

A dissertation on
COMPARISON OF ANALGESIC EFFECT OF SPECIFIC ACUPUNCTURE
AND MOXIBUSTION IN RHEUMATOID ARTHRITS

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Government Yoga & Naturopathy Medical College & Hospital, Chennai from
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LIST OF ABBREVIATIONS

RHUEMATOID ARTHRITIS	RA
HUMAN LEUKOCYTE ANTIGEN	HLA
TUMOUR NECROSIS FACTOR	TNF
PROTEIN TYROSINE PHOSPHATASE NON RECEPTOR TYPE 22	PTPN
SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION 4	STAT4
TUMOUR NECROSISFACTOR ALPHA INDUCED PROTEIN 3	TNFA1P3
CLUSTER OF DIFFERENTIATION	CD4
INTERLEUKIN	IL
INTERFERON	IFN
VASCULAR ENDOTHELIAL GROWTH FACTOR	VEGF
5HYDROXY TRYPTAMINE	5HT
C-REACTIVE PROTEIN	CRP
ERYTHROCYTES SEDIMENTATION RATE	ESR

DYNORPHIN	DYN
ENDOMORPHIN	EM
PREPRODYNORPHIN	PPD
PRO-OPIO MELANO CORTIN	POMC
TRADITIONAL CHINESE MEDICINE	TCM

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ABSTRACT

OBJECTIVE:

To evaluate the analgesic effect of specific acupuncture and moxibustion in Rheumatoid arthritis.

BACKGROUND:

Rheumatoid arthritis is a systemic auto immune connective tissue disease with unknown etiology. RA is characterized by nonspecific, chronic progressive inflammation of joints that leads to progressive destruction of the joints and periarticular tissues. and is the most common persistent inflammatory arthritis. RA causes inflammation in the affected joints which leads to intense pain and decreased range of movement leads to disability and affects day today life. This study was planned to evaluate the analgesic effect of specific acupuncture and moxibustion in Rheumatoid arthritis

DESIGN AND METHOD:

A comparative study performed among 80 patients with Rheumatoid arthritis age ranging between 30-55 years from IP and OP dept of Govt. yoga and naturopathy medical college, Arumbakkam. They were randomly assigned into two groups. Experimental group (n=40) and control group after satisfying the inclusion and exclusion criteria and ACR/EULAR 2010 criteria. Experimental group was given moxibustion at selected acupuncture points and ah-shi points of the affected joint. Control group received

acupuncture on the same acupuncture points.Both groups were assessed at baseline and immediately after treatment by using visual analogue scale(VAS)

RESULTS:

The result when seen with in the group there is significance,but when compared between the groups the datas are not significant.

INTERPRETATION AND CONCLUSION

Experimental group and control group showed significant improvements in pain reduction in onetime exposure to the treatment. Hence, immediate effect moxa and acupuncture in RA patients has shown a positive influence on pain reduction of the human body.when it compared between the groups it shows that both are equal in reducing pain in RA.

KEYWORDS:

Moxibustion, acupuncture, analgesia, rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is characterized by nonspecific, chronic progressive inflammation of joints, which finally leads to gradual destruction of the joints and periarticular tissues. RA expresses a systemic autoimmune connective tissue disease (1) it is a chronic disease that is characterized by non-specific inflammation of the peripheral joints, resulting in the progressive destruction of the joints and periarticular tissues (Scott, 2004). and is the most common persistent inflammatory arthritis that occurs throughout the world and in all ethnic groups. The prevalence is lowest in black Africans and Chinese; in Caucasians it is 1.0–1.5% with a female :male ratio of 3: 1. Disease occurrence rates are higher in monozygotic twins (12–15%) than in dizygotic twins (3%). It is a disease with unknown etiology and it is characterised by chronic inflammation of the affected joints, granuloma formation and joint destruction. The earliest change is hyperplasia and hypertrophy of the synoviocytes. The cells become multilayered, reaching a depth up to 6 to 10 cells. (Kulka et al., 1955; Kulka, 1966). and infiltration of lymphocytes, macrophages and plasma cells in the connective tissue of the affected joint., and the pannus formation (inflammatory granulation tissue) spreads around the articular cartilage, and it causes progressive destruction of the cartilage. Muscles in the affected joints become atrophy and joint is infiltrated with lymphocytes. Subcutaneous rheumatoid nodules are granulomatous lesions consist of fibrinoid material, and it is surrounded by proliferating mononuclear cells. Rheumatoid nodules occur in the sites of pressure prone areas such as

the extensor surfaces of the forearm, Achilles tendon ,and toes of the seropositive patients. Alike nodules may also occur in the pleura, lung and pericardium. Connective tissue is packed with mononuclear cells and forms Russells bodies. (Gardner, 1965) .Changes in the vascular system includes dialatation of venules,increase in the size and number of endothelial cells,leakage of RBC and plasma proteins and obstruction of vessels and also causes arteriolar haemorrhage and thrombosis.(2)

Slow onset of symmetrical arthralgia and synovitis of small joints of the hands, feet and wrists. Large joint involvement, systemic symptoms and extra-articular manifestations such as rheumatoid nodules, vasculitis, pericarditis, keratoconjunctivitis sicca, uveitis and rheumatoid lung.etc [3].

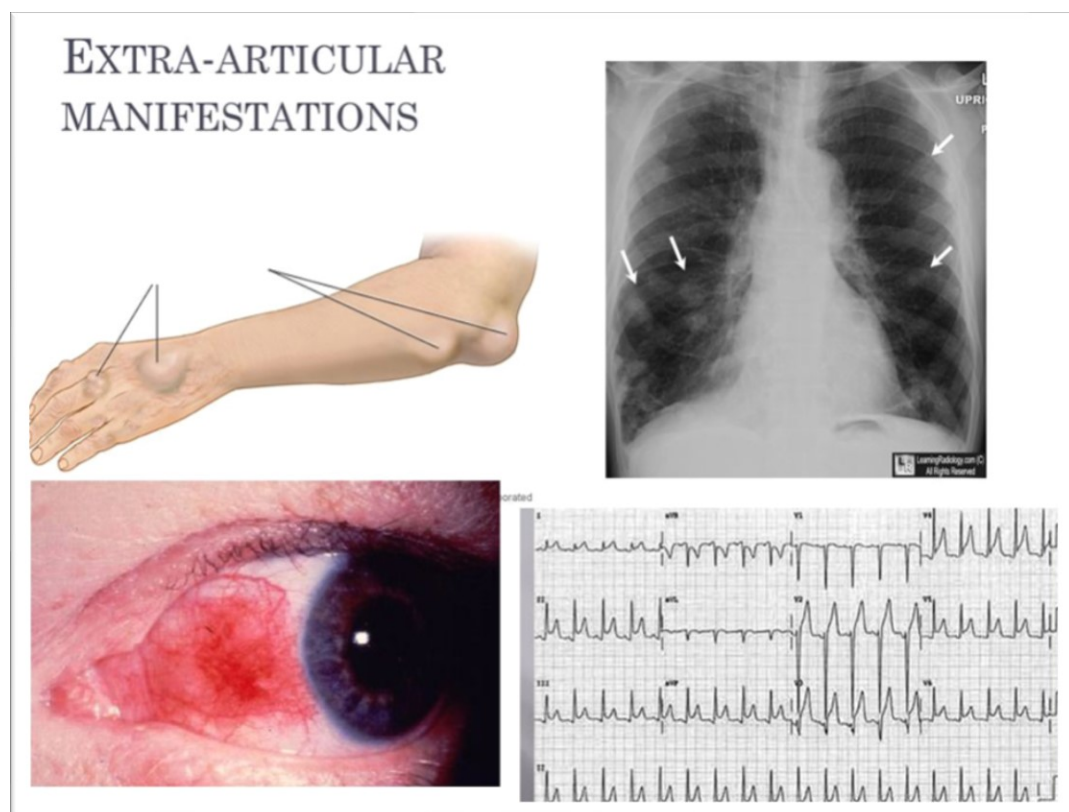


Figure 1: shows extra articular manifestations of RA

Systemic appearances comprise of anemia, acute-phase protein production and cardiovascular disease. RA has a very acute onset in old age with pitting edema, morning stiffness, and polyarthritis. Characteristic deformities develop with prolonged uninhibited disease, including 'swan neck' deformity, the boutonniere ('button hole') deformity, and Z deformity of the thumb. Rupture of fourth and fifth extensor tendons occur due to dorsal subluxation of the ulna at the distal radio-ulnar joint. Trigger fingers may also occur due to the nodules in the flexor tendon sheaths. Dorsal subluxation of the MTP joints leads to pain on the metatarsal heads. Popliteal ('Baker's') Cyst rupture, often by knee flexion and leads to calf pain and swelling. In addition to joint symptoms, osteoporosis, fatigue and depression, Anorexia, weight loss are common.[4,5]

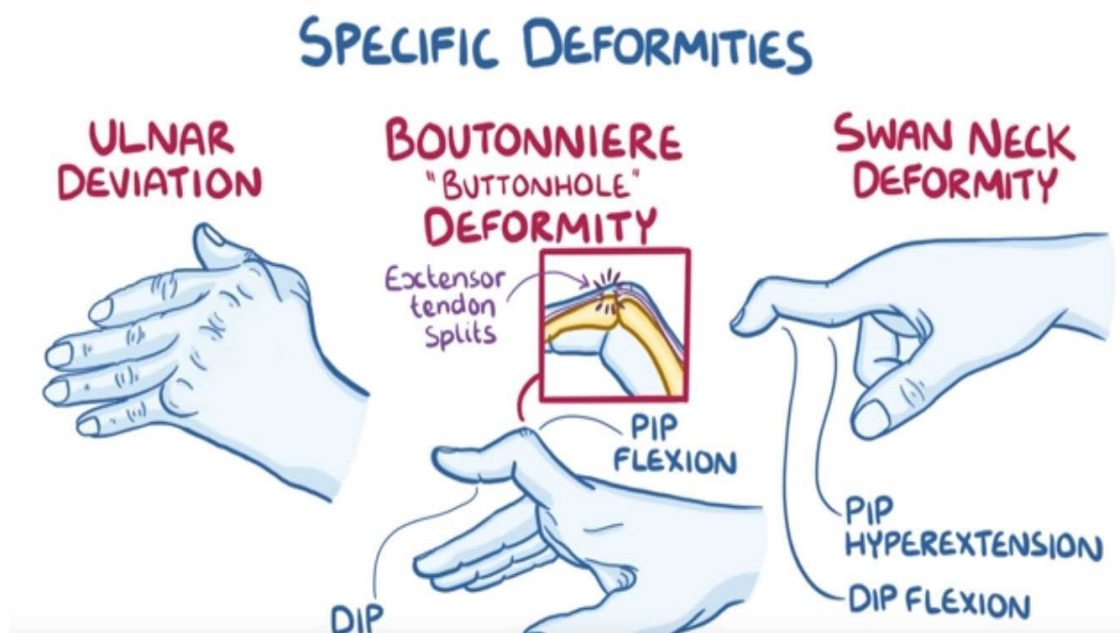


Figure 2 :shows specific deformities of RA.

Recent discoveries show that genetic origin for the development of disease and 80% of patients carry the epitope of the HLA-DRB1*04 cluster. Antigen-presenting cells (dendritic cells, macrophages and activated B cells), present arthritis-associated antigens to T cells. Simultaneously, CD4⁺ T cells secrete IL-2 and IFN- γ . Disease-associated HLA-DR alleles present arthritis-related peptides, leading to the stimulation of autoantigen-specific T cells in the joints and lymph nodes. B cells produce autoantibodies and cytokines and also produce cell surface proteins and differentiation antigens (CD20 and CD22). Autoantibodies stimulate the production of pro-inflammatory cytokines, including TNF- α , through complement and Fc-receptor activation. Within the synovial membrane activated fibroblast-like synoviocytes concentration increased and it also produce inflammatory cytokines, Prostaglandins and Matrix metalloproteinases (MMP). Synoviocytes cause destruction of cartilage and bone by the secretion of MMPs into the Synovial fluid and by direct invasion into these tissues [6]. Patients expressing two HLA-DRB1*04 alleles are associated with increased risk for nodular disease, joint destruction [7].

Additional alleles related to RA risk, found on the conserved A1-B8-DR3 which is found near the HLA-DPB1 gene. Other RA-associated loci are PTPN22, PADI4, STAT4, TRAF1-C5 and TNFAIP3. Other factors like Smoking and infection, also influence the development of disease and its progression. The initial event in RA is activation of dendritic cells by autologous antigen in the innate immune response. Macrophages are

responsible for osteoclastogenesis and secretes cytokines, including TNF- α , IL-1 and IL-6. Cytokines from monocytes activates leukocytes, T cells, endothelial cells, chondrocytes, and synoviocytes.[8]

TNF induces local inflammation and regulates cytokines production in RA. Immune modulators are responsible for the synovial joint damage and covers most intra articular structures . Synovitis is caused by the influx of T cells, B cells, plasma cells, dendritic cells, macrophages and mast cells . The synoviocytes becomes hyperplastic, and the synovial membrane expands and forms villi . pannus formation destroys bone, and enzymes from neutrophils, synoviocytes and chondrocytes degrade cartilage.[9]

cytokines such as IL-10, IL-15, Fibroblast growth factor 1 (FGF 1) found in RA. The concept of T cell role in the pathogenesis of RA has been outdated due to unimpressive clinical results of T cell cytokines. some new cytokines [IL-10, IL-15] found in RA synovial joints. cell to cell interaction provides harmful events in RA. IL-6, and its membrane-bound IL-6R, act by secreting proteolytic enzymes and reactive oxygen intermediates which causes joint inflammation in Rheumatoid arthritis.[9]

