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Review Article

RHEUMATIOD ARTHRITIS: A REVIEW ARTICLE

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INTRODUCTION

Rheumatoid arthritis is a disease of unknown aetiology characterized by a chronic polyarthritis in which the major target tissue is the synovial lining of the joints, bursa and tendons sheath resulting in varying degrees of joint deformities and associated muscle wasting. Despite rheumatoid arthritis is traditionally considered as a systemic, inflammatory, autoimmune disorder but it differs from organ specific autoimmune disease entities in several reports. Enhanced understanding of molecular pathogenesis has enabled development of innovative biological agents that target specific parts of the immune system. These treatments have changed the course and face of rheumatoid arthritis and outcomes for patients and society. New knowledge has emerged of how environmental factors interact with susceptibility genes and the immune system in the pathogenesis of a major subset of rheumatoid arthritis (Klareskog et al, 2009). Considerable advances in recent years in both the clinical and basic research aspects of rheumatoid arthritis have been made. Clinical progress of rheumatoid arthritis has shown considerable development and validation for clinical trials and, consequently, innovative trial designs. In parallel, basic research has provided clues to the pathogenic events underlying rheumatoid arthritis, and advances have facilitated the development of new classes of therapeutics (Josef S et al, 2003).

Epidemiology

The incidence of rheumatoid arthritis as reported in 1993 is 0.2 per 1000 population for males and 0.4 per 1000 for females but virtual absence of epidemiologic data of the under developed or developing countries of the world does not reported the true picture thus epidemiological findings under score the complexity of rheumatic disease (Sherine E, 2009)

Clinical features

Rheumatoid arthritis is a heterogeneous disease does not involve a single entity. Typically small joints of the hands and feet as well as the wrists are affected. But more common representations are diffuse symmetrical joint pain, swelling and stiffness of small peripheral joints.

Treatment

The management of rheumatoid arthritis is a multidisciplinary approach in order to lessen the pain, reduction of inflammation and restoration of joints function. In practical terms suppression of inflammation is the target intensive therapy. Herbal medicines have become popular for the treatment of rheumatoid arthritis worldwide recently.

Research Study on Rheumatoid arthritis in Pakistan

Considering all the above mentioned salient features the past decades has brought many new insights regarding the treatment options for the rheumatic disease with allopathic and herbal medicines.

This article describes the currently available scientific evidence that regarding the safety and efficacy and toxic effects, if known, of *Apium graveolens, Nigella Sativa L., Smilax China, Trigonella foenum graecum L., Zingiber officinale*, *Withania somnifera dunal* and *Colchicum autumnale L*. since these are most commonly used as medicinal agents for the treatment of rheumatoid arthritis or the action of these medicine is likewise Disease Modifying Anti Rheumatic Drugs (DMARD). A study was done to evaluate the efficacy of herbal medicine in comparison with allopathic medicine methotrxate for treatment of rheumatoid arthritis. This case control examination based study was conducted at Shifa-ul-Mulk Memorial Hospital for Eastern Medicine on the patient living in the rural areas of 70 villages surrounding Madinat-ul-Hikmah Hamdard University, Karachi. The study was carried out from September 2006 to August 2008. The patients 50 in number were treated with Arthritin and 50 of Methotrexate for twenty four weeks based on randomized clinical trial. Chi-square test and exact fisher test were used to analyze the statistical difference. Arthritin and Methotrexate were prescribed to 100 patients with rheumatoid arthritis. The primary criteria in evaluating the efficacy was the degree of relief of pain, swelling, stiffness and tenderness how the patients felt after taking the medication. After six months study of patients taking the herbal formulation orally, three times per day, patients reported improved range of motion in their joints and decreased pain, swelling, tenderness, in hands elbows, knees, ankles joints. This study very clearly reveals that in case of rheumatoid arthritis when treated with Arthritin and Methotrexate, the result on the efficacy display that Arthritin is more effective for treatment of rheumatoid arthritis(Owais M. et al 2010).

