Determinants of Treatment Cessation Among Pulmonary Tuberculosis Patients in Khorassan Province of Iran

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Keywords: Pulmonary tuberculosis; Complications; Treatment completion; Treatment cessation; Mortality

Background: Recognizing of factors involved in the cessation and interruption of a disease like tuberculosis are important and can help us to improve the treatment strategy and educational status of the patients. We assessed the causes of treatment cessation in the patients suffering from pulmonary tuberculosis referred to the tuberculosis Center No.2 in Khorasan Province of Iran during the years March 2003 to March 2005.

Methods: A descriptive and retrospective study of case-sheets of all pulmonary tuberculosis' patients who were referred to the Mashhad Health Center No. 2 during the years 2003 to 2005 and the variables like age, sex, nationality, outcome of treatment and causes of treatment cessation and interruption were presented with descriptive statistic.

Results: The total number of the patients were 659. Of these patients, 534 (81%) were smear positive and 125 (19%) were smear negative. Among the 534 smear-positive patients, 43 (8%) have treatment cessation and interruption. The reasons of treatment interruption were mortality due to T.B in 20 patients (3.7%), drug induced hepatitis in 11 (2%), premature sensation of wellbeing in 2 (0.37%), Hearing problems and vertigo in 2 (0.37%), multi drug resistance (MDR) tuberculosis, in 2 (0.37%), purpura in 1 (0.2%), and exacerbation of renal failure in 2 (0.37%). 438 cases (82%) had total cure.

Conclusion: Observation supported the effectiveness of directly observed therapy short course (DOTS) strategy, with first line therapy. The causes of treatment cessation and interruption like drugs' induced hepatitis and premature sensation of wellbeing can be controlled by increasing the awareness of patients about the severity of T.B disease. Efforts to improve patients’ understanding of TB disease and related treatment issues may be an important TB control program strategy and should be emphasized at the initiation of therapy and at intervals throughout the treatment course to minimize treatment interruption.

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Multifocal Tuberculous Spondylitis Caused by Multi-drug Resistant Tuberculosis in a 15-year-old Boy

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A 15-year-old boy presented to the Orthopaedic Department for neck, thoracic and back pain for 6 weeks. The pain progressively worsened and caused difficulty in walking and sitting. His had significant constitutional upset. Examination revealed tenderness and decreased range of movement over the lower cervical spine region and thoraco-lumbar junction. There was no motor or sensory deficit. MRI of the cervical and thoracic spine showed erosion of the anterior vertebral body from C5 to T1 level with paraspinal soft tissue swelling from C4 to T1 level which was compatible with tuberculous spondylitis. Imaging also showed extensive involvement of the thoracic and lumbar spines with paraspinal soft tissue involvement and left psoas abscess formation. Blood tests revealed hypochromic microcytic anaemia, raised ESR and CRP. He was empirically treated with standard antituberculous drugs. Anterior spinal fusion of C7 to T1 level was performed. Despite treatment he had persistent swinging fever. A second operation was performed which consisted of throracotomy and drainage of the abscessed at T7 and the left psoas. Central line was also inserted for administration of drugs and TPN. Pus and granulation tissue collected yielded large number of AFB and PCR was positive for Mycobacterium tuberculosis (MTB) complex. Formal susceptibility testing of the MTB isolate later confirmed multi-drug resistant tuberculosis with resistance to isoniazid, rifampicin, streptomycin and ethambutol while susceptibility testing showed sensitivity to most agents except ofloxacin. Immune function screening showed normal findings. He was HIV negative. The treatment was change to levofloxacin, prothionamide, para-aminosalicylic acid, cycloserine, linezolid and amikacin. In conclusion, tuberculous spondylitis should be considered in any patient who presented with neck pain, back pain and constitutional upset. Prompt isolation of the AFB with susceptibility test for detection of drug resistance is vital to the clinical management. Immune function disorder should be considered in individual case.

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Outcome of Treatment of MDR-TB Patients with Standardized Regimens; Iran's Experience 2002–2006

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Background: MDR-TB imposes a formidable burden on countries health systems. There is not still a consensus on the subject and there are controversies regarding treatment protocols, treatment outcomes and various regimens.

Methods: This study accounts for Iran’s Second National Cohort for treatment of MDR-TB. The study comprises all MDR TB documented cases in Iran referred to our center during the period of 2002–2006. All patients received standardized second-line regimen uniformly consisted of Ofloxacin, Cycloserine, Prothionamide and Amikacin. Based on drug susceptibility tests Ethambutol and Pyrazinamide were added to the regimen.