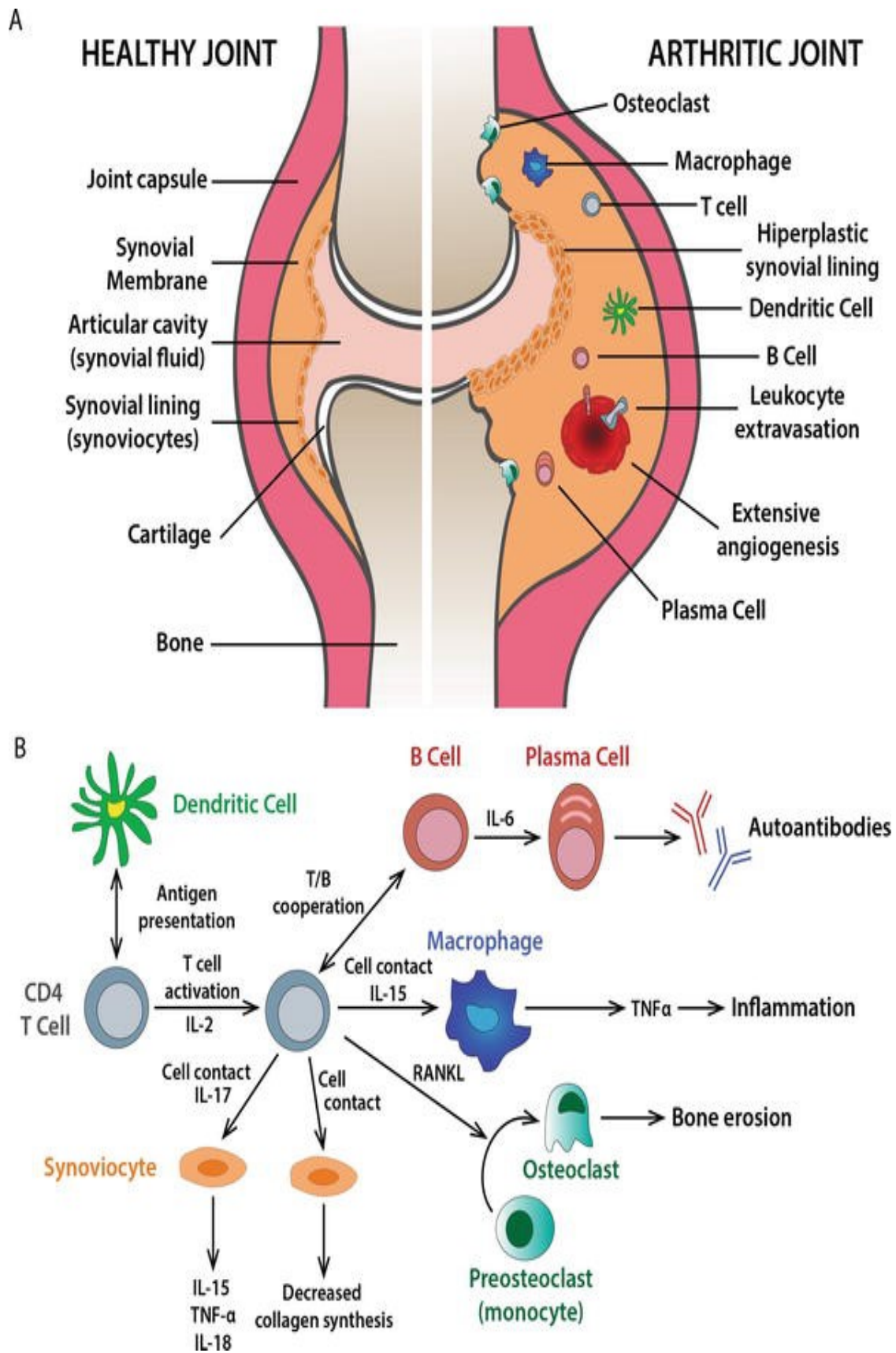


Figure 3: Shows pathophysiology of RA.

absence of IL-2 production improves the T cell function in RA.[10]. Tcells can produce individual cytokines by self regulation.[11] Rheumatoid arthritis is originated by CD4+ T cells, it increases the immune response by stimulating other mononuclear cells, synovial fibroblasts, chondrocytes, and osteoclasts. Cytokines release especially TNF-alpha, interleukin-1, and interleukin-6, promotes synovial inflammation. Joint damage results from the degradation of connective tissue by matrix metalloproteinases and the stimulation of osteoclastogenesis by activated CD4+ T cells. So therapeutic targets should inhibit cytokines to offer an effective approach to reducing inflammation and preventing joint damage[12].IL-6 can directly recruit neutrophils, recruitment occur indirectly through fibroblasts [13].

Osteoclastogenesis involves the presence of macrophage colony-stimulating factor (MCSF) and results from the interaction of the RANK(receptor activator of nuclear factor kappa B) and the RANK ligand (RANKL) [14]. RANKL expression is regulated by pro-inflammatory cytokines such as TNF- α , IL-1, IL-6 and IL-17 [15] pannus formation is found at the interface with cartilage and bone .In RA patients, the VEGF plays the chief role in new blood vessel development. and an inducer of vascular permeability [16]. IL-6 ,IL-6R,IL-1 β and TNF- α , induces VEGF production [17].Cartilage degradation in RA occurs when TNF- α , IL-1 and IL-6 activate synoviocytes, resulting in the secretion of MMPs into the Synovial fluid.Cytokines also activate chondrocytes, leading to the direct release of additional MMPs into the cartilage [18, 19]

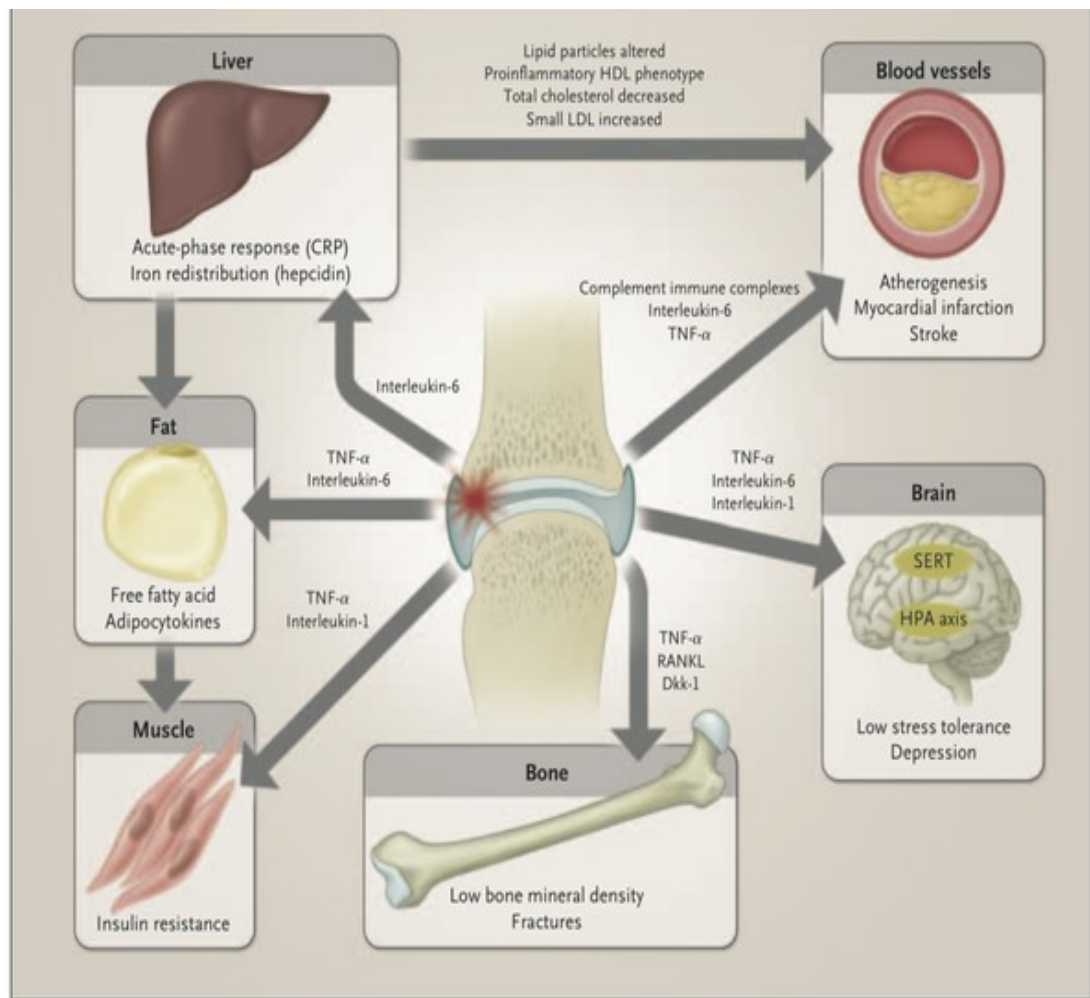


Figure 4:shows complications of RA

ACUPUNCTURE

These points are situated in a regular pattern on the body surface. These points are used to diagnose the different diseases of the body. The line which connect the points associated with particular internal organ is known as a meridian. Traditional Chinese medicine has been developed and practised over centuries. In ancient texts, acupuncture is obtained from continuous critical thinking and clinical observation it has developed its own concept of the body

and mind and also health and disease. It is a holistic method, where body and mind can be treated as a single unit. basic concept of Chinese medicine is balancing or harmonising the energy or chi which flows through the meridian along the body .(Kaptchuk 1983). Blockage of chi flow in a particular area causes pain and disease. this can be prevented by keeping the body energy in a balanced state. [20]

Totally 12 meridians in connection with various internal organs (such as the heart, bladder, kidney, lungs, liver, stomach etc. and also organs not recognized by Western medicine, such as the 'triple warmer'). chinese concept of an organ differs from the western system of medicine. Chinese, consider organs are not only a gross structure, but also a functional unit which connects with other bodily system. chinese are particular about organ function rather than its structure. Usually 4 to 6 acupuncture needles are inserted in the acupuncture points on the meridian pathway and needles are kept in the points for 15 to 20 minutes duration. A thorough understanding of location of acupuncture points and surface anatomy are essential to locate acupuncture points precisely. [20]

Acupuncture is defined as, inserting needles into the skin and underlying tissues at particular sites, known as points, for therapeutic or preventive purposes. The points are stimulated by manually with hand, and also by using electricity, lasers, pressure, heat or ultrasound waves. Acupuncture worldwide accepted intervention for the treatment of a various disease conditions [21]

ACUPUNCTURE ANALGESIA

Before the discovery of endogenous opioids, it was believed that serotonin [5-HT] a neurotransmitter, played an important role in the mediation of acupuncture analgesia [22].

The discovery of endogenous opioid peptides further improve the quality of the acupuncture analgesic study. Enkephalin discovered in the year of 1975, soon after in 1976 beta endorphin discovered. and discovery of dynorphin in 1979. After the long gap fourth endogenous opioid peptide, the endomorphin, in 1997. endomorphin considered as the pure μ opioid receptor agonist [23] and dynorphin the relatively pure kappa opioid agonist [24], the enkephalin and beta endorphin were mixed μ and delta opioid receptor agonists. [25]

Acupuncture is very effective for the treatment of RA. It has analgesic, and anti-inflammatory, immuno modulatory effects in patients suffering from RA. acupuncture can modifies specific and nonspecific cellular influx, activation of cell proliferation and regulation of subsequently involved cells that will result in a complex mechanism of transport, further breakdown and clearance of all bioactive mediators [26]. Another hypothesis is acupuncture inhibits the innate immune system via reflexive action. thus produces anti inflammatory effect. And it decreases inflammatory molecules such as CRP, ESR, and other pro inflammatory cytokines. It increases acetylcholine output and autonomic tone. [13].

RHEUMATOID ARTHRITIS-TCM VIEW:

RA is broadly studied in both Western medicine (WM) and TCM. In traditional Chinese medicine, the condition which is corresponding with arthritis is called "Bi syndrome." Bi syndrome shows as pain, soreness, or numbness of muscles, tendons and joints, and is the result of the body being "invaded" by the external atmospheric factors of Wind, Cold, Heat, and/or Dampness. Manifestation of the symptoms showed by the individual depend on which external pathogenic factor is strongest.

RA is primarily considered as Bi Zheng in TCM, which means "impediment condition". Bodily spaces with the external invasion of pathogenic factors, such as prolonged living in a damp atmosphere and contraction of wind, cold, damp, and/or heat evils, are known causes of RA in TCM. The brief summary of the disease etiology is closely related to the TCM pattern diagnosis in the management of RA. If the RA patient experiences pain with Cold and shows other symptoms (such as possible Cold aversion; loose stools; clear, long urination; pale and thin, white-coated tongue; and a deep and tight pulse), then the RA patient is classified into a TCM pattern known as the 'wind, Cold, and damp impediment' pattern. This pattern is a defensive Qi deficiency caused by a spleen Qi deficiency and it allows the wind, Cold, and/or damp pathogens to invade, resulting in an obstruction. so the goal main

treatment principles should be expelling wind and eliminate dampness, warm the channels, and dissipate Cold from the meridian system. The guiding pathway depends on the exact symptoms. In the treatment of RA patients, body language plays significant role in diagnosis of RA. every gesture, word and feature provides a clue to a person's health and well being. The basic patient questions focus on the following:

- reaction of individual to Heat and Cold (facial color, tongue color and coating, pulse quality, urine color)
- If and when pain or swelling is experienced
- Type of pain and swelling, if any
- Stomach, bowel and bladder function
- Thirst, appetite, and taste sense
- Sleep pattern
- Sexual function, sexual activity, and reproductive history
- General medical history
- General physical activity
- Emotions

RA manifests a number of dissimilar TCM patterns. According to TCM, the larger group of RA is divided into the five common patterns:

- (1) ‘wind, cold and damp impediment’ pattern; the main clinical manifestations demonstrated in RA.
- (2) ‘wind, damp and heat impediment’ pattern; this pattern is seen in those with an early, active stage of RA. There is joint swelling, pain, heaviness, and limited movement. Coolness improves pain.
- (3) Enduring impairment transforms Heat and damages the yin pattern; this pattern is also called the ‘mixed Cold and Heat’ pattern.
- (4) Qi and blood form dual vacuum, phlegm and stasis in a equally binding pattern; this pattern is observed in the later stages of RA so there is joint rigidity and deformation.
- (5) Liver blood–kidney yin and yang emptiness with phlegm and stasis in a mutually binding pattern[27].

MOXIBUSTION

Moxibustion is an ancient form of heating therapy and it has been practised in China for 3000 years. It spreads to more than 160 countries for its good effects in pain, nausea, vomiting, etc.[28].studies have proved the analgesic effect of acupuncture from analysing neurophysiology, neurochemistry, molecular biology, and brain functional imaging[29-33].

It is a twin therapy of acupuncture, moxibustion is effective in alleviating visceral pain.acupuncture decreases pain by increasing the concentration of dynorphin (Dyn) and endomorphin (EM) [34,35]., moxibustion treating

visceral pain by modifying the dynorphin and endomorphin concentrations in the spinal cord fragments. In particular, moxibustion applied with moxa can employ a warming effect, dredge the meridians, tonify yang, strengthen deficiency, strengthen the spleen and support the kidney, and lift yang. Due to its easy operation, very low-cost, highly safe with no side effects, moxibustion is easy to be accepted and learnt and can be used widely, and is the first option for "treating subclinical conditions[36].

Moxibustion at Zusanli (ST 36) and Shenshu (BL 23) resists inflammation, relieves pain and swelling around joints, reduced serum tumor necrosis factor (TNF), alters immunological disorders, balances the metabolism of free radicals, enhances the micro-structure of synovial cells, and lessened inflammatory reactions. Moxibustion at Shenshu (BL 23) and Zusanli (ST 36) in treating RA rat models and it produces warming and unblocking effect, and improving cytokines of RA rats and inducing apoptosis of synovial cells. Moxibustion has profound effect of analgesia, anti-inflammation, and relieving swelling on RA rats, and enhances the RA rats' immune function[37]

Moxa cone and stick are the needed materials of moxibustion. By igniting moxa at exact acupoints or affected areas, moxibustion helps to warm meridians and dissipate cold, clear meridians and collaterals, and harmonize and normalize qi and blood through the infiltration of heat. Moxa leaf (*artemisia vulgaris*) is warm and hot in nature, and functions to clear meridians, dissipate cold and resolve dampness. Fire can reinforce its effect of warming meridians to encourage qi activity, and dissipating cold to dredge meridians and

collaterals. The warm stimulation produced by ignited moxa directly or indirectly works on specific superficial areas of the human body, along with the function of meridians and collaterals, to cause local or distal effect.