Anti-inflammatory cooperativity of corticosteroids and norepinephrine in rheumatoid arthritis synovial tissue in vivo and in vitro

Corticosteroids (CS) and norepinephrine (NE) support each other's biological effects. Thus, deficiency of cortisol and reduced synovial sympathetic innervation (SSI) may be proinflammatory in rheumatoid arthritis (RA). This study tested the anti- inflammatory cooperativity of CS and NE in human RA synovial tissue. In an in vivo study, 32 patients with RA (with prior CS therapy/without SSI: n=7; without prior CS therapy/with SSI: 6; with prior CS therapy/with SSI: 19) were investigated for synovial inflammation. In an in vitro study with synoviocytes from RA and OA patients, the separate and combined effects of cortisol and NE were studied. In the in vivo study, patients with prior CS therapy/with SSI showed lower secretion of synovial IL-8 than the other groups, lower synovial density of T cells and macrophages, and lower overall inflammation. In the in vitro study, a cooperative suppressive effect of NE (10-6 M to 10-8 M) and cortisol (10-6 M and 10-7 M) on secretion of IL-8 and TNF from primary early culture mixed RA synoviocytes was observed. This cooperative effect was not observed in OA synoviocytes. In the same RA and OA patients, the cooperative effect was lost in 3rd passage synovial fibroblasts. This study demonstrates the cooperativity of cortisol and NE for inhibition of proinflammatory mediators produced in the synovial tissue of RA patients. These results underscore that coupling of an efficient secretion of systemic cortisol together with local production of NE is important in order to lower synovial inflammation (Straub et al, 2002).

Treatment of Rheumatoid Arthritis with Methotrexate Alone, Sulfasalazine and Hydroxychloroquine, or a Combination of All Three Medications

In this study 102 patients were enrolled with rheumatoid arthritis and poor responses to at least one disease-modifying drug in a two-year, double-blind, randomized study of treatment with methotrexate alone (7.5 to 17.5 mg per week), the combination of sulfasalazine (500 mg twice daily) and hydroxychloroquine (200 mg twice daily), or all three drugs. The dose of methotrexate was adjusted in an attempt to achieve remission in all patients. The primary end point of the study was the successful completion of two years of treatment with 50 percent improvement in composite symptoms of arthritis and no evidence of drug toxicity.

Fifty of the 102 patients had 50 percent improvement at nine months and maintained at least that degree of improvement for two years without evidence of major drug toxicity. Among them were 24 of 31 patients treated with all three drugs (77 percent), 12 of 36 patients treated with methotrexate alone (33 percent, P<0.001 for the comparison with the three-drug group), and 14 of 35 patients treated with sulfasalazine and hydroxychloroquine (40 percent, P = 0.003 for the comparison with the threedrug
group). Seven patients in the methotrexate group and three patients in each of the other two groups discontinued treatment because of drug toxicity. In patients with rheumatoid arthritis, combination therapy with methotrexate, sulfasalazine, and hydroxychloroquine is more effective than either methotrexate alone or a combination of sulfasalazine and hydroxychloroquine(James R et al, 1996).

Total condylar knee replacement in patients who have rheumatoid arthritis. A tenyear follow-up study.

In this study, eighty knee replacements with a total condylar prosthesis in patients who had rheumatoid arthritis were followed for ten years. At ten years, nineteen knees needed revision and sixty-one prostheses were still functioning. The major reasons for revision were loosening of the tibial component or late bacteremic seeding from another site. Radiolucency at the bone-cement interface adjacent to the tibial component was statistically related to malposition of the tibial component. According to the system of The Hospital for Special Surgery, the mean scores were 64 points preoperatively and 85 points postoperatively. Synovitis recurred in only 3 per cent of the knees. When revision, pain, or radiographic evidence of loosening were considered an indication of failure, the ten-year cumulative survival was 75 per cent (Laskin RS, 1990).

Etanercept in Children with Polyarticular Juvenile Rheumatoid Arthritis

In this study , Patients 4 to 17 years old received 0.4 mg of etanercept per kilogram of body weight subcutaneously twice weekly for up to three months in the initial, open-label part of a multicenter trial. Those who responded to treatment then entered a double-blind study and were randomly assigned to receive either placebo or etanercept for four months or until a flare of the disease occurred. A response was defined as an improvement of 30 percent or more in at least three of six indicators of disease activity, with no more than one indicator worsening by more than 30 percent. At the end of the open-label study, 51 of the 69 patients (74 percent) had responses to etanercept treatment. In the double-blind study, 21 of the 26 patients who received placebo (81 percent) withdrew because of disease flare, as compared with 7 of the 25 patients who received etanercept (28 percent) (P=0.003). The median time to disease flare with placebo was 28 days, as compared with more than 116 days with etanercept (P<0.001). In the double blind study, there were no significant differences between the two treatment groups in the frequency of adverse events. It was concluded that treatment with etanercept leads to significant improvement in patients with active polyarticular juvenile rheumatoid arthritis. Etanercept is well tolerated by pediatric patients(Daniel J et al, 2000)

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