural depolarization in the brain due to stimuli from the senses. These electrical patterns obtained from the surface of the skull are the result of the graded potentials on the dendrites of the neurons in the cerebral cortex and other parts of the brain, as they are influenced by the firing of other neurons that impinge on these dendrites. When the transmission of the signals to the synapses is impaired, the communication between the cells fail and this leads to abnormalities like epilepsy that is characterized by seizures. When a seizure occur the body of the person becomes rigid and he/she immediately falls to the ground. The muscles then relax and tighten rhythmically causing the person to convulse. At the start of the Seizure the person may bite their tongue or cry out. Breathing becomes difficult and the person

chokes. The seizures may last for 2- 5 minutes or even more depending upon the amount of energy released. These seizures may sometime lead to death if immediate medical aid is not provided. Seizures are generally classified into Partial Seizures and Generalized Seizures. Further they are classified into as said earlier all these types of seizures causes either rhythmical twitching of one limb or part of a limb, or unusual tastes or sensations such as pins and needles in a specific part of the body, change in awareness as well as automatic movements such as fiddling with clothes or objects, mumbling or making chewing movements, or wandering about and general confusion. Under such circumstances the patient is under high risk of injuring himself.

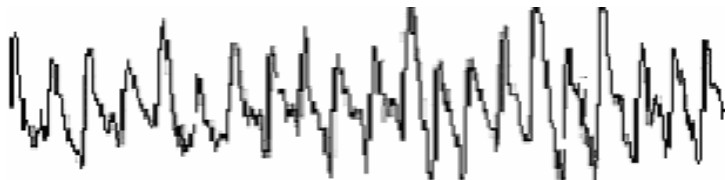


Figure 1

There are several types of seizure spikes that arise from the brain. These Spikes are known as the anterior temporal spikes, the frontal spikes and the rolandic sharp waves.

A New Device

To help the victims of seizure attack, there arises a need for a device, which the Patient can always carry with him while driving a Two-Wheeler. Though several portable health monitoring device for the cardiac patients had been developed, there is still no effective portable device for the monitoring the brain signals. This paper brings out the design of a device that would help the above purpose. During a seizure the brain releases large bursts of electrical energy.

On an EEG these bursts of energy appears as sharp waves or spikes. These spikes have very short time duration and arise mostly from the anterior temporal, frontal, or Centro temporal

regions of the brain. Thus taking the above fact into consideration, the device is designed with three electrodes positioned exactly in the above three regions. Since a real time monitoring of EEG signals is not required, the conventional 10-20 system of placing electrodes is not used as it makes the design of the cap complex with an increasing number of electrodes. Four electrodes placed in the above four regions is sufficient to detect the abnormal signals. The diagram below shows the areas where the electrodes are placed and also the seizure spikes.

Explanation of Device

Electrodes

In order to prevent accidents when seizures occur while driving, the patient is connected to the electrodes in the mentioned regions as showed in the figure.

The device consists of four electrodes which are linked to a comparator each. Electrode-1 is connected to comparator-1 and electrode-2, 3, 4 to Comparator-2, 3, 4 respectively.

Comparators

Reference values are pre-set in the comparator. These reference values are the normal waves which is non-epileptic. The output from the electrodes is received by the respective comparators, which compares the received signal with the pre-set values in each comparator. When the difference in the received signal and the pre-set signal is very large in any of the comparator, it sends a signal to the Multiplexer (MUX).

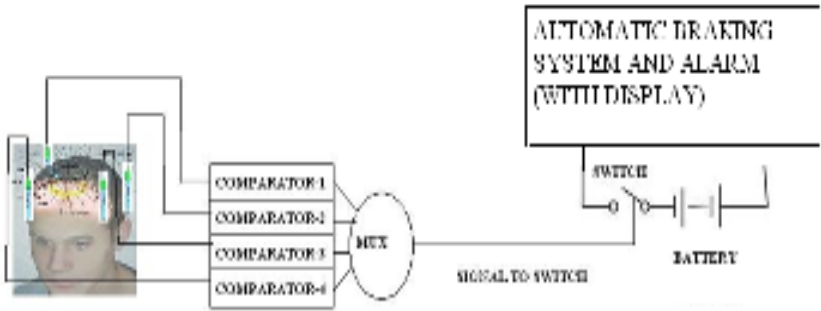


Figure .2

Multiplexer

It receives the signal from the comparators. When it receives input from even one of the comparator, the circuit gets closed in the battery.

Making a Vehicle Stop

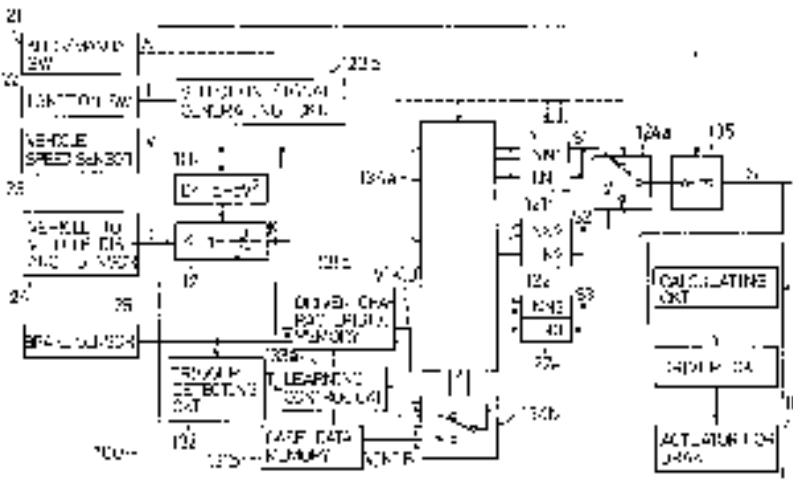


Figure 3

An automatic braking system brakes a driving vehicle according to a target brake control amount calculated by a neural network. The system detects the vehicle speed of the driving vehicle and detects the actual distance between the driving vehicle and the vehicle ahead of it.

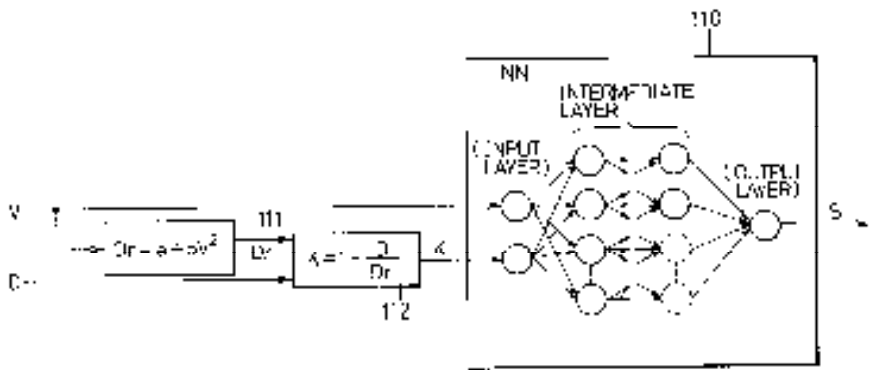


Figure 4

Figure 4 is a block diagram showing a function for normalizing a vehicle to vehicle distance in an automatic brake control system according to present invention.

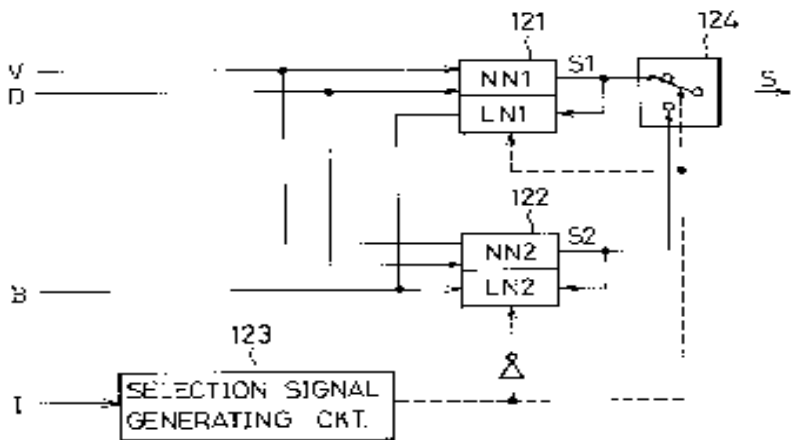


Figure 5

Figure 5 is a block diagram showing a function for simultaneously executing a control and learning in an automatic brake control system according to the present invention.

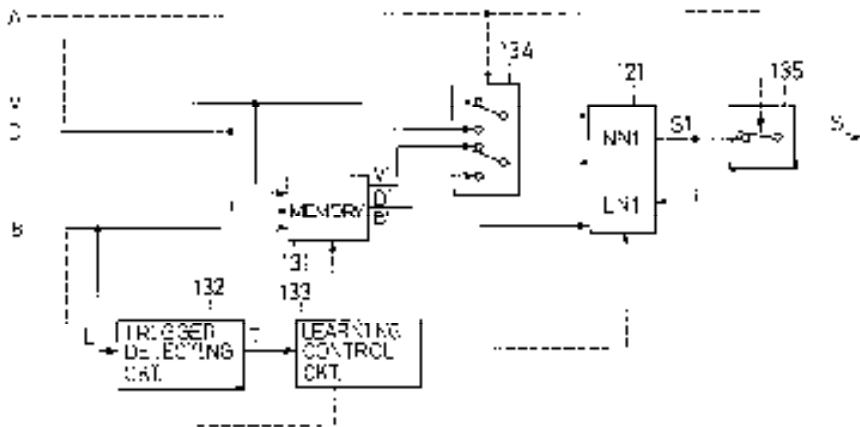


Figure 6

Figure 6 shows the function for selectively learning data when a braking operation is done in an automatic brake control system.

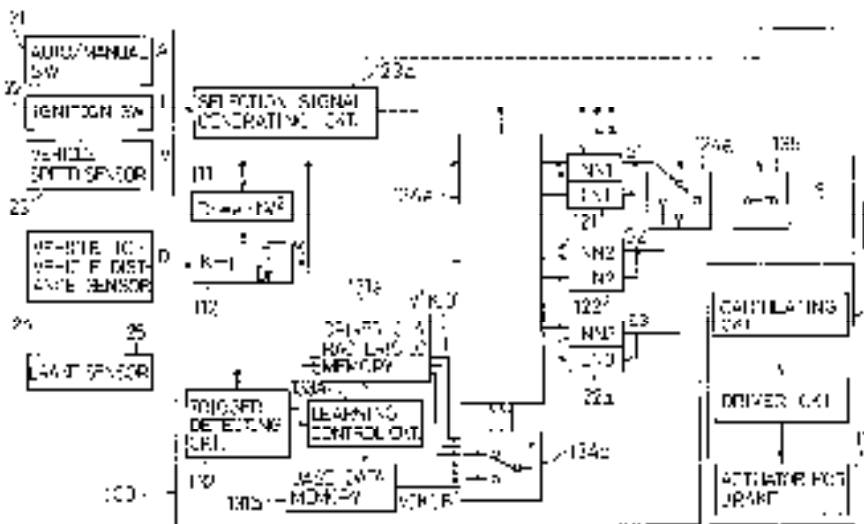


Figure 7

Figure 7 is an embodiment of an automatic brake control system, applied to a vehicle.

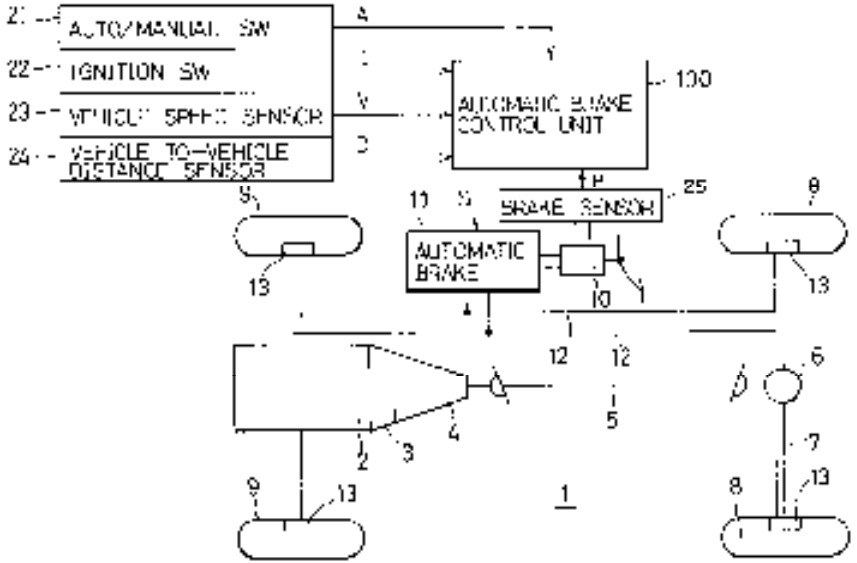


Figure 8

Figure 8 is a schematic diagram of a vehicle incorporating an automatic brake control system.

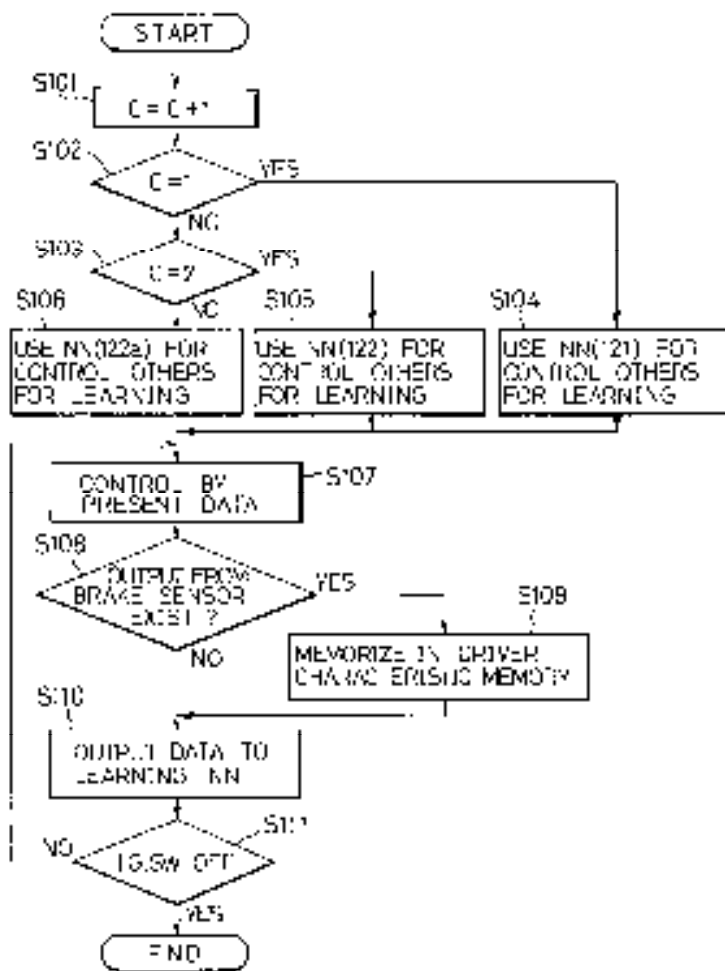


Figure 9

Figure 9 is a flowchart of the control in an automatic brake control system.

Conclusion

Thus, by implementing this method, several road-accidents due to epileptic seizures while driving can be prevented. The

patient is secure once the vehicle stops and later the matter can be informed to his physicians and relatives.

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Wound Healing Activity of Aqueous Extract of *Allium* *Sativum* L. in Rats

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Abstract

The aqueous extract of garlic (*Allium sativum*) was evaluated for wound healing activity in rats. The animals were divided equally into four groups of six each (n=6). All animals were experimentally wounded in the posterior neck area. A thin layer of blank Vaseline was applied topically to wounds of Group 1 rats as a negative control. Wounds of Group 2 and Group 3 animals were treated with a thin layer of Vaseline containing 5% and 10% aqueous *Allium sativum* extract, respectively. A thin layer of solcoseryl jelly was applied topically to wounds of Group 4 animals as reference. The effects of these topical applicants on the rate of wound healing were assessed. Wounds treated with Vaseline containing garlic extracts, or solcoseryl jelly significantly ($P<0.05$) accelerate wound healing activity

compared to wounds treated with blank Vaseline. Wounds treated with Vaseline containing 10% plant extract also significantly healed faster than wound treated with Vaseline containing 5% garlic extract, or solcoseryl jelly. The histological examination of healed skin showed that the original tissue regeneration was much greater with Vaseline containing 10% plant extract and solcoseryl jelly groups. We conclude that *A.sativum* aqueous extract significantly enhanced the acceleration rate of wound enclosure in rats.

Keywords: Wounds healing, *Allium sativum*, Solcoseryl jelly, histology

Introduction

Burn trauma and wounds are still a major problem in developing countries, often having severe complications and involving high costs for therapy. An important aspect of the use of traditional medicinal remedies and plants in the treatment of burns and wounds is the potential to improve healing and at the same time to reduce the financial burden. Several plants and herbs have been used experimentally to treat skin disorders, including wound injuries, in traditional medicine (Suguna et al., 2002, Rane et al., 2003, Shirwaikar et al., 2003).

Allium sativum (garlic), a member of the lily family, is most commonly used worldwide for flavorful cooking; much of the clinical literature on garlic has focused on its potential antioxidant activity (Sundaresan and Subramanian, 2003), anti-platelet, and fibrinolytic effects (MacDonald et al., 2004); and microcirculatory effects (allicin and ajoene for use in hypertension and hyperlipidemia) (Al-Qattan et al., 2003). Garlic derivatives are also frequently used for antibacterial (Dikasso et al., 2002); antifungal activity (Lemar et al., 2002), anti-inflammatory (Hofbauer et al., 2001), antiparasitic activity (Lun et al., 1994) hypoglycemic properties (Roman-Ramos et al., 1995) and may have anticancer activity (Berges et al., 2004). The use of herbal medicine is widespread and growing with the

increasing number of herbal products available in conjunction with, or as replacement for, conventional medicine. To our knowledge, nothing is known about the effect of garlic on the rate of wound healing. Therefore, the purpose of the present study was carried out to assess the effects of *Allium sativum* aqueous extracts on the rate of wound-healing activity in rats.

Materials and methods

Vaseline (100% pure petroleum jelly)

Vaseline is a brand of petroleum jelly originally produced by Chesebrough-Pond's, USA, and currently by Unilever. Vaseline is obtained from the local pharmacy.

Solcoseryl^R jelly

Solcoseryl^R jelly manufactured by Solco Basle Ltd, Birsfelden-Basle (Switzerland) bought from pharmacy. The jelly used for the promotion of granulation and epithelization of wounds.

A. sativum and preparation of extract

Fresh, unprocessed garlic was obtained from the local market, and identified by comparing with specimens available at the Herbarium of Rimba Ilmu, Institute of Science Biology University Malaya. It was fully grinded by blender, and then 50 g of blended garlic were weighted and placed into 1000 ml flask. The water was added in ratio 1:20. After that, mixing it with 800 ml of sterile distilled water in a conical flask using a ratio of 1:20. It was then heated and stirred on a hotplate for 3 hours. Next, using filter paper and filter funnel filtered it. The step was followed by rotor vaporized to remove the water. Then, it was mixed with blank Vaseline in a concentration of 5% w/w (5 g extract/95 g of blank Vaseline).and 10% w/w (10 g extract/90 g of blank Vaseline).

Experimental animals

Sprague Dawley rats were obtained from the animal house, Faculty of Medicine, University of Malaya, Ethic No. PM 28/-9/2006 MAA (R). The rats were divided randomly into 4

groups of 6 rats each. Each rat that weighted between 180-200 gm was housed separately (one rat per cage). The animals were maintained on standard pellet diet and tap water.

Experimentally induced wounds

The animals were anesthetized by diethyl ether. The skin shaved, disinfected with 70% alcohol and injected with 1 ml of Lignocaine HCl (2%, 100 mg/5 ml). An area of uniform wound 2 cm in diameter was excised from the nape of the dorsal neck of all rats with the aid of round seal as described by Morton and Melone (1972) (Figure 1). Avoided incision of the muscle layer and tension of skin was kept constant during the procedure.



Figure 1: 2 cm diameter excision skin wound on day 0 before application of vehicle

Topical application of vehicles

A thin layer of blank Vaseline was applied topically twice daily to the wounds of Group 1 animals; a thin layer of Vaseline containing 5% and 10% extracts of *A. sativum* each was applied topically twice as daily dressing to the wounds of Group 2 and Group 3 rats, respectively. Thin layer of solcoseryl jelly was

topically applied twice daily to Group 4 animals. The wound enclosure was observed daily until complete wound-healing process occurs.

Measurement the diameter of wounds

Measurements of the diameter were performed on first day and then an interval one day until complete healing.

Histology of healed wounds

After the wounds were completely healed, all rats were killed from each group. The rat's skins were incised ~2cm X 2cm from healed wound. The areas of healed wounds were fixed immediately in freshly made buffer formalin (10%), for 4-6 hours, and processed in the automated machine. Biopsies were embedded in freshly made Paraplast. 5 μ m thick were cut with rotary microtome using disposable knife blades and stained with Hematoxylin and Eosin. The structural change of healed wound of each group was observed by light microscope at 10x magnification in 0.15mm² areas.

Statistical analysis of data

All values are reported as mean + S.E.M. and the statistical significance of differences among groups were assessed using one-way ANOVA. A value of $P < 0.05$ was considered significant.

Results

Wounds treated with aqueous extracts of garlic, and wounds treated with solcoseryl jelly showed considerable signs of dermal healing and significantly ($P < 0.05$) healed earlier than those treated with blank Vaseline (Table 1; Figure 2 and Figure 3).

Table 1: Time required for healing of wounds in experimental animals

Animal groups	No of animals	Type of dressings	Healing time (days) (Mean \pm S.EM)
Group 1	6	Blank Vaseline (Control)	19.67 \pm 0.33 ^a
Group 2	6	5% garlic extract + Vaseline	15.33 \pm 0.49 ^b
Group 3	6	10% garlic extract + Vaseline	12.00 \pm 0.37 ^c
Group 4	6	Solcoseryl Jelly	14.67 \pm 0.49 ^b

All values were expressed as mean and \pm standard error mean. Mean with different superscripts were significantly different ($P < 0.05$)



Figure 2: Complete wound healing with Vaseline containing 10% *Allium sativum* on day12.



Figure 3: Wound healing with blank Vaseline on day 18 after topical application.

Wounds treated with Vaseline containing 10% garlic extract significantly accelerate wound healing compared to wounds treated with 5% garlic extract or wounds treated with solcoseryl jelly. There were no significant differences between wounds treated with 5% garlic extract and solcoseryl jelly in the term of duration of wound healing (Table 1). The histological examination of healed skin showed that the original tissue regeneration was much greater with Vaseline containing 10% plant extract and solcoseryl jelly groups without any edema, congestion or inflammatory changes. The skin of these treated wounds were thick and hyperkeratotic and regular / slightly regular with hair follicles present, whereas negative control (Vaseline alone) has thin, irregular epidermis and in the dermis area were granulation and numerous inflammatory cells (Figure 4 and Figure 5).

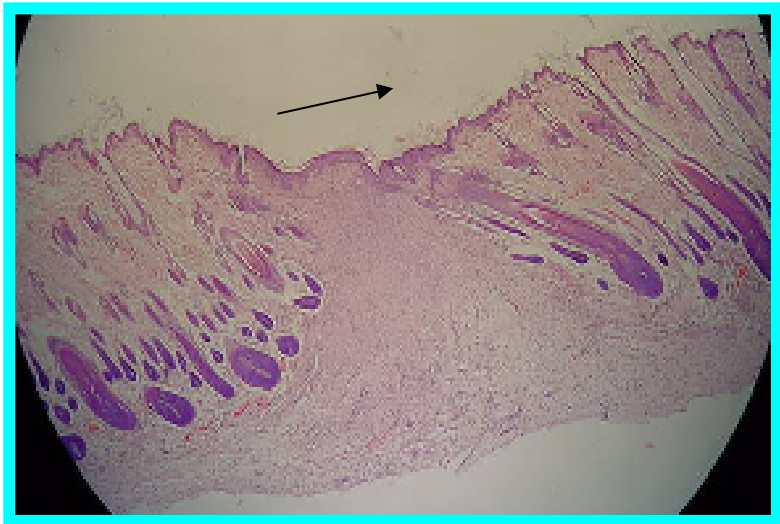


Figure 4: Histological section of complete wound healing treated with Vaseline containing 10% aq extract of *A. sativum*. Narrow scar at the closure wound (H&E stain, 10x)

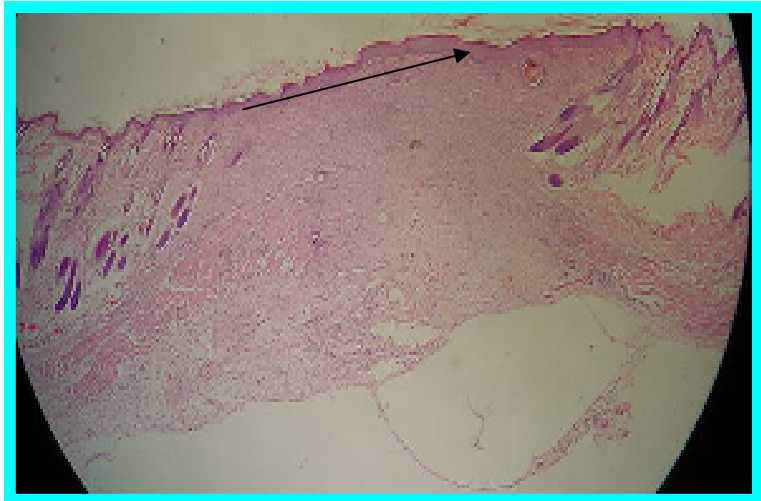


Figure 5: Histological section of complete wound healing treated with blank Vaseline. Wide scar at the closure wound (H&E stain, 10x)

Discussion

The majority of the world's population relies on traditional medicine for their health care. This is also the case in the treatment of wounds. In developing countries, remedies prepared from herbal plants have been widely used for the treatment of soft tissue wounds and burns by medical personnel trained in western medicine as well as by traditional practitioners. The results of the present study showed that the usage of Vaseline containing 10% garlic aqueous extract as topical applicants of wounds dressing significantly ($P<0.05$) accelerated wound healing activity. Garlic has been used for medicinal purpose for centuries. The most active ingredient in garlic is allicin (contain sulfur, and combined with breakdown products, give garlic its characteristic smell). Crushing the garlic clove activates the enzyme allinase, which converts allin to allicin (Ness et al., 1999). It has been found by (Dikasso et al., 2002) that garlic has a strong antibacterial activity, and the active principle of garlic (allicin) with its antimicrobial activity could attribute to wound healing process in the present study. Garlic extract, with higher concentration of diallyl sulphides, showed greater antimicrobial activity (Tsao and Yin, 2001), that they may be useful in the prevention or treatment of variety of infection (Lemar et al., 2002). The antioxidant properties of garlic were well documented (Sundaresan and Subramanian, 2003). Garlic administration experienced a significant reduction in lipid peroxidation, which attributes to wound healing properties in the current study. Garlic caused an increase in fibrinolytic activity, inhibited platelet aggregation, and lowered cholesterol (Beaglehole, 1996). It has been used historically to enhance circulation, fit stress and fatigue, and stimulate immune function. In conclusion, garlic aqueous extract appeared to have several important properties that make it useful ideal as a dressing agent for wounds and ulcers.