Modern researches illustrate that with the large volume of heat produced by burnt moxa, moxibustion produces a photothermal radiation effect. There was a study finding that during moxibustion, the subcutaneous temperature changed in a different way from the temperature of muscle, indicating that the stimulation of moxibustion may involve a variety of layers of the body. The analgesic effect of moxibustion and increase of the concentration of Dyn and EM in spinal cord were demonstrated, which partially explained the mechanism of the analgesic effect of moxibustion in management of visceral pain. Moxibustion has been adopted in China for its analgesic effect. Researches have revealed its analgesic effect in treatment of primary dysmenorrhea, knee osteoarthritis, rheumatoid arthritis and cancer pain. Moxibustion accomplishes its analgesic effect via multiple pathways and levels. Spinal cord is the primary integrating center which receives moxibustion signal first then it increases the concentrations of Dyn and EM in spinal cord and induces post-synaptic inhibition and pre-synaptic inhibition, and then blocking the further transmission of pain signal. Researches shown that midbrain periaqueductal gray descending inhibitory system includes at least three transmitters: Endogenous Opioid Peptides, 5-hydroxy tryptamine and Nor adrenaline. Moxibustion stimulation improves the synthesis and release of central EOP endorphin (dynorphin and endomorphin) and other

neurotransmitters (5-HT) in the spinal dorsal horn neurons or nociceptive primary afferents, exerting analgesic effects. moxibustion can markedly reduce the pain and improves the pain threshold in arthritis rats with chronic visceral hyperalgesia, and the analgesic effect by increased concentrations of Dyn and EM in spinal cord. There are very less studies in comparison of analgesic effect of acupuncture and moxibustion in RA patients.[38]

AIM:

To evaluate the analgesic effect of specific acupuncture and moxibustion in rheumatoid arthritis.

OBJECTIVES OF THE STUDY:

To compare the effect of specific acupuncture and moxibustion on pain management in Rheumatoid arthritis.

LITERATURE REVIEW:

Baozhu Zheng conducted a study on Moxibustion and he states that moxibustion has an analgesic effect and increases hypothalamic POMC and PDYNmRNA expression levels and plasma β -EP content in RA rats. The analgesic effect in moxibustion group II is better than another group.[39] Noriko uryu conducted a study and concluded that, repeated moxibustion treatments are required for pain relief in the present rat experimental knee osteoarthritis model and showed the involvement of sustained inhibitory modulation mediated by endogenous opioids [.40]

The author sun hua reviews that treatment of rheumatoid arthritis(RA) with acupuncture and moxibustion can dredge meridians and collaterals,regulate Qi and blood,eliminate wind,cold and dampness,remove blood stasis and promote blood circulation and relieve pain.,it has been proved to be effective to treat RA with acupuncture and moxibustion.Studies on mechanisms indicate that acupuncture can regulate immune system,improve blood rheology and eliminate free radicals.Also the author brings forward that key points of treatment of RA with acupuncture and moxibustion[41].Zukow conducted a study and the results show a significant positive effect with acupuncture treatment,when it is compared with the sham acupuncture[42]

Yang and his colleagues conducted a animal study on moxibustion in RA .and he states that Moxibustion can resist inflammation and eliminate swelling in RA rabbits, which may be closely with its effect in inhibiting abnormal activation of JAK-STAT pathway in synovial cells.[43]Dr.luo states that Moxibustion can protect the immune organs (thoracic gland and spleen) from injury and improve pathological changes of the ultrastructure of local synoviocytes in RA rats.[44]Dr.xie xx observed the therapeutic effect of Spreading moxibustion in rheumatoid arthritis.and he concluded that spreading moxibustion has an significant therapeutic effect on rheumatoid arthritis[45].Wei zhou done experiment on effect of different temperature of moxibustion.In this study, it is suggested that the higher the temperature of moxibustion, the better the analgesic effect in chronic inflammatory mice; in neuropathic pain, the higher temperature (47°C or 52°C) of moxibustion

produced stronger analgesic effect than lower temperature (37°C or 42°C), in which similar effect was displayed between 47°C and 52°C or 37°C and 42°C.[46]

Chuanying states that Mainly by its anti-inflammatory and immune effects, moxibustion therapy can be supposed to improve immune functions, inhibit the secretion of the synovial cells factors in the joints, control the proliferation of the synovial cells, and induce apoptosis of the synovial cells in the synovitis, and promote the apoptosis of the fibroblast, so as to play a therapeutic role in the treatment of rheumatoid arthritis. The therapeutic effect is obtained by the comprehensive effect created from integration between the physical factors and herbal factors in burning moxa wool and the special functions of the acupoints and meridians.[47]

Xiao done experimental study on influence of acupuncture and moxa in RA patients. and the results have shown that the decrease of IL-2 in patients with RA should be one of main causes of internal environment disorder, acupuncture and moxibustion as a stress stimulation exerts an influence on the immunity system through neuroendocrine system to improve the IL-2 production.[48]Tao yi concluded that the present study provides the first demonstration that moxibustion could release enkephalins in the spinal cord in irritable bowel syndrome rats. Through the action of enkephalins in the spinal cord, moxibustion could relieve chronic visceral hyperalgesia in irritable bowel syndrome rats, which is similar to the mechanism of acupuncture analgesia.[49]

Xulu Lei conducted a study on moxibustion with zanthoxylum bungeanum cake .and he concluded that the anti-inflammatory effect of ZBCS-moxi on rheumatoid arthritis rats for the first time and found that ZBCS-moxi could decrease the paw swelling and inhibit the expression of IL-1 β and TNF- α in RA rats, which might contribute to its anti-inflammatory effect on RA. Our results indicated that ZBCS-moxi is effective in improving the symptoms of RA rats through suppressing the expression of cytokines, which could be used as an alternative therapy and this study provides an experimental basis for the clinical application of Zanthoxylum bungeanum-cake-insulated moxibustion.[50]

Matsumoto and shinohara study reveals the improvement of blood flow has been considered one of the basic mechanisms of acupuncture and moxibustion action. The vicious cycle originating with a strained muscle contraction has been widely accepted as the cause of muscle pain, and the accumulation of various algescic or sensitizing substances produced by muscle contraction under ischemic conditions is considered the direct cause. Increased blood flow caused by acupuncture and moxibustion may flush out the algescic or sensitizing substances and induce pain relief. There have been several reports suggesting that acupuncture increases local and remote muscle blood flow in human subjects [51, 52].

Kawakita,in his review he discussed the important role of the polymodal receptors, which are responsive to both acupuncture and moxibustion. The morphological and functional characteristics of the polymodal receptors can

explain the nature of so-called acupuncture points and trigger points. Immediate effects of acupuncture and moxibustion may be explained, at least in part, by the axon reflex via the polymodal receptor. The existence of various endogenous pain inhibitory systems was also pointed out for understanding the immediate effects of acupuncture and moxibustion.[53]

Cao states that ElectroAcupuncture could induce the expression of preproenkephalin (PPE) mRNA, preproopiomelanocortin (POMC) mRNA in many painmodulation-related nuclei, such as caudate nuclei, amygdala, hypothalamus, PeriAqueductal Grey matter, in the brain, when EA was combined with Droperidol, the expression of PPE mRNA and POMC mRNA was further enhanced. In spinal dorsal horn, EA enhanced the preprodynorphin (PPD) mRNA expression, and the combination of EA with DRO further promoted the expression. The above mentioned results could explore the mechanism of potentiating effect of Droperidol on Acupuncture Analgesia at molecular level. The above studies suggested that the further activation of opioid peptidergic system from presynaptic (EOP release and gene expression) to postsynaptic (opioid receptors) level as well as the antagonism of dopaminergic system were involved in the mechanisms of Acupuncture Balanced Anesthesia[54].

Zhao states that Acupuncture analgesia is manifest only when the intricate feeling of acupuncture (soreness, numbness, heaviness and distension), so-called “De-Qi”, occurs. Such a “De-Qi” feeling mainly originates from acupuncture-induced impulses from local muscle contraction beneath the

acupoint. Types of afferent nerve fibers activated by acupuncture depend upon the manipulation methods and individual differences in sensitization. Manual acupuncture stimulates afferent fibers and activates them to conduct the signal. Electroacupuncture (EA): electrical current via acupuncture needles at intensities strong enough to excite Ab and part of Ad type afferents can induce an analgesic effect. Acupuncture analgesia is essentially a manifestation of integrative processes at different levels of the CNS between afferent impulses from the pain regions and impulses from acupoints. Segmental mechanisms in the spinal cord contribute to the functionally relative specificity of acupoints. Spinal pathways of acupuncture impulses from acupoints ascend mainly through the ventrolateral funiculus. A complex network of many brain structures is involved in processing acupuncture analgesia, including the VRM (mainly NRM), PAG, Locus coeruleus, Arcuate nucleus, amygdala, etc. Most of nuclei are constitutive parts of the endogenous descending inhibitory system in the CNS. Activity in most nuclei mediates acupuncture analgesia, except for the Hyper anxiety behaviour and LC, which antagonize it. Various signal molecules are implicated in acupuncture analgesia, such as opioid peptides (m- μ - and κ -receptors), cholecystokinin octapeptide (CCK-8), glutamate, 5-hydroxytryptamine and noradrenalin. Among them, opioid peptides and their receptors play a pivotal role in mediating acupuncture analgesia. The release of opioid peptides evoked by EA is frequency-dependent. EA at 2 and 100 Hz induce release of enkephalin and dynorphin in the spinal cord, respectively. In

accord with the effect of morphine analgesia, CCK antagonizes acupuncture analgesia[55].

Zhang conducted a study ,In this study,he concluded that the combination of moxibustion and acupuncture can invigorate yang qi, strengthen pathogenic qi to eliminate vital factors, remove the obstruction from the meridians and collaterals. Concerning the mechanism of analgesic function of acupuncture, modern study still lacks of clear conclusion. Han thinks that the mechanism of analgesic function of acupuncture lies in that needling may trigger the pain sensation regulation system of the body to control the reception and transmission of hurting information at all central levels, needling can invigorate the endogenous analgesic mechanism of the body, produce an integrative regulatory and control process of needling information from peripheral to the central nerve system of all levels against the reception and transmission of hurting information'[56]Yi G conducted a study on moxa and acupuncture in cancer pain and he states that, Warming-yang moxibustion technique in combination with acupuncture in the treatment of cancer pain is not only featured with quick effect, absence of side effect, and long duration of effect, but also can regulate yin and yang of the body, so it is significantly important for improving the quality of life of patients with cancer pain[.57]

H.Chen concludes that Effect of moxibustion has thermal stimulation effect. The generally accepted view is that the meridian system combines with moxibustion physical and chemical effects to produce comprehensive effects. When physical and chemical factors act on the acu- point receptors, the signal

enters the central nervous system through the peripheral pathways and outgoes after being integrated, adjusting the nerve-endocrine-immune network and circulatory system, so as to regulate the internal environment of the body, in order to achieve the effects of preventing and curing diseases [58].

R.Chen states that ,though lots of research works have been carried out and made some progress, there is still a great distance from fully understanding the mechanism of moxibustion. Therefore, he proposed the following views on the study of mechanism of moxibustion in the future. First, value the importance of whole, moxibustion cannot be separated from the theory of TCM. More than a simple stimulus, meridian and acupoint system of the human body is the key of efficacy of moxibustion. The studying of mechanism of moxibustion from the overall level, based on the further understanding of the meridian system or even of the TCM system, is indeed very difficult. But on the other hand, maybe the studies of moxibustion should be helpful to the understanding of acupoint, meridian, and TCM [59]

X.Yong fi states that , it is a useful exploration of extending the study perspective from the part to the whole with moxibustion as the breakthrough point. Second,he insists to pay more attention to scarring moxibustion (suppurative moxibustion). Scarring moxibustion had been the favorite to ancient doctors, “where there is moxibustion sore, there is cure.” Modern clinical practice has also shown that scarring moxibustion, compared with other moxibustions, has advantage of curative effect in the treatment of some chronic refractory diseases. And he staets to introduce new technologies and disciplines

into the mechanism research of moxibustion effect, such as bioheat transfer theory, the interdisciplinary focus heat transfer phenomena in living organisms; in order to reveal the energy transport in the living organism. Thus the interdisciplinary approach promote the research of moxibustion [60] and the study on the mechanism of moxibustion should be oriented to promote its clinical application. Many research achievements have already been applied in clinic, such as the applications of 650 nm–10.6 μm combined laser moxibustion on knee osteoarthritis and bradycardia [61, 62]

Shen and zhao findings say that the multifunctional moxibustion instrument which simulate the 6 Evidence-Based Complementary and Alternative Medicine traditional moxibustion by heating artificial moxa (contains effective components of moxa) with electromagnetic-heating device [63]. There are enough reasons to believe that, with the progress of mechanism research, the new achievements will surely provide a larger space to improve the patient experience and the curative effect of moxibustion.

Zhang conducted a study on mechanism of moxibustion in RA. RA belongs to the "Bi-obturation syndrome" in Chinese medicine, deficiency in constitution and excess in symptoms. Moxibustion has the effects to replenish the kidney, strengthen yang, warm up and unblock the meridians, dissipate wind, disperse cold and remove dampness, suitable for the patients with long-term "Bi-obturation syndrome" in particular. Moxibustion is a heat radiation reaction and is supposed to influence the metabolism and functions of the neurological system by warming and stimulating the skin receptors.

