ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-5 | MAY - 2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

Dexamethasone and Leflunomide drug's Effect on rheumatoid arthritis

Medicine

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KEYWORDS:

The prevalence of rheumatoid arthritis is approximately 0.8% of the population (range 0.3 to 2.1%) (Lipsky, 2001). In India the prevalence is 0.75% and a rough calculation indicates that over seventy lac people are affected with this disorder (Malaviya et al., 1993, Chopara et al, 1997).

PATHOGENESIS OF RHEUMATOID ARTHRITIS

Phase	Pathological Changes	Clinical Feature
I	Interaction of genetic and environmental agents	None
II	Antigen presentation	None
III	Inflammatory cascade	Polyarthritis, juxta-articular osteopenia
IV	Cartilage and bone destruction	Severe arthritis, erosions, deformities
v	Vasculitis etc	Extra articular feature

The propagation of rheumatoid arthritis is an immunologically mediated event. The inflammatory process in the tissue is driven by the CD_4+ T cells infiltrating the synovium. (Lipsky and Davis, 1998).

Within the rheumatoid synovium the CD_4+ T cells differentiate predominantly into Th l -like effectors cells producing the proinflammatory cytokine IFN-y and appear to be deficient in differentiation into Th2-like effectors cells capable of producing the anti inflammatory cytokine IL-4. As a result of the ongoing secretion of INF-y without the regulatory influences of IL-4, macrophages are activated to produce the proinflammatory cytokine IL-1 and TNF-a and also increase expression of HLA molecules. CD 154 produce a variety of cytokines that promote p cell proliferation and differentiation into antibody forming. The resultant production of the immunoglbulin and rheumatoid factor can lead to immune complex formation with consequent complement activation and exacerbation of the inflammatory process by the production . · of the anaphylatoxins C_3a and C_5a and the chemotactic factor C_5a ·

CLINICAL FEATURES OF RHEUMATOID ARTHRITIS:

Extra-articular manifestations of Rheumatoid arthritis (Pispati, 2003) Systemic • Low grade fever • Loss of appetite • Loss of weight • Fatigue	Cardiac • Pericarditis • Myocarditis • Endocarditis • AortitisIaortic regurgitation • Conduction disturbances
Respiratory • Pleural effusion • Fibrosing alveolitis • Nodules • Bronchiolitis • Caplan' s syndrome	Haematological • Anaemia • Thrombocytosis • Eosinophilia • Felty 's syndrome • Splenomegaly
Skin • Subcutaneous nodules • Vasculitis • Ulcers • Gangrene • Pyoderma gangrenosum • Nail fold infarcts	Neurological • Entrapment syndromes • Cervical compression • Peripheral neuritis • Mononeuritis multiplex
Eye • Sicca syndrome • Scleritis • Scleromalacia • Episcleritis	Musculoskeletal • Muscle wasting • Bursitis • Tenosynovitis
Others • Systemic vasculitis (skin, CNS, lungs etc) • Amyloidosis -	

LABO RA TORY FINDINGS IN RHEUMATOID ARTHRITIS

- Anemia - nromochromic or hypochronic, normocytic.
- Thrombocytosis.
- Raised erythrocyte sedimentation rate (ESR).
- Raised C-reactive protein concentration (CRP).
- Raised ferritin concentration as acute phase protein.
- Low serum iron concentration.
- 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 (Dexamethasone 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 Dexamethasone 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 m age range 18 to 70 years who were treated with loading dose of leflunomide l OOmg 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 Dexamethasone.

INCLUSION CRITERIA

Patients of either sex, with age range 18 to 7Q years with active RA based on American College of Rheumatology Criteria (ACR) and ACR functional class I, II, III were included. The stable doses of NSAIDs and low dose Dexamethasone were allowed and treatment with other DMARDs was discontinued 4 weeks prior to enrolment.

EXCLUSION CRITERIA :

Following patients were excluded from the stl!dy viz.:

1. Infective, go.uty or traumatic arthritis.
2. Patients who were unwilling to give informed consent.
3. Pregnant and lactating women.
4. Patients (including men) planning a family.
5. Active GI tract, renal, hepatic or coagulation disorders.
6. Uncontrolled diabetes or hypertension.
7. Recent serious cardiovascular event.
8. Any condition that may interfere with patients self-assessment ability.

1. TENDER JOINT COUNTS OF SUBJECTS STUDIED

G rou p	Tender Joint Count (Mean±S.D.)				Mean Change	P value baseline v/s end point
	Time in weeks					
	0 baseline	4	8	12 end point		
Dexame thasone	19.67±5.32	20.54±5.04	20.54±4.82	21.13±4.82	1.46±0.50	> 0.05 N.S.
Lefluno mide	20.05±4.34	20.94±5.20	20.28±5.04	21.22±5.45	1.17±1.11	< 0.001 H.S.

2. SWOLLEN JOINT COUNTS OF SUBJECTS STUDIED

G roup	Swollen Joint Count (Mea n±S.D.)				Mean changes	P value baseline vis end point
	Time in weeks					
	0 baseline	4	8	12 end point		
Dexame thasone	21.24±5.76	20.70±5.44	19.94±4.88	21.67±4.79	0.43±0.97	< 0.05
Lefluno mide	21.33±4.22	21.16±4.41	20.5±4.28	20.55±4.23	-0.78± 0.01	< 0.001 H.S.

3. PAIN INTENSITY IN SUBJECTS STUDIED

Group	Pain intensity in mm (VAS) (Mean± S.D.)				Mean Change	P value base line v/s end point
	Time in weeks					
	0 baseline	4	8	12 End point		
Dexame thasone	42.02±12.94	44±13.31	41.64± 11.64	43.18±12.47	1.16±0.47	> 0.05 N .S.
Lefluno mide	45.63±10.84	47.47±11.53	43.80±12.18	42.22±10.72	-3.41±0.12	< 0.001 H .S.

SUMMARY & CONCLUSION

This study was carried out in 108 patients of classical or definite R.A. proved by A.R.A. criteria (1987).

- All the patients in group A (Dexamethasone),B (Leflunomide) are identical in all the aspects like age,sex .
- In group A 36 patients treated with high dose IV pulse dexamethasone 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 therepy, the:·ir functional capacity class increased, and duration of morning stiffness decreased ,
- In group B (Leflunomide group) 36patients who had Leflunomide drug therepy showed sustained effect up to 6 months. Their functional capacity class was improved , and the duration of morning stiffness Richie' s joint score and rheumatoid antibody titre were decresed.
- It is concluded from the study that dexamethasone is effective in patient's global assessment and physician's global assessment.
- 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, platlet 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.