Acknowledgements

This study was supported by the University of Malaya through the grand SAGA 66-02-03-0046.

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Doppler Studies in the Individuals with Injuries around the Hip- Immediately after Injury and after Treatment

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Abstract

Background: Deep Venous Thrombosis (DVT) is one of the most common, potentially serious and preventable complications of major injuries and major surgeries of lower limbs. In terms of morbidity, DVT delays discharge from the hospital by approximately 5 days while pulmonary embolism (PE) necessitates an additional week of hospitalization. The true incidence of postoperative DVT and its pattern of distribution in Indian patients are not well highlighted. A few studies place the incidence at 6%-75%. The risk of fatal pulmonary embolism (PE) after major lower limb surgery ranges from 0.19%-3.4%.

Aims and Objectives: This cross sectional study was undertaken primarily to study the prevalence of DVT in patients undergoing treatment for injuries around the hip-

mainly proximal femur fractures-as detected by Color Doppler Sonography, to find out the pattern of thrombosis therein & to estimate if there is any association between the age, type of injuries, the type of treatment undertaken and the type of anesthesia used on the one hand and the occurrence of deep venous thrombosis on the other

Patients/Methods: A cross sectional study of 40 patients fulfilling inclusion criteria, admitted for injuries around the hip, was carried out at Indira Gandhi Government Medical College Nagpur. On admission, standard all-patient-treatment was initiated and informed consent obtained. Compression ultrasonography with Color Doppler scan was done when the patient was suitably comfortable. Demographic details, type and mode of injury, nature of treatment, type of anesthesia and risk factors were noted. Before and after treatment patients were closely observed for signs of DVT. Color Doppler Scan with compression ultrasonography was repeated between 4th day upto day of discharge (average 6th day), only on the affected limb and not on contralateral leg and findings noted. Doppler results were interpreted as being positive or negative for DVT and failure of deep vein to flatten when compressed with ultrasound transducer was considered a definitive diagnosis of DVT. Response on distal augmentation (pressure on calf), color flow images, patency of saphenofemoral and saphenopopliteal junctions were used to support the diagnosis. No prophylaxis was given to any patient and all patients were mobilized within 48 hours of treatment-as is the practice routinely followed in this institute. Analysis was done by comparison of prevalence of DVT with exposure and prevalence of DVT without exposure. Fisher's Exact test was used to detect association between variables & student's t-test to compare means. Analysis was done using online resources & Excel worksheets.

Results: 6 out of 40 patients (15%) showed presence of DVT. Of these, 5 had proximal thrombi and 1 had isolated distal thrombus. No significant difference was found between the mean ages of patients with and without DVT. Prevalence of

DVT in patients undergoing Dynamic Hip Screw fixation was 21.05 % as compared to 9 % in patients undergoing other treatments. It was 21.73 % in patients having fracture Intertrochanteric Neck Femur (versus 5 % in other fractures around hip), and 14.8 % in patients over age 50 years (versus 15.38 % in age < 50 years). There was no significant association found between DVT and the three variables mentioned above, as also spinal anesthesia. 1 patient showed no clinical signs of DVT, the rest presented with limb edema or fever. None of the patients had a fatal outcome directly related to DVT or pulmonary embolism.

Conclusions: The high prevalence of DVT found in this study indicates the need for routine screening of patients with injuries around the hip, using compression ultrasonography with color Doppler scanning, and early mobilization-irrespective of age or absence of signs of deep venous thrombosis.

Keywords: Deep Venous Thrombosis, Doppler Sonography, Hip Injury

Introduction

Deep venous thrombosis (DVT) is one of the most common, potentially serious and preventable complications of major lower limb surgeries like Total Hip Replacement and Total Knee Replacement (Agarwala, Bhagwat, Modhe, 2003, and McNally, Bahadur, Cooke, Mollan, 1997). Depending on the studies and their protocol, the published incidence of deep venous thrombosis without prophylaxis varies widely but has been found to be in the range of 40-84% in the West, with highest rates found in Total Knee Arthroplasty (Agarwala et al. 2003, Dhillon, Askander, Doraisamy, 1996, Hull & Raskob, 1986). About 20 million cases of lower extremity deep venous thrombosis occur in USA alone. Although in Asian (and especially Indian) patients, the true incidence of postoperative deep venous thrombosis and its pattern of distribution are not

well highlighted, a few studies have placed the incidence at 6%-75%(Agarwala et al. 2003).

The etiology of deep venous thrombosis is multifactorial and the risk factors include advanced age, male patients, prolonged immobility, previous history of heart failure and deep venous thrombosis, obesity, estrogen therapy, malignancy, etc (Davidson, Mazzu, Gage, Jeffrey, 1996, and Hull & Raskob, 1986). In Western literature, the pattern of thrombosis is mainly proximal while in South-East Asians, involvement of distal veins is more common (McNally et al.1997). Proximally placed thrombi are potentially more dangerous in their ability to cause Pulmonary Embolism (PE) (Ciccone et al. 1998) -the risk of fatal pulmonary embolism after major lower limb surgery has ranged from 0.19% to 3.4% (Freedman, Brookenthal, Fitzgerald, Williams, Lonner, 2000). Though distal thrombi appear to be benign, they have a potential for proximal propagation and subsequent embolization (Agarwala et al. 2003). In terms of morbidity deep venous thrombosis delays discharge from the hospital by approximately five days while pulmonary embolism necessitates an additional week of hospitalization (Lieberman & Geertz, 1994).

Hence, to “nip the evil in the bud”, it is necessary to reconsider whether postoperative screening and prophylaxis against deep venous thrombosis should or should not be recommended routinely.

The lack of reliability of clinical signs in early detection of deep venous thrombosis is well known (Dhillon et al. 1996). Hence a multitude of diagnostic methods like ¹²⁵I-fibrinogen scanning, Doppler Sonography, impedance plethysmography, venous ultrasonography and contrast venography have been used over the course of time (Lieberman & Geertz, 1994, Hull & Raskob, 1986).

Contrast venography has been the traditional choice for the diagnosis of deep venous thrombosis. Although it gives direct visible evidence of thrombi and is equally sensitive and specific for diagnosis of proximal and distal deep venous thrombosis (whether occlusive or non-occlusive), it does have its

disadvantages like contrast-medium-induced phlebitis, allergic reactions, inability to cannulate the veins of a swollen foot, development of thrombosis secondary to venography itself, time consuming, painful and subject to technical inadequacies and to interobserver error. ¹²⁵I-fibrinogen scanning and impedance plethysmography have limited accuracy in detection of proximal thrombi (Ciccione et al. 1998, Clarke, Green, Harper, Gregg, 1997, Lieberman & Geertz, 1994).

On the other hand, Color Doppler Sonography has emerged as a highly accurate test with acceptable reproducibility for detection of deep venous thrombosis-especially in the calf veins (Atri et al. 1996, Davidson et al. 1996). Being non-invasive, convenient, relatively inexpensive, and with no known complications due to the procedure itself, it has achieved increasing popularity over the past 30 years. But it is limited in its inability to detect thrombi of iliac veins and its dependence on the skill of the operator (Lieberman & Geertz, 1994).

Routine prophylaxis against deep venous thrombosis after lower limb surgery remains controversial-not only in terms of which method or agent to be used but whether it should be recommended at all (Hull & Raskob, 1986). Although a wide variety of mechanical and pharmacological methods have been tried in this respect-only a few like the Arterio-Venous Impulse foot pump, intermittent pneumatic compression and warfarin have been documented to be of value by several studies (Freedman et al. 2000, Warwick et al 1998).

This study was undertaken primarily to study the prevalence of deep venous thrombosis in patients undergoing treatment for injuries around the hip-mainly proximal femur fractures- as detected by Color Doppler Sonography which is non-invasive and easily accessible and to find out the pattern of thrombosis therein. It is hoped that such a study will help in decisions regarding patient management and routine use of screening and prophylaxis for deep venous thrombosis.

Brief Review of Literature

Creager & Dzau (2005) explain that "the presence of thrombus within a superficial or deep vein and the accompanying inflammatory response in the vessel wall is termed as venous thrombosis or thrombophlebitis. Initially the thrombus is composed principally of platelets and fibrin. Red cells become interspersed with fibrin and the thrombus tends to propagate in the direction of blood flow. The inflammatory response in the vessel wall may be minimal or characterized by granulocyte infiltration, loss of endothelium and edema" (p. 1491).

Pathogenesis

Deep venous thrombosis results from the classic Virchow's triad of:

1. Venous stasis
2. Hypercoagulability
3. Endothelial injury

This triad comes into play perioperatively. Positioning the limb during the procedure, localized post-operative swelling and reduced mobility after the operation are responsible for venous stasis. Hypercoagulability occurs, because the trauma of the procedure itself results in a sustained activation of tissue factors and other clotting factors, along with postoperative reduction in the levels of antithrombin III and inhibition of endothelial fibrinolytic system. Endothelial injury is due to torsion and complete occlusion of the femoral vein during dislocation of hip joint and insertion of the prosthesis; operative positioning and use of a tourniquet on the thigh may result in foci of vascular damage that provide a nidus for the thrombus (Lieberman & Geertz, 1994).

The reported incidence of post-operative deep venous thrombosis varies widely depending on the studies and their protocol. In the Western literature, the incidence of post-operative deep venous thrombosis where no prophylaxis was

used ranges from 40% to 84% while in Asian patients it was found to be 6% to 75%.

Materials and Methods

This cross sectional study was carried out at Indira Gandhi Government Medical College, Nagpur during the period of 10 May – 10 June 2005 in the department of Orthopaedics. It included a total of 47 patients admitted for injuries around the hip. The study protocol was submitted to the Institutional Ethics Committee (IEC) and received its approval.

After patient was admitted to the ward, standard all-patient-treatment was initiated which included immediate assessment of neuro-vascular status, radiographic evaluation (X-ray pelvis – Antero-posterior and Lateral views) and provisional immobilization by applying below-knee skin traction. The following patients were included in the study – fractures of femur neck, pubis, ilium, ischium, sacro-iliac joint, and acetabulum. Patients were excluded if they had fracture of shaft and lower end of femur. All patients were informed about the research project & were included only after their informed consent was obtained in their language. The scan was done when the patient was suitably comfortable for shifting, and the findings noted.

The Doppler Ultrasound scan used for the purpose had the following specifications- G.E. logiq-3 pro-scan based machine with 2, 3, 3.5, 5 MHz interexchangeable multifrequency convex array and 6,7.5,8,10 MHz interexchangeable multifrequency convex linear array.

For each patient, a complete protocol included demographic details, type and mode of injury, nature of treatment, type of anesthesia and any risk factors observed. A predesigned case proforma and consent form were used.

Management was done based on clinical opinion, patient's general condition, presence of risk factors, and availability of implants.

Before and after treatment, patients were observed closely for signs of deep venous thrombosis. Depending on the availability

of personnel and adequate pain relief for the patient, Color Doppler scan with compression ultrasonography was done between 4th day upto the time the patient was discharged (average 6th day), only on the affected limb and not on the contralateral leg, and findings noted.

The Doppler results were interpreted as being positive or negative for deep venous thrombosis. Any additional findings like subcutaneous edema, enlarged lymph nodes, and dilated superficial veins were also noted. Failure of deep vein to flatten when compressed with ultrasound transducer was considered a definitive diagnosis of deep venous thrombosis. (See figure 1)

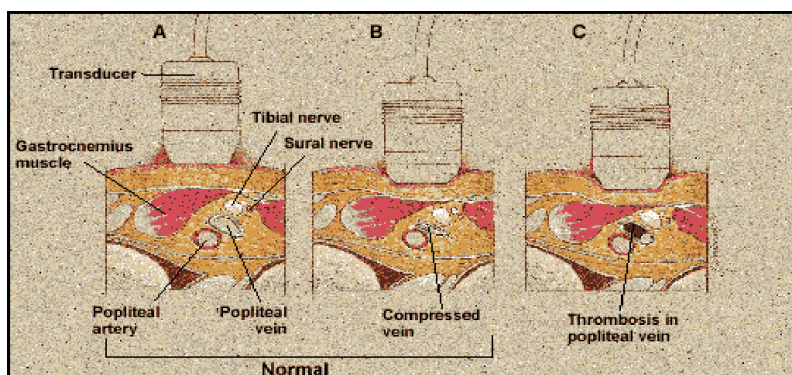


Figure 1. Responses of normal and abnormal popliteal veins to compression (transverse axis). (A and B) With compression, the normal vein completely collapses. (C) In the vein with deep venous thrombosis, the popliteal vein resists compression, and the lumen persists (Barloon, Bergus, Seabold, 1997).

Further, response on distal augmentation (by pressure on calf), and Color flow images were also used to support the diagnosis. Patency of saphenofemoral and saphenopopliteal junctions was also tested.

No prophylaxis was given to any patient except that all patients were **mobilized within 48 hours** (2nd day onwards) of the treatment- as is the practice routinely followed in this institute.

Analysis was done by comparison of prevalence of DVT with exposure and prevalence of DVT without exposure. Fisher's exact test was used to detect association between variables & student's t-test to compare means. Analysis was done using online resources & Excel worksheets

Observations and Results

Of the total 47 patients enrolled for the study, there were 6 dropouts, and 1 patient died due to aspiration pneumonia before treatment. Thus, 40 patients were available for analysis. The Age and Sex distribution of cases is shown in Table 1.

Table 1: Age and Sex distribution of cases

Age Group	Males	Positive cases	Females	Positive cases
11-20 years	3	0	0	0
21-30 years	2	1	0	0
31-40 years	3	0	1	1
41-50 years	5	0	0	0
51-60 years	5	0	5	0
61-70 years	8	1	4	2
71-80 years	2	1	2	0
Total	28	3	12	3

Out of 40 patients, there were 28 males with 3 positive cases (10.71%), and 12 females with 3 positive cases (25%). Majority of the patients belonged to age group of 61-70 years and the age range was 14 – 75 years.

Of the 40 patients, 6 (15%) showed evidence of deep venous thrombosis, of whom 5 had proximal thrombi and one had only distal thrombus.

The prevalence of deep venous thrombosis varied for different groups – formed according to the type of injury and type of treatment. (See Tables 2 & 3)

Table 2: Prevalence of deep venous thrombosis in different types of injuries

Type of injury	Number	Positive cases	% of positive cases
# ITNF	23	5	21.73 %
# ICNF	11	1	9.09 %
# Subtro.	5	0	--
# Ilium/acetab	1	0	--
Total	40	6	
# ITNF – Fracture inter trochanteric neck femur			
# ICNF – Fracture intra capsular neck femur			
# Subtro. – Fracture subtrochanteric neck femur			
# Ilium/acetab – Fracture of ilium or acetabulum			

Fracture intertrochanteric neck femur was the most commonly found injury and percentage of deep venous thrombosis in this group was 21.73%, while that in fracture intracapsular group was 9.09%.

Table 3: Occurrence of deep venous thrombosis in different types of treatment

Type of treatment	Number	Positive cases	% of positive cases
DHS	19	4	21.05 %
AMP	9	1	11.11 %
MBH	4	1	25 %
CC Screw Fixation	2	0	--
PFN	4	0	--
Conservative	2	0	--
Total	40	6	
DHS – Dynamic Hip Screw			
AMP – Austin Moore Prosthesis			
MBH – Modular Bipolar Hip			
CC Screw – Cortico- Cancellous Screw			
PFN – Proximal Femoral Nail			

Dynamic Hip Screw was the most frequently performed procedure, and the percentage of Deep Venous Thrombosis in

this group was 21.05% (See Table 3) as compared to that in the Prosthetic Replacement Group (15.28%), comprising of Modular Bipolar Hip group (25%) and Austin-Moore Prosthesis Group (11.11%).

Table 4: Occurrence of deep venous thrombosis according to type of anesthesia

Type of anesthesia	Number	Positive cases	% of positive cases
Spinal	34	6	17.64 %
Combined spinal +Epidural	4	0	--
None (conservative)	2	0	--
Total	40	6	

All the 6 positive deep venous thrombosis cases had been given Spinal anesthesia (See Table 4). Out of the 6 patients, 1 showed no clinical signs of deep venous thrombosis (asymptomatic), while the rest presented with either limb edema or fever.

The 3 patients, in whom deep venous thrombosis was detected preoperatively, had history of immobilization for 7 to 10 days prior to coming for treatment in this institute. On following up postoperatively, it was found that 2 of them had partial recanalization of the veins while one showed proximal extension of thrombus. The summary of the data can be seen in Table 5.

Table 5: Table of Baseline Characteristics

Variable	Measured data – Study Population (n= 40)	
Age (years)	53.87 +/- 16.51	Standard error 53.87 +/- 2.61
		(CI 48.76 - 58.98)
Age in Males	50.28 +/- 17.75	Standard error 50.28 +/- 2.8
		(CI 44.8 – 55.76)
Age in females	62.25 +/- 8.58	Standard error 62.25 +/- 1.35
		(CI 59.61 - 64.89)
Type of injuries		
# ITNF	23 (57.5 %)	
# ICNF	11 (27.5 %)	
# Subtroc & #Ilium/acetab	6 (15%)	
Type of Treatments		
DHS	19 (47.5%)	
AMP	9 (22.5 %)	
Others	12 (30 %)	
Type of Anesthesia		
Spinal	34 (85%)	
Combined spinal and epidural	4 (10%)	
DVT	6 (15%)	

The association between various variables and DVT was estimated with the help of 2x2 tables (p value significant at 0.05 level).

Table 6: DVT in patients undergoing DHS fixation

Dynamic hip screw fixation	Deep venous thrombosis		
	Present	Absent	Total
Done	4	15	19
Not done	2	19	21
Total	6	34	40

Prevalence of DVT in patients undergoing DHS fixation was 21.05 % as compared to 9 % in patients undergoing other treatments. (See table 6) Using Fisher's Exact test, p value = 0.282 . Thus, there was no significant association found between DVT and DHS fixation. Similarly, prevalence of DVT in patients with # ITNF was 21.73 % as compared to 5 % in patients with other injuries. p value = 0.175 (See table 7). Thus, there was no significant association found between DVT and # ITNF.

Table 7: DVT in patients with # ITNF

# ITNF	Deep venous thrombosis		
	Present	Absent	Total
Present	5	18	23
Absent	1	16	17
Total	6	34	40

Also, prevalence of DVT in patients aged greater 50 yrs was 14.8 % as compared to 15.38 % in patients aged less than 50 yrs. p value = 0.707 (See table 8). There was no significant association found between DVT and age >/< 50 yrs.

Additionally, there was no significant difference in the mean age between patients with (55.6%) and without deep venous thrombosis (53.5 %) as calculated by student's t-test.

Table 8: DVT in patients with age >/< 50 years age

Age	Deep venous thrombosis		
	Present	Absent	Total
Age >50 yrs	4	23	27
Age <50 yrs	2	11	13
Total	6	34	40

Similarly with p value = 0.35, there was no significant association found between DVT and use of spinal anesthesia.(See table 9)

Table 9: DVT in patients given spinal anesthesia

Spinal anesthesia	Deep Venous thrombosis		
	Present	Absent	Total
Present	6	28	34
Absent	0	6	6
Total	6	34	40

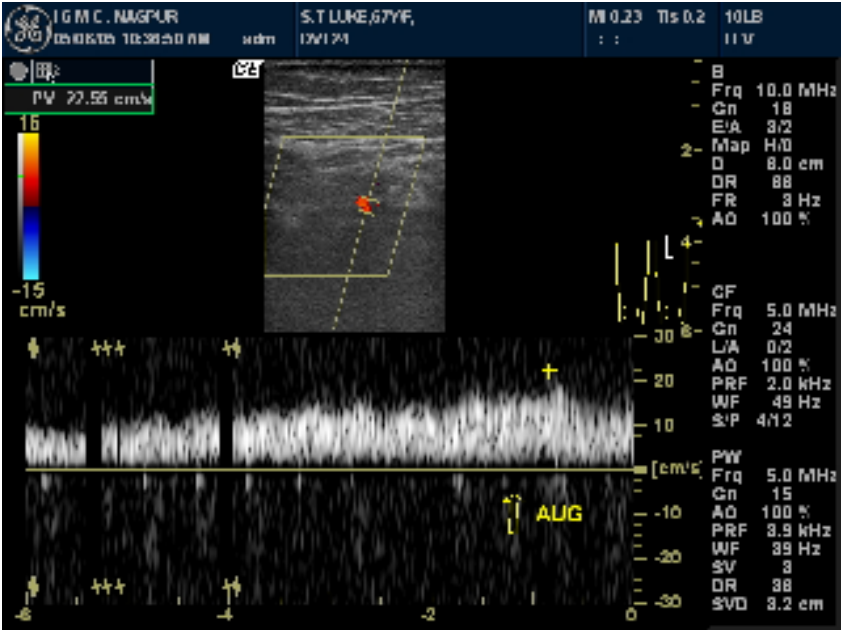


Figure 2: Color Doppler image of Patient S, 65 Yrs Female, a postoperative deep venous thrombosis positive patient in this study. The figure shows loss of augmentation in the common femoral vein on compression of the calf, due to thrombus in the popliteal vein. There is also marked loss of blood flow.

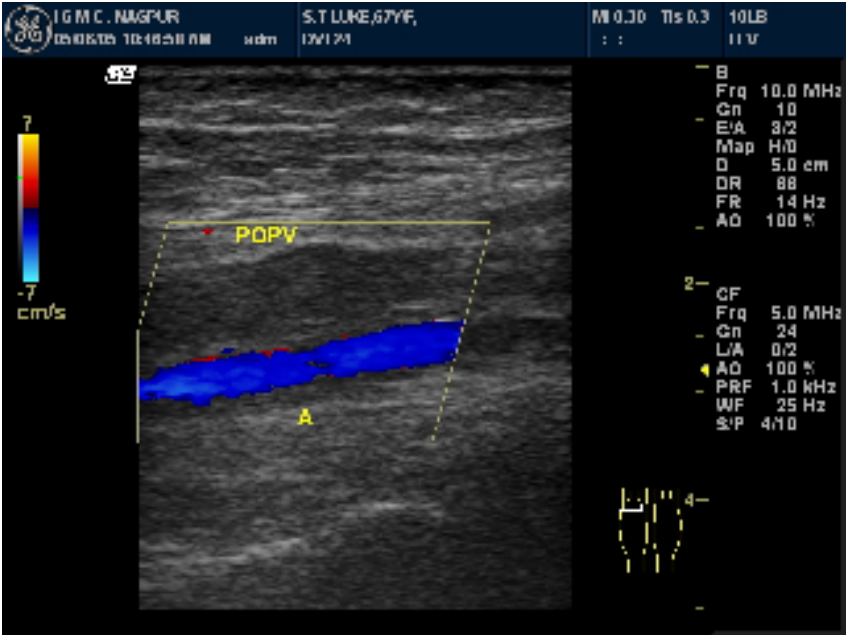


Figure 3: Color Doppler image of the same patient showing incompressibility of the Popliteal vein on compression by ultrasound transducer, due to presence of thrombus

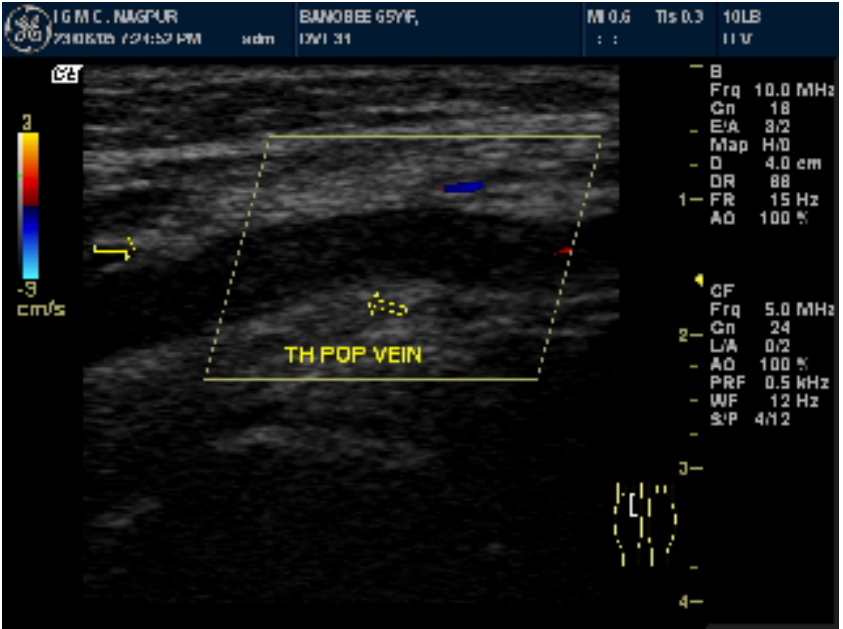


Figure 4: Color Doppler image of Patient B, 65Yrs Female, a postoperative deep venous thrombosis positive patient. This figure shows presence of thrombus in the Popliteal vein as evidenced by loss of blood flow

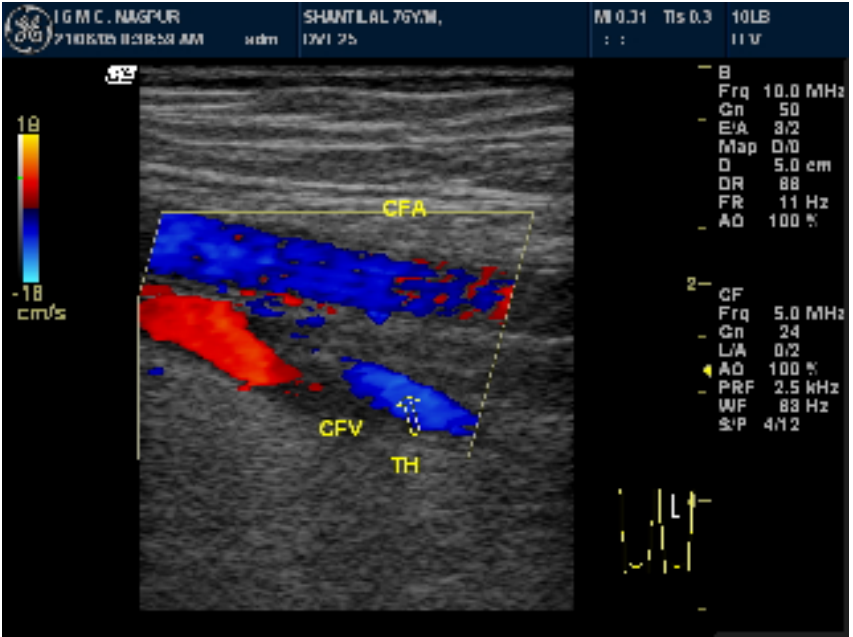


Figure 5: Color Doppler image showing thrombus in the Common Femoral Vein in Patient SN, 76 Yrs Male.