Moxibustion effect is a comprehensive effect created from integration between the physical factors and herbal factors in burning moxa wool and the special functions of the acupoints and meridians. Mainly by improving the immune functions, inhibiting secretion of cellular factors of the articular synovium, controlling the excessive proliferation of the synovial cells, inducing the cell apoptosis of the synovial inflammation and promoting apoptosis of fibroblast, moxibustion gives a therapeutic effect to RA. RA is a complicated and intractable chronic disease, involving many systems of the whole body pathologically. Moxibustion is just one of the therapeutic methods and must be combined with acupuncture, or with herbal medicine, or with cupping method clinically, in order to enhance the therapeutic effect further. Its internal pathological mechanism and other mechanisms of moxibustion for RA need to be explored. It has been proved by the pathological observation that moxibustion could relieve congestion and edema of the articular synovium, infiltration of inflammatory cells, proliferation of the synovial cells, and tissue thickening, indicating that moxibustion plays a therapeutic role for arthritis by inhibiting synovitis. It is the main mechanism to inhibit occurrence and release of inflammatory cellular factor and to induce apoptosis of the synovial cells in the treatment of RA by moxibustion.[64]

Okada states that one cannot entirely reject the roles of thick afferent fibers in the production of analgesia via gate control mechanisms; however, mechanoreceptors innervated by thick fibers cannot be activated by thermal stimuli such as moxibustion. It should be stressed that the fundamental

mechanism of acupuncture and moxibustion is based on moxibustion-sensitive input. Polymodal types of nociceptors that respond to mechanical, thermal and chemical stimulation are particularly sensitive to capsaicin, and innervated by the afferent C fibers in the skin, as well as by both A-d and C fibers in the muscle. These polymodal receptors seem to be the most reasonable candidates for acupuncture and moxibustion; they are not purely nociceptors, but they are responsive to non-noxious stimuli such as scratching the skin. This functional characteristic of polymodal receptors may be vital for further investigations. . Analgesic effects of acupuncture have been well explained by experimental studies and the participation of various endogenous opioids and their receptors has been widely accepted. Moreover, the nature and development of acupoints remains as an important issue to be resolved by acupuncture and moxibustion research. Sensitization of the polymodal receptors has been proposed as a rational explanation of the nature of acupoint formation. However, more actual evidence is required from future investigations [65]

Murase conducted a study on antinociceptive property of acupuncture and moxa in rats. In this study it states that acupuncture and moxibustion works through diffuse noxious inhibitory controls. Thus it gives anti-nociception action. [66] In this review, Mr. Lee states acupuncture is beneficial for treating RA, possible mechanisms of action include anti-inflammation, autonomic nervous system modulation or analgesic effects of acupuncture in patients suffering from RA. And acupuncture influences specific and non-specific cellular influx, activation of cell proliferation and regulation of subsequently

involved cells that will result in a complex mechanism of transport, further breakdown and clearance of all bioactive mediators. Another hypothesis is that the anti-inflammatory actions of acupuncture are mediated via the reflexive central inhibition of the innate immune system. Acupuncture increases autonomic tone and acetylcholine output while decreasing inflammatory molecules including cytokines, CRP and ESR. Anti-inflammatory effects explained by modulation of autonomic nervous system and acupuncture changes the function of the hypothalamic–pituitary–adrenal axis. Acupuncture combined with moxibustion, reduce pain through stimulating the serotonergic, noradrenergic and opioid system in pain conditions. Another possibility is the synergetic effects of heat from moxibustion on the stimulation of acupuncture[67]

In this study, moxibustion given on Dazhui (GV 14) strengthening ability to the phagocytic effect in mice with low immunoglobulin and it enhance the non-specific immune function in mice. In the systematic summary of the relevant study on the anti-inflammatory immune effects of moxibustion, Tang Zhao-liang, et al, found out that inflammation was closely related to immunity and observed that moxibustion helps for an obvious anti-inflammatory and antihydopic effect to the rats with adjuvant arthritis and it relieve or slow down inflammatory reaction. Moxibustion on Shenshu (BL 23)) and Zusanli (ST 36) activate and boost the immune system, improving the response levels of the immune system, and firming anti-inflammatory ability. Moxibustion has an antigen-like immune effect and can avert and release delayed and multiple

arthritis in the mice with adjuvant arthritis. It has the effect to counterattack hypersensitivity and can reestablish and promote the activity of spleen lymphatic cells, strengthen immune functions, and encourage and help secretion of internal IL-2, and can prevent secretion of IL-1 from unusually activated phagocytes. It also has the ability of blocking release of TNF inflammatory factors, and improve the immune strength of the organism, thus protecting the immune organs [thymus and spleen] there by correcting metabolic disturbances of free radicals in inflammation, regulating the imbalance of NO, NE and 5-HT neurotransmitters and help the steadiness of the internal environment. The anti-inflammatory immune function of moxibustion is the functional foundation of moxibustion therapy in supporting anti-pathogenic ability and helps to eliminate pathogens, and in treating and preventing diseases.[68]

Dr. peng and his colleagues conducted a study and states that Moxibustion at Shenshu (BL 23) and Zusanli (ST 36) decreases pro-inflammatory cytokines, balances immune system, corrects the metabolism of free radicals, initiates apoptosis of synovial cells, and hormonizes the inner environment. Spleen and thymus gland are two inevitable immune organs in human body. During aging process immune organs will atrophy to varying degrees. Certainly moxibustion helps to repair the atrophy . This study shows that moxibustion at Shenshu (BL 23) and Zusanli (ST 36) improve the local and general symptoms of RA rats, improve thymus index, reduce spleen index, and enhance body immunity. The binding of Fas and FasL initiate apoptosis of Fas carrier cells. As a major

apoptosis-inducing factor, Fas can be expressed in synovial cells of RA and osteoarthritis (OA) patients. Fas binding with anti-Fas antibody can induce apoptosis of synovial cells, suggesting that Fas retained on synovial cells may function to transmit the apoptosis signal, and produces joint damage in RA is possibly related to the apoptosis mediated by Fas. Moxibustion is effective in treating RA, by regulating the expression of Fas/FasL and inducing apoptosis of synovial cells. Compared with moxa oil treatment, moxibustion more significant effect in enhancing body weight, paw circumference, thymus and spleen indexes, and the expression of Fas/FasL in synovium of RA rat's joint; moxibustion is more effective than cigarette in enhancing the expression of Fas/FasL, while their effects in improving symptoms and thymus index are similar, indicating that the heat stimulation produced during moxibustion maybe one of the mechanisms of moxibustion in achieving its effects.[37]

Moxibustion treatment can lessen inflammation reactions in RA rats, which is closely associated with its effects in promoting plasma ACTH, downregulating serum CS level and synovial NF-kB p 65 immunoactivity, and the intact hypothalamus-pituitary-adrenal axis (HPAA).[68]

MATERIALS AND METHODS:

SUBJECTS:

100 patients with RA age group 30-55yrs were recruited from the patients visiting Govt. yoga and naturopathy medical college. In that, 80 patients were

selected on the basis of inclusion and exclusion criteria and 2010 ACR/EULAR criteria of Rheumatoid arthritis.

CRITERIA FOR SELECTION:

Subjects recruited for the study fulfilled the selection criteria of inclusion and exclusion criteria and 2010 ACR/EULAR criteria of Rheumatoid arthritis. 80 subjects selected from the out patient and in patient dept of the Government yoga and Naturopathy medical college. the subjects were included in the study after obtaining informed consent.

INCLUSION CRITERIA:

- Age group 30-55 years
- Both genders
- People who are ready to give their consent
- People who are having Rheumatoid arthritis more than 6 months

EXCLUSION CRITERIA

- Pregnancy
- children
- other types of arthritis
- SLE
- Sjogren's disease
- Lactating women
- Skin ulcers

2010 ACR-EULAR classification criteria for rheumatoid arthritis

Target population Patients who have at least 1 joint with definite clinical synovitis (swelling) with the synovitis not better explained by another disease

Classification criteria for RA (score-based algorithm: add score of categories A - D; a score of $\geq 6/10$ is needed for classification of a patient as having definite RA).

The metacarpophalangeal joints, proximal interphalangeal joints, the interphalangeal joint of the thumb, second through fifth metatarsophalangeal joint and wrist as *small joints*, and shoulders, elbows, hip joints, knees, and ankles as *large joints*

A. Joint involvement

1 large joint	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)	5

B. Serology (at least 1 test result is needed for classification)

Negative RF <i>and</i> negative ACPA	0
Low-positive RF <i>or</i> low-positive ACPA	2
High-positive RF <i>or</i> high-positive ACPA	3

C. Acute-phase reactants (at least 1 test result is needed for classification)

Normal CRP <i>and</i> normal ESR	0
Abnormal CRP <i>or</i> abnormal ESR	1

D. Duration of symptoms

<6 weeks	0
≥ 6 weeks	1

Table 1: Shows ACR/EULAR criteria

ALLOCATION OF SUBJECTS:

100 were screened initially from the In Patient and Out Patient department of Govt.yoga and naturopathy medical college, Arumbakkam. Among 100 subjects, 80 subjects who met the inclusion criteria were participated in the study. Subjects were assigned as two groups i.e., experimental group as moxa (n=40) and control group as acupuncture (n=40).

DEMOGRAPHICS: Gender wise distribution in RA

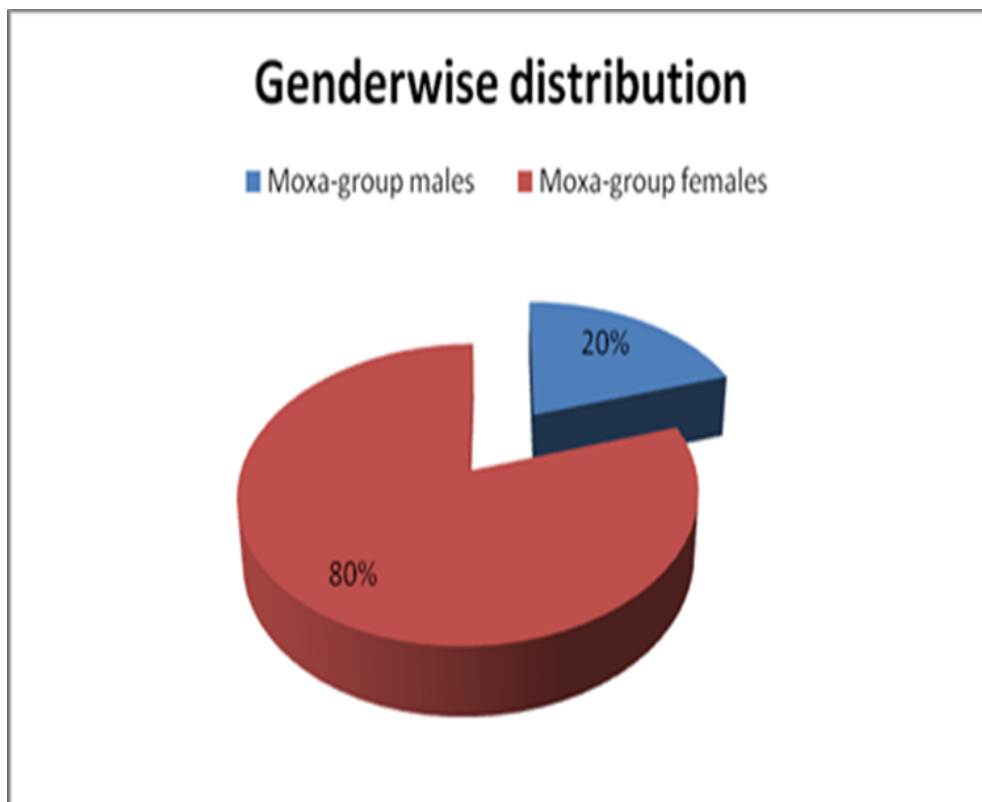


Figure 5:shows gender distribution in moxibustion

Average age group in moxibustion is 43.

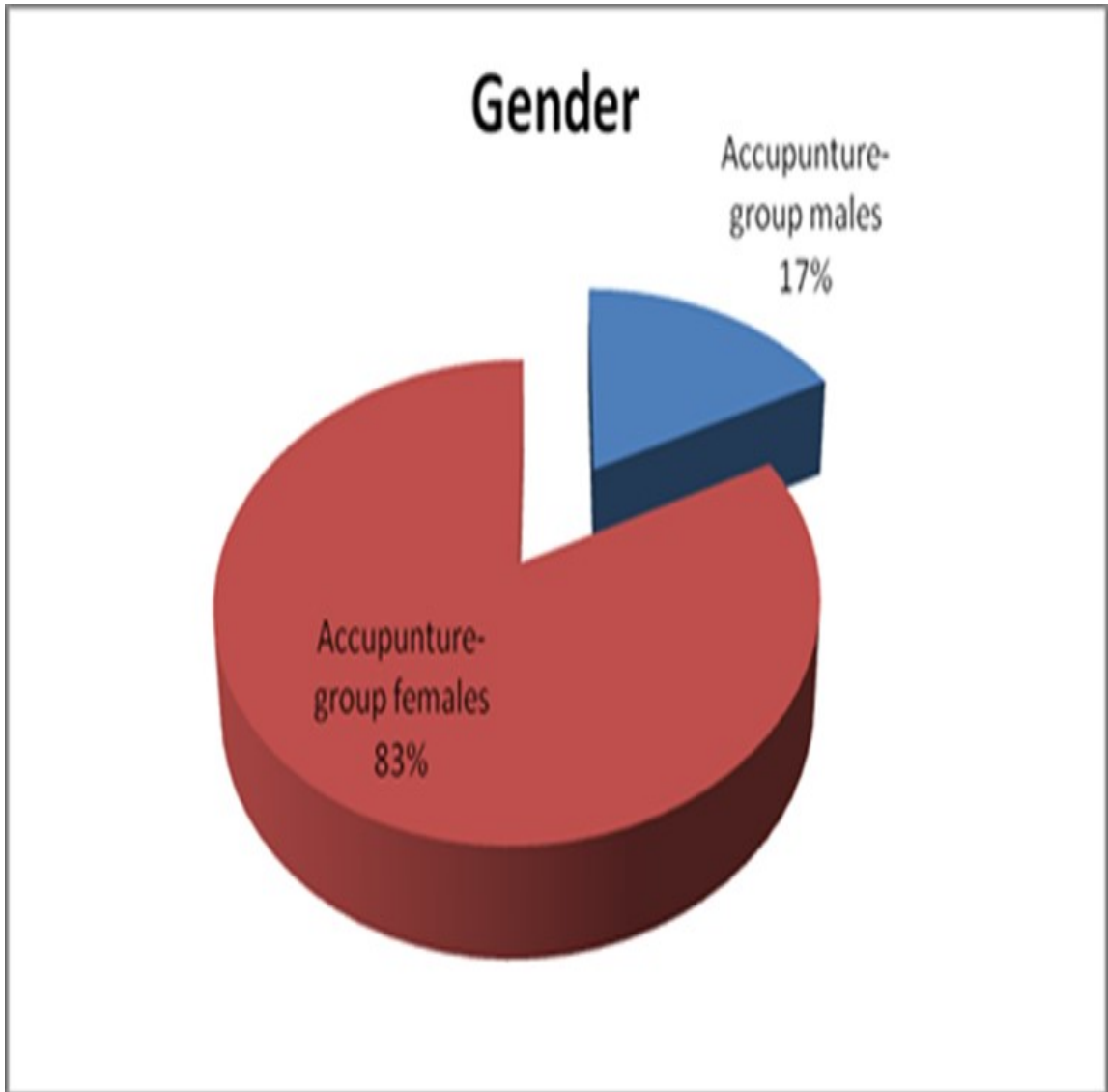


Figure 6:shows gender distribution of acupuncture

Average age group in acupuncture is 43

ETHICAL CONSIDERATION:

Subjects who fulfilled inclusion criteria were appraised about the purpose of the study and their rights as research subjects. Informed consent form was administered in English. As all the subjects understood spoken English, there was no requirement of translating the signed informed consent form into native language i.e., tamil .Adequate time was given to each patient to go through the information sheet and their queries were answered. Their right to withdraw anytime from the study and the need for willingness to participate voluntarily in the study was explained. All the subjects expressed their willingness to participate in the study by giving a signed informed consent. (A sample information sheet and consent form is enclosed as **Annexure-1**) Ethical clearance was obtained from the Institutional Ethical Committee prior to the start of the study and the approval for the same was granted.

STUDY SETTING:

The subjects were divided into two groups- experimental group and control group. The experimental group was given an moxibustion on selected acupuncture points for 15 mins for one day whereas the control group received acupuncture treatment on the same selected acupuncture points for 15 mints..

