



LEFLUNOMIDE AND METHOTREXATE DRUG'S EFFECT ON RHEUMATOID ARTHRITIS

Pharmacology

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ABSTRACT

Rheumatoid arthritis is a chronic autoimmune disorder. This study compares the efficacy and safety of Leflunomide and Methotrexate in active cases. Seventy two (72) patients with active disease were randomly assigned to receive either Methotrexate or Leflunomide for twelve weeks. Clinical and laboratory parameters including morning stiffness, joint counts and inflammatory markers were monitored. Both groups showed significant improvement but Leflunomide was found to be more effective and safer than Methotrexate.

KEYWORDS

Rheumatoid arthritis, Leflunomide, Methotrexate, DMARDs, joint pain, inflammation, clinical trial

The prevalence of rheumatoid arthritis is approximately 0.8% of the population (Lipsky, 2001). In India the prevalence is 0.75%	Skin <ul style="list-style-type: none"> Subcutaneous nodules Vasculitis Ulcers Gangrene Pyoderma gangrenosum 	Neurological <ul style="list-style-type: none"> Entrapment syndromes Cervical compression Peripheral neuritis Mononeuritis multiplex
	Eye <ul style="list-style-type: none"> Sicca syndrome Scleritis Scleromalacia, Episcleritis 	Musculoskeletal <ul style="list-style-type: none"> Muscle wasting Bursitis, Tenosynovitis
	Others <ul style="list-style-type: none"> Systemic vasculitis (skin, CNS, lungs etc) Amyloidosis 	

Pathogenesis Of Rheumatoid Arthritis

The propagation of rheumatoid arthritis is an immunologically mediated event. The inflammatory process in the tissue is driven by the CD₄⁺ T cells infiltrating the synovium. (Lipsky and Davis, 1998).

Within the rheumatoid synovium the CD₄⁺ T cells producing the proinflammatory cytokine IFN- γ and capable of producing the anti-inflammatory cytokine IL-4. As a result of the ongoing secretion of IFN- γ without the regulatory influences of IL-4, macrophages are activated to produce the proinflammatory cytokine IL-1 and TNF- α and also increase expression of HLA molecules, produce a variety of cytokines that promote p cell proliferation and differentiation into antibody forming. The resultant production of the immunoglobulin and rheumatoid factor can lead to immune complex formation with consequent complement activation.

Laboratory Findings In Rheumatoid Arthritis

- Anemia - normochromic or hypochromic, normocytic.
- Thrombocytosis.
- Raised erythrocyte sedimentation rate (ESR).
- Raised C-reactive protein concentration (CRP).
- Raised ferritin concentration as acute phase protein.
- Raised serum globulin concentrations.
- Presence of rheumatoid factor.
- Raised serum alkaline phosphatase activity.

The present study was conducted in 72 patients of active rheumatoid arthritis at J.L.N. Medical College and Associated Group of Hospitals, Ajmer. The subjects for study were taken from patients attending medical outdoors and admitted in various wards.

Group I (Methotrexate Group; n=36)

This group consisted of age, sex, BMI matched patients of active RA in age range 18 to 70 years who were treated with Methotrexate with or without stable doses of NSAIDs.

Group II. (Leflunomide Group; n=36)

This group consisted of age, sex, BMI matched patients of active RA in age range 18 to 70 years who were treated with loading dose of leflunomide 100 mg once a day for 3 days and then 20mg once a day for

12 weeks with or without stable doses of NSAIDs and low dose Methotrexate.

1. Tender Joint Counts Of Subjects Studied

Group	Tender Joint Count (Mean \pm S.D.)				Mean Change	P value
	Time in weeks					
	0 baseline	4	8	12 end point		
Leflunomide	20.05 \pm 4.34	20.94 \pm 5.20	20.28 \pm 5.04	21.22 \pm 5.45	1.17 \pm 1.11	< 0.001 H.S.
Methotrexate	19.62 \pm 5.77	19.02 \pm 5.60	19.72 \pm 5.25	20.97 \pm 5.59	1.35 \pm 0.18	> 0.05 N.S.

2. Swollen Joint Counts Of Subjects Studied

G roup	Swollen Joint Count (Mea n \pm S.D.)				Mean change	P value
	Time in weeks					
	0 baseline	4	8	12 end point		
Leflunomide	21.33 \pm 4.22	21.16 \pm 4.41	20.5 \pm 4.28	20.55 \pm 4.23	0.78 \pm 0.01	< 0.001 H.S.
Methotrexate	20.75 \pm 5.44	20.70 \pm 5.19	20.16 \pm 4.69	20.32 \pm 4.40	0.43 \pm 1.04	< 0.05

Thus there was a statistically highly significant improvement in swollen joint count in leflunomide group as compared to (p < 0.001) and Methotrexate group, improvement in swollen joint count at week 4 and 8 is also significant in leflunomide group as compared to Methotrexate group.

SUMMARY & CONCLUSION

This study was carried out in 72 patients of classical or definite R.A. proved by A.R.A. criteria (1987).

- In group A 36 patients treated with Methotrexate alone showed initial clinical response with decrease in their functional capacity class, decrease in duration of morning stiffness and decrease in Ritchie joint score and rheumatoid antibody titre for about 1-2 months only. After 6 months of therapy, their functional capacity increased, and duration of morning stiffness decreased. In group B (Leflunomide group) 36 patients who had Leflunomide drug therapy showed sustained effect up to 6 months. Their functional capacity class was improved, and the duration of morning stiffness, Ritchie's joint score and rheumatoid antibody titre were decreased.
- Leflunomide drug therapy was highly effective in improves remission, improves functional capacity class and joint score and it reduced the rheumatoid antibody titre in all the cases. Leflunomide is highly effective in swollen joint count reduction, pain intensity reduction, decrease in ESR, low C-Reactive protein, Good ACR response rate, lower risk of anemia, no increase of Total leucocyte count, platelet count was unchanged, lowest elevation or unchanged S. creatinin, S. bilirubin, SGOT, SGPT and low risk of adverse reaction. No serious side effects were observed with Leflunomide.
- Hence the routine use of Leflunomide therapy is recommended for the management of rheumatoid arthritis, as it was found to be more effective and well treated by the patient in our study.

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