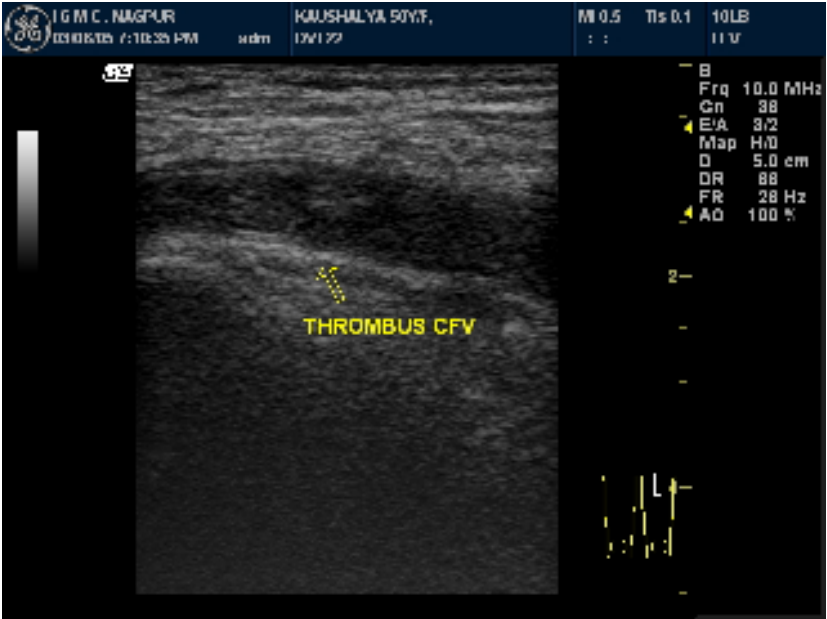


Figure 6: Deep vein thrombosis in the Common Femoral Vein (Patient K, 50 Yrs Female)

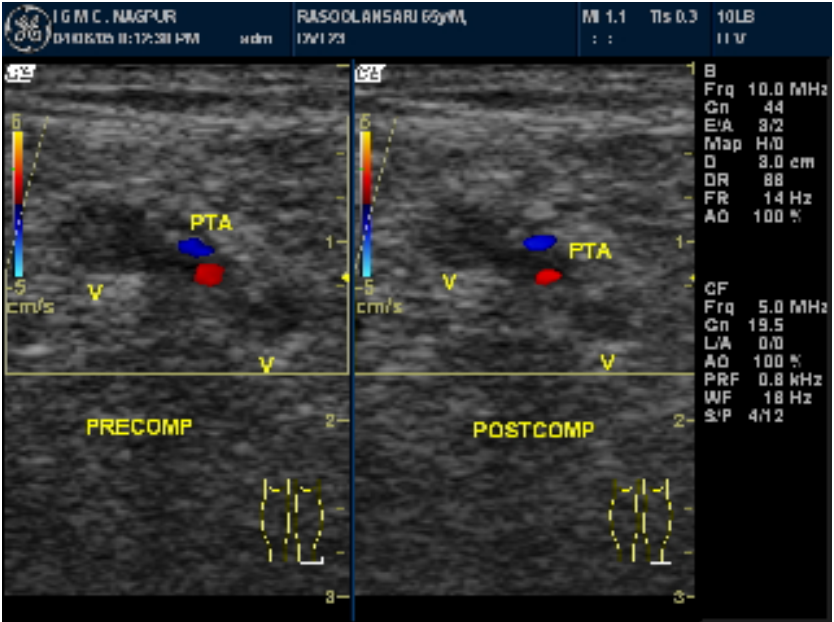


Figure 7: Color Doppler image showing thrombosis of the posterior tibial vein. Precompression and postcompression images show loss of compressibility (Patient R, 65 Yrs Male)

Discussion

Dhillon et al. (1996) found no significant difference in the mean age between patients with and without deep venous thrombosis. In the present study too, there was no significant difference in the mean age between patients with (55.6%) and without deep venous thrombosis (53.5 %). A few studies mention age as a significant risk factor (Davidson et al. 1996, Lieberman & Geertz, 1994, Hull & Raskob, 1986).

The prevalence of deep venous thrombosis of 15 % found in this study matches that found in some other studies (see Table 10).

Table 10: Incidence of Deep Venous Thrombosis found in previous studies (Only those studies in which no prophylaxis was used have been included in the table)

Study by	Number of Patients	Year	Incidence found
Cunningham & Yong	-	1974	2.6 % - 53.3 %
Mok et al.	53	1979	
Nandi, Wong, Wei, Ngan, Ong	-	1980	
Inada, Shirai, Hayashi, Matsumoto, Hirose	256	1983	
Atichartakan, Pathepchotiwang, Hirose	50	1988	4 %
Kim & Suh	146	1988	10 %
Mitra, Khoo, Ngan	72	1989	9.7%
Lieberman & Geertz	-	1994	40% - 60%
Dhillon et al.	88	1996	62.5 %
Freedman et al.	Meta-analysis 10929	2000	39 % – 74 %
Agarwala et al.	104	2003	60 %
Present study	40	2005	15 %prevalence

Prevalence of DVT in patients undergoing DHS fixation was 21.05 % as compared to 9 % in patients undergoing other treatments. It was 21.73 % in patients having # ITNF (versus 5 % in other fractures around hip), and 14.8 % in patients over age 50 years (versus 15.38 % in age < 50 years).

There was no significant association found between DVT and the three variables mentioned above, as also spinal anesthesia Compression ultrasonography with Color Doppler scan was used in this study because it was available in this institute and because of its gradual establishment as the non- invasive method of choice for detecting deep venous thrombosis (Atri et al. 1996, Bates & Jaffrey, 2004, Davidson et al. 1996, Fraser & Anderson, 2004, Steele, Dodenhoff, Ward, Norse, 2005).

There could be several reasons why the prevalence found in this study does not match that found in some other studies:

1. All patients in this study were mobilized right from 2nd day after operation (within 48 hours based on their ability to stand with support).

2. Most other studies have reported incidence of deep venous thrombosis after a major operation like Total Hip Replacement or Total Knee Replacement (Agarwala et al. 2003, Freedman et al. 2000, Lieberman & Geertz, 1994), especially in elderly patients. On the other hand, in this study, no age limit was fixed for inclusion of patients and the operations undertaken included Dynamic Hip Screw, Austin – Moore Prosthesis etc., which are not as major operations as Total Hip Replacement. This translates into lesser vascular trauma and stasis, and reduced immobilization period.

3. Almost all the patients were from lower socioeconomic group, with poor diet as compared to the western population and their affluent counterparts in this country. Diet has been found to play a role in the incidence of DVT/PE. (Steffen et al. 2007).

Thus, early mobilization and dietary variation may have had an effect on the prevalence, although there is no evidence currently to support this hypothesis.

Majority of the patients in this study suffered from fracture of proximal femur, with inter trochanteric neck fractures showing prevalence of deep venous thrombosis to be 21.73 %, and intracapsular neck femur – 9.09%. Dhillon et al. (1996) reported an incidence of deep venous thrombosis upto 50 % in the proximal femur fracture group.

As far as relation of deep venous thrombosis to type of treatment is concerned, this study found Modular Bipolar Hip to be associated with 25 % prevalence, Dynamic Hip Screw with 21.05 % and Austin Moore Prosthesis with 11.11 % prevalence.

Davis et al. (1989) found that spinal anesthesia reduced the risk of postoperative thromboembolism in total hip replacement, while Dhillon et al. (1996) and Agarwala et al. (2003) found no significant correlation between the two. In the present study, all the deep venous thrombosis positive patients had been

administered spinal anesthesia, but no statistical association was found.

Five of the 6 patients with proven deep venous thrombosis showed limb edema. The pattern of thrombosis was proximal in 5 of them, while one showed distal venous involvement. This contrasts with the finding by Agarwala et al (2003) that the predominant involvement in Indian patients is distal.

Being a cross sectional study, the following limitations apply to this study:

Prevalent cases may not be representative of all cases of DVT (selection bias). Also, this study was hospital based and without a control group. It is not possible to establish a temporal relationship between exposure and outcome using a cross sectional study, hence no causation can be inferred. It can only suggest association. Sample size was small due to time and funding constraints. Also, findings of Doppler Scans are operator-dependent (Observer bias)

Although the sample size in this study was small, and there was no control group for comparison, the results obtained suggest an important role for early mobilization in the management of patients with injuries around the hip.

Conclusions

1. The prevalence of deep venous thrombosis found in this study is as high as 15 %. It indicates the need for routine screening of patients with injuries around the hip using compression ultrasonography with Color Doppler scanning – irrespective of age or absence of signs of deep venous thrombosis.
2. Almost all the patients in the present series had unilateral, single trauma. It is very likely that patients with polytrauma on one or both the limbs may have a higher prevalence of deep venous thrombosis. Such patients - whether symptomatic or asymptomatic – should therefore be specially considered for routine screening.

3. Age, type of neck fracture, type of intervention (among those covered in this study), may not always be associated with development of DVT.
4. None of the patients in this study had a fatal outcome directly related to deep venous thrombosis or pulmonary embolism. This, alongwith the fact that chemical prophylaxis is expensive and may lead to bleeding complications, points to a need for reconsideration regarding routine use of prophylaxis in such patients.
5. For better results, there is a need for such a study with longer follow up period and including a control group.

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Cinnamtannin B1: A Small Compound Having Antidiabetes Properties

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Abstract

Type 2 diabetes mellitus is a chronic metabolic disease that results from defects in insulin secretion and insulin receptor kinase. Investigation of novel small active molecule that can potentiate insulin action or having a similar action as insulin is important in the treatment of diabetes. World ethnobotanical information on medicinal plants reports almost 800 plants used in the treatment of diabetes mellitus. However, only a small number of them have been studied thoroughly. Recent study conducted on *Cinnamomum* reported that it has a great activity in activating insulin receptor kinase and inhibiting insulin

receptor phosphatase leading to increased insulin sensitivity and function as a mimetic for insulin. Our study was designed to investigate insulin-mimetic activity of cinnamtannin B1 isolated from *Cinnamomum zeylanicum* on adipocyte cells. The insulin-mimetic activity of cinnamtannin B1 was evaluated by monitoring preadipocytes differentiation, glucose uptake and phosphorylation of insulin receptor β -subunit in 3T3-L1 adipocytes. To determine whether cinnamtannin B1 able to promote differentiation of preadipocytes, we cultured 3T3-L1 preadipocytes in the presence of cinnamtannin B1, or combination of cinnamtannin B1 and insulin, and then cell proliferation was measured at several points during the course of growth. Investigation of role of cinnamtannin B1 on tyrosine phosphorylation of insulin receptor of 3T3-L1 cells was done by immunoprecipitation of cells lysate with anti-insulin receptor β -subunit antibody and the immunocomplex samples were subjected to SDS-PAGE, transferred to nitrocellulose membranes, and immunoblotted with monoclonal anti-phosphotyrosine antibody. Evaluation of glucose uptake by adipocyte cells after treatment with cinnamtannin B1 was carried out by analyzing of radioactive glucose uptake with liquid scintillation counter. Based on these experiments, it was found that, a mixture cinnamtannin B1 with differentiation cocktail was able to induce differentiation of preadipocytes cells. Cinnamtannin B1 was found to active to stimulate phosphorylation of insulin receptor β -subunit by positively exhibited phosphorylation at 170-kDa. The mixture of cinnamtannin B1 was also able to stimulate glucose uptake from a basal value. The results demonstrated that activity of cinnamtannin B1 on adipocyte cells was found to mimicking insulin action. It acted directly on insulin receptor β -subunit by activation of PI3-kinase that stimulates glucose transporter-4 (GLUT-4) translocation. Stimulation of GLUT4 translocation therefore stimulates glucose uptake lead to glucose disposal process in adipocytes. Based on the work that has been carried out, it was suggested that cinnamtannin B1 could be one of the

potential lead drug compound in the treatment of type 2 diabetes.

Keywords: Cinnamtannin B1, *Cinnamomum zeylanicum*, adipocytes, antidiabetic properties

Background

Type 2 diabetes mellitus is a metabolic disorder of carbohydrate and lipid (Nadler and Attie, 2001). There are two important characteristics of this disease are insulin resistance and failure of pancreatic β -cells to produce insulin in response to increasing of glucose levels. Obesity is one of significant factor for the development of type 2 diabetes mellitus. An extremely lean and lipoatrophic models have revealed a similar predisposition to developing diabetes. Although it may seem paradoxical that both increased adiposity and severely reduced fat mass cause diabetes, a common pathophysiologic process in fat may be responsible for the predisposition to develop hyperglycemia in both conditions (Kim *et al.*, 2001; Nadler and Attie, 2001).

The response of cell to insulin is mediated through the insulin receptor (IR), which is a tetrameric protein consisting of two identical extracellular α -subunits that bind insulin as well as two identical transmembrane β -subunits that have intracellular tyrosine kinase activity (White, 1997). Insulin resistance is important feature of type 2 diabetes which manifested as attenuated IR signaling in response to insulin binding. A drug that promotes the initiation of IR signaling by enhancing IR autophosphorylation will be useful for treating type 2 diabetes.

In order to discover a non peptide, small active compound that exhibited insulin-mimetic activity. Salituro *et al.* (2001) screened over 50,000 samples of natural extracts for their ability to mimic insulin activity. They recently discovered a small non-peptidyl molecule (L-783,281) from a fungal (*Pseudomassaria*) extract (Zhang *et al.*, 1999; Ding *et al.*, 2002; Qureshi *et al.*, 2000). Purification of the active compound

revealed that demethylasterriquinone B1 (known as L-783,281) structurally belong to quinone-like structure of natural product. L-783,281 seems to bind directly to the intracellular β -subunit of the insulin receptor containing the insulin receptor tyrosine kinase activity. Binding leads to a conformational change resulting in activation of the kinase and induction of the insulin signaling cascade downstream of the receptor at micromolar concentrations. L-783,281 leads to phosphorylation of a number of proteins of the insulin signaling pathway including the β -subunit of the insulin receptor, the insulin receptor substrate-1 and the Akt-kinase (or protein kinase B). In addition, it stimulates phosphoinositol 3-kinase. L-783,281 was also shown to increase glucose uptake in primary adipocytes and in soleus muscle.

Cinnamtannin B1 (Fig. 1) is a double-linked proanthocyanidin isolated from stem bark of *Cinnamomum zeylanicum*. Cinnamtannin B1 is water soluble compound found in acetone extract after soxhlet extraction. The compound is giving sweet taste and exhibited an interesting activity on adipocytes cells. In our research we did evaluate its activity for preadipocytes differentiation, glucose uptake and phosphorylation of insulin receptor.

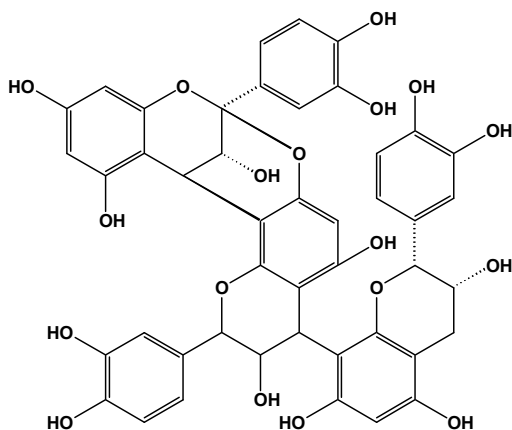


Figure 1: Chemical structure of cinnamtannin B1

Cinnamtannin B1 induces adipocyte differentiation

Cinnamtannin B1 was evaluated for its activity to induce adipogenesis. It was used to induce differentiation of preadipocytes into adipocytes. Two days post confluent (day-0), preadipocytes were induced with the cocktail of dexamethasone (0.25 mM) and 3-isobutyl-1-methylxanthine (0.5 mM) containing cinnamtannin B1 (100 µg/mL) and/or insulin (1 µg/mL).

On the day-two post confluent, preadipocytes were treated with different inducers as summarized in Table 1. On the day-11, preadipocytes differentiation was terminated and stained with oil red O. Fat droplets in these cells were visualized and photographed.

Figure 2 shows that replacing insulin with cinnamtannin B1 exhibited high density of lipid droplets. This result indicated that cinnamtannin B1 was able induce adipocyte differentiation of 3T3-L1 preadipocytes.

Table 1: Composition of inducer agent to convert 3T3-L1 preadipocytes to 3T3-L1 adipocytes

Day	Negative control	Positive control	Treatment
Inducers added at day 0	No inducer	Dex. 0.25 mM IBMX 0.5 mM Insulin 1 µg /mL	Dex. 0.25 mM IBMX 0.5 mM Cinnamtannin B1 100 µg/mL
Inducers added at day 2	No inducer	Insulin 1 µg /mL	Cinnamtannin B1 100 µg/mL

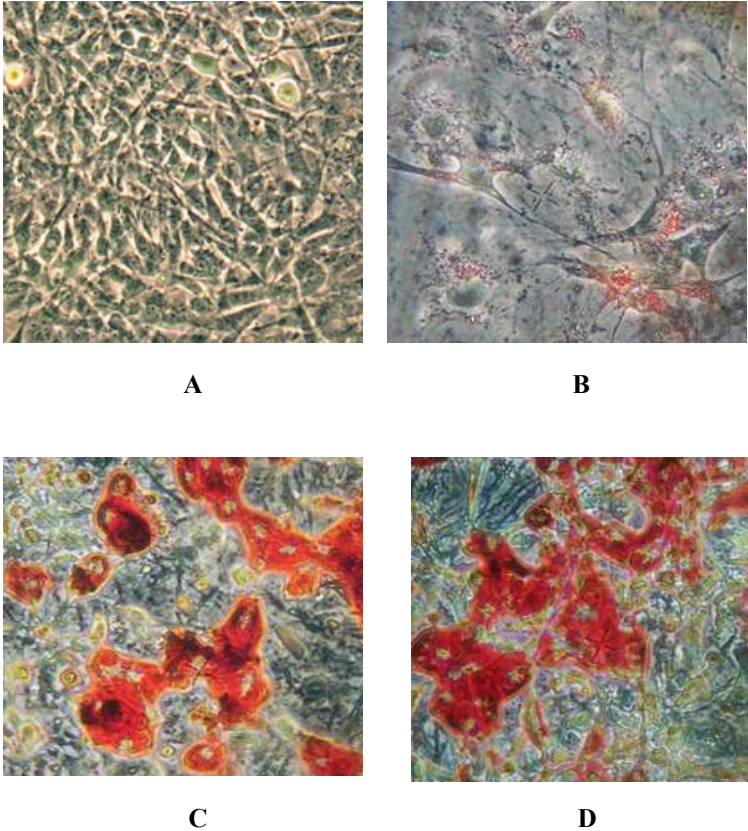


Figure 2: Effects of cinnamtannin B1 on adipogenesis of 3T3-L1 preadipocytes.

Differentiation is induced by addition inducers as indicated in Table 1. After day-11, preadipocytes differentiation was terminated and stained with oil red O. The figure shows the lipid accumulation can be seen in all the induced samples. **A**= the confluent of undifferentiated preadipocytes (unstained), **B**= non-induced, **C**= control, containing (insulin + dexamethasone + isobutyl methylxanthine), **D**= treatment, containing (cinnamtannin B1+ dexamethasone+ isobutyl methylxanthine). Red areas show lipid droplets.

The stained cells were then extracted with 1 ml of 4% Igepal CA-630 in isopropanol and measured with ultraviolet spectrophotometer to quantify the concentration of oil red O. Figure 3 shows an increment of lipid droplets in the samples treated with inducers as compared to negative control.

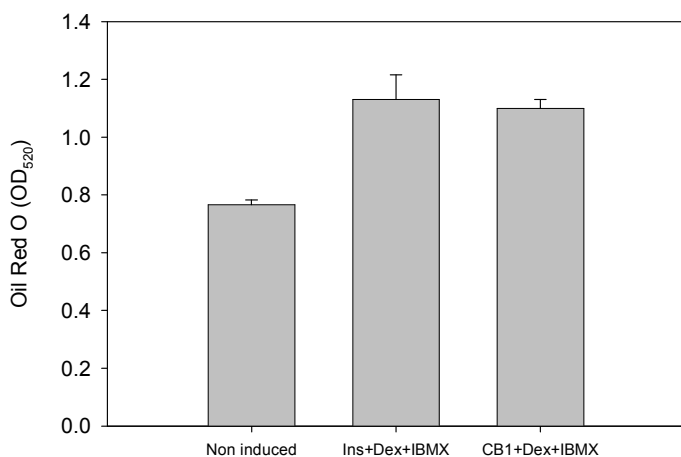


Figure 3: Adipogenesis assay

After day-11, preadipocytes differentiation was terminated and stained with oil red O and extracted with isopropanol and measured with UV spectrophotometer. Results are means \pm SE of three experiments.

Before induction, 3T3-L1 cells free of any fat droplets in cytoplasm. On the day-three after induction, fat droplets were observed in the cytoplasm of 3T3-L1 cells and cells having two nuclei were detected. On the day-eight after induction by hormones and the cinnamtannin B1, about 90% cells differentiated, and there were fat droplets in the cells, which were bigger and circular. It was observed that some adipocytes, which had two nuclei, were dividing into two cells, and also there were significant fat droplets in both dividing cells.

Cinnamtannin B1 stimulates glucose uptake

The use of 3T3-L1 cells to investigate the regulation of the glucose transport system offers several advantages. Fully differentiated 3T3-L1 adipocytes are particularly responsive to insulin. In contrast to isolated adipocyte suspensions, which lose cell viability rapidly, 3T3-L1 adipocytes can be studied in stable cell monolayers which maintain cell viability and hormonal responsiveness for extended periods of time (Frost and Lane, 1985).

It was observed that upon stimulation of adipocytes by insulin, a membrane-associated intracellular pool of glucose transporters was translocated to the plasma membrane, thereby increasing the rate of hexose uptake. The increased V_{\max} for sugar uptake in the presence of insulin was, therefore, attributed to an increased number of glucose transporters at the cell surface (Frost and Lane, 1985).

In muscle and adipose tissue, insulin accelerates the uptake of glucose by facilitating the translocation of the glucose transporter-4 (GLUT-4) to the cell membrane. Deoxyglucose uptake rate by mature 3T3-L1 adipocytes is achieved within 3-4 min after activation by insulin and then proceeds at a constant rate for at least 10 min. In the saturating insulin level, deoxyglucose uptake was activated by insulin 17-fold (Frost and Lane, 1985).

Several recent clinical studies have confirmed that some antidiabetic agent such as vanadium salts improve insulin action and reduce hyperglycemia. Vanadium is a nonspecific inhibitor of phosphatases, and potent inhibition of the phosphatases that dephosphorylate and deactivate insulin receptor tyrosine kinase activity provides a mechanism for enhanced insulin action. It is likely that this is not the only mechanism through which vanadium compounds can enhance insulin action.

These compounds increase glucose transport in skeletal muscle when the recognized pathway of insulin stimulated glucose transport via insulin receptor substrates-1 and -2 (IRS1/2),

phosphatidylinositol 3-kinase (PI 3-kinase) and protein kinase B has been blocked. Accordingly, vanadium compounds have been reported to act via an alternative signaling pathway to increase the translocation or activity of glucose transporters (Bailey, 2000).

Glucose transport across the cell plasma membrane is the first step of glucose metabolism in the target tissue. To determine that effect, the activity of the cinnamtannin B1 on glucose uptake was investigated.

After incubation of the cells with 100 µg/mL cinnamtannin B1, the radioactive labeled glucose uptake into cells was analyzed. As shown in Figure 4, 100 nM insulin maximally stimulated glucose uptake in adipocytes and cinnamtannin B1 also significantly stimulated glucose uptake at 100 µg/mL. However, a combination of cinnamtannin B1 with the maximal effective concentration of insulin exhibited no significant effect in increasing stimulation of glucose uptake compared to cinnamtannin B1 or insulin alone.

Cinnamtannin B1 stimulated glucose uptake in 3T3-L1 adipocytes significantly increased by the treatment time. At 15 minutes post treatment, activity of the compound was not significant. After 15 minutes, its activity was increasing gradually. After 60 minutes, there was a significant increase in the uptake by a one and half of basal uptake. As expected, insulin stimulated glucose uptake was similar to that of the cinnamtannin B1 activity. The combination of the compound with insulin result in similar effect compared to uptake by insulin or the compound alone. It was suggested that cinnamtannin B1 exerted insulin-mimetic activities in adipocytes.

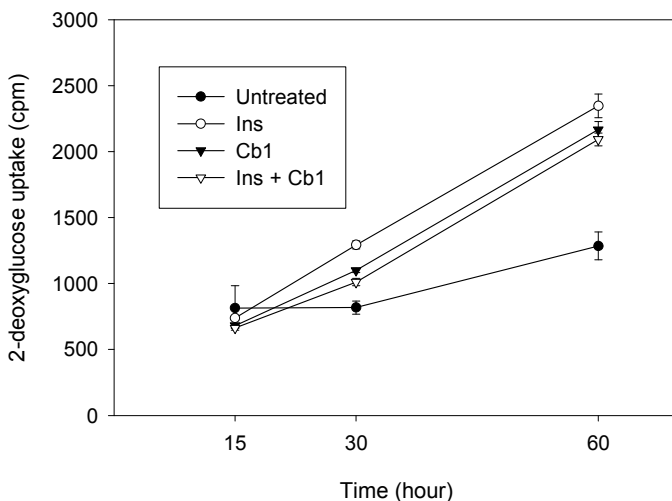


Figure 4: Effect of cinnamtannin B1 in stimulating glucose uptake.

3T3-L1 adipocytes in 25 cm²-T flask were incubated with 100 nM insulin, 100 µg/mL cinnamtannin B1 and 100 nM insulin + 100 µg/mL cinnamtannin B1. 2-deoxy-D-[³H] glucose uptakes were assayed using liquid scintillation counter. Results are means ± SE of three experiments.

Cinnamtannin B1 stimulates insulin receptor phosphorylation

Protein-tyrosine phosphorylation plays a central role in regulating a variety of fundamental cellular processes. The current hypothesis of insulin action proposes that interaction of insulin with its receptor leads to phosphorylation its own receptor with subsequent activation of the receptor tyrosine kinase activity. Immunoprecipitation of insulin receptor demonstrated that two major subunits of insulin receptor phosphorylated with molecular weights of 135,000 and 95,000 that correspond exactly to the position of the α- and β-subunit of the insulin receptor, respectively (Kasuga *et al.*, 1982 and Zick *et al.*, 1983).

Insulin binding to the insulin receptor activates a series of signal transduction events that result in specific biological actions in sensitive tissues. The signaling cascade starts with autophosphorylation of the insulin receptor through its tyrosine kinase activity and subsequent phosphorylation of insulin receptor substrates (IRS). Phosphorylation of IRS leads to activation of the phosphatidylinositol 3-kinase (PI3K) and the mitogen-activated protein kinase (MAPK) pathways. Stimulation of glucose transport and disposal, glycogen synthesis, and inhibition of lipolysis are mediated by PI3-K activity, whereas MAPK promotes cell growth (Saltiel and Kahn, 2001).