STUDY DESIGN

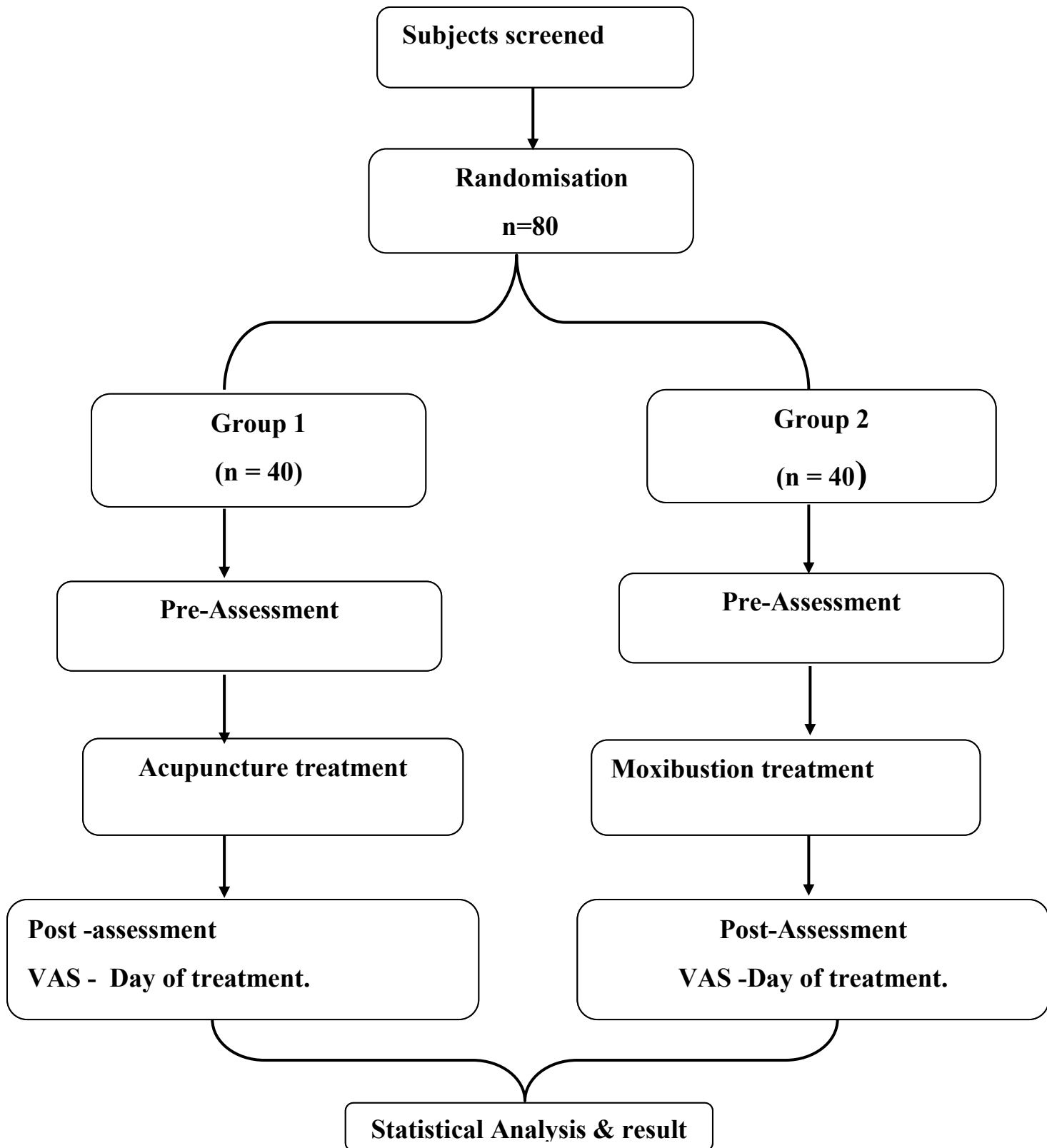
Type of the design:

The study design adopted was a comparative study. Eighty RA patients were selected and they were divided into experimental group and control group by using computer generated randomisation lottery method. Visual analogue scale given to the patient .pre assessment taken for both groups.Study group received moxibustion on selected acupuncture points Sp-5, LI-4, UB60, St-36, LU10, SP2, ST41, GB38 and ah-shi points of the affected joint for 15 mins for one day. ignited moxa cigar shown to the acupuncture points in the distance of 3-4 cm from the skin for 15 mints.at the end of treatment visual analogue scale given to the patient.and the post assessment of pain noted whereas the control group received acupuncture treatment on the same selected acupuncture points along with ah-shi points of the affected joints for 15 mints.needles left in the acupuncture points of the body for 15 mints. Then acupuncture needles removed from the acupuncture points gently from the site of insertion by using cotton swab. Then Visual analogue scale given to the patient. Then the post assessment of pain noted. After the assessment the patient asked to visit the OP dept every week for the follow up treatment. All the subjects were assessed at baseline and immediately after the treatment .

DATA POINTS:

The data was collected before the treatment , and immediately after the treatment.

STUDY PLAN:



ASSESSMENT

The baseline and post-intervention assessments was done for two groups.

PRIMARY OUTCOME VARIABLE:

Visual analogue scale

The **visual analogue scale** or **visual analog scale (VAS)** is a psychometric response scale which can be used in questionnaires. It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end-points. The VAS provides a continuous scale for subjective magnitude estimation and consists of a straight line, the limits of which carry a verbal description of each extreme of the symptom to be evaluated. The line is usually 10 cm long and vertical, though different lengths and orientations have been employed and proven satisfactory. The VAS is often used to evaluate the analgesic properties of various treatments and accomplishes this by measuring either pain relief or pain severity.

The pain visual analog scale can be self-completed by the patient. Instruct the patient to point to the position on the line between the faces to indicate how much pain they are currently feeling. The far left end indicates "no pain" and the far right end indicates "worst pain ever." The patient is asked to place a line perpendicular to the VAS line at the point that represents their pain intensity. After the patient has marked, using a ruler, the score can be

determined by measuring the distance (mm) on the 10-cm line between the “no pain” anchor and the patient’s mark. The scores can be from 0–100.

0–10 Numeric Pain Rating Scale

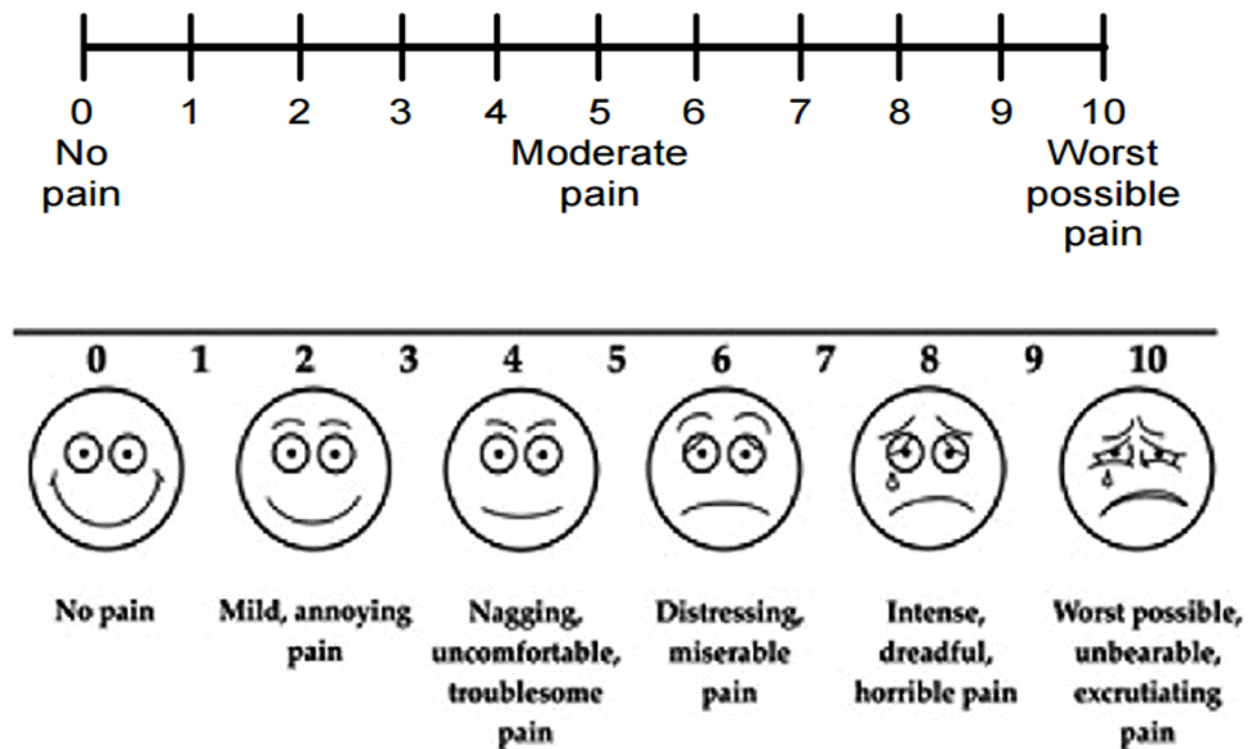


Figure 7: shows visual analogue scale

Using a ruler, the score is determined by measuring the distance (mm) on the 10-cm line between the “no pain” anchor and the patient’s mark, providing a range of scores from 0–100. A higher score indicates

greater pain intensity. Based on the distribution of pain VAS scores described pain intensity as none, mild, moderate, or severe, the following cut points on the pain VAS have been recommended: no pain (0–4 mm), mild pain(5-44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm) (11). Normative values are not available. The scale has to be shown to the patient otherwise it is an auditory scale not a visual one.[69]

INTERVENTION:

EXPERIMENTAL GROUP:

Experimental group received moxibustion on the selected acupuncture points and ah-shi points of the painful joints. moxa or mug wort (*artemisia vulgaris*) rolls are used for the treatment.ignited moxa roll gently shown 3-4 cm from the skin over the selected acupuncture points. The given acupuncture points are Sp- 5,LI-4,UB- 60,ST -36,LU- 10,SP-2,ST-41,GB-38. Moxa rolls are used for the treatment .each point received moxibustion therapy. Duration of moxibustion therapy is 15 mints. Utmost care given to the patient while taking treatment.



Figure 8 :shows moxa treatment and moxa stick

CONTROL GROUP:

Control group received acupuncture treatment at the selected acupuncture points and ah-shi point of the painful joints. copper headed half cun needles are used for the treatment purpose. Acupuncture points were located properly. then by holding the head of the needle, it is gently inserted into the patients skin. then needle is kept in the acupuncture points for 15 mints. after 15 mints that needle is removed gently from the acupuncture point with utmost care by using cotton swab.

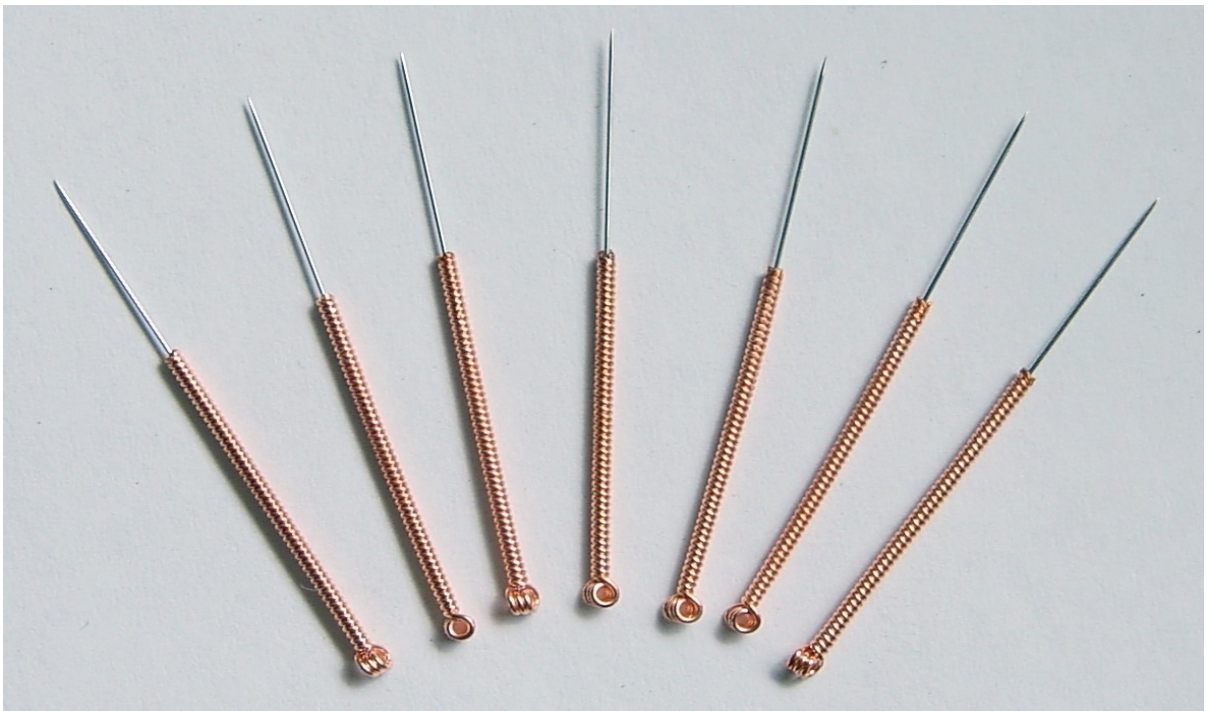


Figure 9: shows acupuncture needles

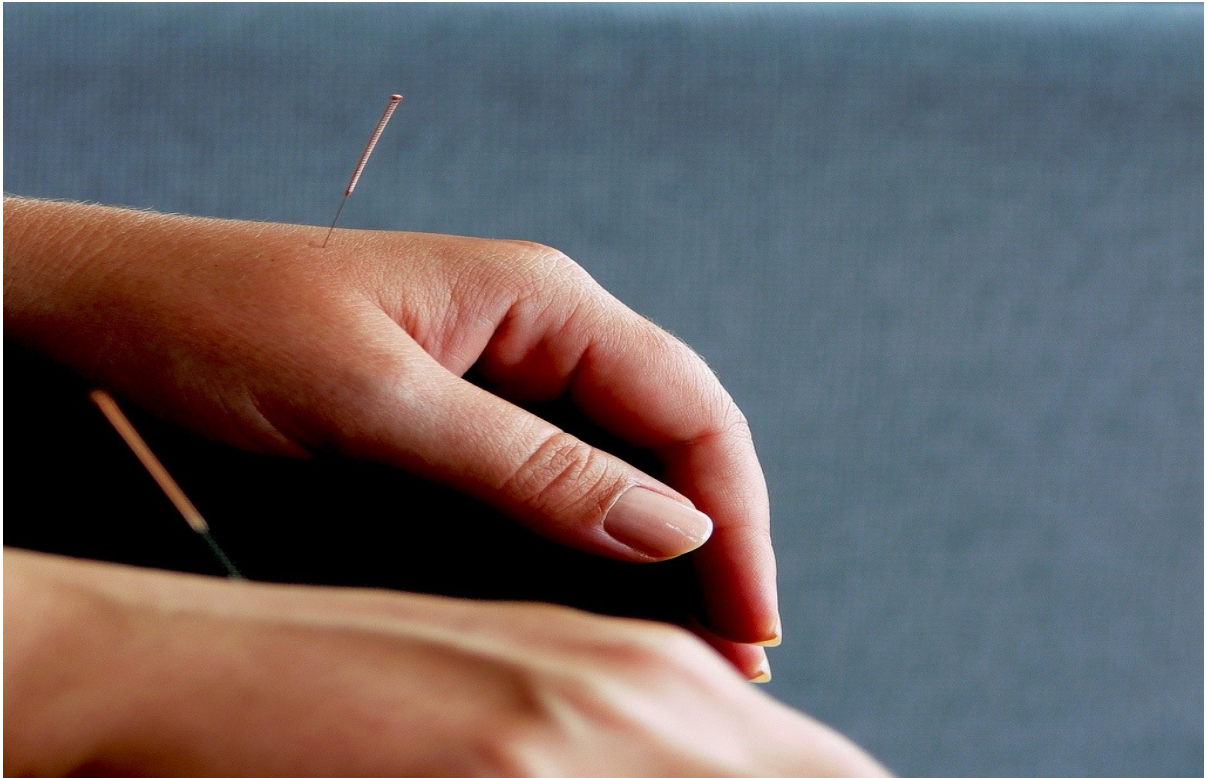


Figure 10 :shows acupuncture needle and treatment

ACUPUNCTURE POINTS:

The selected acupuncture points are SP 5,LI 4,UB 60,ST 36 ,LU 10,SP 2,ST 41,GB

38.