Results: Finally, 43 patients with diagnosis of MDR-TB were involved for treatment, among those 27 (62.8%) were male. Mean age was 44.38 ± 19.05. Twenty three (53.5%) of them were Iranians and the remaining were Afghan. All patients were secondary MDR-TB cases. Of total 43 cases, 25(58.1%) experienced major and clinically significant adverse effects. 29(67.5%) had successful outcome. Conversely, overall 14 (32.5%) showed poor outcome (Treatment Failure in 6(14%) and Death in 8(18.6%). Mortality was...
higher in Iranians (P-value: 0.039) and in patients whose initial regimen was changed due to adverse drug reaction. (P-value: 0.01) Conclusion: MDR-TB treatment using standardized regimen showed favorable outcome in our study, comparing with previous studies.

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42.011
Investigations of Polymorphisms Associated with Cytochrome P4503a5 and MDR1 in Patients with Severe Leprosy Reactions Treated with Cyclosporin A

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Background: The only treatment available for severe leprosy Type 1 Reactions (T1R) is prednisolone but a significant number of patients do not respond to treatment. There have been 2 case reports of successful treatment of non-responsive T1R with cyclosporin A (CyA). This study uses an Indian microemulsion formulation of CyA (Panimune) as monotherapy to treat patients with severe T1R. Evidence is now available showing that some ethnic groups metabolise CyA differently. Genetic differences have also been identified in the genes responsible for CyA metabolism (cytochrome P450) in various ethnic groups. It is important to identify any groups that metabolize or absorb CyA differently as this will help in deciding the optimal dose to be used.

Aims: To identify any differences in dose requirements for CyA treatment of severe leprosy T1Rs in the 2 racial groups and whether these differences were related to genetic variations.

Methods: 33 Ethiopian and 12 Nepali patients with severe T1Rs were recruited and treated with CyA at a dose of 5–10 mg/kg/day; dose increases were dependent on clinical improvement. Trough blood concentrations of CyA were analysed using a Liquid Chromotography/Tandem Mass Spectrometry assay. Pharmacokinetic studies were carried out on a subgroup of patients. DNA was extracted from whole blood and samples genotyped using PCR and restriction length polymorphism (RFLP). For CYP3A5, AA, AG and GG genotypes were identified and for MDR1, CC, CT and TT genotypes were identified.

Results: 77% Ethiopian patients needed a higher dose of CyA than the Nepalis to show a clinical improvement. Patients with the TT and GG genotypes achieved a higher Cmax and area under the curve (AUC) for CyA than those with CC/CT or AG/AA genotypes respectively.

Conclusion: Polymorphisms in CYP3A5 and MDR1 may explain variation in dose requirements for CyA in different racial groups. This is important for all drugs that are heptatically metabolised and in particular HAART medication.

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Vaccines Pre-Clinical (Poster Presentation)

43.001
Can Outer Membrane Vesicle of Group B Meningococci be Applied as an Adjuvant in Immunization of the Rabbit Against Serogroup A Neisseria Meningitidis?

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Keywords: OMV; Adjuvant; Neisseria meningitidis serogroup A & B; Bactericidal activity

Background: Since the use of new adjuvants in designing new vaccines against most of infectious diseases should be improved, many candidates are recommended for modulating an immune response to an antigen. Neisseria meningitidis serogroup B outer membrane vesicle (OMV) has been used previously by Siadat et al (2007), as a carrier for polysaccharide immunogens. In this study OMV was used as an adjuvant for group A meningococcal capsular polysaccharide (GAMP) and was tested in Newzeland white rabbit for bactericidal antibody activity induction.

Methods: The complex of OMV with GAMP, in no covalent form, and control were injected intramuscularly into groups of four rabbits with boosters on day 14 and 28 after primary immunization. The following groups were used as control: 1.GAMP, 2.OMV and 3.normal saline. The serum samples collected on days 0, 14, 28 and 42 and tested by complement mediated bactericidal assay against serogroup A and B meningococci according to the world health organization protocol.

Results: Rabbits given three dose of the complex of serogroup B meningococcal OMV with GAMP developed high level of serum bactericidal activity against serogroup A meningococci after 42 days in comparison with the GAMP and OMV control group (P<0.005). Bactericidal titer against serogroup B meningococci of the GAMP plus OMV complex showed no significant difference in comparison with the OMV containing control (P>0.005).

Conclusion: The results indicate that the combination of OMV with GAMP, in non covalent form, would be able to induce a high level of bactericidal antibody response in comparison with GAMP. The OMV of Neisseria meningitidis is a potent protein carrier in the induction of immune system but in this article the role of OMV is studied as an immune system promotor in non-covalent form and without any conjugation process(as an adjuvant) in order to induce immune response against three prevalent serogroups of Neisseria meningitidis.

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