A metabolite (LY78,3281) from a *Pseudomassaria* fungus stimulates insulin receptor tyrosine kinase activity with high specificity without inhibition of phosphatases, presenting another means to enhance insulin action (Zhang *et al.*, 1999). Given the recent evidence that defective phosphorylation of IRS-1 and IRS-2, PI 3-kinase and PKB are all implicated in the development of insulin resistance (Krook *et al.*, 2000).

This work investigated the role of cinnamtannin B1 tyrosine phosphorylation of insulin receptor of 3T3-L1 cells. Cell lysates were subjected to immunoprecipitation with anti-insulin receptor β -subunit antibody and the immunocomplex samples were subjected to SDS-PAGE, transferred to nitrocellulose membranes, and immunoblotted with monoclonal anti-phosphotyrosine antibody (4G10).

Figure 5 demonstrated the typical insulin stimulated tyrosine autophosphorylation of insulin receptor β -subunit. EGF-stimulated A431 cell lysate was positively exhibit phosphorylation at 170-kDa. Untreated cells was not exhibit phosphorylation of insulin receptor except for molecular weight of 55-kDa that expressed by all cell lysates. Treatment with 100 nM insulin expressed phosphorylation of insulin receptor β -subunit at 95-kDa. 100 $\mu\text{g}/\text{mL}$ cinnamtannin B1 alone augmented phosphorylation of insulin receptor. To investigate the ability of cinnamtannin B1 to potentiate the phosphorylation of insulin receptor, the cells were treated with

the combination of cinnamtannin B1 and insulin. Treatment of the cells with combination of cinnamtannin B1 and insulin activated phosphorylation similar to that of insulin alone. It was suggested that insulin and cinnamtannin B1 may be reacted competitively to insulin on receptor β -subunit.

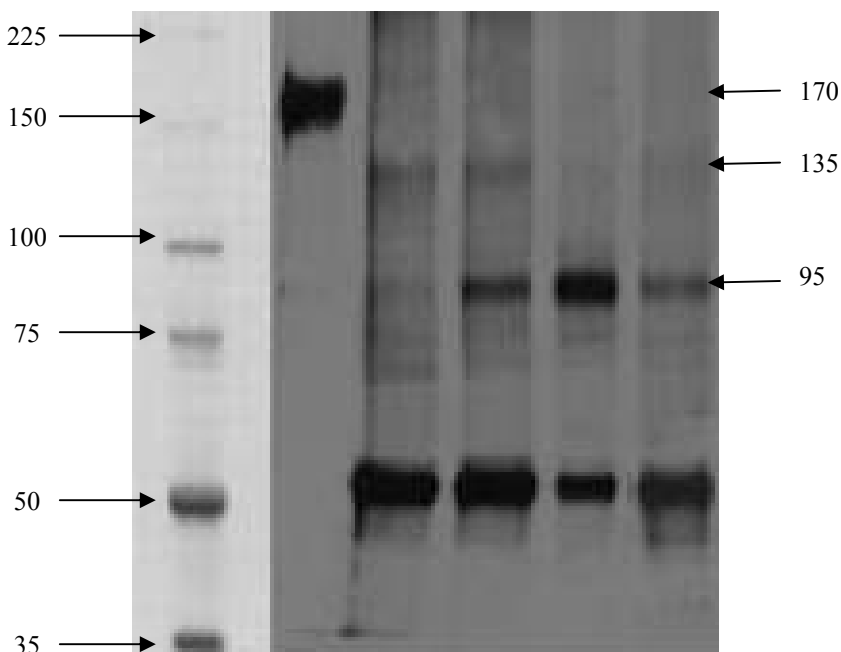


Figure 5: Effect of cinnamtannin B1 on phosphorylation of insulin receptor of 3T3-L1 adipocytes.

3T3-L1 adipocytes cells were left untreated, or treated with 100 nM insulin (Ins), 100 μ g/mL cinnamtannin B1 (Cb1), M= marker. Proteins were separated by electrophoresis, blotted onto a membrane, and detected with an antibody to phosphotyrosine (4G10).

Conclusion

In order to discover small molecules that activate the insulin receptor tyrosine kinase (IRTK), a cell-based assay has been

established and utilized to screen antihyperglycemic activity of cinnamon products. This approach was similarly to that of identification of a nonpeptidyl, small molecule, insulin-mimetic compound (demethylasterriquinone B-1, DMAQ-B1) that was isolated from a mixture of metabolites produced by a tropical endophytic fungus, *Pseudomassaria* sp. This compound induced human IRTK activation and increased tyrosine phosphorylation of IR β -subunit. It mediated insulin-like effects, including insulin receptor substrate-1 (IRS-1) phosphorylation and activation of phosphatidylinositol 3-kinase and Akt kinase. DMAQ-B1 also exhibited an insulin-like effect on glucose uptake in adipocytes and skeletal muscle (Salituro *et al.*, 2001).

It was proposed that mechanism of action of cinnamtannin B1 was similar to that of insulin (insulinomimetic). It postulated acts through activation of the β -subunit tyrosine kinase resulting autophosphorylation of β -subunit residues. The phosphorylation insulin receptor (IR) activated receptor phosphorylation of the endogenous substrates such as insulin receptor substrates (IRS)-1 and -2. IRS proteins recruit additional adaptor proteins that initiate multiple signaling cascades. Akt and MAPK are two divergent kinases, which are downstream of IRS and are activated by both insulin and IGF-I.

Then, IRS-2 activated PI 3-kinase, a lipid kinase that has key element in the pathway leading to metabolic effects of insulin. Activation of PI 3-kinase followed by translocation of glucose transporter to plasma membrane leading to stimulation of cellular glucose uptake. IRS-1 appears to be an important mediator in adipocytes differentiation. This signaling molecule appears to exert its unique role in differentiation via activation of PI3-kinase and its downstream target, serine/threonine protein kinase (Akt), and its upstream of the effects of peroxisome proliferators-activated receptor gamma (PPAR γ) and CCAAT/enhancer-binding protein alpha (C/EBP α).

In summary, it was found that cinnamtannin B1, a nonpeptidyl, small molecule that act directly on the IR β -subunit and

stimulated glucose uptake and adipocyte differentiation. Pathogenesis of type 2, non-insulin-dependent diabetes mellitus (NIDDM) is complex, involving progressive development of insulin resistance and a defect in insulin secretion. Several studies have shown that patients in NIDDM decrease in insulin receptor number. Decreasing in insulin stimulated receptor tyrosine kinase activity and defects in receptor-mediated IRS phosphorylation or phosphatidylinositide (PI) 3-kinase was found muscle or fat tissues from NIDDM patients or rodent NIDDM models. Cinnamtannin B1 that augmenting insulin receptor could be an important breakthrough in the treatment of diabetes and insulin resistance.

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Injury Surveillance System Trial for Medical College Hospital Thiruvananthapuram

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Abstract

Background: Modern day control programs aiming at reducing both communicable and non-communicable diseases have been setup in most parts of the world. But in the developing nations like India, no specific surveillance systems have been established for injuries. Such a system could potentially bring down the injury load by providing data for acting at the level of causation. Since injuries tend to affect mostly the productive age group, such measures hold special meaning for developing nations across the world. Such a system provides data regarding which area needs to be worked upon.

Objectives:

- To introduce the concept of Injury surveillance and demonstrate its importance.
- To draw out the pattern of Injuries in the casualty Medical College Hospital Thiruvananthapuram.

Methodology: This is a case series study using the definition of injury as provided by WHO guidelines for Injury surveillance. Data related to injury was collected using a

precoded questionnaire from the Triage area of the casualty for one month and analysed.

Results: It was seen that majority of injuries were caused by traffic accidents (49.3%) followed by fall (36%), assault (3.8%), Burns (2.4%), Poisoning (0.5%), and others.

Injuries mostly occur in age group 21-30(31.8%) and 31-40(18.2%). Sex wise - Males (74.3%).

90.3% of injuries were unintentional. Self injuries were 4.5% and assault 5.1%.

Among Traffic accidents, only 8.7% of persons were using safety measures out of 63% persons to whom they were applicable. 22.8% had suspected alcohol consumption.

Location data showed the area distribution of RTAs.

41.3% of injuries occurred to those using bike out of which 30.4% were riding the bike & 10.9% were pillion riding. 28.3% occurred to pedestrians. Opposite vehicle involved was bike - 22.8%, car and other light motor vehicles -26.1%, bus & other heavy vehicles 17.4% and Skidding or hitting a stationary object -15.2%.

The average time taken to report to casualty is 1 hour and 20 minutes.

Among intentional injuries(assault) the background was of quarrel or pre-existing rivalry (75%), Involved were mostly male (75%), age groups involved were mainly 21-30 and 31-40(75%) and 62.5% of them used a heavy sharp weapon. Among them, 12.5% had suspected alcohol consumption.

Among burn victims, 28% were of age group 21-30 years, intent was mainly self harm (60%), assault (20%).

Conclusion: From the results, Traffic accidents form the majority case load (52.3%), safety measures usage needs to be improved (currently 8.7%), and location data collected on them can be used for city planning.

Likewise, other areas to be worked upon can be identified. Improvement in the fields would be indirectly reflected in the serial data collected.

Regarding feasibility of introducing such a system, we found that data collection can be introduced without any change in the existing setup, but analysis needs participation of trained personnel. Results obtained can be used for various planning purposes.

Keywords: Injury surveillance, Hospital based, Surveillance system

Introduction

Injuries have been described as the biggest epidemic of the 21st century killing more than 5 million people worldwide each year and causing many more cases of disability. People from all economic groups suffer fatal injuries, but death rates due to injury tend to be higher in those in the lower income groups. The poor are also less likely to make a full recovery following an injury. Injuries have traditionally been regarded as random, unavoidable

“Accidents”. Within the last few decades, however, a better understanding of the nature of injuries has changed these old attitudes, and today both unintentional and intentional injuries are viewed as largely preventable events.

To develop effective prevention strategies, most countries need better information. In particular, countries need to know about the numbers and types of injuries that occur and about the circumstances in which those injuries occur. Such information will indicate how serious the injury problem is, and where prevention measures are most urgently needed.

Recent years have witnessed a rapid increase in motorization, industrialization, migration, and urbanization consequent to the larger globalization in India. As a result, life styles and value systems of people have changed. In consonance with these changes, injuries are emerging as a leading cause of deaths, hospitalizations, disabilities and socioeconomic losses in India. Systematic and scientific efforts in injury prevention and control are limited or yet to begin. While injuries have been on

the decline in many developed parts of the world, it is on a constant increase in India. The lessons learnt from High Income Countries are crucial for injury prevention in India to avoid repetition of mistakes and to make appropriate decisions with recognition of principles. Last four decades of research and policy developments across the world have shown that injuries are predictable, preventable and needs a systems approach. In the absence of coordinated, integrated and intersectoral approaches, injury prevention and control is at cross roads and without direction in India. Comprehensive information on injuries are often lacking or, at best, patchy. Good quality, reliable and representative information is very vital to formulate injury prevention programs in India, a country which lacks such systems till date. Thus, time is appropriate to give a major push and direction for this area in India.

What is Injury?

The standard definition of an “injury” as used by WHO is: “Injuries are caused by acute exposure to physical agents such as mechanical energy, heat, electricity, chemicals, and ionizing radiation interacting with the body in amounts or at rates that exceed the threshold of human tolerance. In some cases (for example, drowning and frostbite), injuries result from the sudden lack of essential agents such as oxygen or heat (Baker et al., 1992).

The energy causing an injury may be:

- mechanical (e.g. an impact with a moving or stationary object, such as a surface,
- knife or vehicle)
- radiant (e.g. a blinding light or a shock wave from an explosion)
- thermal (e.g. air or water that is too hot or too cold)
- electrical
- chemical (e.g. a poison or an intoxicating or mind-altering substance such as alcohol

or a drug).

Whereas the above definition of an injury includes drowning (lack of oxygen), hypothermia (lack of heat), strangulation (lack of oxygen), decompression sickness or “the bends” (excess nitrogen compounds) and poisonings (by toxic substances), it does NOT include conditions that result from continual stress, such as carpal tunnel syndrome, chronic back pain and poisoning due to infections. Mental disorders and chronic disability, although these may be eventual consequences of physical injury, are also excluded by the above definition.

What is surveillance?

The standard definition of “surveillance” as used by WHO is (Injury Surveillance guidelines, 2001): “Surveillance is the ongoing, systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of health practice, closely integrated with the timely dissemination of these data to those who need to know. The final link of the surveillance chain is in the application of these data to prevention and control. A surveillance system includes a functional capacity for data collection, analysis and dissemination linked to public health programs (CDC, 1988).

Active versus passive surveillance

In *active surveillance*, injury cases are sought out and investigated; injured persons are interviewed and followed up. Active surveillance usually requires large expenditures of human and financial resources (Injury Surveillance guidelines, 2001).

In *passive surveillance*, relevant information is collected in the course of doing other routine tasks. That is to say, the generation of data is not necessarily the primary function of the system that yields the data. In most settings, the use of well-designed forms and, perhaps, the addition of just a few extra

steps to an established routine, means that surveillance adds little in the way of costs.

Why do surveillance?

Without reliable information, health care planners are severely handicapped. They are unable to allocate resources so as to achieve the greatest impact in preventing injuries, reducing the harm they do, and treating and rehabilitating injured persons (Injury Surveillance guidelines, 2001).

Injury profiles vary greatly from country to country, with large differences in the total numbers of injuries, types of injuries, numbers of deaths and serious disabilities, and levels of intervention.

Trends vary from country to country. Injury profiles can change suddenly in response to economic ups and downs, social upheaval, and rapid shifts in the levels of industrialization, urbanization and motorization.

Injury problems tend to be greatest in those countries with the fewest resources.

Low-income countries especially, are plagued by a greater number and variety of potential hazards, yet have the least capacity to prevent and treat injury.

Objectives

- To study the pattern of Injuries reported to the Casualty of Medical College hospital Thiruvananthapuram.
- To introduce the concept of Injury surveillance and demonstrate its importance.

Methodology

- Study design: Case Series Study
- Study Setting:

The Casualty of Medical College Hospital Thiruvananthapuram- A tertiary care centre.

- Period of Study: 10th Dec 2008 to 10th Jan 2009
- Study Subjects:
All patients reporting with injuries at the Casualty of Medical College hospital, Thiruvananthapuram. The total case load incurred was 260 patients.

Inclusion criteria:

- All patients attending The Casualty of Medical College Hospital, Trivandrum.
- For the same person with multiple injuries of various causes, all injuries are accounted for.
- Repeated visits for treatment of injuries due to different causes.

Exclusion criteria:

- Repeated visits for treatment of same injury.
- Cases with unreliable information and those with unavailable information

- Study Variables
 - Age
 - Sex
 - Time delay in presentation
 - How the injury was inflicted
 - Intent
 - Alcohol consumption
 - For Traffic injuries
 - Place of occurrence
 - Activity at time of injury
 - Opposite vehicle involved

- Safety measures used
- For Assault
 - Place of occurrence
 - Context
 - Relationship of assaulter with victim
 - Object used for assault

Results

I. General Data

1) Pattern of injuries

The general pattern of injuries are as follows

Table: 1

How injury occurred	Percentage
RTA	49.3
Assault	3.8
Fall	36
Burns	2.4
Choking/Hanging	0.9
Poisoning	0.5
Other Blunt Forces	6.6
Others	0.5

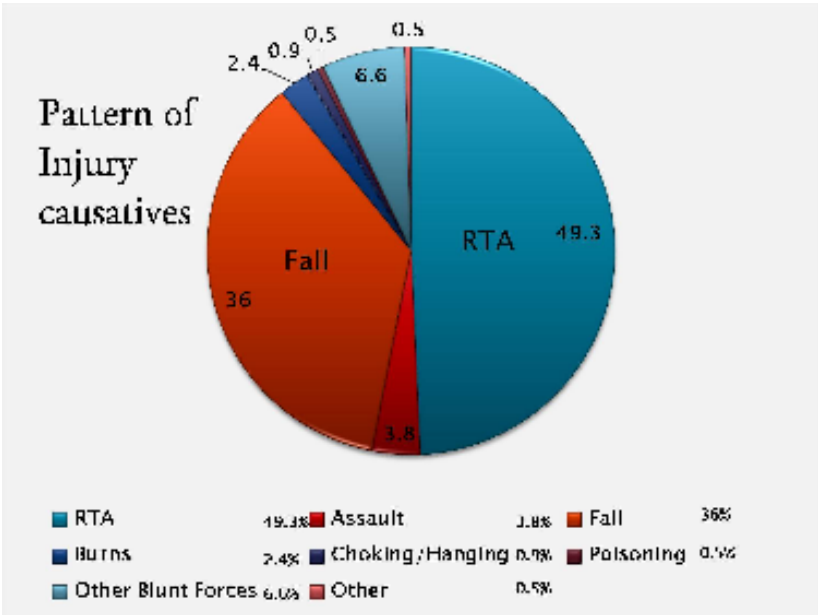


Figure 1

This data (Table 1) indicates that about half of the injuries are due to RTA which are indeed preventable if proper interventions are done.

2) Intent

Definition: The role of human intent in the occurrence of the injury incident.

Table 2

Intent	Percentage
Unintentional (accidental)	90
Intentional (Assault)	5.7
Intentional (Self Harm)	4.3

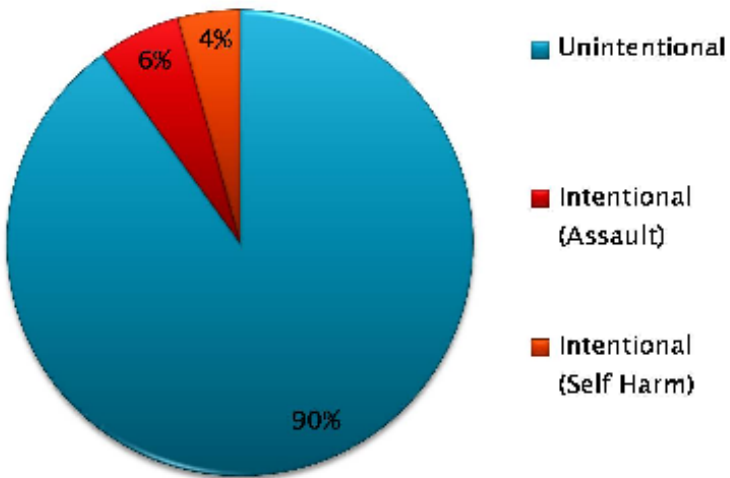


Figure 2

Fig: 2 reflects the general pattern for injury but its different when each injury is analyzed individually. This result is shown here is for comparison with individual results obtained.

Time delay in presentation

Time delay in presentation reflects the time difference between occurrence of the injury and presentation of case to the casualty.

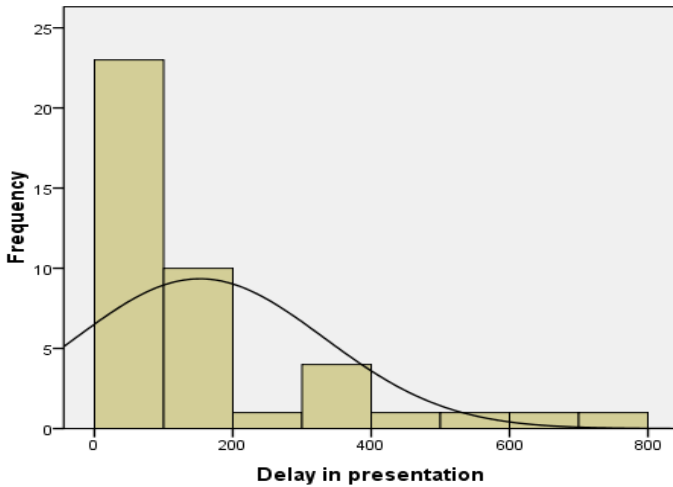


Figure 3

Median Time delay: 1 hour 15 minutes

Since the median time delay is more the 1 hour (Figure 3) it exceeds the *Golden hour concept* of intervention. This indirectly reflects the current status of pre hospital care.

Nature of Injury

Definition: The physical nature of the injury, real or suspected, which brought the person to the agency. If more than one injury, both are accounted for.

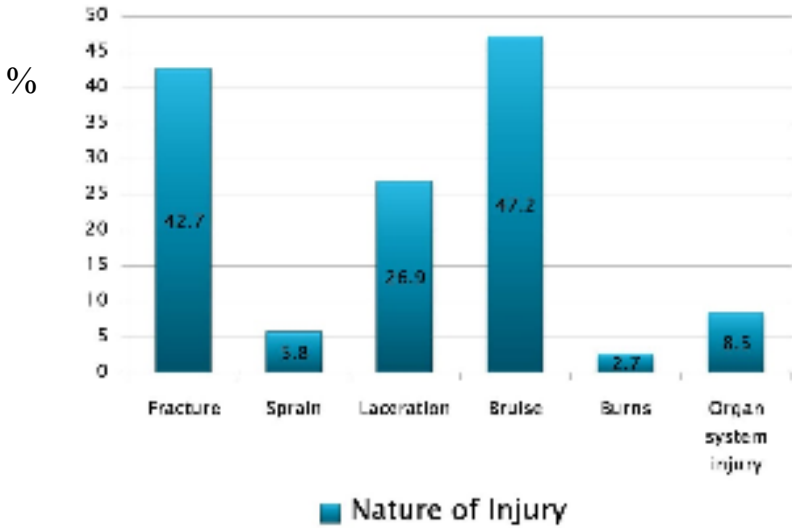


Figure 4

Table 3

Nature	Percentage
Fracture	42.7
Sprain	5.8
Laceration	26.9
Bruise	47.2
Burns	2.7
Organ system injury	8.5

About half of the injury caused are fractures which reflects the referral pattern to our hospital.

II. Road Traffic Accidents (RTA)

Definition: A road traffic accident (RTA) is any injury due to crashes originating, terminating or involving a vehicle partially or fully on a public highway (WHO, 1992).

1) Age pattern

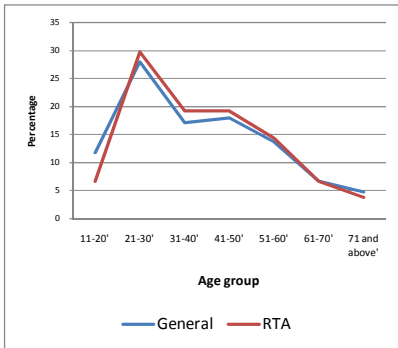


Figure 5

Table 4

Age(in years)	General Pattern (%)	RTA (%)
11-20	11.8	6.7
21-30	28	29.8
31-40	17.1	19.2
41-50	18	19.2
51-60	13.7	14.4
61-70	6.6	6.7
71 and above	4.7	3.8

Age pattern shows a peak at age group between 21-30 yrs similar to the general pattern.

2) Sex pattern

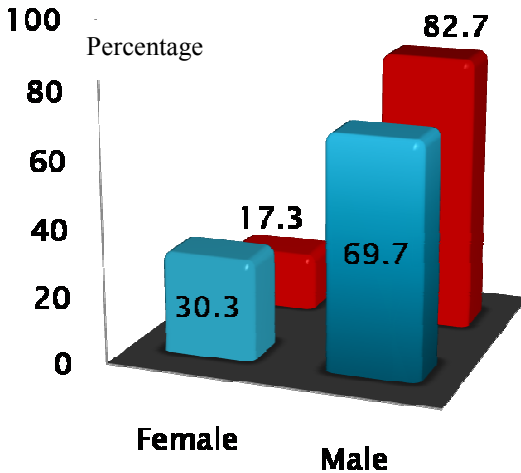


Figure 6

Table 5

Sex	General pattern (%)	RTA (%)
Female	30.3	17.3
Male	69.7	82.7

Males constitute about 82.7% which is a little more than the general pattern of sex distribution in our study.

Mode of transport

Definition: How the injured person travelling at the time of the injury event (Injury Surveillance guidelines, 2001).

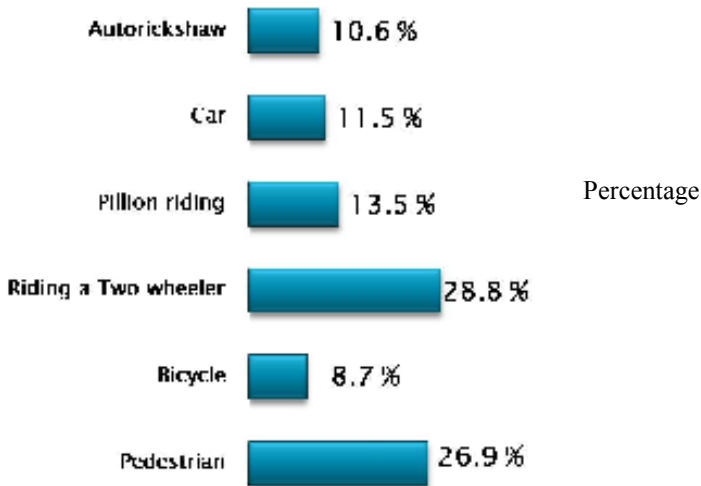


Figure 7

Results indicates that pillion riding and riding a two wheeler together (42.3%) constitute the majority of cases while pedestrians comes next (26.9%).

5) Opposite Vehicle involved

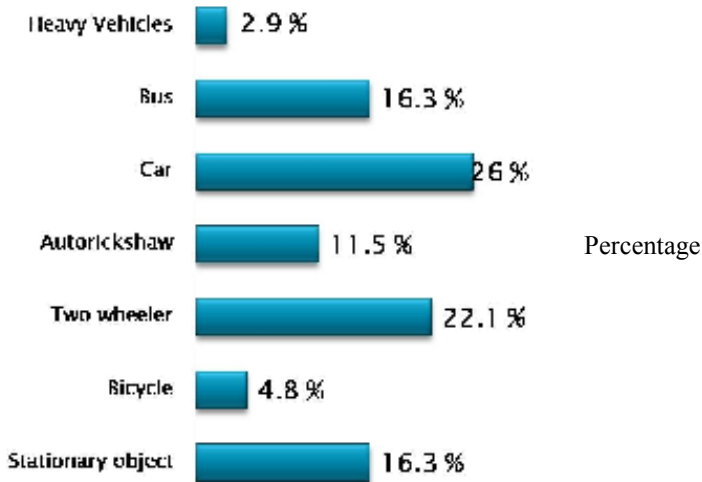


Figure 8

Results indicate that cars constitute the highest percentage (26%) and two wheelers came next at 22.1%.

Alcohol Consumption

Definition: Suspicion or evidence of alcohol use before the injury event, by the injured person or others directly involved in the incident (Injury Surveillance guidelines, 2001).

The tool here used is only the smell of alcohol as detected by the triage physician at time of presentation to the casualty.