SP 5:

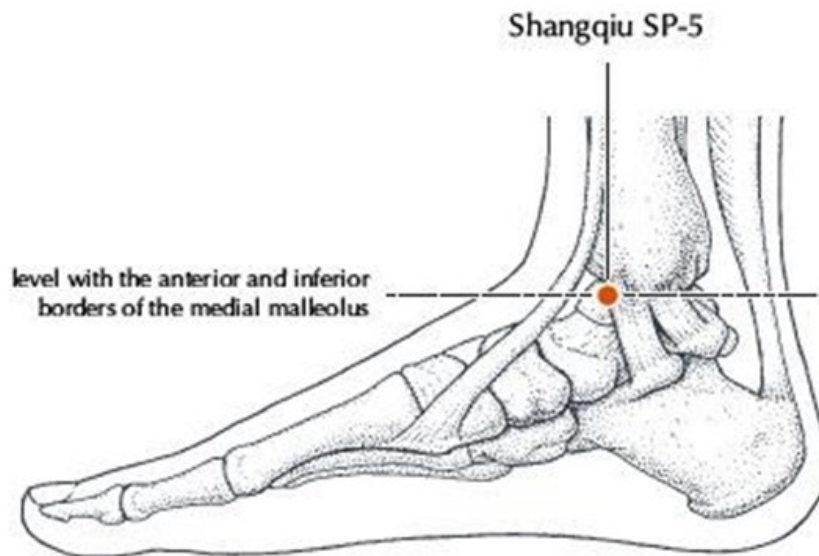


Figure 11: shows location of spleen 5

Location

In the depression at the junction of a vertical line drawn along the anterior border and a horizontal line drawn along the lower border of the medial malleolus. Or: In the depression halfway between the highest prominence of the medial malleolus and the tubercle of the navicular bone. SP-5 is located in a depression anterior and inferior to the medial malleolus, at the junction of a vertical line drawn along the anterior border and a horizontal line drawn along the inferior border of the medial malleolus. SP-5 is located distal to the tendon of

the tibialis anterior muscle. Located in a comparable position on the lateral aspect of the foot is → G.B.-40 (in a depression at the junction of a vertical line drawn along the anterior border and a horizontal line drawn along the inferior border of the lateral malleolus).

Needling

0.3–0.6 cun vertically, obliquely or transversely (subcutaneously) deep to the tendons towards → ST-41

Actions/Indications

- Tonifies the Spleen, eliminates Dampness, benefits the tendons and bones
- Moves Qi locally
- Calms the shen

Special features

Jing-river point, Metal point, sedation point. Important point for treating Damp bi-syndrome.

LI 4

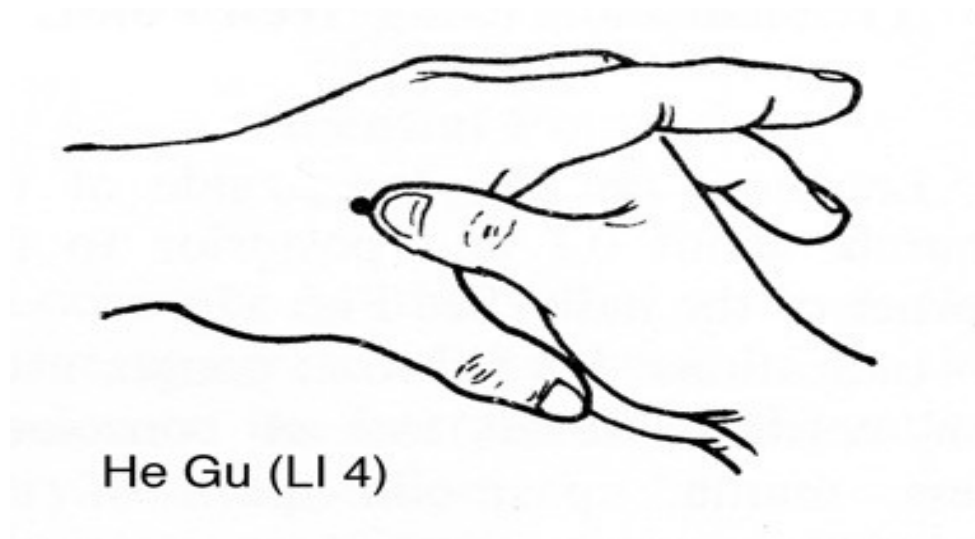


Figure 12: shows location of large intestine 4

Location:

On the radial aspect of the hand, between the 1st and 2nd metacarpal bones, closer to the 2nd metacarpal bone and approximately at its midpoint. To find the point press the thumb and index finger together, the adductor pollicis and the interosseus dorsalis muscles will form a bulge. Needle L.I.-4 at the highest point of the bulge and push it further towards the inferior aspect of the second metacarpal bone. Or: Spread the thumb and forefinger and place the distal phalanx of the thumb of the other hand on the webbed border. When flexing the thumb, its tip will point to L.I.-4. Or: Insertion on the angle bisector between the 1st and 2nd metacarpal bones, needling in the direction of the towards the palmar aspect of the hand.

Caution:

Reducing needle techniques are contraindicated during pregnancy; exception: to induce labour.

Needling

0.5–1 cun vertically or slightly obliquely

Actions/Indications

- Releases the Exterior (main point!)
- Regulates the face and head
- Regulates the Defensive Qi (wei qi) and sweating
- Opens the channel and luo-connecting vessels
- Alleviates pain
- Promotes labour

Special features

Yuan-source point, Gao Wu command point for the head and mouth, Ma Dan Yang Heavenly Star point, entry point according to some authors. Most

important analgesic point for the whole body. Most important single distal point for disorders of the face and sensory organs. It is the most commonly used point in clinical practice. The combined bilateral needling of L.I.-4 and → LIV-3 (between the 2nd and 3rd metatarsal bones) is known as si guan (Four Gates): they strongly regulate the Qi and Blood, stop pain and relieve spasm.

UB 60

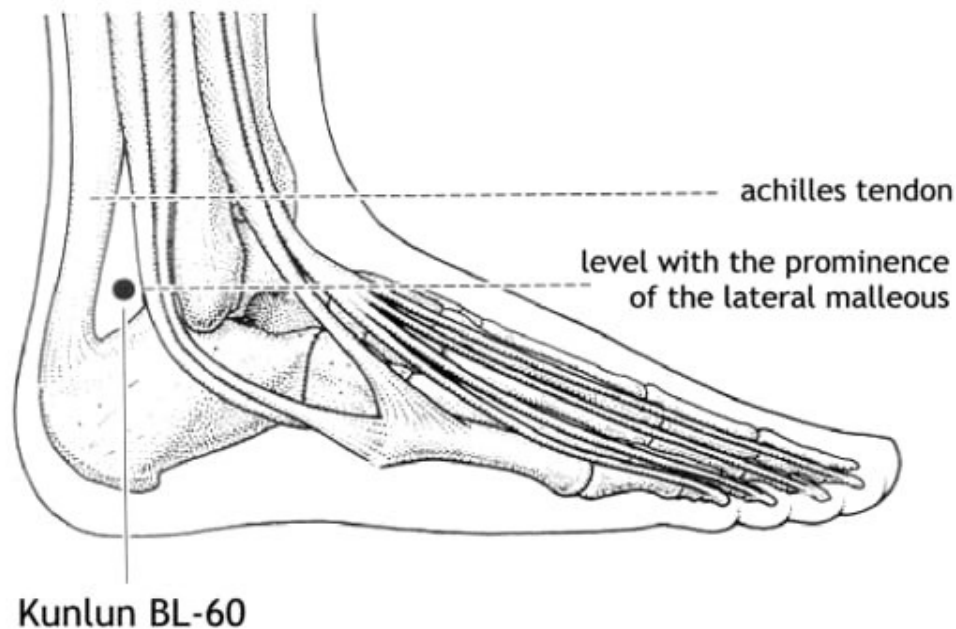


Figure 13:shows location of bladder 60

Location

Location In the depression on the line connecting the Achilles tendon and the highest prominence of the lateral malleolus.

How to find:

Locate the highest prominence of the lateral malleolus ,From there, palpate horizontally towards the Achilles tendon and locate BL-60 in a depression anterior to the tendon.

Needling

Vertically 0.5–1 cun.

Caution:

Reducing needle techniques contraindicated during pregnancy.

Exception:

A supportive point during labour

Actions/Indications

- Clears Heat, subdues Yang and Wind and eliminates excess, especially in the head
- Opens the channel, alleviates pain, relaxes the tendons, strengthens the lumbar region
- Promotes labour

Special features

Jing-river point .Fire point.

Ma Dan Yang Heavenly Star point

Important distal point for the cervical, thoracic and lumbar spine

Useful for chronic cases.

Helps in labor pain

useful in headache,dizziness,epistaxis

Helps in infantile convulsions.

ST36

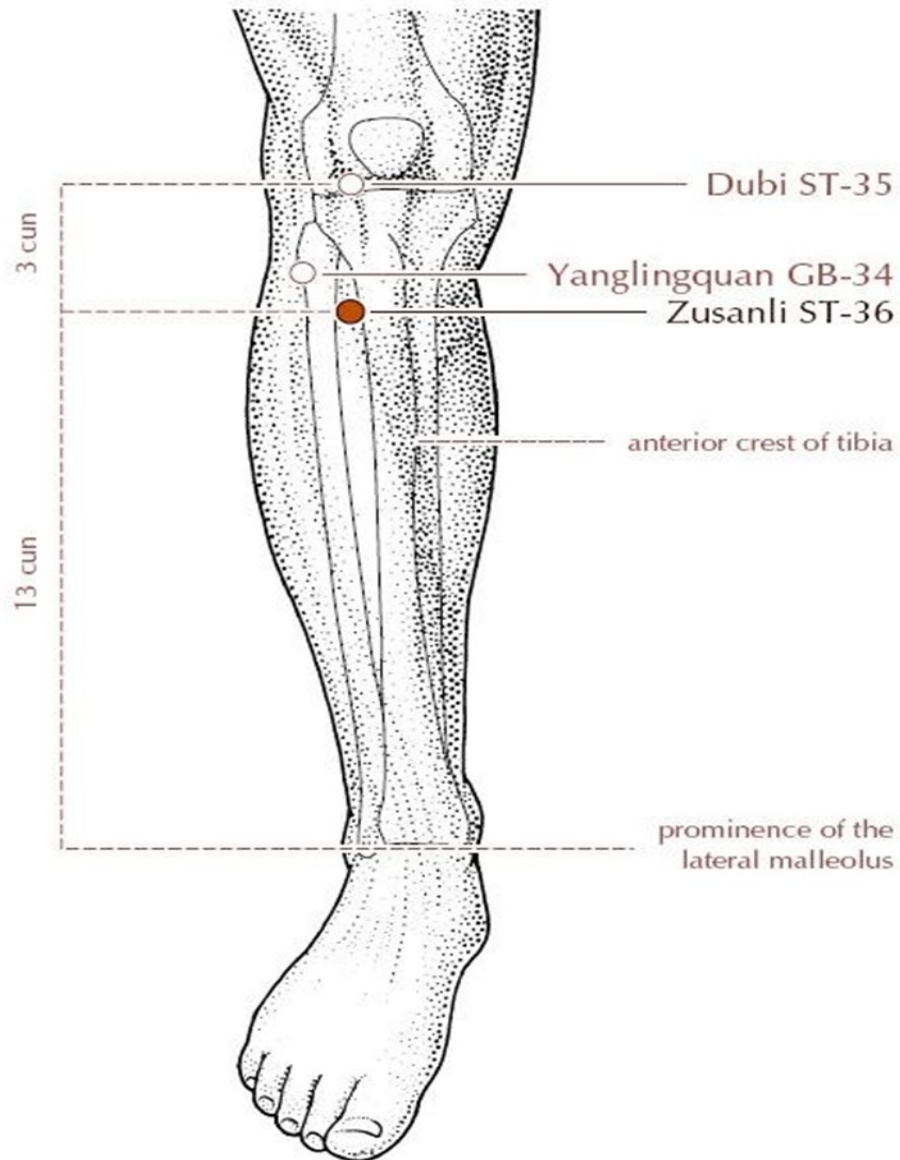


Figure 15 :shows location of stomach 36

Location

3 cun distal to → ST-35 ('lateral eye of the knee') and 1 fingerbreadth lateral to the anterior crest of the tibia, on the tibialis anterior muscle.

How to find

First, locate → ST-35 ('lateral eye of the knee', at the level of the knee joint space). From → ST-35, palpate 3 cun (1 handbreadth) down and 1 fingerbreadth towards lateral by placing the middle finger adjacent to the tibial crest. There, ST-36 is located in a depression, which can be palpated 'dynamically' (choose the point according to pressure sensitivity). Or: Palpate the lower border of the tibial tuberosity and 'dynamically' locate ST-36 one fingerbreadth lateral to it.

Needling

Vertically 1–1.5 cun. Moxibustion is often used on this point.

Actions/Indications

- Regulates the Stomach, strengthens the Spleen, transforms Dampness
- Tonifies Qi and Yang, nourishes the Blood and Yin
- Calms the shen
- Opens the channel

Special features

He-sea point, Earth point, ben point (Five Phases point), lower he-sea point of the Stomach, Gao Wu command point for disorders of the abdomen, Ma Dan Yang point, Sea of Water and Grain point. Main point to tonify Qi and Blood for general weakness. Very important point

LU 10

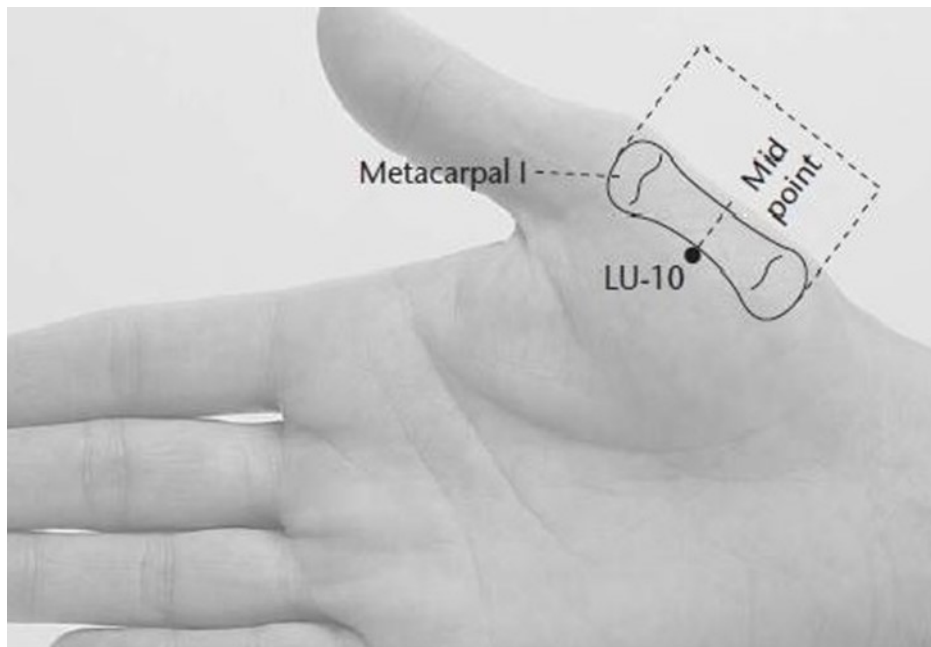


Figure 15 :shows location of lung 10

Location

the midpoint of the palmar border of the 1st metacarpal bone.

How to find

With the thumb relaxed, palpate the ‘belly’ of the thenar eminence from palmar to lateral (radial), then palpate the first metacarpal bone. LU-10 is

located at the midpoint of its palmar 'border'. → L.I.-4 is located on the dorsal aspect of the hand, close to the 2nd metacarpal bone.

Needling

Vertically 0.5–1 cun.

Caution

Painful point.

Actions/Indications

- Regulates the Lung Qi
- Cools Blood Heat
- Expels pathogenic factors from the throat
- Descends rebellious Qi
- Harmonises the Stomach and Heart

Special features

Ying-spring point, Fire point, important distal point for sore throat caused by Wind-Heat.

SP 2

Location

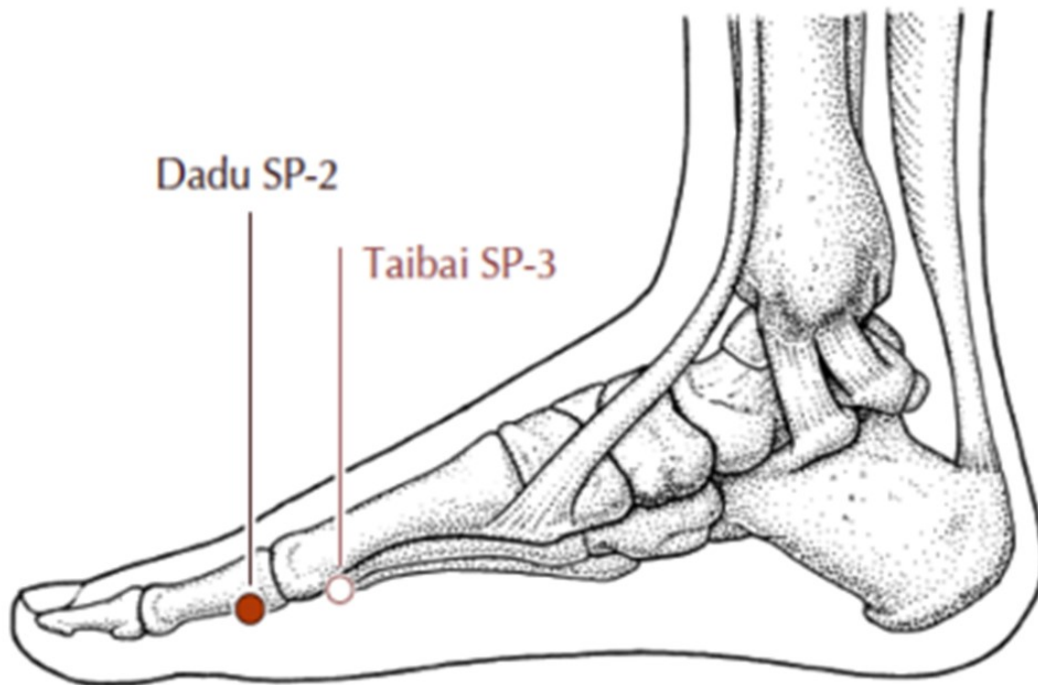


Figure16: shows location of spleen 2

On the medial aspect of the big toe, at the junction of the shaft and the base of the proximal phalanx, distal to the 1st metatarsophalangeal joint.

How to find

On the medial aspect of the big toe, palpate from distal to proximal towards the metatarsophalangeal joint, until you can feel the junction of the shaft with the base of the proximal phalanx. SP-2 is located distally to the base of the bone, which forms a distinct step, and slightly inferiorly to its outer curvature, at the border of the red and white skin (sole/dorsum of the foot). Located in

comparable positions are → BL-66 on the lateral border of the foot, → L.I.-2 on radial aspect and → S.I.-2 on the ulnar aspect of the hand.

Needling

0.2–0.5 cun vertically or obliquely, just below the lower border of the bone.

Caution:

Painful point.

Actions/Indications

- Regulates and supports the Spleen, harmonises the Lower Burner and clears Heat

Special features

Ying-spring point

Fire point

tonification point.

ST 41

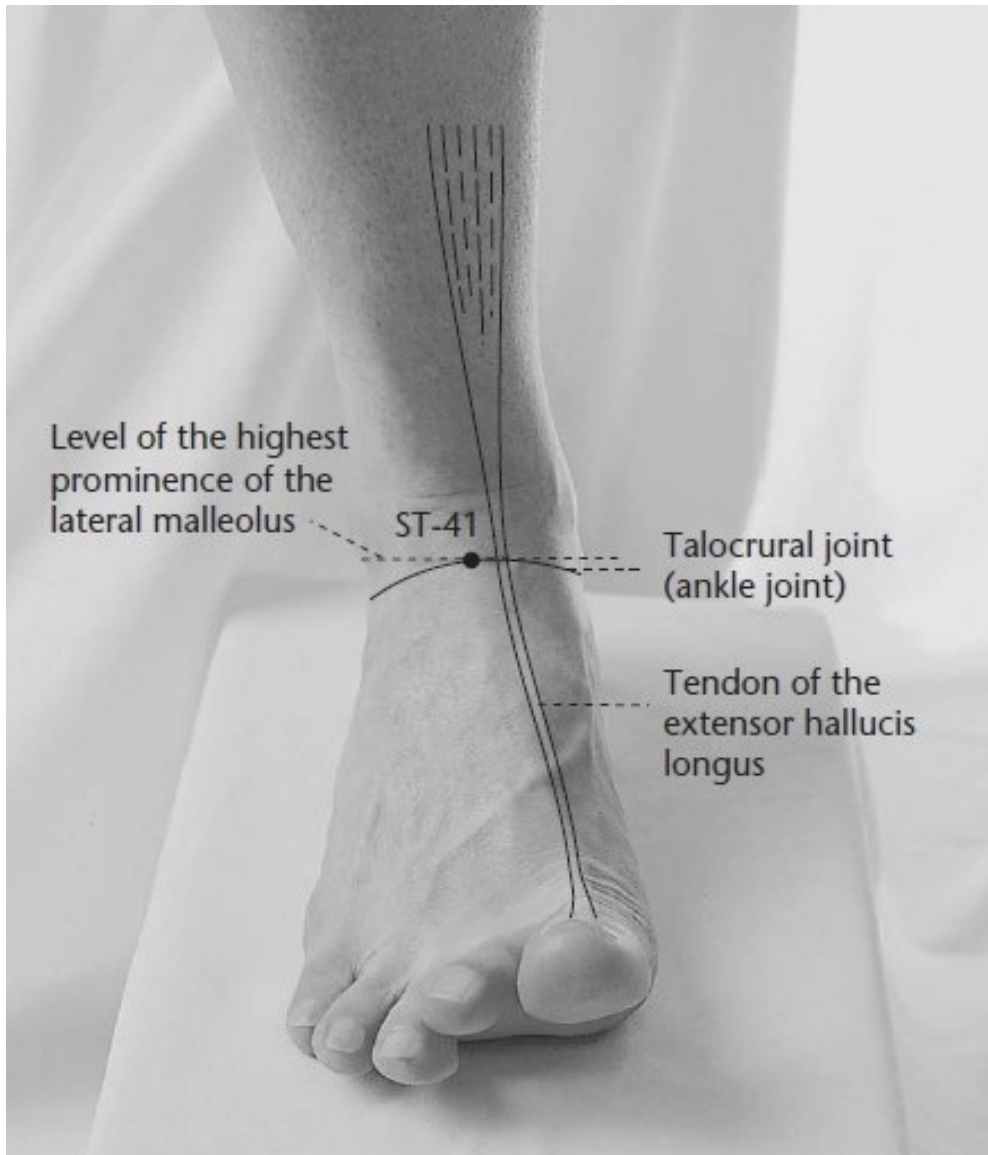


Figure 17:shows location of stomach 41

Location

On the ankle, on the level of the highest prominence of the lateral malleolus, in the depression between the tendons of the extensor digitorum and the extensor hallucis longus.

How to find

With the patient extending their big toe against resistance, the tendon of the extensor hallucis longus muscle will become more distinct. ST-41 is located lateral to this tendon, in an obvious depression on the level of the highest prominence of the lateral malleolus and ankle joint space. Located on the same level is → LIV-4 (medial to the tendon, halfway between → SP-5 and ST-41).

Needling

0.5–1 cun vertically or obliquely deep to the tendons in a medial direction towards → SP-5 or in a lateral direction towards → G.B.-40

Caution

Tibial artery/vein/nerve lie deep to this point.

Actions/Indications

- Clears Heat from the Stomach and Stomach channel

- Calms the shen
- Opens the channel and lu vessels alleviates pain

Special features

Jing-river point.

Fire point.

tonification point.

Important local point for disorders of the ankle joint.

Important distal point for frontal headaches caused by Stomach Heat or Stomach Fire.

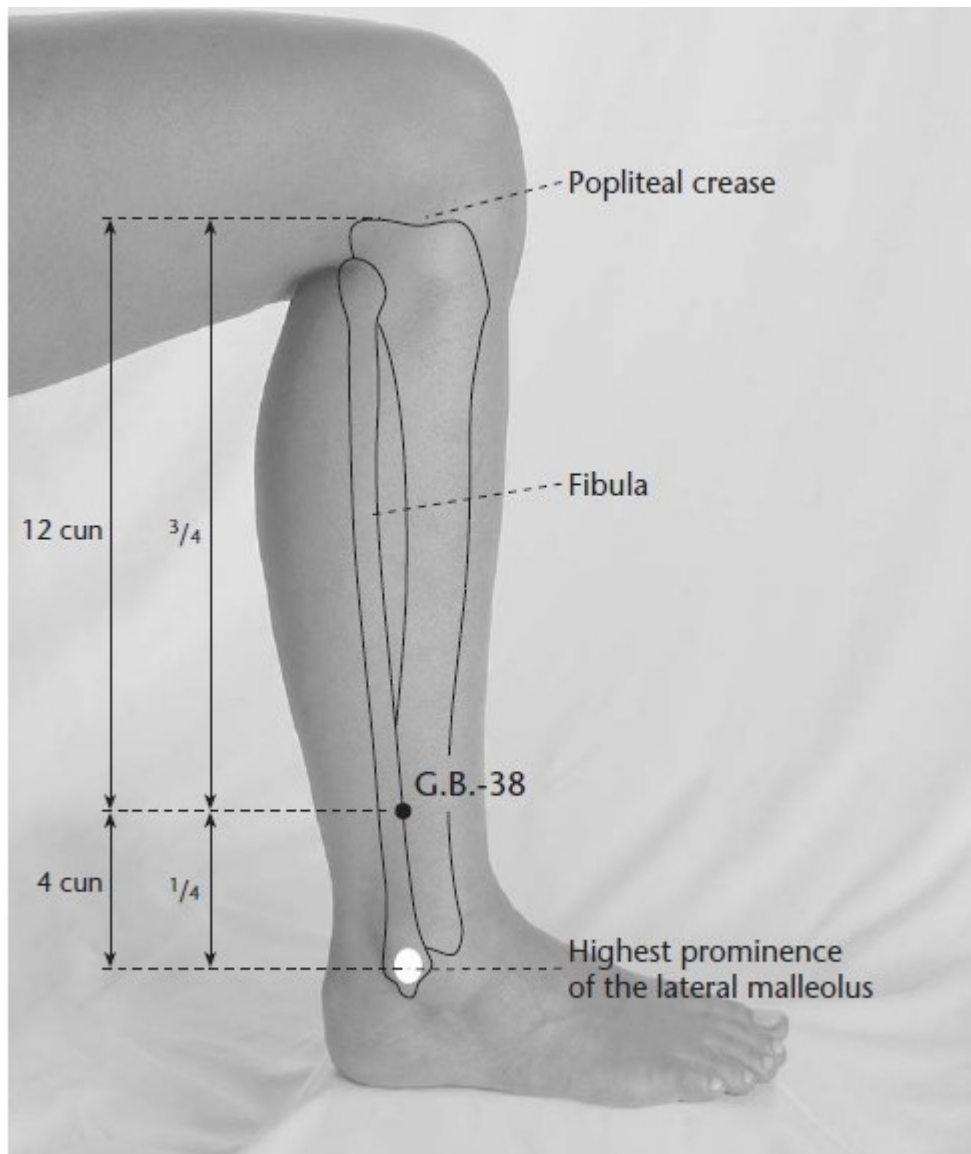


Figure18:shows location of gall bladder 38

GB 38

Location

4 cun proximal to the highest prominence of the lateral malleolus, on the anterior border of the fibula

How to find

First, locate the prominence of the lateral malleolus and, from there, measure 4 cun in a proximal direction. There, locate G.B.-38 on the anterior border of the fibula. Or: On the lateral aspect of the lower leg, the distance between the prominence of the lateral malleolus and the popliteal crease is 16 cun. Divide this distance into quarters and locate G.B.-38 one quarter of the distance from the lateral malleolus. The borders of the fibula are deep to the peroneus brevis muscle and are often not easily palpable. For this reason, it is suggested to palpate the anterior border of the fibula just superior to the ankle and then locate the point on an imaginary line running to the head of the fibula.