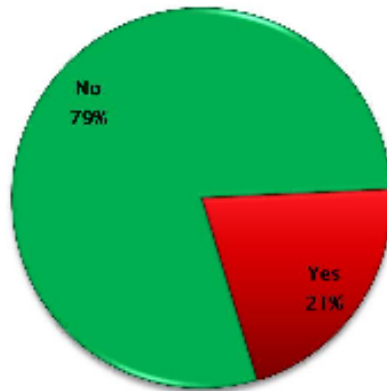


Figure 9

Positive cases recorded were 21%, but in due consideration with median time delay in presentation, accurate results on diagnosis of consumption of alcohol could not be assured.

Safety measures

Safety measures here taken into account are those which are established by law (Govt of India) viz helmet in case of two wheelers and seat belt in case of four wheeler, but certain cases do not require the same as in cases persons travelling in auto rickshaw and bus etc which constitute the not applicable group.

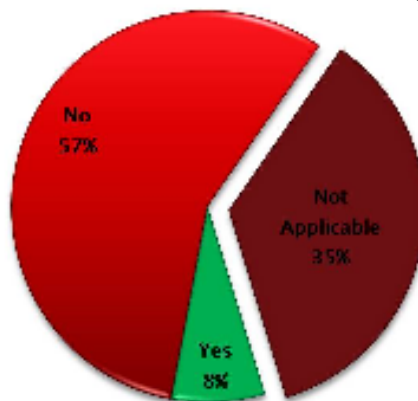


Figure 10

To the 65 % of cases to whom they were applicable, only 8% used the safety measures.

Geographical distribution of RTA in Thiruvananthapuram City, Kerala

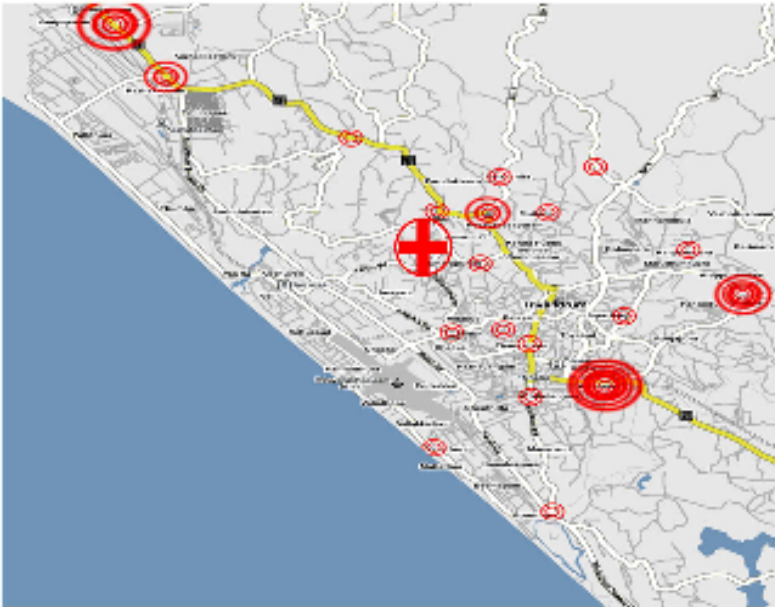


Figure 11

Shown above is the satellite based mapping system of Thiruvananthapuram city. Based on the location data collected, the areas where accidents occur were plotted. This indicates the relative frequency of accidents at a particular area and the radius of circle indicates the relative number of cases occurring at that particular area/ junction.

The yellow line indicates the national highway (NH47) through the district and red cross indicates medical college Thiruvananthapuram.

III. Assault

Definition: "The intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, mal development, or deprivation (WHO, 1996)"

1) Context

Definition: The factor(s) that precipitated the assault.

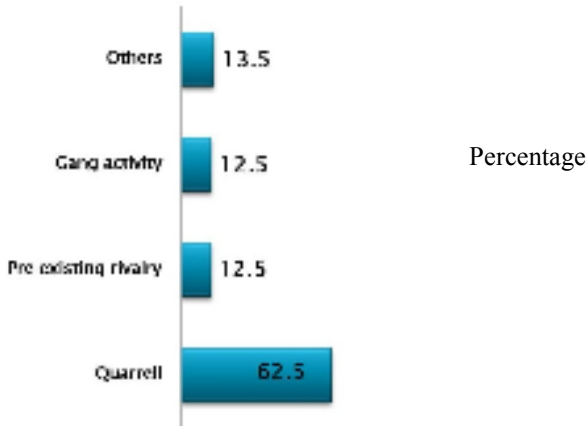


Figure 12

Majority (62.5%) of cases of assault resulted due to quarrel as indicated by the data collected.

2) Perpetrator/Victim Relationship

Definition: The relationship of the perpetrator to the victim.

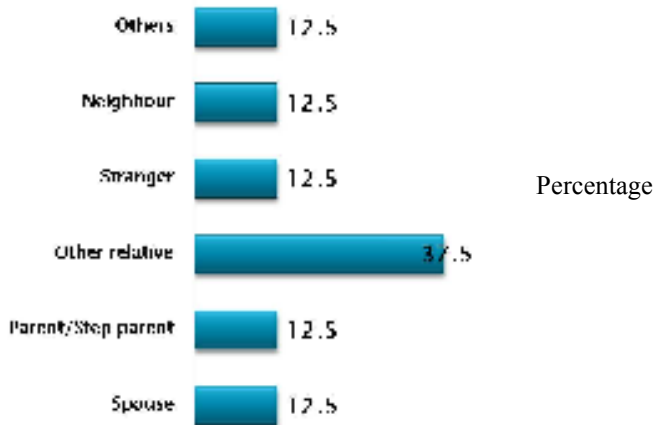


Figure 13

The data given above is indicative that assault mainly occurs between family members.

3) Age wise pattern

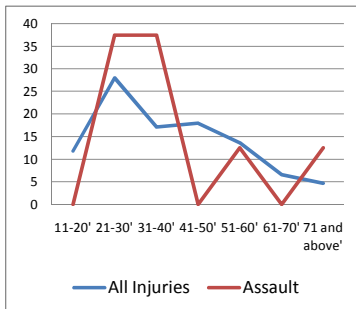


Figure 14

Table 6

Age Group (years)	General pattern (%)	Assault (%)
11-20	11.8	0
21-30	28	37.5
31-40	17.1	37.5
41-50	18	0
51-60	13.7	12.5
61-70	6.6	0
71 and above	4.7	12.5

There is a high peak at age group between 21-40 yrs.

4) Sex distribution

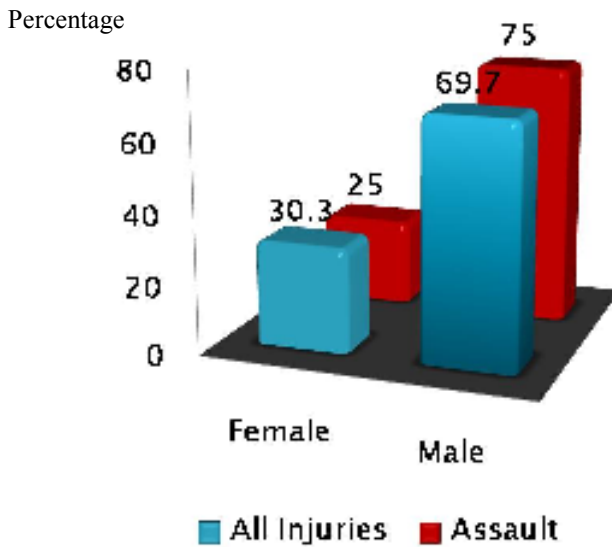


Figure 15

Sex distribution does not show much of a difference from the general pattern.

IV. Fall

Definition: Fall is a case of primary impact of the body with the ground.

Fall-related deaths and non-fatal injuries exclude those due to assault and intentional self-harm. Falls from animals, burning buildings and transport vehicles, and falls into fire, water and machinery are also excluded (WHO, 1992).

1) Age Distribution

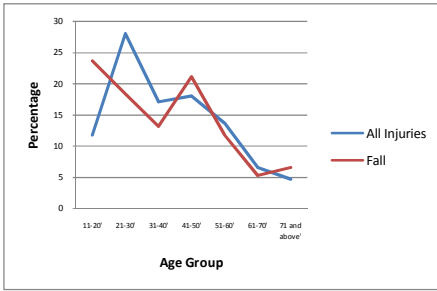


Figure 16

Table 7

Age group (years)	General Pattern (%)	Fall (%)
11-20	11.8	23.7
21-30	28	18.4
31-40	17.1	13.2
41-50	18	21.1
51-60	13.7	11.8
61-70	6.6	5.3
71 and above	4.7	6.6

The analysis showed that the cases of fall were distributed towards the younger and middle age group.

2) Sex Pattern

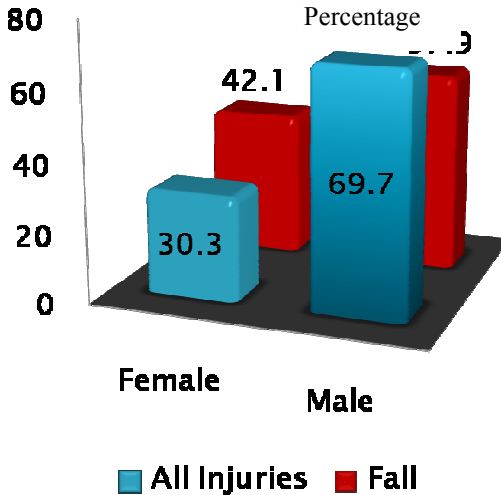


Figure 17

Female percentage (42.1%) for cases of fall is higher than that for the general pattern of injuries.

V. Burns

Definition: A burn occurs when some or all of the different layers of cells in the skin are destroyed by a hot liquid (scald), a hot solid (contact burns) or a flame (flame burns). Skin injuries due to ultraviolet radiation, radioactivity, electricity or chemicals, as well as respiratory damage resulting from smoke inhalation, are also considered to be burns (WHO, 1994).

1) Age wise Distribution

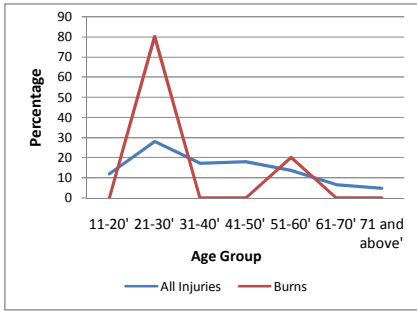


Figure 18

Table 8

Age group (years)	General Pattern (%)	Burns (%)
11-20	11.8	0
21-30	28	80
31-40	17.1	0
41-50	18	0
51-60	13.7	20
61-70	6.6	0
71 and above	4.7	0

The analysis shows that most cases fall within the age group of 21 to 30 years. The younger age groups are mostly affected in this preventable form of injury.

2) Sex distribution

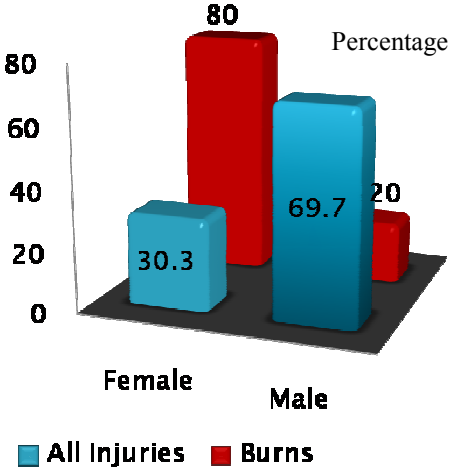


Figure 19

Contrary to the general pattern, the sex distribution data showed that cases of burns occurs mostly to females (80%).

3) Intent

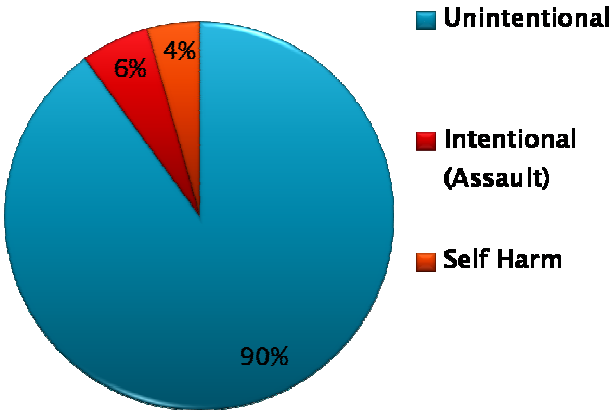


Figure 20

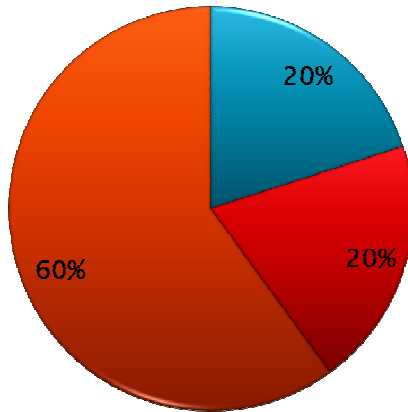


Figure 21

For cases of burns, the data regarding intent showed a contrasting difference. While for general pattern of injuries, 90% were unintentional, for cases of burns, only 20% were unintentional, and the rest- 60% was intended as Intentional assault, and 20% was intended as Intentional self harm.

VI. Choking/ Hanging

Definition: A form of injury caused by suspension of the body by a ligature which encircles the neck, the constricting force being the force of the body. It constituted 0.9% of all cases of injury. The details were not analyzed due to limitations due to the sample size.

VII. Poisoning

Definition: The category “poisoning” as used here refers to all unintentional poisoning-related deaths and non-fatal outcomes caused by exposure to noxious substances. Those which are intentional or for which the intent is undetermined as well as those resulting from reactions to drugs are excluded from the definition as used here (WHO, 1992). It constituted 0.5% of all cases of injury.

VIII. Other Blunt forces

Definition: Any injury caused due to a blunt trauma that cannot be included in the above. It constituted 0.5% of all cases of injury.

Inference

From the results which we obtained the areas where preventive interventions for injury can be effectively implemented are as follows:

1) Time delay (Median): 1 hour 15 minutes

Evaluate current pre hospital care .the time delay in presentation brings the patients to the hospital outside what is called the golden hour of injury that is time in which intervention is most effective

2) Two wheelers constituted the mode of transport of the majority (42.3%) of victims of RTA. The reason needs to be looked into and measures formulated to reduce this.

3) 21% of victims of RTA were suspected of alcohol consumption- This area needs to be looked into and more control brought about on drunken driving.

4) Safety measures used by only 8% of cases

This area has much scope for improvement

Despite the strict law implemented the current usage of safety measures is below par ,the cause of this needs to be evaluated .and if the surveillance system if established would help in indirectly reflecting the level of usage of safety measures in the community.

5) Geographical distribution data obtained can be used for effective planning measures.

6) In case of burn victims, the most injuries were seen among the 21-30 age group (80%), females (80%), and were mostly intended as self harm (60%). This indicates the need for studies into the mental health status of the population at risk.

Conclusion

From our experience of introducing this new system of hospital based surveillance of injuries, we could generate data on the major forms of injuries that affect the community.

The data collection for the system could be introduced without any change in the existing setup. But the data entry and analysis needs participation of trained personnel, the provision of which could break a potential barrier for its establishment.

Such a system if established could provide data which analyzed on a large enough time scale would give the seasonal trends and variation of injuries.

Results can be potentially used as guidelines for hospital development, city planning, law enforcement and planning of public health programs without adding much burden on the existing setup.

Limitations

Sample size proved a hurdle in analyzing the complete data on all the types of injury that we recorded.

The study period was one month which accounts for the small sample size and also for the reason why a seasonal trend could not be generated. Such results would need data collection for longer time duration.

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Application of Conducting Polymer Polyaniline in Biomedical Monitoring

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Abstract

Background: Electrically conducting polymers are interesting and very prospective class of new organic materials that combine solubility, processability and flexibility of plastics with electrical and optical properties of metals and semiconductors. These polymers have attracted remarkable attention in the recent decades and have been used and studied extensively in wide variety of applications including batteries, capacitors, smart windows, light emitting diodes, sensors, biosensors, drug delivery systems, electrochromic devices, switchable membranes, anticorrosive coatings, etc..

Aims & Objectives: of this paper were to make review of the incorporation of conducting polymers within biosensors, with special accent on polyaniline, one of the most widely investigated conducting polymers ever in order to increase research interest of polyaniline in Balkan especially in Bosnia and Herzegovina(B&H).

Methods/Study Design: Method we used for collecting data were collecting all available information from scientific

literature and articles in English, published until 2008, a method of theory analysis, a method of observation and a descriptive method.

Conclusions: These devices are used for the determination of clinical parameters (lactate, glucose, cholesterol, urea, etc.) in biological fluids, such as blood, urine and serum, and play very important role in clinical biology, food-processing industries and in sports medicine. Because of considerable flexibility in chemical structure and redox characteristics, they have been used as transducers in unmediated electrochemical biosensors

Suggestions: Concerning temporarily situation in Balkan and B&H, it is necessarily to choose professional and qualitative educated people for leading and taking responsibility in order to do more research in field of polyaniline and also to get some grants from the government so we could continue our research.

Keywords: Conducting polymer, polyaniline, biosensor

Introduction

Biosensors

Needs of today's world, especially in medicine, for detection of very different compounds had great impact for the development of sensor technologies, such as smart sensors, fiber-optical sensors, and thin film devices, etc. Biomedical monitoring of physiological liquids (blood glucose levels, presents of antibody, etc.) has provided a reliable and convenient method to diagnose, monitor and follow cases of different kind diseases, such as diabetes, AIDS, accidental poisoning, or detections of drugs, neurotoxins, microbial contamination and carcinogens.

Biosensors, due to their high sensitivity and selectivity, portable field-based size, possibility to determine various substances with different properties in 'real-life' samples, rapid response time and low-cost, are unavoidable for the measurement of

analytes of interest in modern medical diagnosis, environmental monitoring and food analyses.

Biophysical definition of biosensors is: these are, portable and simple for use, devices which detect, record and transmit information regarding physiological change or process.

Biosensors are in general analytical devices that measure the presence or concentration of biological molecules (analyte), by translating a biochemical interaction at the sensor surface into a measurable physical response.

Most biosensors consist of three principal components:

1.) *biological receptor (bioreceptor)* capable of recognizing the analyte of interest with a high degree of selectivity and specificity (enzymes, tissue slices, micro-organisms, antibodies, nucleic acids like deoxyribonucleic acid (DNA) strand, whole cell receptors, immunochemicals, organelle, or biologically derived materials or a biomimic component) (Saxena et al., 2003). Biological sensing element (bioreceptor) is usually integrated into a transducer and have the role of the sensing probes in biosensors.

2.) *transducer*, making possible the translation of the binding event (generation of: electrons, protons or physical changes in: conductivity, optical absorbance and fluorescence). Transducer may be electrochemical, thermometric, optical, piezoelectric or magnetic. Biological receptor and transducer could be seen as biosensor membrane.

3.) *method* for amplifying and measuring the change detected at the transducer, converting and displaying this into useful information.

Conducting polymers

There's a lot of vitality in this field (conducting polymers), and lots of new ideas still emerging from the simple fact that what you have here are materials with the electronic and optical properties of metals and semiconductors, while retaining the processing advantages and mechanical advantages of polymers.

Alan J.Heeger

Conducting polymers such as polypyrroles, polythiophenes and polyanilines have been projected for applications for a wide range of biomolecular electronic devices such as optical, electronic, drug-delivery, memory and biosensing devices.

Conducting polymers are interesting for sensor and biosensor applications because they can directly convert the binding event into an electrical signal and have been receiving great and broad interests in clinical diagnosis (Kan et al., 1997). They can also be modified chemically with appropriate functional groups for specific recognition and detection of different biological molecules and be scaled all the way down to the nanoscale. There are many advantages in preparing sensors with conducting polymers, such as efficient transfer of electric charge, and considerable flexibility in available chemical structure.

The use of biologically active dopants in conductive polymers allows the polymer to be tailored for specific applications.

Among all conducting polymers, polyaniline has recently achieved importance because of its unique conduction mechanism, easy synthesis, environmental stability, and easy procesability in its non-conductive base form. A relatively durable conjugated polymer such as polyaniline is considered as a three-dimensional network of intrinsically conducting macromolecular wires, which are able to transfer electrical signals. The advantage of using polyaniline for the biosensor development lies in its capability as a biomolecule (e.g. enzyme) entrapment matrix. (Wang et al., 1999).

There are evidences that redox enzyme could be doped within polyaniline (Borole et al., 2007), matrices immobilized on the surface of Pt and Au electrodes (Pan et al., 2004).

Aims

It is known that in the recent years number of published articles about polyaniline has exponential growth. The main idea of this work was to determine the way of growth in number of published articles, on the limited set of worldwide

relevant articles about polyaniline and biosensors, and also to investigate number of articles about polyaniline for the part of Balkan region in the same period.

Method

In this Review Paper it is shown an exhaustive inquiry of published articles in English from ACS (American Chemical Society) database of the most cited peer-reviewed journals in the chemical and related sciences. From 34 research journals published from ACS only 17 had articles (abstracts) with demanded key words:

- 1.) Accounts of Chemical Research (Acc. Chem. Res.)
- 2.) American Chemical Society Nano (ACS Nano)
- 3.) Analytical Chemistry (Anal. Chem.)
- 4.) Bioconjugate Chemistry (Bioconjugate Chem.)
- 5.) Biomacromolecules
- 6.) Chemistry of Materials (Chem. Mater.)
- 7.) Chemical Reviews (Chem. Rev.)
- 8.) Environmental Science and Technology (Environ. Sci. Technol.)
- 9.) Industrial and Engineering Chemistry Research (Ind. Eng. Chem. Res.)
- 10.) Journal of Agricultural and Food Chemistry (J. Agric. Food Chem.)
- 11.) Journal of the American Chemical Society (J. Am. Chem. Soc.)
- 12.) The Journal of Physical Chemistry A (J. Phys. Chem. A)
- 13.) The Journal of Physical Chemistry B (J. Phys. Chem. B)
- 14.) The Journal of Physical Chemistry C (J. Phys. Chem. C)
- 15.) Langmuir
- 16.) Macromolecules
- 17.) Nano Letters (Nano Lett.)

Key English words for search criteria were: polyaniline and biosensors in date range between January 1977 and December

2008. Resulted sample has 228 articles divided on this types: Research Article (212), News, Features and Commentary (16). Searching time interval started with 1977 due to published article C. K. Chiang, C. R. J. Fincher, Jr., Y. W. Park, A. J. Heeger, H. Shirakawa, E. J. Louis, S. C. Gau, A. G. MacDiarmid, 'Electrical conductivity in doped polyacetylene,' Physical Review Letters 1977, 39, 1098 in which possibility of creating controlled electrical conductivity of polimers is presented.

The second search criterion was: conducting polymers and biosensors in the same date time range. This resulted sample has 469 articles.

For the part of Balkan region, we investigated these databases:

- 1.) Hrvatska znanstvena bibliografija CROSBİ,
- 2.) COBISS.BH - virtual library of Bosnia and Herzegovina,
- 3.) COBISS.SR – virtual library of Serbia,
- 4.) COBISS.MK – virtual library of Macedonia,

in English, Bosnian, Croatian, Macedonian and Serbian in the period from 1991 till 2008.

Key word for this part of searches in Bosnian was *polianilin* and in English was *polyaniline*.

Searching for key words of polyaniline and biosensors has no results.

These bases are not completed, as mentioned at the preface of it, so we've made additional searches and supplement results. In this searches are taken into consideration all references which we have find, including articles, poster presentations, doctoral theses and master works.

Results

ACS database

Number of collected publications with regarding to: conducting polymers and biosensors in ACS database during period from 1977 to 2008 was 469 (Fig.1), while that number

for polyanilin and biosensors in the same database was 228. The first article in that database regarding conducting polymers and biosensors are issued 1984 (Dennis et al., 1984), while the first one about polyaniline and biosensors are issued four years later (Pierre et al., 1988).

A few published articles in the beginning have increasing linear trend till 2000, when two chemists (H. Shirakawa, A. G. MacDiarmid) and a physicist A.J. Heeger were awarded the Nobel Price in Chemistry for tremendous contribution in the field of conducting polymers. After that, interest for this kind of polymers shows enormous growth in the whole world, in science and industries as well, what resulted with exponential growth in number of published articles about conducting polymers, especially about polyaniline.

After our research, the fact of exponential growth of number of published articles about conducting polymers & biosensors and polyaniline & biosensors in ACS database till the end of 2008, could be seen on the diagram below (Figure 1).

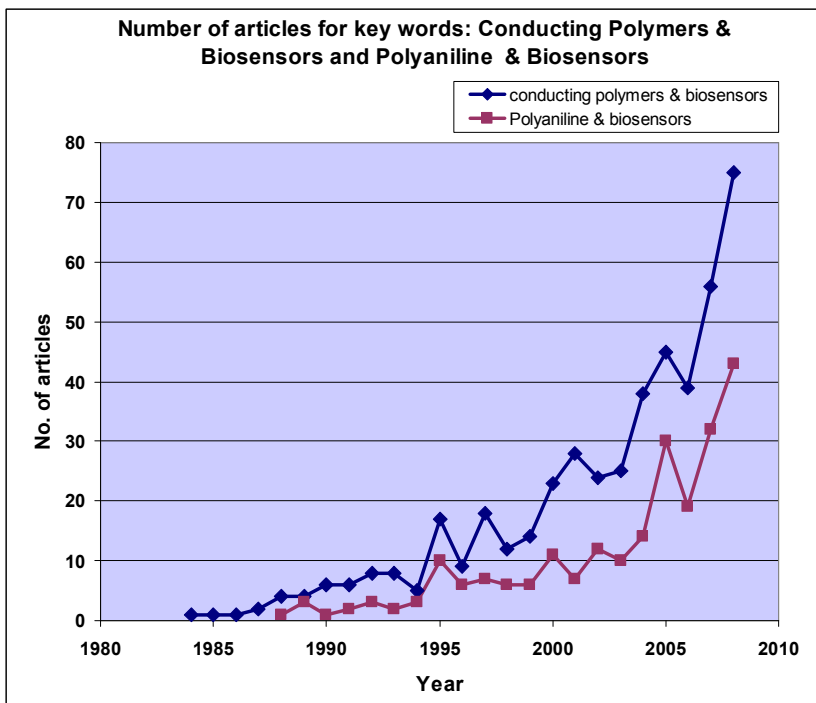


Figure 1: Number of articles in ACS database in the period (1980 – 2008), with key words: a.) conducting polymers, biosensors b.) polyaniline, biosensors

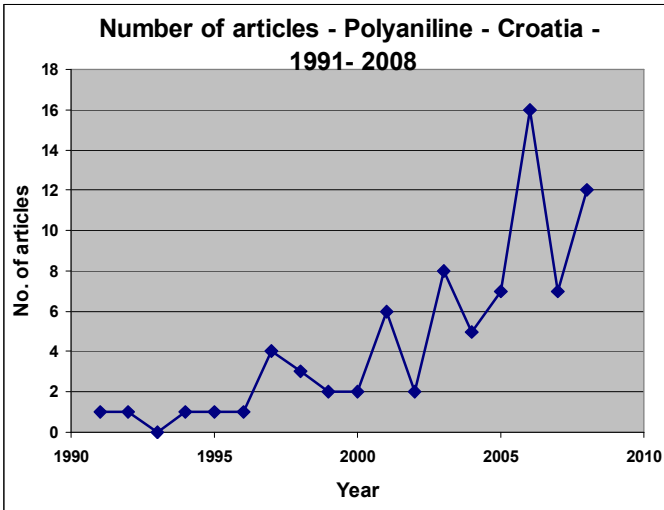


Figure 2: Number of articles in Croatia database in the period (1990 – 2008), with key words: polyaniline (eng.), polianilin (cro.)