Needling

Vertically 0.5–1.5 cun

Actions/Indications

- Opens the channel
- Clears Wind and Heat

Special features

Jing-river point, Fire point, sedation point

RESULTS :

80 RA patients are selected after satisfying inclusion and exclusion criteria and 2010 ACR/EULAR CRITERIA.

Paired Samples Test								
	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 moxaprevas - moxapostvas	2.525	1.198	.189	2.142	2.908	13.330	39	.000
Pair 2 accpprevas - accppostvas	1.775	1.230	.194	1.382	2.168	9.129	39	.000

Table 2: shows paired sample T test

Paired sample T- test is used to determine the difference between pre and post datas of each acupuncture and moxibustion. comparison of moxibustion pre and post datas significant with p value<0.000.by comparison of acupuncture pre and post datas also highly significant with p value<0.000.

Pain had reduced statistically significance immediately after moxa application to particular points in rheumatoid arthritis.

Immediately after acupuncture also the pain got reduced statistically significant.

Paired Samples descriptive Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	moxaprevas	6.45	40	1.679	.265
	moxapostvas	3.92	40	1.845	.292
Pair 2	accpprevas	5.72	40	1.768	.280
	accppostvas	3.95	40	1.724	.273

Table 3 :shows paired samples descriptive statistics

Paired sample descriptive statistics shows mean value is higher in moxa group.

Descriptive Statistics

		N	Mean	Std. Deviation	Std. Error Mean
dvvas	1	40	3.92	1.845	.292
	2	40	3.95	1.724	.273

Table 4 :shows descriptive statistics

1=moxa group, 2=accup group

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
dvvas	Equal variances assumed	.105	.746	-.063	78	.950	-.025	.399	-.820	.770
	Equal variances not assumed			-.063	77.642	.950	-.025	.399	-.820	.770

Table 5 :shows independent samples test

Levene's test for equality of variances is used to determine the differences between immediate effect of acupuncture and moxa . and the result shows the value of $p < 0.7$ which is not significant.

Acupuncture and moxibustion two groups results are highly significant
But when comparing statistically it is not proven as significant

DISCUSSION

Moxibustion has an analgesic effect and increases hypothalamic POMC and PDYNNmRNA expression levels and plasma β -EP content in RA rats.(39) Repeated moxibustion treatments are required for pain relief and showed the involvement of sustained inhibitory modulation mediated by endogenous opioids in the present rat experimental knee osteoarthritis model [40]

Treatment of rheumatoid arthritis(RA) with acupuncture and moxibustion can dredge meridians and collaterals, regulate Qi and blood, eliminate wind, cold and dampness, remove blood stasis and promote blood circulation and relieve pain.,it has been proved to be effective to treat RA with acupuncture and moxibustion. Studies show that acupuncture can regulate immune system,improve blood rheology and eliminate free radicals[41]. Moxibustion can resist inflammation and eliminate swelling by inhibiting abnormal activation of JAK-STAT pathway in synovial cells.[43]Dr.luo states that Moxibustion can protect the immune organs (thymus gland and spleen) from injury and improve pathological changes of the ultrastructure of local synoviocytes.[44]

Dr.xie xx observed the therapeutic effect of Spreading moxibustion in rheumatoid arthritis.and he concluded that spreading moxibustion has a significant therapeutic effect on rheumatoid arthritis[45] It is suggested that the higher the temperature of moxibustion (47°C or 52°C) produces stronger analgesic effect than that lower temperature (37°C or 42°C)[46].

Moxibustion therapy improve immune functions, inhibit the secretion of the synovial cells factors in the joints, control the proliferation of the synovial cells, and induce apoptosis of the synovial cells in the synovitis, and promote the apoptosis of the fibroblast, so as to play a therapeutic role in the treatment of rheumatoid arthritis. The therapeutic effect is obtained by the comprehensive effect created from integration between the physical factors and herbal factors in burning moxa wool and the special functions of the acupoints and meridians.[47]

RA patients have shown that the decrease of IL-2 should be one of main causes of internal environment disorder, acupuncture and moxibustion as a stress stimulation exerts an influence on the immunity system through neuroendocrine system to improve the IL-2 production.[48]Tao yi concluded that moxibustion could release enkephalins in the spinal cord which helps , relieve chronic visceral hyperalgesia in irritable bowel syndrome rats.it is similar to the mechanism of acupuncture analgesia.[49]

Zanthoxylum bungeanum-cake-insulated moxibustion could decrease the paw swelling and inhibit the expression of IL-1 β and TNF- α in RA rats and it is effective in improving the symptoms of RA rats via suppressing the expression of cytokines .[50]

Acupuncture and moxibustion can improve blood flow. Increased blood flow caused by acupuncture and moxibustion may flush out the algescic or sensitizing substances and induce pain relief. There have been several reports

suggesting that acupuncture increases local and remote muscle blood flow in human subjects [51, 52].

Kawakita discussed the important role of the polymodal receptors, which are responsive to both acupuncture and moxibustion. The morphological and functional characteristics of the polymodal receptors can explain the nature of so-called acupuncture points and trigger points. Immediate effects of acupuncture and moxibustion may be explained, at least in part, by the axon reflex via the polymodal receptor. The existence of various endogenous pain inhibitory systems was also pointed out for understanding the immediate effects of acupuncture and moxibustion.[53]

ElectroAcupuncture induce the expression of preproenkephalin (PPE) mRNA, preproopiomelanocortin (POMC) mRNA in many painmodulation-related nuclei, such as caudate nuclei, amygdala, hypothalamus, PeriAqueductal Greymatter, in the brain. In spinal dorsal horn, EA enhanced the preprodynorphin (PPD) mRNA expression.. The above studies suggested that the further activation of opioid peptidergic system from presynaptic (EOP release and gene expression) to postsynaptic (opioid receptors) level as well as the antagonism of dopaminergic system were involved in the mechanisms of Acupuncture Balanced Anesthesia[54].

Acupuncture analgesia is manifest only when the intricate feeling of acupuncture (soreness, numbness, heaviness and distension), so-called “De-Qi”, occurs. “De-Qi” feeling originates from acupuncture-induced impulses

from local muscle contraction beneath the acupoint. Types of afferent nerve fibers activated by acupuncture depend upon the manipulation methods and individual differences in sensitization. Manual acupuncture stimulates afferent fibers and activates to conduct the signal. Electroacupuncture excite Ab and part of Ad type afferents can induce an analgesic effect. Acupuncture analgesia is essentially a manifestation of integrative processes at different levels of the CNS between afferent impulses from the pain regions and impulses from acupoints. Spinal pathways of acupuncture impulses from acupoints ascend mainly through the ventrolateral funiculus[55].

A complex network of many brain structures is involved in processing acupuncture analgesia, including the VRM (mainly NRM), PAG, Locus coeruleus, Arcuate nucleus, amygdala, etc. Most of nuclei are constitutive parts of the endogenous descending inhibitory system in the CNS. But Hyper anxiety behaviour and LC antagonize acupuncture analgersia. Various signal molecules are implicated in acupuncture analgesia, such as opioid peptides (m- d- and k-receptors), cholecystokinin octapeptide (CCK-8), glutamate ,5-hydroxytryptamine and noradrenalin. Among them, opioid peptides and their receptors play a pivotal role in mediating acupuncture analgesia [55].

Moxibustion and acupuncture invigorate yang qi, strengthen anti pathogenic qi to eliminate pathogenic factors, remove the obstruction from the meridians and collaterals. Acupuncture needling trigger the pain sensation regulation system of the body to control the reception and transmission of hurting information at all central levels, needling can invigorate the

endogenous analgesic mechanism of the body, produce an integrative regulatory and control process of needling information from peripheral to the central nerve system of all levels against the reception and transmission of hurting information'[56] Warming-yang moxibustion technique combined with acupuncture in the treatment of cancer pain provides quick effect, absence of side effect, and long duration of effect, regulate yin and yang of the body .[57]

Moxibustion has thermal stimulation effect. When physical and chemical factors act on the acu- point receptors, the signal enters the central nervous system through the peripheral pathways and outgos after being integrated, adjusting the neuro endocrine immune network and circulatory system [58]. Scarring moxibustion has advantage of curing chronic refractory diseases. [60]

Zhang conducted a study on mechanism of moxibustion in RA. RA belongs to the "Bi-obturation syndrome" in Chinese medicine, deficiency in constitution and excess in symptoms. Moxibustion has the effects to replenish the kidney, strengthen yang, warm up and unblock the meridians, dissipate wind, disperse cold and remove dampness, suitable for the patients with long-term "Bi-obturation syndrome" in particular[64].

Moxibustion is a heat radiation reaction and is supposed to influence the metabolism and functions of the neurological system by warming and stimulating the skin receptors. It has been proved that moxibustion could relieve congestion and edema of the articular synovium, infiltration of

inflammatory cells, proliferation of the synovial cells, and tissue thickening, indicating that moxibustion plays a therapeutic role for arthritis by inhibiting synovitis. It inhibit occurrence and release of inflammatory cellular factor and to induce apoptosis of the synovial cells in the treatment of RA by moxibustion.[64]

Okada states that acupuncture produces analgesia via gate control mechanisms. however, mechanoreceptors innervated by thick fibers cannot be activated by thermal stimuli such as moxibustion. It should be stressed that the fundamental mechanism of acupuncture and moxibustion is based on moxibustion- sensitive input. Polymodal types of nociceptors that respond to mechanical, thermal and chemical stimulation are particularly sensitive to capsaicin, and innervated by the afferent C fibers in the skin, as well as by both A-d and C fibers in the muscle. These polymodal receptors seem to be the most reasonable candidates for acupuncture and moxibustion; they are not purely nociceptors, but they are responsive to non-noxious stimuli such as scratching the skin. This functional characteristic of polymodal receptors may be vital for further investigations.Sensitization of the polymodal receptors has been proposed as a rational explanation of the nature of acupoint formation. [65]

Acupuncture is beneficial for treating RA, possible mechanisms of action include an anti-inflammation, autonomic nervous system modulation or analgesic effects of acupuncture in patients suffering from RA. And acupuncture influences specific and non-specific cellular influx, activation of cell proliferation and regulation of subsequently involved cells that will result

in a complex mechanism of transport, further breakdown and clearance of all bioactive mediators. Another hypothesis is that the anti-inflammatory actions of acupuncture are mediated via the reflexive central inhibition of the innate immune system. Acupuncture increases autonomic tone and acetylcholine output while decreasing inflammatory molecules including cytokines, CRP and ESR. Anti-inflammatory effects explained by modulation of autonomic nervous system and acupuncture changes the function of the hypothalamic–pituitary–adrenal axis. Acupuncture combined with moxibustion, reduce pain through stimulating the serotonergic, noradrenergic and opioid system in pain conditions. Another possibility is the synergetic effects of heat from moxibustion on the stimulation of acupuncture[67]

Overall acupuncture and moxibustion works through diffuse noxious inhibitory control, and activation of polymodal receptors and A- delta and C fibers of the muscle. Thus it give anti-nociception action.[65,66]. Our results also show that acupuncture and moxa show significant result in immediate pain reduction in RA patients. while comparison of moxibustion and acupuncture, statistically both are equal in immediate analgesic effect in RA Patients.

Overall moxibustion and acupuncture have significant effect in immediate analgesic effect in RA patients. But when compared between the groups both are not significant.

CONCLUSION

The present study showed that acupuncture and moxibustion shown significant result in pain reduction in RA patients. The results when seen with in the groups they are significant, but when compared between the groups the datas are not significant.

Limitations

- The sample size is relatively smaller. Hence, generalizing the study outcomes to a larger population would not be definitely conclusive.
- Room temperature was not maintained during the assessment.
- Diurnal variations might have influenced the results.
- Other activities acted as confounding factors during the study.
- Variables like NRS(Numerical rating scale),VDS(verbal descriptor scale),NVDS(numerical descriptorscale),MPQ(McGillpain questionnaire)have not been used in this study.

Directions for future research

This study should be replicated with a larger sample size.

The study was conducted for very short duration.

This study is specified only on immediate analgesic effect in RA

SUMMARY:

Acupuncture is a system of ancient healing. It is believed that 4000 years old tradition of China. Stimulation of particular points on the surface of the body affects the function of an internal organs. Rheumatoid arthritis is a systemic auto immune connective tissue disease with unknown etiology. It is characterized by nonspecific, chronic progressive inflammation of joints. Acupuncture and moxibustion helps in reducing pain and inflammation in RA.

A comparative study performed among 80 patients with Rheumatoid arthritis age ranging between 30-55 years from IP and OP dept of Govt. yoga and naturopathy medical college, Arumbakkam. They were randomly assigned into two groups. Experimental group (n=40) and control group (n=40) after satisfying the inclusion and exclusion criteria and ACR/EULAR 2010 criteria. Experimental group was given moxibustion at selected acupuncture points and ah-shi points of the affected joint. Control group received acupuncture on the same acupuncture points. Both groups were assessed at baseline and immediately after treatment by using visual analogue scale (VAS)

The result when seen within the group there is significant with p value $p < 0.000$, but when compared between the groups the data are not significant. So it is proven that both are effective in immediate analgesic effect in RA patients.

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ANNEXURE

INFORMATION SHEET

- We are conducting a study on Rheumatoid arthritis among patients attending Government yoga and naturopathy medical college Chennai and for that, your participation may be valuable to us.
- The purpose of this study is to compare ANALGESIC effect of specific acupuncture and moxibustion in rheumatoid arthritis
- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period.

Signature of Investigator

Signature of Participant

Date:

INFORMED CONSENT FORM

Title of the study : Comparison of analgesic effect of specific acupuncture and moxibustion in rheumatoid arthritis

Name of the Participant :

Name of the Principal Investigator : Dr. G.Yasodha

Name of the Institution : Government Yoga & Naturopathy Medical College,
Chennai – 600 106

Documentation of the informed consent

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.
8. I have not participated in any research study within the past _____ month(s).
9. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
10. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.
12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
13. I have understood that my identity will be kept confidential if my data are publicly presented.
14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form, I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature / thumb impression of the participant (or legal representative if participant incompetent)

Name _____ Signature _____

Date _____

Name and Signature of impartial witness (required for illiterate patients):

Name _____ Signature _____

Date _____

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature _____

Date _____

INFORMATION TO PARTICIPANTS

Investigator: Dr. G. Yasodha

Name of Participant:

Title: Comparison of analgesic effect of specific acupuncture and moxibustion on Rheumatoid arthritis”

You are invited to take part in this research/ study / procedure. The information in this document is meant to help you decide whether to take part. Please feel free to ask if you have any queries or concerns.

You are being asked to participate in this study being conducted in Government Yoga and Naturopathy Medical College, Chennai.

What is the Purpose of the Research?

The purpose of the research is to compare the analgesic effect specific acupuncture and moxibustion in Rheumatoid arthritis

The Study Design

80 adults from both gender with rheumatoid arthritis will participate in the study.

Study Procedures

The study involves needling specific and ashi points of painful joints will be given to one group. other group receives moxibustion at specific and ashi points of painful joints.

Possible Risks to you - Nil

Possible Benefits to you- joint pain will be relieved

Possible benefits to other people

The result of the research may provide benefits to the society in terms of use of acupuncture and moxibustion as an alternative approach to rheumatoid arthritis instead of taking drugs and medicines. The effectiveness of the acupuncture needling and moxibustion can also be differentiated.

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, IEC and any person or agency required by law like the Drug Controller General of India to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decisions to not to participate in this research study will not affect your medical care or your relationship with investigator or the institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment