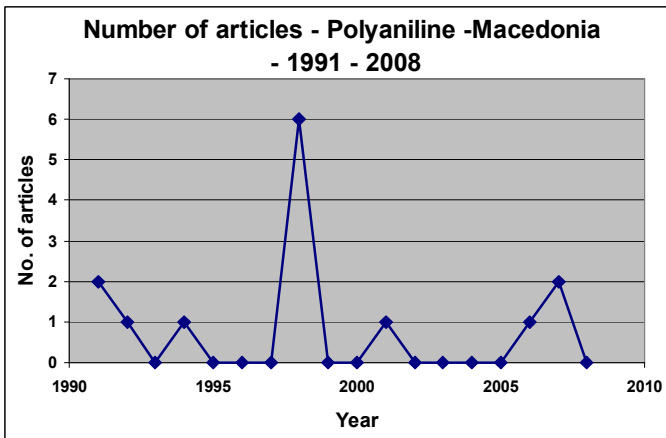


Figure 3: Number of articles in Macedonia database in the period (1990 – 2008), with key ward: polyaniline

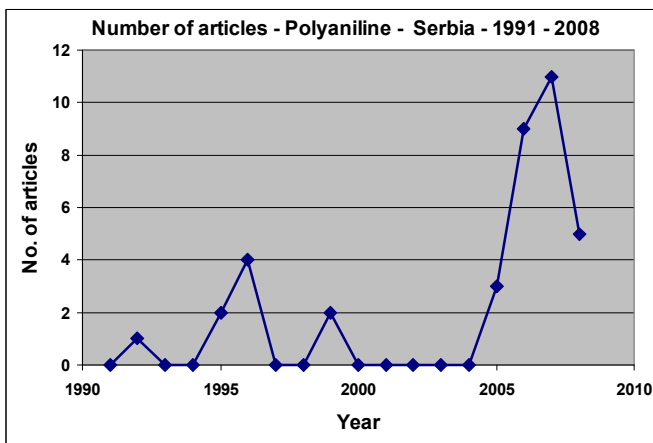


Figure 5: Number of articles in Serbia database in the period (1990 – 2008), with key wards: polyaniline (eng.), polianilin (srb.)

The first article about polyaniline, published in central Balkan area (ex- Socialist Federative Republic of Yugoslavia), was in Bosnia and Herzegovina in Collection of abstracts from The XII Yugoslav conference of electrochemistry, with the title: „*The influence of media on the initiation reaction of the electrochemical polymerization of aniline*” Duić Ljerka, Mandić Zoran, held from 06/03/1991 to 06/08/1991, Igman near Sarajevo (SVIBOR, 2008).

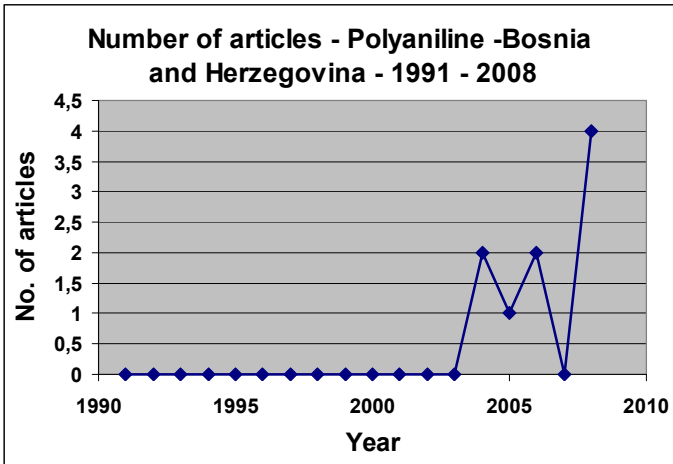


Figure 4: Number articles in Bosnia and Herzegovina database in the period (1990 – 2008), with key words: polyaniline (eng.), polianilin (bosnian)

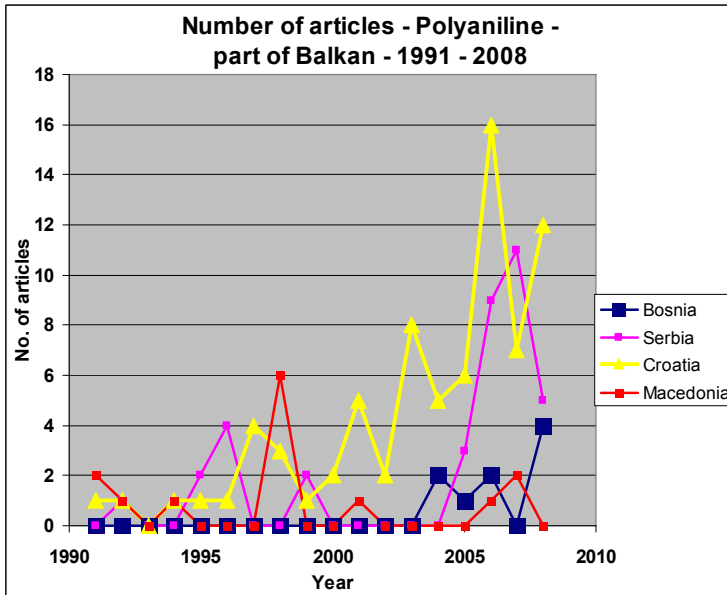


Figure 6: Number of articles in Bosnia & Herzegovina, Croatia, Serbia and Macedonia databases in the period (1990 – 2008), with key words: polyaniline, polianilin

Unfortunately, the war in Bosnia (1992-1995) stopped possibilities to start researches of conducting polymers, while Croatia and Macedonia each have four publications and Serbia three articles during the same period. After 1995, the number of articles in this area is increased.

It is clear from the Fig.2 that in Croatia there is, with some variations, continual significant increasing of published articles with maximum (16) in year 2006.

Researchers in Serbia, issued 9 articles in the period 1990 – 2000, and start with publishing again in year 2005. From 2005 till the end of 2008 they issued 28 new publications (Fig.5).

However, in Macedonia, there isn't still continuity in investigations and publications of articles about polyaniline, so they issue articles from time to time. Total amount of articles in this country is 14, with maximum (6) in year 1998.

Interest of investigations of polyaniline and its applications in Bosnia and Herzegovina started in year 2004 as a result of particular attempts of scientists (Gazdic; Muharemovic) from Faculty of Natural Science and Mathematics University of Tuzla, Department of Biophysics of Medical Faculty in Sarajevo and Department of Physical Chemistry of Faculty of Natural Science and Mathematics University of Sarajevo.

It should be emphasized that researchers from Bosnia had big support of colleagues from Department of Solid States Physics and Polymers of Natural Science and Mathematics University of Zagreb, Croatia, leading with prof.dr.sc. Dinko Babic. That international collaboration would be continued.

Conclusions

It's necessary to emphasize that number of publications about conducting polymers and especially polyaniline is connected with researches and reveals unique properties of conducting polymers, as a low density, variety of producing methods, high anisotropy of electrical conductivity, and possibility of controlled changing of electrical conductivity, optical absorbance, permeability, charge depositing, change of length

and volume. This possibility of controlling properties of materials had significant impact on construction of different devices, such as biosensors.

Number of published articles, in ACS database, about polyaniline and biosensors (43) in 2008 year represents 57,3 % of all published articles about conducting polymers and biosensors (75) in the same year, what is the confirmation (on this limited sample) that polyaniline with its extraordinary properties is the most applicable conducting polymer in biosensors.

Total amount of published articles about polyaniline in the period from 1991 till 2008 year connected with these four countries of Balkan is 136. In last four years the number is 79 articles, and represents 58% out of it. It indicates increasing interest for research in field of conducting polymers, especially polyaniline, in the central Balkan region. The fact that, in this list of publications, there is no article about application of polyaniline in the production of biosensors, points at necessity (in whole region) to continue research in this field of science and technology, for which is said that today present, the leading technology of 21st century. We could hope it would be recognized from Ministries of Education in these countries, especially in Bosnia and Herzegovina, where, after terrible war only education and science could give chance for improvement of lives for all people.

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Students' Opinion about Training in Primary Health Care

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Abstract

Teaching of basic clinical skills in primary care during the preclinical course help produce an integrated curriculum and introduce students to the community health problems. This study aims to evaluate students' opinion and suggestions about training in primary health care. An anonymous self-administered questionnaire was completed after the end of the program. The response rate was 93% of the fourth year medical students of Al-Hassa College of medicine, Saudi Arabia. Students showed high satisfaction with most of the training facilities. They reported many skills as the result of such training especially data collection, entry and analysis as well as communication skills. Students' suggestions included proper coordination with facilities to be visited, longer training duration and actual practice in PHC centers; and improving transportation. These suggestions need to be considered.

Keywords: Field training, Primary health care, Communication skills

Background

In the last few decades community-based medical education has been promoted increasingly (Morrison, 2006). Teaching and learning in the community has the potential to deliver a

major and positive contribution to undergraduate medical students (Bradley, 2001).

Community-based education is an educational approach that aims to prepare students for future professional work at community level (Schmidt, 2000). This educational activity takes place within a community or in a variety of health services settings at the primary health care (PHC) level (WHO, 1987). Teaching of basic clinical skills in primary care during the preclinical course help produce an integrated curriculum (Thistlethwaite et al., 2007a).

The use of primary care as a teaching base has been extended in many medical curricula (Howe, 2000). In North America, evaluation of several medical schools' curricula supported primary care as a valuable setting for medical education (Halos, 2005; Hansen et al., 1992). Early community clinical experience has been shown to motivate students and help them acclimatise to clinical environments, develop self-reflection and appraisal skills and develop professional identity (Dornan, 2005). Students can also appraise the communication systems that team members use in professional interactions with colleagues and patients (Thistlethwaite et al., 2007b). PHC can offer medical students access to a large pool of patients with opportunity to study diseases in their natural context through an holistic, problem solving approach to patient management (Illife, 1992).

The College of Medicine in Al-Hassa, King Faisal University, Saudi Arabia endorses the concept of integration and coordination between family and community medicine. During the fourth year, students are introduced to the concept and elements of PHC. Fieldwork provide experience in the logistics of running PHC activities and performing small-scale PHC-oriented research. Although field training in community medicine is applied in many school in Saudi Arabia, opinion and satisfaction of students on the contents and schedule of this educational program has not been evaluated. Students' satisfaction has been associated with their later professional attitudes, career commitment and retention. So students'

satisfaction is an outcome of educational process (Stitth et al., 1998).

Study Objective

This study aims to evaluate students' opinion and suggestions about the PHC field training program.

Methods

Target population:

All the 57 fourth year male students enrolled in PHC field training program during the Academic year 2007-2008 G.

Settings:

The Ministry of Health affiliated PHC facilities in Al-Hassa and College of Medicine in Al-Hassa, King Faisal University, Saudi Arabia.

Research committee of Al-Hassa college of Medicine approved the study as there is no ethical committee at the moment.

Approach:

At the end of the program students, after their verbal consent, were requested to fill an anonymous self-administered English questionnaire to evaluate the program and give their suggestions for future improvement.

Program description:

The program aims to introduce students to community health needs, to be acquainted with the functions, activities, implemented national programs and organization of PHC; to develop communication skills with patients and attendants; and to collect and enter data into Statistical Package for Social Sciences (SPSS) program with preliminary analysis.

Schedule:

Six days visits, 6 hours daily, to PHC facilities. Half a day visit to each of the following facilities: PHC administration and preventive medicine department in Al-Hassa, smoking control

clinic, Center of vector control and tuberculosis center. One day visit to each of school health unit and a PHC center. The last two days were devoted to data collection for two field projects to be implemented in PHC centers.

During each visit a PHC staff working in the facility explained to the students all activities, showed them the forms and records to be used in PHC and reviewed with them the most recent statistical data of the facility. Each student submitted a written report on one of the visited facilities following conventional styles of scientific report writing.

Research projects:

Each student completed 20-30 questionnaires in each project. They entered data into SPSS file and performed preliminary data analysis under guidance of staff.

Project I: Assessment of infants growth

*Study type: A record-based

*Target population: infants who completed their first year of life.

*Study design: systematic sample of 20 family files per day. All infants of the families were included. Relevant data were abstracted from growth curve and family files.

Project II: Physical activity among Saudi males attending PHC centers

*Study type: an interview study

*Target population: male attendants of PHC centers aged 15-60 years.

*Study design: depending on work load all or a sample of (up to 15 per day) male attendants were interviewed.

Students evaluation:

Field training program was assigned a total of 30 marks (out of 100 marks of six credit hours). Element of evaluation included attendance (6 marks), conduct (4 marks), report writing (5 marks); and data collection, entry and preliminary analysis (15 marks).

Results

Fifty-three students returned the questionnaire (response rate = 93%). Students cited that the most useful training sites were PHCCs (96.2%), vector control center (96.2%), smoking control clinic (84.9%), primary health care administration (75.5%) and school health unit was the least useful (52.8%).

Minority of students see that program contents was poor (3.8%), with unsuitable schedule (1.9%). However, 11.3% of them reported that elements of evaluation were not fair. Furthermore, 26.4% see that its duration is short. About two-thirds of students reported that the research projects were clear and reflect the community health problems. More than half of them stated that the variables are clear and easy to collect and time of data collection was adequate (table 1).

Table (2) shows that skills acquired included data entry and analysis using SPSS program (60.4%), data collection (52.8%), communication/interview skills (37.7%), becoming familiar with PHC services (34.0%) and report writing (22.6%). The most frequently cited suggestions to improve the program are proper coordination with facilities to be visited, actual practice in PHC centers, improve transportation, long duration for the program and use project questionnaires in Arabic

Table1: Students' opinion about field training program

Program elements	Number (%)
Contents: Adequate	21(39.6)
Fair	30(56.6)
Poor	2(3.8)
Duration: Adequate	39(73.6)
Short	14(26.4)
Schedule: Suitable	51(98.1)
Unsuitable	1(1.9)
Evaluation elements: Fair	47(88.7)
No fair	6(11.3)
Overall program: Good	23(43.4)
Fair	29(54.7)
Poor	1(1.9)
Research projects:	
Clear	36(67.9)
Reflect community health problems	35(66.0)
Questionnaires are well designed	31(58.5)
Variables are clear and easy to collect	28(52.8)
Time of data collection was adequate	29(54.7)

Table 2: Skills acquired by students and their suggestions for improvement

	Number (%)*
Skills acquired	
Data entry and analysis using SPSS	32(60.4)
Data collection	28(52.8)
Communication/interview skills	20(37.7)
Becoming familiar with functions of PHC services	18(34.0)
Report writing	12(22.6)
Suggestions	
No suggestions	8(15.1)
Proper coordination with facilities to be visited	11(20.8)
Theoretical background about disease/programs to be exposed to during field visits	5(9.4)
Improve transportation	6(11.3)

Field training ought to be one day per week throughout the semester (longer duration)	7(13.2)
There should be actual practice in PHC centers	7(13.2)
Refresh training in SPSS	2(3.8)
Use Arabic questionnaire for projects	6(11.3)

*Categories are not mutually exclusive

Discussion

Although students may not be the best judges of their educational needs, their input remains an important element in design and evaluation of curricula (Al-Shehri et al., 1998; Leed et al., 2008). The idea of students learning in community setting and general practice is not a new concept (Thistlethwaite et al., 2007a). PHC offers a unique perspectives and training opportunity for medical students who, relative to the need of the communities in which they are based, receive a disproportionate amount of their undergraduate experience from hospital-based teaching (Parry et al., 2001).

More than two-fifths (43.4%) of students viewed the overall program as good, others evaluated it as fair (54.7%) or poor (1.9%). It appears that PHC has long way to go before it is perceived by medical students as providing a valid learning experience as the hospital environment (Jones et al., 2001).

Program elements were perceived differently by students. Despite the finding that more than half of students responded positively to research projects 11.3% of them suggested that it is better to use project questionnaire in the Arabic language. Although English is formal teaching language in the college, students may feel it is better to use the local language when dealing with community. Also it is probable that these students are not mastering the English as they translate it into Arabic during conversation with patients or attendants.

About 11% of students see that evaluation elements were not fair. Students assessment in the community setting presents problems for medical teachers e.g. lack of test standardization due to varying field condition, and difficulties in assessing the contribution of individual members to group work. Students'

assessment and feedback are important in program evaluation. If it is relevant to the program's primary objective, the results will have a direct impact on the way the program is operated and further developed (Magzoub & Mustafa, 1998).

An important finding is that more than a quarter of students see the program is of short duration, however only 13.2% suggested a longer duration for future training. Difficulties in providing the program included organization of student travel and coordination with PHC facilities before the due date of visit. Also students had no opportunity to practice examination skills or see patients relevant to their basic medical science course.

There has been much written about the need for medical education to be more relevant to local health care systems (Parry, 1983) and to develop more medical schools based on community-oriented learning (Rolfe et al, 1999). Training in primary health care provided a chance for students to learn in an environment similar to the one they are going to face in the future. The use of community-oriented approach can introduce the student to the problems of the community and deepens his understanding of the socio-economic and environmental background of various health matters (Milaat, 2003). More than one-third of students got benefit of becoming familiar with functions of PHC services. Furthermore, 13.2% of them suggested that they should practice these services. Morrison and Murray (1996) suggested that students should be given a chance to have practice in those activities in which they are expected to be competent, such as examining and interviewing patients as well as performing practical procedures.

Communication skills are taught as an integral part of the curriculum in all medical schools (Lloyd-Williams, 2001) and have achieved a considerable amount of attention (Cegala et al., 2003). More than one-third of students (37.7%) reported they acquired communication/interview skill during the program. It was commented that good communication skills may improve the physician-patient relationship and are related to positive health outcomes for the patients (Charon, 1994; Stewart, 1995).

In their qualitative study, O'Sullivan et al (2000) found that community-based learning was perceived as appropriate for improving communication skills and forms a greater proportion of the undergraduate medical experience.

Sudy limitation

The study was carried out in one college and included small number of male students enrolled in the program during an academic year. There is no female students in the fourth year at the time of study. The results can not be generalized to other colleges and students all over the Kingdom. The evaluation is incomplete without structured enquiry of the PHC tutors. Also there is no standardised evaluation tools to be applicable under different situations of training.

Recommendation

There is a need to modify the existing program with consideration of students suggestions. PHC tutors, mostly general practitioners working in these centers, should be trained, oriented and motivated about the aim of the course and how and what to teach to students at the fourth year level. They should be involved in planning, execution and evaluation of the program and students. For PHC to be a quality learning environment, the team and administrative staff must be enthusiastic about the presence of students (Thistlethwaite et al, 2007b).

We emphasize on active students participation on PHC activities. As suggested by Morrison & Murray (1996) students should be given a chance to have practice in those activities in which they are expected to be competent, such as examining and interviewing patients as well as performing practical procedure. More PHC centers and tutors are needed for the future increasing number of students. This requires adjustment and change in learning style. The entire family and community medicine curriculum should be examined in the light of these findings. There is a need for longitudinal prospective study to assess the impact of PHC training in career choice and work

satisfaction of students. Different issues might emerge in a longer term follow-up. The problem of is how to assess students' performance is urgent and must be addressed. Success of training program depends on close collaboration with Ministry of Health.

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Student's Mental Health Literacy and Attitudes toward Depression: findings from a survey conducted at a Malaysian University

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Summary

Objective

To determine the knowledge and perception toward depression among students of University Sains Malaysia (USM), in Pulau Penang, Peninsular Malaysia.

Methodology

This study was a questionnaire based survey undertaken in June 2007 at a public university, Penang, Malaysia. A face to face interview was conducted among the university students at University Sains Malaysia (USM). A cluster random sampling method was adopted, on an average fifty students were approached from every discipline. The ethical approval from the Research Ethics Committee, University Sains Malaysia was granted for this study.

A prevalidated 21 Item questionnaire was used to evaluate the student's knowledge attitudes and perception toward depression. The reliability scale was applied to all the variables comprising the knowledge domain i.e. knowledge about symptoms, awareness about causes/ prevention and diagnosis and therapy, the reliability of the tool was estimated on the basis of Cronbach's Alpha ($\alpha = 0.76$). The questionnaire was comprised of two parts; the demographic part and the part evaluating the student's knowledge and perceptions toward depression. The demographic variables considered in the study tool were race, age, religion and gender. However, knowledge about depression was assessed using the correct symptoms of depression as mentioned in the Diagnostic Statistical Manual (DSM IV). In addition to the symptoms the perception toward the causes of depression was also evaluated. The knowledge toward the depression therapy was evaluated using the names of medications used to treat depression. Knowledge was evaluated on the basis of symptoms of depression. The responses about symptoms of depression were scored in order to classify the knowledge in sub-level, this classification provide information about the level of recognition towards

depression and its symptoms. Every right answer adds one score to the respondent's knowledge level. Those unable to recognise any symptoms of depression scored zero and ranked very poor, afterwards one to two (poor), three to four (moderate), five to six (good) and seven and over were graded with a very good knowledge levels.

Data Analysis

The statistical package for social sciences (SPSS15.0®) was used for data analysis. The χ^2 test was used to test the difference between proportions. Further more as a rule of thumb, if 25% or more of the cells have expected cell count less than 5, then Fisher's exact test was preferred over the chi square. However, in some cases where data set was large and exact computation require great computer time and memory, to cope this error Monte Carlo simulation in SPSS 15® was used [34]. For the comparison of knowledge level among two groups i.e (gender and personal experience of depression) Mann-Whitney U test was applied. A p -value of less than 0.05 was considered significant. Some of the questions had multiple choice options; therefore, the sum of percentages is not always 100%.

Results

The total number of students responded to this study were 500, of whom 24.6% (123) were male and 75.4% (377) were females. The majority of the respondents were Malay 50.0% (250), followed by Chinese 44.0% (220), and Indians 6.0% (30). The mean ages of them were 22 years (SD: \pm 3.70). About 13.0% (65) of the respondents have never heard of a disease called depression; 11.4% (57) of the sample reported having had personal experience of depression, of whom 59.6% (34) were female ($\chi^2=8.605$, $p=0.003$). In response to a multiple options question about the type of depression, the majority 77.2% (386) has prioritised tension as main type of depression followed by sadness 49.8% (249), change in behaviour 29.0% (145) and 20.8% (104).

The respondent's knowledge about the symptoms of depression was assessed using a nine-item symptoms scale. Findings demonstrated that Chinese have a better knowledge toward depression symptoms in comparison to Malays and Indians. In order to clarify the association of gender and personal experience of depression with knowledge level further analysis was carried out. Personal experience of depression were found statistically significant ($Z = -2.394$, $p = 0.017$). However, in term of gender the findings were non-significant ($Z = -0.252$, $p = 0.801$) but further exploration proved that the personal experience of depression were significant among female ($\chi^2 = 8.605$, $p = 0.003$). Female respondents were found to have a better knowledge toward depression.

In response to the question about the causes of depression, most of the respondents have cited familial and educational issues as the key possible causes of depression. Table 4 illustrated the details of the responses in this regard. The findings revealed some gender base difference in responses toward causes of depression, female respondent were found more inclined toward the family related problems. Majority 51.6% (258) prioritising death of loved one as a cause of depression were female, followed by relationship problems 47.6% (238) and home and family harmony 42.0 % (210). Whilst evaluating the student perception toward the biological causes of depression, 32.6 % (163) cited chemical imbalance in brain as a cause of depression, of whom 74.8% (122) were females.

Whilst question evaluating the knowledge about the medication for depression, majority 31.4% (157) has mentioned the use of tranquilizers as the first drug of choice for treating depression followed by herbs 136 (27.2%), vitamins 12.4% (62), diazepam 9.8% (49) nerve tonic 9.4% (47) and Fluoxetine 33(6.6%). In addition to these medications about 20.4% (102) has recommended the use of alternative medicines. Further analysis

was carried out to look at the attitudes toward alternative medicine in terms of gender and race of the respondents. In terms of help seeking behaviour, the majority revealed to consult both psychiatrist and general practitioner. However, segregation of responses showed that about 65.6% (n=328) were willing to seek help from psychiatrist, and about 49.6 % (n=248) has preferred to consult a general practitioner. Professional help seeking responses was found associated with gender, majority 65.6% (328) has preferred to consult psychiatrist of whom, 50.2% (251) were female.

Conclusion

The findings of this study will be beneficial for the health policy maker and public health department. Majority of the students have a moderate level of knowledge about symptoms and a poor knowledge toward depression therapy. Better knowledge of depression was found significantly associated with personal experience of depression. Majority has associated social issues as the causes of depression; however, very few have focus on the biological causes of depression.

Keywords: Depression, alternative medicine, knowledge, perception

Sleep Habits and Academic Performance in Medical Students

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Summary

Introduction: Sleep habits and disturbances have been shown to negatively affect school performance at the level of school – aged students. However, limited numbers of studies have assessed the effect of sleep habits and disturbances on the academic performance among medical students as a specific group.

Objectives: This study was designed to assess the effect of sleep patterns /habits and other daily habits on academic performance among medical students (males and females) at different academic levels.

Methods: Participants in this cross sectional study were healthy medical students in the first, second and third academic levels of the college of medicine, King Saud University, Riyadh, Saudi Arabia. The study was conducted during December 2008. A self administered questionnaire was distributed to students to assess age, academic level, academic performance based on the accumulative grades, sleep-wake schedule, naps, quality of sleep based on self-satisfaction with sleep, total sleep time at night and day time sleepiness using the Epworth Sleepiness Scale (ESS). Day time sleepiness was defined as an ESS score of >10. Students who didn't report their accumulative grades, have chronic illnesses or drink alcohol were excluded.

Results: The final analysis included 410 students (273 males & 137 females) with the mean age were 20.37 ± 1.13 years and the body mass index (BMI) was 25.01 ± 8.6 kg/m². One hundred and fifteen students (28%) were defined to be in group1 (those with accumulative grade of A) and 295 students (72%) to be in group2 (those with accumulative grades of B, C or D). Group1 students go to bed earlier during weekdays (23.8 ± 1.70) compared to those in group2 (00.2 ± 1.5), $P=0.018$. Also, they had longer total sleep time (TST) at night during weekdays (6.28 ± 1.45 hours) than students in group2 (6.02 ± 1.25), $P=0.073$. ESS score was significantly less in group1 students (6.88 ± 3.64) than group2 students (8.03 ± 3.89), $P=0.007$. Additionally, 24 students (20.9%) of group1 reported that they had chronic sleep complaints versus 101 students (34.2 %) in group2, $P=0.008$. Sixty three of students (55.3%) in group1 felt sleepy during daytime in comparison to

198 (68.8%) of group 2 students, $P=0.011$. Only one smoker (0.9%) in group1 versus 23(7.9%) smokers in group2, $P=0.007$. Obesity was significantly more common in group2 students (16.3%) than group1 students (7.8%), $P=0.026$.

Conclusion: The present study showed that lower academic performance can be associated with the presence of sleep complaints, poor sleep habits, shortened total sleep time at night and daytime sleepiness.

Keywords: Sleep habits, Academic performance, medical students

Information Technology Knowledge in Nursing Profession

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Abstract

Nursing students and practitioners are required to have an in-depth understanding of information systems in medical science, Informatics in patient care and patient safety. It is beyond any reasonable doubt that nurses are the key to the implementation of informatics in all areas of health care. Nurses are the largest group of health professionals, need to be technologically savvy, and have the patients' best interest and safety at heart.

In this study, the authors will introduce about an on-line course at Indianan University, USA which covers general computing literacy concepts as well as application of technology and Informatics in the Nursing profession.

The course includes several discussions and contents on:

- General Technology Concepts
- Typical Decision Support Applications within Healthcare profession
- Real life examples of how new breed of hardware and software can assist nurses to improve patient care
- Real life examples of how new forms of technology can assist nurses to improve patient safety and privacy
- The role of Internet and on-line communication
- The infrastructure of global networks and applications such as holographic transmission of images to fulfill the nursing shortage from outsourced stations in other nations.
- How Nursing educators all over the world are attempting to educate nurses in the understanding of Computing and Informatics in Healthcare

Authors believe that the above mentioned subject matter will not only influence the audience to reconsider Nursing education, research practices, curriculum design and outcome objectives, but the course has potential to contribute towards global efforts to further improve intellects of the students in medical and nursing studies as well as educate emerging nursing leaders for strategic management of an informed labor force and improvement of patient outcome.

Keywords: Information Technology, Nursing, Healthcare, Online Course, Indianan University

Alpha-lipoic acid and quercetin protect against methotrexate induced-hepatotoxicity in rats

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Abstract

Background: Methotrexate (MTX), a folic acid antagonist, is widely used as cytotoxic chemotherapeutic agent for malignancies as well as in the treatment of various inflammatory diseases. The efficacy of this agent is often limited by severe side effects and toxic conditions. Regarding the mechanism of these side effects, several hypotheses have been put forward, among which oxidative stress is noticeable.

Aims & Objectives: The present study was undertaken to determine whether α -lipoic acid or quercetin, potent free radical scavengers, could ameliorate MTX-induced oxidative liver injury and modulate immune response. The study also aimed to investigate the possible role of nitric oxide (NO) and tumor necrosis factor- α (TNF- α) in the pathogenesis of MTX-induced hepatotoxicity.

Study design/Methods: Rats were randomly divided into four experimental groups beside a normal control group consisting each of 8 animals. Following a single injection of MTX (20 mg/kg; i.p), experimental groups were allowed to

receive either α -lipoic acid (50 mg/kg/day; orally), quercetin (10 mg/kg/day; i.p in dimethylsulphoxide (DMSO)) or the vehicle DMSO alone. Treatment was carried out for 5 consecutive days. On the sixth day, blood serum was separated and used for the determination of TNF- α level as well as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities to assess the hepatic function. Liver tissue samples were collected for the estimation of tissue malondialdehyde (MDA), reduced glutathione (GSH) and nitric oxide (NO) levels, myeloperoxidase (MPO), superoxide dismutase (SOD) and catalase (CAT) activities as well as for histological examination. Results obtained were statistically analysed by one way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison test. Significance was considered at $p < 0.05$.

Findings: MTX caused a significant reduction in hepatic GSH level, SOD and CAT activities while MDA and MPO activities were significantly increased. Hepatic NO as well as serum TNF- α levels were markedly elevated following MTX treatment. Only ALT rather than AST activity was significantly increased. These changes were significantly reversed by either α -lipoic acid or quercetin treatment. Similarly, histological analysis revealed that both treatments were effective in attenuating tissue damage. However, the effect of α -lipoic acid was more pronounced.

Conclusion: The study indicates that oxidative stress, NO as well as TNF- α may play an important role in the pathogenesis of MTX-induced hepatotoxicity. α -Lipoic acid and quercetin have protective aspects in this process through their antioxidant and anti-inflammatory effects. These data imply that antioxidant therapy may be of therapeutic potential in alleviating hepatotoxicity in patients receiving MTX treatment.

Keywords: Methotrexate, α -Lipoic acid, quercetin, nitric oxide, TNF- α , oxidative stress

Can CA 19-9 and CEA Predict Operability and Survival in Pancreatic Malignancies?

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Abstract

Introduction: Pancreatic cancer is a leading cause of death in the developed countries. CA 19-9 and CEA, when combined they have a specificity of 95% in detecting pancreatic cancer. A CT-Scan examination is used to find out the extent, local and distant spread of the disease- and is used for preoperative staging of the disease. However, the tumor markers have not been studied to predict Operability and Survival in these patients.

Aim: To evaluate the efficacy of CA 19-9 and CEA to predict Operability and Survival in patients with pancreatic malignancies.

Methods: This study was carried out a tertiary care center which has a high patient load. All the patients who presented to the department with obstructive jaundice, abdominal lump and those who were concluded to have a pancreatic cancer were included in this study. Levels of CA 19-9 and CEA were measured (Pre and Post operatively) in 49 patients of pancreatic malignancy. CECT (Contrast Enhanced Computed Tomography Scan) was performed by a senior radiologist for diagnosis and staging of the tumor. Patients having vascular invasion, metastasis to the liver, retro-peritoneal lymph nodes, peritoneum were concluded to be inoperable. A senior surgeon determined the operability on surgical exploration. The levels

of tumor markers were then correlated with the operability and the survival based on CECT and intra-operative findings.

Results: Of the 49 patients, 24 were found to be operable and 25 were found to be inoperable. Male: Female was 3:1. The mean age of all the patients was 55 years. The normal values of CA 19-9 and CEA are 0-37U/ml and 0-2.5ng/ml respectively. 16/24 (67%) patients with CA 19-9 levels (<2times) and 19/24 (79%) patients with CEA levels (<2times) were found to be operable. 22/25 (88%) patients having elevated CA 19-9 levels (pvalue-0.0002-significant) and 17/25(70%) patients having elevated CEA levels (pvalue-0.0031-significant) were found to be inoperable. Of the 27 patients, found operable on CT-Scan, 5 were inoperable intra-operatively. All of these had elevated levels of CA 19-9 and 4/5 (80%) had elevated levels of CEA. Only 5/21 (23%) inoperable patients, with elevated levels of CA 19-9 were surviving at 1 year follow up. Of the 12 inoperable patients with CA 19-9 levels >1000U/ml none survived beyond 6 month follow-up. Similarly, only 3/17 patients having elevated levels of CEA were surviving at 1 year follow-up. No evidence of any recurrence was obtained on any of the patients following surgery.

Conclusion: Levels of tumor markers CA 19-9 and CEA (<2 times) predict better chances of the tumor being operable. Elevated levels of CA 19-9 and CEA (>2 times) predict increased chances of inoperability and poor survival in pancreatic tumors. Levels of tumor markers (>3times) predict increased chances of inoperability even in patients deemed operable on CT-Scan. Levels of CA 19-9 (>1000U/ml) indicate a dismal survival in inoperable group of patients. Elevated levels of tumor markers do not help in predicting the recurrence of pancreatic cancers following surgery.

Discussion: In patients who have levels of CA 19-9 and CEA (>3 times) and are concluded to be Operable on CT-Scan findings, it is recommended that a diagnostic laparoscopy be done prior to taking the patient for any surgical exploration.

This should be done to pick up any metastasis to the peritoneum or to the diaphragm or to the liver which could not be evident on CT-Scan. A diagnostic laparoscopy if reports any metastasis, then a palliative intervention like an endoscopic stenting of possible should be attempted to reduce the morbidities associated with a surgery. Patients having highly elevated levels of CA 19-9 are generally associated with a poor survival rate and metastasis. Neo-adjuvant therapy in such patients to reduce the load of the tumor, if possible should be attempted to increase chances of survival.

Keywords: Pancreatic malignancies, CA 19-9, CEA

Peculiarities of Vascular Component of Communicative Systems in Rectal Adenomas

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Objectives & Aims

Molecular mechanism of colorectal cancer development is well-studied and adenomas are assumed to be the precursors. The most important determinants of colorectal cancer risk include the size of adenoma, histological type and the degree of epithelial dysplasia.

In the past two decades, in Smolensk regional institute of pathology, there has been an active study of neoplastic processes that were focused on the evaluation of peculiarities of quantitative and qualitative combination of distribution of cell populations with the use morphometric methods. In the course of these studies, there had been an attempt to introduce microcirculatory vessels and vegetative nerve terminals as points of reference in the methodology of morphometric study. Microcirculatory vessels are the active parts of the cell redistributions and nerve elements are the integrative units between influencing factors and eventual reaction of the tissue. The cell populations, which determine the peculiarities of regulation of trophic processes in the tissues in normal

conditions and in pathological processes, are liable to a huge variability than vessels and nerves. Thus, communicative systems can be defined as follows. Communicative systems are open systems containing the whole structural and functional units: microcirculatory vessels, nerve terminals, cell microenvironment of these structures that are localized in the histophysiological correlation, providing a structural basis of homeostasis.

Mathematical analysis of cellular microsurrounding of vascular and nerve component of communicative systems allows revealing on the light-microscopic level of those intercellular correlations, which usually are interpreted on a more deep level of investigation. Also it is revealed that the changes in the stroma of a tumor may predict its behavior. Therefore a study of parenchymal and stromal interactions explains the mechanisms of tumor progression and further assumes the prognostic factors.

Our aim was to study the peculiarities of vascular component of communicative systems in different histological types of rectal adenomas.

Materials and Methods

A study of surgical and biopsy materials of tubular (TA), tubulovillous (TVA) and villous (VA) rectal adenomas — 30 cases of each histological type was performed. 20 biopsies of rectal mucosa were studied as a control group. The material was microscopically analyzed using Hematoxylin and Eosin and Picrofuchsin by van Gieson. Histotopographically distinct capillaries were selected, the area around which did not overlap with the corresponding area of surrounding capillaries. Absolute number of cellular elements around the capillaries was counted in 10 different fields of view with a magnification of x 900 (oil immersion applicable).

Proliferative activity of epithelial cells (10 cases from each group) and structure of vascular bed (5 cases from each group) were estimated immunohistochemically with the use of polyclonal rabbit antibodies to human antigen Ki-67 and CD31

(“Dako”, Denmark). Immunopositivity was revealed by detecting the dark-brown nuclei (Ki-67) and membranes (CD31) staining of antigen. In each case, Ki-67 immunopositive cells were counted among 1500 epithelial cells, and their ratio in multiples of 100, was calculated as an index of proliferative activity (IPA). Area of vascular bed was calculated by micromorphometry with the use of Glagolev’s ocular net. Differences in distributions between variables were calculated using nonparametric methods (U-Test, Kruskal-Wallis test). Probability values < 0.05 were considered significant. Correlations were calculated using Spearman rank correlation coefficients ranging from -1 to +1. All data analysis was done with the statistical package Statgraphics Plus, version 5.0.

Results

Study of case reports of patients revealed that adenomas were detected mainly in the age group 50–69 years (68.9% of cases). Age of patients varied from 19 to 83 years (mean 52.3 ± 3.4 years). In 67.8% of patients the process was revealed for the first time. Endoscopic investigation confirmed that the adenomas were localized mainly in the distal part of rectum (5–10 cm from anus), prevalent size was upto 1 cm (54.5%) and large tumors (more than 2 cm) were noted in 22.2% cases.

Localization of proliferating epithelial cells had the following distribution: normal mucosa in basal parts of crypts, TA in basal and middle parts of crypts, and in VA proliferation was active on the surface of villi and the upper third of the crypt. Positive immunostaining (Ki-67) of epithelial cells was observed in villous structures of TVA, similarly as in VA and had a diffused pattern. IPA in the control group comprised of 20.9 ± 0.7 , 26.6 ± 0.3 in TA, 36.8 ± 1.3 in TVA, 47.1 ± 1.7 in VA. The reliable significant differences ($p < 0.05$) in proliferative activity of epithelial cells in the following adjacent pairs of tumors were revealed: TA–TVA, TVA–VA.

Rectal mucosa and adenomas were exclusively abundant with capillaries. In adenomas, numerous microvascular structures like blood and lymphatic capillaries and sinusoids were

observed. Area of vascular bed was characterized by following indices: 30.7 ± 0.9 in control group, 41.1 ± 1.1 in TA, 82.2 ± 1.3 in TVA, 274.3 ± 7.3 in VA. The reliable significant differences ($p < 0.05$) in the intensity of vascularization in the following adjacent pairs of tumors were revealed: TA–TVA, TVA–VA.

Micromorphometric study of cell population was carried out around the blood capillaries. In the following sequence “normal mucosa \rightarrow TA \rightarrow TVA \rightarrow VA” there is a gradual increase in the absolute number of all the studied cell populations. At the same time an increase in the following positions ($p < 0.05$) in the adjacent pairs is statistically reliable: epithelial cells and fibroblasts (control — TA), epithelial cells, plasma cells and fibrocytes (TA — TVA), epithelial cells, lymphocytes, plasma cells and polymorphonuclear leukocytes (TVA — VA).

Correlation analysis of cell interaction in capillary microenvironment helps to determine the following peculiarities of intrastromal intercellular relations. In control group, there is a positive relation between haematogenous and histogenous cell populations, where fibroblasts, macrophages, lymphocytes and fibrocytes actively participate in its formation. In the initial stages of tumor growth (TA), an increase in the number of correlations and activation of cell regulator such as macrophage, which along with fibroblast encloses the number of positive cell relations, is noted. In TVA, as the number of correlations decrease, the macrophage undergoes a peculiar isolation from other cells. In VA, for the first time at the stages of tumor progression, the number of intercellular correlations reaches to minimum, but isolation between haematogenous and histogenous population does not occur.

Conclusion

A positive correlation between transitions from one morphological category to another exists with an evident increase in the absolute number of parenchymal and stromal cells. In the course of a tumor progression “normal mucosa \rightarrow TA \rightarrow TVA \rightarrow VA” there is a gradual loss of correlations

between cell elements of stroma that are isolated from each other. In a number of cases, according to the state of cellular infiltrate, degree of evident changes in the epithelial cells can be predicted. A full-value estimation of prognostic factors of rectal adenomas is possible only with a parallel study of parenchyma and stroma of the tumors.

Acknowledgement

The study was performed by the financial support of Russian Humanitarian Scientific Foundation in frame of scientific research project No. 07-06-58606a/C.

Chronic Infections and management setting in Drug addicts of MMT program in Pinang, Malaysia

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Abstract

Background: The authors sought to identify the prevalence of blood-borne chronic infections and determine the appropriate management therapy setting among the drug addicts of methadone maintenance treatment (MMT) program. The purpose to identify such factor is to know the quality of health of respondents active to MMT program and possibly predict the risk reduction of relapse during the treatment.

Methodology: As it was known that government of Malaysia allowed MMT on large scale at 2005, so a year retrospective with six months prospective study (from Jan 2007 to May 2008) was conducted in three methadone clinics of Pinang state, Malaysia. All the registered patients were included in the study and data was collected through special design data collection form by reviewing the medical profiles.

Results: Findings showed HIV/AIDS was found in 2.3%, HCV 76.3%), HBV 3.3%, while 37.7% respondents were identified impaired liver function. The risk combination was HCV with impaired liver function identified in 39.5% respondents. None of them receives any supportive management treatment for the current chronic infectious condition.

Conclusion: This study highly recommends producing necessary resources for the management treatment of Drug addicts for such chronic infection, as further delay can possibly increase the risk to transmit the infection in the society.

Keywords: Blood-borne infection, Drug abuse, Addiction, MMT, Drug abuse and infections.

Postmortem Investigations Following Human Immunodeficiency Virus Infection

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Abstract

Background: HIV/AIDS is a global disease and despite intensive research it is one of the main causes of human death. Postmortem studies have proven accurate in determining the various pathologies in these patients.

Aims & Objectives: Our aim was to analyze the post mortem results of individuals who died after HIV infection in the same geographical region. We evaluated the most frequent opportunistic diseases and their clinical and morphological outcomes.

Methods: We studied case reports and autopsy research data from 32 patients who died after HIV infection in Smolensk, Russian Federation, between 2003 and 2008. All patients had been diagnosed with HIV infection before death, using HIV-

specific enzyme linked immunosorbent assay (ELISA) and immunoblotting. Autopsy specimens of various organs were examined histologically and microbiologically.

Findings: The mean survival period from the moment of detection of seropositivity in all the patients was less than five years. Twelve patients had a parenteral mode of contact, six had been infected by sexual contact, and 14 patients had unknown modes of infection. Most patients (69%) had chronic hepatitis C. The main causes of death were various infectious diseases. The most common were generalized miliary tuberculosis and progressive secondary tuberculosis of the lungs. Three (9%) patients had tuberculosis of the meninges and five (16%) had peritoneal infections, but tuberculous peritonitis had not been diagnosed before death. Six patients had pulmonary tuberculosis and bacterial pneumonia simultaneously. Two (6%) patients died from bacterial sepsis as a result of cervical lymphadenitis, and eight (12.5%) from abscess-forming pneumonia. The opportunistic infections revealed were *Pneumocystis carinii* pneumonia (eight patients), cytomegaloviral pneumonia (three), bronchopulmonary aspergillosis (one) and mucosal candidiasis (three). In three patients, the causes of death were advanced neoplastic processes: two cases of leukemia and one case of cervical cancer.

Conclusions: Tuberculosis was the most widespread among the opportunistic infections, which often had affected the entire lung and had a destructive form. In the morphological picture of tuberculous inflammation, alterative and exudative changes dominated. Moreover, HIV infection had a characteristically broad spectrum of causative agents of pneumonia, including bacteria, viruses, fungi, and protozoa.

Keywords: HIV infection, Morphology, Opportunistic infections, Secondary neoplasms

Emerging Community-Acquired Methicillin-Resistant Staphylococcus Aureus Pneumonia

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Abstract

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) has been an important nosocomial pathogen worldwide for more than four decades. Community-acquired MRSA infections, generally occurring in previously healthy persons without recognizable risk factors for health care setting-related MRSA, are emerging as serious clinical and public health concerns. The most frequent of these community-based infections include skin and soft tissue infections and necrotizing pneumonias. A majority of causative community-acquired MRSA (CA-MRSA) isolates are associated with genes that encode the virulence factor, Pantone-Valentine leukocidin (PVL) toxin.

Aims & Objectives: To describe six cases of CA-MRSA pneumonia recently admitted to our community hospital in

Florida, and discuss the epidemiology, clinical features, and management of these expanding infections.

Methods/Study Design: The medical records of six patients with radiographically-confirmed pneumonia and positive sputum cultures for MRSA at the time of hospitalization at the Lawnwood Regional Medical Center and Heart Institute, Fort Pierce, Florida, from December 2006 through January 2007, were retrospectively reviewed. All patients were seen by one of the authors (DO), an infectious diseases consultant. Lawnwood Regional Medical Center is a 341-bed, acute care institution and regional referral center for four counties of Treasure Coast, FL. The hospital institution review board gave permission for this study.

Results/Findings: Six patients (5 men, 1 woman) with CA-MRSA pneumonia were identified. The mean patient age was 57 years (range, 32-79 years). Three patients had no history of previous hospital admission, while two patients had been last hospitalized two years prior to the study admission. Three elderly patients had known co-morbidities predisposing to pneumonia including carcinoma of the lung (2 patients), and cirrhosis, diabetes mellitus, chronic renal failure, COPD, and cardiomyopathy (1 patient each). Sputum samples were collected at the time of admission and all grew MRSA. Two isolates were resistant only to oxacillin, while four were also resistant to levofloxacin (3 isolates), erythromycin (2 isolates), ciprofloxacin (1 isolate), and/or clindamycin (1 isolate). One patient had concurrent *Pseudomonas* bacteremia, and another had *Pseudomonas* isolated from sputum culture in addition to MRSA. All patients had abnormal chest radiographs; three had focal unilateral pneumonia, two had bilateral pneumonia, and one had a lung abscess. The latter patient also had evidence of metastatic infection with sternal osteomyelitis. Three patients required ventilatory support; two of these subjects died and one was discharged to hospice care. None of the six patients had any epidemiologic connection to one another.

Conclusion: CA-MRSA is becoming an increasingly important cause of community-acquired pneumonia in many

parts of the world, and in these regions empiric antibiotic treatment guidelines should be reconsidered.

Keywords: Pneumonia, community-acquired, Staphylococcus aureus, MRSA

Nitric Oxide and eNOS Gene in Essential Hypertension

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Abstract

Background: Currently hypertension grips around 25% of the entire world population. More than 90% of the hypertensive patients suffer from essential hypertension. In Asian Indians hypertension is the predominant risk factor for Coronary Artery Disease among others. Nitric Oxide (NO) is synonymous with endothelial derived relaxation factor. Acting via cGMP (cyclic guanosine monophosphate) it causes smooth muscle relaxation, prevents platelet aggregation and acts as an anti-inflammatory agent. iNOS (inducible Nitric oxide synthase), nNOS(neuronal nitric oxide synthase) and eNOS (endothelial nitric oxide synthase) are the three enzymes producing the gas nitric oxide in the human body. eNOS is the main source of NO under physiological conditions. It is known to have a number of polymorphisms. The most well known ones being the G to T polymorphism in exon 7, the T to C polymorphism in the promoter region and the a/b polymorphism in the intron 4. While the G to T polymorphism

has been associated with hypertension in many races including the north Indian population, the association of other polymorphisms has been more of a controversy. Not much study has been done on the Asians especially those in India regarding these polymorphisms.

Aims: To elucidate the association between the intron4a/b polymorphism in the eNOS gene and nitric oxide levels and essential hypertension.

Objectives:

1. To determine the genotype frequencies of the above mentioned polymorphism in patients and controls
2. To study the levels of NO in the plasma of the patients and controls
3. To find out correlation if any between this polymorphism and plasma NO levels
4. To find a correlation if any between this polymorphism and essential hypertension

Materials and Methods: The study design was a case control study. 10 ml of venous blood was taken from 45 patients (selected from the department of Cardiology All India Institute of Medical Sciences, ages between 25 to 55 yrs and not on any antihypertensive medications) and controls (healthy volunteers with normal blood pressure, ages between 25 to 55 yrs, not on antihypertensive treatment, not having any diabetes mellitus or endocrine disorder or any acute illness and responding to a publicized call. It was separated into plasma and packed cells. The alleles were identified by method of Wang et al with slight modification using PCR and Agarose Gel electrophoresis with 2.7% agarose. The nitric oxide was measured using levels of the surrogate marker, nitrite by the simple and economical method of Ding et al using Griess reagent. The Data was analyzed using SPSS software. The level of significance was fixed at $p < 0.05$.

Results/Findings: The patient and control populations were found to be in Hardy Weinberg equilibrium [p value (patient) = 0.05, p value(control) > 0.05]. The mean level of nitric oxide in the patients was found to be 42% less than that of the controls.

The majority of patients (76%) had plasma nitrite levels below 5uM. On the other hand a majority of controls (64%) had plasma nitrite levels more than or equal to 5uM. The fraction of patients with nitrite levels below 5uM (76%) was more than double that of the controls (34%). The patients were equally distributed between the lower two groups. The controls however showed two peaks the higher one being that of greater than 7uM.

There was no significant difference (p value= 0.79) in the genotype distribution between patients and controls. There was also no significant difference between in the levels of nitrite between ab and bb genotypes in both patients and controls.

Conclusion: The levels of nitrite were found to differ significantly between patients and controls. Although no statistically significant correlation could be found in the present study a trend towards higher frequency of a allele could be envisaged among the patients of essential hypertension. A detailed study with a larger sample size is needed to establish or refute the role of this polymorphism in essential hypertension in the Indian population.

Keywords: Essential Hypertension, Nitric Oxide, eNOS gene intron 4a/b polymorphism

Tungiasis: A Neglected Health Problem in Rural Cameroon

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Summary

Tungiasis is a neglected, ectoparasitic disease common to resource-poor communities of the developing world. The disease arises when the fertilised female jigger flea, *Tunga*

penetrans, burrows into the epidermis of its host, feeds on lymph and swells as the eggs grow. Infestation mostly occurs in the hands and feet but ectopic lesions have been reported. Areas subjected to this health problem include South America, Caribbean, Sub-Saharan Africa and parts of South Asia.

In areas of jigger flea habitation, tungiasis is not regarded as a serious threat to health. Unfortunately this is a common misconception. Tungiasis results in significant morbidity, manifesting itself in a number of symptoms such as severe local inflammation or deformation and loss of nails. There is also substantial risk of secondary infection; many lacking immunisation are vulnerable to tetanus (*Clostridium tetani*), often proving fatal. Complaints of insomnia are also not uncommon due to the intolerable itchiness of the infestation.

Aware of its presence in Africa, the study aimed to ascertain the prevalence and impact of Tungiasis in a number of rural settings in the North West Province of Cameroon. Each individual involved in the study was inspected for Jigger flea lesions and interviewed using a comprehensive, piloted questionnaire. Following this, we aimed to identify any risk factors or preventative measures and assess their impact on this well known, but poorly handled, health problem.

This cross sectional study was carried out for 45 days in July/August 2008 among townships within the Ndu subdivision of the Northwest Province of Cameroon, an anglophone region lying 300km from the capital city, Yaounde. During this time, a total of 1151 people (occupying a representative sample of 50 randomly selected compounds) were interviewed and inspected. The total population of the Ndu subdivision was 86,322 inhabitants. This fertile area is renowned for its large tea plantations and agriculture is the main occupation.

The houses in this region are found on large compounds, which are governed by traditionally elected chiefs or 'Fons'. In general, the buildings have a very basic structure with dusty, mud floors, no running water or electricity. To understand the

living conditions better, a questionnaire regarding each compound was completed.

Prior to obtaining any results, draft questionnaires were piloted and all aspects of the study were discussed and explained at meetings with the Fons of each village. At an individual level, the study was explained and oral consent was obtained before any data collection proceeded. Participation in the study was completely voluntary and anonymous. Furthermore, this study was approved by the Ethics Committee of the Royal Geographical Society.

Having completed the inspection and interview, written data were entered into the Epi Info software package. This was then double-checked against the original questionnaires. The data were exported to Microsoft Excel for analysis. Fisher's exact test was applied to determine the significance of difference of relative frequencies. Use of median and interquartile range data indicated where results were not normally distributed.

In terms of results, we obtained a representative sample of 1151 individuals (50 compounds, nine villages) over the 45 day period. Of these individuals 567 (49%) were male and 584 (51%) were female. In total, 610 were infested with *Tunga penetrans*, resulting in a point prevalence of 53%, although 65% had experienced the flea in the past month. 336 males (59%) and 274 females (47%) were infested, indicating a significant difference in prevalence between the two sexes ($P=0.004$).

Lesions were found on the feet of all infected individuals. In total, 3103 parasitic lesions were recorded; 2991 (96%) of which presented on the feet and 112 (4%) on the hands, resulting in a mean parasite intensity of 5.1 and a median parasite intensity of 2 (interquartile range 2-5). Males showed a much higher parasite load than females. The maximum number of fleas on an individual was 102.

For those who did not consider tungiasis a disease, infestation did appear to be more apparent. Prevalence in the illiterate (59%) was greater than in the literate (50%). Despite these findings, there is no conclusive evidence to show that not

regarding tungiasis as a disease has any marked effect on the prevalence or severity of infestation.

Physical removal of the flea using a sharpened stick was the most common treatment method and was used by 98% of the sample. Although symptoms of tungiasis can be debilitating and painful, 59% would not consider visiting a medical centre for treatment.

This report has demonstrated that tungiasis is endemic to this region of Cameroon. The jigger flea impacts heavily on the rural and agricultural communities around the town of Ndu. The parasite inhibits progress and development in the poverty stricken; farmers and other breadwinners find it more difficult to work and are held back by the associated morbidity such as difficulty in walking, persistent itching and the resulting insomnia.

Our study shows that tungiasis in Cameroon is a problem stretching beyond mere nuisance or irritation; it is associated with severe morbidity and is an issue which needs to be addressed. Health officials, medical doctors, churches, schools, chiefs and the sufferers themselves must all become involved if we are to tackle this disease. Numerous other studies have emphasized the need to keep animals, such as pigs and dogs from domestic settings, by containing them within appropriate enclosures.

Tungiasis is clearly problematic, and despite its associated morbidity and growing awareness, it is not recognised on a local or international level as a serious health issue. Educating people about the risk factors and potential causes is paramount in addressing this problem.

Keywords: Tungiasis, Tunga penetrans, jigger flea, epidemiology, parasite, Cameroon

Prevalence of Depression and its Correlates among Unskilled Workers in Al Ain, United Arab Emirates

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Abstract

Background: The UAE recruits most of its construction and other labour from overseas, especially from the Indian subcontinent. Many live in labour camps separated from their families for many years. There have been media reports about several cases of suicide but reliable data on mental stress and depression are lacking.

Objectives: The study aimed to assess the prevalence & risk factors for depression among labor camp residents in Al Ain, UAE.

Methods: We conducted a cross-sectional survey and a random sample (n=318) from a sampling frame of labor camps of various sizes located in Al Ain. We used Urdu, English and Arabic translated versions of Depression Anxiety and Stress Scale (DASS-42) to assess depression and suicidality among the study participants. Final year medical students visited selected labor camps to conduct the survey.

Results: Out of 318 study participants, 239 completed and returned the survey. The prevalence of depression was 25.1% (60/239). The highest prevalence of depression was noted

among laborers from Bangladesh (40%), followed by non-national Arabs (37.5%), Pakistani (30%), and Indians (13.8%). Depression was associated with physical illness (adjusted odds ratio-AOR 2.9; 95% CI 2.27-5.18), working in construction (AOR 2.2; 95%CI 1.59-3.83), earning less than 500 DHR per month (AOR 1.8; 95%CI 1.33-3.16), and working more than 8 hours a day (AOR 1.4; 95%CI 1.08-2.52). About 7% of the study participants reported thoughts of suicide and 8 (3%) had attempted suicide.

Conclusions: Laborers are experiencing a substantial burden of depression, suicidality and attempted self-harm. Policy level intervention needed to improve minimum wages, limit working hours, and devise population-based health strategies to address these issues in this vulnerable population.

Keywords: Labourers, Depression, Suicide

Adverse events following immunization (AEFI) surveillance in Tehran West Health Centre between march 2006 to October 2008

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Abstract

Background: As vaccine-preventable infectious diseases continue to decline, people have become increasingly concerned about the risks associated with vaccines. Furthermore, technological advances and continuously increased knowledge about vaccines have led to investigations focused on the safety of existing vaccines which have sometimes created a climate of concern.

Aims & Objectives: To describe the magnitude, trends, geographic distribution, clinical characteristics of AEFI cases reported to TWHC Registry of Reports.

Methods/Study Design: This is a Retrospective Cohort Study and we analyzed all important data's of our reported cases by SPSS.

Limitation: AEFI surveillance system in our limitation area is new and our under cover centers (hospitals & health care centers is not so familiar to detect all of AEFI's. But the most important limitation of this study is our staff in centers, they still are afraid to report AEFI cases (because of law problems) that it has been caused by inadequate knowledge and attitude about AEFI .

Results/Findings: Totally 321 AEFI reported to us. 21%cases were Serious Adverse Effects¹. In total Serious AEFI cases 32% caused by MMR, 24% DTP and 2% B.C.G. Vaccination center of cases in 78% were health care centers and in 21% cases were vaccinated in hospitals. 87% our reported cases show AEFI earlier than one month after vaccination, also in 9%cases adverse effects has been reported between 30 to 100 days after vaccination. 34% cases vaccinated with MMR, 39% with DTP and 1% with HEPATITIS B. The most important vaccine related adverse effect was encephalitis (11% cases) that 81% of them have been vaccinated with MMR and 19% with DTP. 23% AEFI cases classified as program error (73% B.C.G.) Mean time of first onset of AEFI and vaccination date in B.C.G was 104.5(CI: 89.930 -119.069) days. This statistic value for DT was 1.6 (CI: .279-2.920), for D.T.P. was 8.840 (CI: 5.176- 12.50), for MMR was 4.009 (CI: 2. 89-5.12) days.

Conclusion: There is no such thing as a "without adverse effect" vaccine. Effective vaccines (i.e. vaccines inducing protective immunity) may produce some undesirable side effects which are mostly mild and clear up quickly. The majority of events thought to be related to the administration of a vaccine are actually not due to the vaccine itself - many are simply coincidental events, others (particularly in developing countries) are due to human, or programme error²(see table 1). Alternatively, vaccine-associated adverse events should be promptly identified to allow additional research and appropriate action to take place.

It is not possible to predict every individual who might have a mild or serious reaction to a vaccine, although there are a few contraindications to some vaccines. By following contra indications the risk of serious adverse effects can be minimized.

¹Serious adverse effect is a "CDC" classification for adverse effect which should be investigated immediately with involvement from central levels including epidemiological and/or clinical expertise.

² Event caused by an error in vaccine preparation, handling, or administration.

Keywords: Adverse Effect, vaccine, twch

Recommendations for preventing Programme errors adverse events:

- Usage of new disposable syringe or needle for every person;
- Properly sterilizing syringe or needle;
- Non use of reconstituted vaccine at subsequent session;
- Reconstitution vaccine with correct or recommended diluents;
- No storage of drugs in vaccine or diluents refrigerator;
- Immunization injection in recommended site(example: intradermal for BCG);
- Transportation /storage correctly;
- Consideration of Contraindications

Table1: Programme errors leading to adverse events






Programme errors		Adverse event
Non sterile injection. <ul style="list-style-type: none"> • reuse of disposable syringe or needle • improperly sterilized syringe or needle • contaminated vaccine or diluent • reuse of reconstituted vaccine at subsequent session 		Infection (e.g. local suppuration at injection site, abscess, cellulitis, systemic infection), sepsis, toxic shock syndrome, transmission of blood borne virus (HIV, hepatitis B or hepatitis C)
Vaccine prepared incorrectly <ul style="list-style-type: none"> • vaccine reconstituted with incorrect diluent • drugs substituted for vaccine or diluent 		Local reaction or abscess from inadequate shaking. Fatal if drug (e.g. muscle relaxant, insulin)
Immunization injected in wrong site. <ul style="list-style-type: none"> • subcutaneous instead of intradermal for BCG • too superficial for local vaccine (DPT, DT, TT) • buttocks 		Local reaction or injection site abscess Severe nerve damage (=injection vaccine-hepatitis H)
Vaccine transported/stored incorrectly.		Increased local reaction from frozen vaccine (and ineffective vaccine)
Contraindications ignored.		Avoidable severe vaccine reaction.

Table 2: Vaccination center type * reporter center type Cross tabulation (Pearson Chi-Square =21.412 ;Df=3;P value<0.05)

Vaccination center type	reporter center type		Total
	Hospital	Health center	
health center	13.3%	86.7%	100.0%
hospital	9.0%	91.0%	100.0%
private	13.4%	86.6%	100.0%
Total	13.4%	86.6%	100%

Pearson Chi-Square =43.55325 ;Df=4;P value<0.05

Table3: type of vaccine * hospital admission Cross tabulation

History of admission in hospitals		
Vaccine	YES	NO
BCG	1.4%	98.6%
DT	0	100%
DTP	8.8%	91.2%
HB	0	100%
MMR	32.4%	67.6%
Total	14.6%	85.4%

Tabel 4: Incidence of AEFI 'S after B.C.G (P Value<0.05)

TYPE	Percentage	Count
Osteo myelitis	1.40%	1
Lymphadenitis	98.60%	69
Total	100%	70

Table 5: Incidence of AEFI 'S after D.T

Type	Percentage	Count
faint	20.00%	3
Artropathy	6.70%	1
Mild Local Reaction	53.30%	8
Sever Local Reaction	20.00%	3
Total	100%	15

Table 6: Incidence of AEFI 'S after D.P.T.

Type	Percentage	Count
Abscess-inf	1.6%	2
Abscess-sterile	1.6%	2
anxiety	2.4%	3
fever	16.8%	21
convulsion	3.20%	4
diareaha	4%	5
Faint	0.8%	1
Meningo Encephalitis	5.6%	7
long cry	1.60%	2
Mild local reaction	42.4%	53
sever local reaction	15.2%	19
Rash	0.8%	1
Vomiting	3.2%	4
Lymphadenitis	0.8%	1
Total	100%	

Table 7: Incidence of AEFI 'S after H .B.

TYPE	PERCENTAGE	Count
Mild local reaction	66.70%	2
Sever local reaction	33.30%	1
TOTAL	100%	3

Tabel 8: Incidence of AEFI 'S after M.M.R

TYPE	PERCENTAGE	Count
Diarrhea	0.9%	1
Parotiditis	43.5%	47
Fever	9.3%	10
Hematuria	0.90%	1
Convulsion	2.8%	3
Arteropathy	1.9%	2
mild local reaction	2.80%	3
sever local effect	1.90%	2
Meningo encephalitis	27.80%	30
Rash	8.3%	9
Total	100.00%	108

Table 9: Descriptive analysis of Time between Vaccination and AEFI onset

Mean	21.3738
Std. Error of Mean	2.70563
Median	2.0000
Mode	.00
Std. Deviation	48.47542
Variance	2349.86606
Range	354.00
Minimum	.00
Maximum	354.00

Table 10: Ferequensis of recieved vaccines in AEFI cases (P value<0.05)

	Responsible Vaccine					Total AEFI
	BCG	DT	DTP	HB	MMR	
Count	70	15	125	3	108	321
Percentage in AEFI	21.80%	4.70%	38.90%	0.90%	33.60%	100.00%

Table 11: Cross tabulation between type of vaccine * sever effect
 Pearson Chi-Square =43.55325; Df=4; P value<0.05

Vaccine	Freq.	Sever effect ³		Total
		Yes	No	
BCG	Count	1	69	70
	Percentage	%1	%99	%100
DT	Count	0	15	15
	Percentage	%0	%100	%100
DTP	Count	15	110	125
	Percentage	%12	%88	%100
HB	Count	0	3	3
	Percentage	%0	%100	%100
MMR	Count	33	75	108
	Percentage	%31	%69	%100
Total	Count	49	272	321
	Percentage	%15	%85	%100

Table 12: Cross tabulation between vaccination center type * sever effect (Pearson Chi-Square =16.207; Df=2; P value<0.05)

Type of vaccination centre	Freq.	Sever effect		Total
		yes	no	
Health center	Count	43	209	252
	% within vaccination center type	17	83	100
	% within sever effect	88	77	79
Hospital	Count	4	63	67
	% within vaccination center type	6	94	100
	% within sever effect	8	23	21
Private	Count	2	0	2
	% within vaccination center type	100	0	100
	% within sever effect	4	0	1
Total	Count	49	272	321
	% within vaccination center type	15	85	100
	% within sever effect	100	100	100

³ Sever adverse effects are vaccine related effects which ministry of health classified as urgent AEFI (need to report immediately to ministry of health).

Table 13: Cross tabulation between vaccination center type * AEFI

	Freq.	Abscess-if	Abscess-sterile	anxiety	arthopathy	convulsion	diarceha	Faint	fever	hematuria	long cry	lymphadenitis	Meningo Encephalitis	mild local reaction	osteomyelitis	parotiditis	rash	sever local reaction	vomiting	Total
Health center	Count	2	2	3	3	6	6	4	29	1	2	15	33	63	0	46	10	23	4	252
	percentage	1	1	1	1	2	2	2	12	0	1	6	13	25	0	18	4	9	2	100
Hospital	Count	0	0	0	0	1	0	0	2	0	0	55	2	3	1	1	0	2	0	67
	percentage	0	0	0	0	1	0	0	3	0	0	82	3	4	1	1	0	3	0	100
Private	Count	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	2
	percentage	0	0	0	0	0	0	0	0	0	0	0	100	0	0	0	0	0	0	100
Total	Count	2	2	3	3	7	6	4	31	1	2	70	37	66	1	47	10	25	4	321
	percentage	1	1	1	1	2	2	1	10	0	1	22	12	21	0	15	3	8	1	100

Defining Health

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Summary

WHO (1946) defined health as

“...a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”.

Over the last 66 years many questions arose from time to time around this definition which remains unanswered even to date. Is the ‘complete’ a static state or an ever-evolving state or phenomenon? What does ‘complete’ denote? What does ‘well-being’ denote? Also, who decides what this ‘complete’ and ‘well-being’ look like? Which of the many definitions and understandings of ‘complete’ and ‘well-being’ is to be followed while talking about health?

One message was clear from this definition that it is not just the absence of disease or illness. However, here also no one was made clear about what absence denoted, e.g. was this absence at a macroscopic level that others could see, feel or touch. Alternatively, was this absence at a microscopic level that scientists could look at through microscopes of various kinds? Furthermore, was this absence of a third kind that could be noticeable only through sophisticated equipment by certain groups of specially trained and educated people with their sophisticated advanced biotechnological machines, e.g. a magnetic resonance imaging and technetium nuclear scans?

The definition if explored logically, it leaves a big hole. One wonders if health is a perception of the individuals, or the families, or the community. Or, is it something that can be qualified and quantified only by experts in the field of medicine and, or the social sciences for others and for self as could be derived from the WHO's definition?

While thinking about this definition we also have to decide if there is, or was any time in a person's life when there was nothing that was leading him or her to some disease or ill-health or death? Simply put, as is well known to science for a long time, every moment of the time one or the other part, e.g. cell, of our body is sick and dying and being replaced by a newer generation. These changes could be identified through sophisticated methods by scientists in the field with the help of advanced equipment and genetic studies, etc. Any visible infirmity today has its roots in ones genes and or, ones environment, therefore everyone has some abnormality that is leading one to the end result of macroscopically visible ill-health. Would we like to take this as an unhealthy body for every living organism at all the times?

Moreover, does the definition of health like the WHO's definition give no value to a particular space, context and time? As an example, people living on very high altitude will have more red blood cells (polycythemia) and if they were relocated and started living at the sea level they will get lesser number of red cells. Would polycythemia be considered ill-health? When we take the time, space and context in our exploration, it is not a disease. Similarly, what one thinks of good health at age 14 is different to what s/he will think five years later. Moreover, for someone whose thinking and writing power is great and that's what s/he is living for (context), the person would likely feel very healthy, though s/he may have an ailing body, a least concern of that person. Could health, hence the definition of health, be time, space and context free as the definition above has been?

Roy (1984), on the other hand, defined health as “...a state and a process of being and becoming an integrated and whole person” (p. 39). Roy and Andrews (1986) later defined a whole person as the “...one with the highest possible fulfillment of human potential” (p. 8), and that lack of integration (adaptation) leads to lack of health.” Such a premise is derived from Bertalanffy’s (1968) General Systems Theory that reinforces the idea of interdependence and interrelationships of a person with his or her environment. In addition it derives from Helson’s (1964) adaptation level theory that tells that behavior is adaptive within adaptors’ environment.

The above definition brings in the notion of incoming stimulus and the adaptation level of a person, which reflect upon the health and fitness of a person. Though more nearly the complete definition of health, it leaves certain gaps, too. Who decides what a healthy adaptation level in a person is? Would it be different for different people, and if so, how the definition of health could be generalized? Moreover, would not such a definition focus our actions and us more on individual level? What about those who do not wish to adapt, or those who wish to confront the stimuli and like to either suffer as a consequence, or bring in the notion of opposing the stimuli to bring in a healthy change? What is or was a healthy adaptation or change? Who and on what grounds one decides the meaning of a healthy change or an unhealthy change or adaptation?

Building from the various viewpoints we have been studying and discussing in different national and international forums, and deriving from my personal life experiences with numerous patients and well persons, I have come to an understanding that any definition of health needs to encompass the following aspects:

- Individual, family and community, and everything else, the Totality, or Nature or Universe all encompassing

- Self perceptions, i.e. of the individuals, families and, or the communities
- Individual centered, family centered and community centered, however time, space and context dependent
- Perceptions of others, especially those that can impact upon the perceptions of the individuals, families and, or the communities
- Physical, mental, social and spiritual aspects, as perceived by the person, or persons concerned, individually and, or collectively
- Capacity to live harmoniously (consciously and, or unconsciously) within and outside the individual, the family and, or the community, and to cope with various internal and external stimuli (adaptation), maintenance of interrelationships
- And, or capacity to purposefully (consciously) not accept or adapt to some selected stimuli so as to bring about a change in a manner deemed necessary by the individual, a family and, or a community. When others perceive one, or a family, or a community to be unwell, and when any of those find no reason to get influenced, it should be considered positive health for the people concerned
- Perceptions, values, beliefs and aspirations of the individuals, families and, or the communities, and the level of value they give to various aspects of life and living

Health; As I see it

Perceptions of others about an individual, a family or a community cannot define health per se, though they partly contribute towards a comprehensive understanding of health. These others are the source of different behaviors for different people. This collective of others constructs the norms of any society and accordingly tends to influence the perceptions of an individual, a family and, or a community. Needless to say that as perceptions are influenced by many factors (social

construction), these are generally different for different people, at the same time capable of being quite similar in similar or dissimilar societies in certain aspects.

Deficiency or abnormality in the expected perception for a person, a family and, or a community is the first indication of one's ill health, which may or may not be perceived by others. However, perception of this deviation may not lead to disease once the mind or the body is capable of adjusting to it physically and, or mentally, or purposefully confronting it to bring about a change if the outcome perceived turns out to be expected. Any dissonance at this level may lead to ill health, especially when a body and, or a mind fails to either successfully cope, or successfully confront it as expected.

Moreover, change is the rule of life. Whole universe is changing; no moment is like any other moment. Every person, every family, every community, every species and everything else we could think of is changing its characters, therefore health and its parameters are continuously changing, too. If the understood or perceived state of mind, body and relationships is changing as it has to, then the definition of health is true only for a particular moment rather than for ever unless it incorporates **'ever evolving'** and for a **'particular time, space and context.'**

The purpose of looking at the various notions of health is to bring out the political power-relations struggle that goes on while developing any health related policy, implementation plans and related operational activities at the governance, executive and provider levels. Clearer understanding of health and what is involved in it becomes an important premise on which health related policy with strict, yet fluid, ever evolving guidelines could be developed and practiced. Recent developments and slogans of 'patient-centred', 'family-centred', 'community-centred' medicine that is more of a lip-service,

could never become a reality if our philosophical underpinning is still influenced by the 1846 WHO's definition of health.

Health, like education is a fundamental right of every human being and it requires a comprehensive definition of health that is clear, and universally adoptable that has a great potential to reduce the hegemonic struggle that goes on while developing and implementing health related policy.

Simplified to a comprehensive statement, based on the above notion, here is the definition of health I developed in 1995 with refinements done over the last 13 and a half years,

“...health (or ill-health) is an ever evolving state of mind, body and relationships perceived by an individual, a family, a group, or a community for self in a particular space, time and context.”

Attitude and Awareness of Male Attendees of a Tertiary Care Level Hospital in India Regarding Prevention of Parent to Child Transmission of HIV Infection

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Abstract

Background: Knowledge and information are the primary needs for prevention of HIV. Ignorance about the disease and transmission of the virus can be the greatest hurdle in eliminating the disease from the population.

Aims & Objectives: 1. Assess the level of awareness and the attitude of male patients aged 20-40 years about HIV infection, its modes of transmission and prevention of vertical spread.

2. Assess the level of awareness and the attitude of male partners of pregnant patients attending the Gynecology OPD and undergoing PPTCT counselling, about HIV infection, its modes of transmission and prevention of vertical spread.

Methods/Study Design: A cross-sectional study conducted for a period of 2 months in 2008 on a total of 135 people. 100 male patients admitted to the hospital who belong to the reproductive age group of 20-40 years (controls) were assessed about their knowledge about HIV, the transmission modes and prevention of spread using a semi-structured questionnaire. 35 male partners of the pregnant women attending the Gynaecology OPD who were counselled regarding prevention of parent to child transmission of HIV, (cases) were also

surveyed with the same questionnaire. The results were statistically analyzed.

Results/Findings: 62 % of the controls were aware of the “term” HIV/AIDS and NOT the disease. Only 12% controls knew about the various modes of transmission of the disease. Only 3% control knew about availability of medicine to HIV positive mothers. 100% controls were aware of the disease, the modes of transmission and methods of prevention. Almost everyone admitted that they had scanty knowledge about the disease before the counselling session and that they were benefited from this counselling. However 54.3 % of cases were unsure whether to opt for MTP or use of Nevirapine.

Conclusion: PPTCT counselling can markedly improve the level of awareness and knowledge regarding the disease HIV/AIDS. A proper counselling by trained personnel can help reduce the spread of the disease through vertical transmission so that we can have an HIV/AIDS free future generation. A compulsory PPTCT counselling is highly recommended for the male partners of the pregnant women.

Keywords: PPTCT, counseling, male

Rethinking the Rules of the Game: Leadership and Strategic Planning Process in Health Development - A Universal Message

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Abstract

The purpose of this paper is to examine a conceptual model of strategic planning process in health and health policy development and implementation. The model looks at the process of community 'consultation' and 'participation' in policy development and implementation. Taking a historical approach, it explores and looks critically at how New Zealand health reforms have been conceptualized, developed and implemented. The paper argues that New Zealand health policy leadership did not take into account the "rules of the game" of either economic rationality or social reality, while each government believed in each of the policies. Finally, it proposes that policy makers rethink future processes in order to create a more supportive environment which involves the community, and other stakeholder groups, in decision-making process at all levels of policy formation and implementation. Bureaucracy is there only to bring your policies to fruition, not to rule the professionals.

A Common Surgical Condition with a Devastating Outcome in Rural Australia: a case report on a mis-diagnosed appendicitis

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Abstract

Purpose: This case report highlights how common surgical conditions in rural settings where resources are scarce, may have delayed presentation, missed diagnosis with resultant higher morbidities and long-term complications.

Case report: A 22 year-old woman presented to a local medical practitioner one week after the onset of vague lower abdominal pain, nausea and vomiting. These non-specific symptoms opened up many differential diagnoses, including several gynaecological pathologies more prevalent in young women. The diagnosis of a "non-sexually acquired pelvic inflammatory disease" was made. The patient's symptoms soon worsened and she became septic. She later self presented to her small local hospital where no imaging modalities were available. The woman was soon transferred to a regional hospital. A computed tomography (CT) scan showed appendicitis complicated by two large multilocular pelvic abscesses. She received intravenous antibiotics and underwent two CT guided percutaneous abscess drainage. She

was later discharged with drains left in situ. She was scheduled for an interval appendicectomy, and was counselled about possible long-term complications such as infertility.

Conclusions: Many studies have identified the challenges faced by the medical practice in rural Australia. They often focus on topics such as demographics and socioeconomic status. However, few studies have related these disadvantages to a specific clinical scenario where a common and easily manageable pathology, in this case appendicitis can have a devastating outcome and complications in a rural setting.

Keywords: Appendicitis, pelvic abscess, complications

Predictors of Mortality and Morbidity in Clostridium Difficile Infection

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Abstract

Background: Clostridium Difficile (CD) is implicated in 20 to 30% of patients with antibiotic-associated diarrhoea, in 50 to 70% of those with antibiotic-associated colitis and in more than 90% of those with antibiotic-associated pseudomembranous colitis¹⁻⁴. The incidence of CD associated diarrhoea ranges from 1 in 100 to 1 in 1,000 hospital discharges depending on the antibiotic prescribing habits of the hospital⁵⁻⁷.

Aims: The primary objective of our study was to determine the baseline characteristics of in-patients with hospital acquired Clostridium difficile and to ascertain their eventual outcomes, and thus evaluate the effectiveness of disease severity in predicting mortality, morbidity at discharge and discharge destination.

Secondary aims included an analysis of the epidemiology of the infected population and if antibiotic-related infection varied in prognosis to sporadic (antibiotic-unrelated) infection.

Methods: All patients with diarrhoea admitted to a 24-bedded (cohort) ward in at Whiston Hospital, Merseyside – UK over a four week period (May 2008) were prospectively identified and their case-notes were retrospectively reviewed.

Results: 16 patients with confirmed CD infection were identified during the period of the study. The mean age of the infected population was 80 years (age range: 59-89 years, median: 82 years).

Discussion: The study confirms that CD is a disease that affects a predominantly elderly and frail population with multiple co-morbidities and poor performance status, and carries a large mortality and morbidity burden.

Rural Community Health Carnival: Screening for Chronic Disease Risk Factors in Jeli, Kelantan, Malaysia

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Abstract

In Malaysia, chronic diseases which include heart diseases, strokes, cancers, diabetes and mental disorders are the major cause of death and disability. They account for 71% of all deaths and 69% of the total burden of disease. Obesity, diabetes mellitus, hypertension and high blood cholesterol level are well known cardiovascular risk factors. Health screening is

urgently needed to identify risk factors of chronic diseases. Health carnival is a special event which is designed to bring together a variety of screening services at one place simultaneously. In the present study, a health carnival was implemented as an important role in the early detection of these diseases and their risk factors. This carnival was held in Jeli, Kelantan, which is located 98 km from Kota Bharu. Activities such as house visits were held prior to the health carnival day in order to promote health carnival program. During the two days of the carnival, 141 participants aged 14 years and above received health check-up. Data on body mass index (BMI), waist circumference, blood pressure and random blood sugar were analyzed. In this study, 5.0% of respondents had raised blood sugar. 37.6% of participants had a body mass index of $25\text{kg}/\text{m}^2$ or greater. Furthermore, 60 participants had high blood pressure. Based on these results, about half of residents are considered have one chronic disease risk factor or more. Thus, these data emphasize that more screening tests are needed to increase awareness of chronic diseases and promote healthy lifestyle among rural residents.

Keywords: Malaysia, rural community, health screening, chronic diseases, hypertension, disease risk factor, Jeli