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Clinical outcome of dexamethasone and methotrexate drugs on rheumatoid arthritis

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KEYWORDS :

The mechanism of action of methotrexate in RA is currently not completely understood but seems to be more than an effect on purine biosynthesis,and appears to be not cell type specific.

Leflunomide group	Methotrexate group
inhibition of IFN-alpha but not of IL6	inhibition of IFN-alpha and IL6

Serum IL6 levels of patients with RA have been associated with disease outcome, The T cell derived cytokine IFN-alpha is also produced by natural killer cells (NK cells) and is involved in nearly all phases of inflammation and in the regulation of inflammatory responses. It has effects on macrophage, B cell, and neutrophil function. The inhibition of IFN-alpha, as seen in this study, might be the result of inhibition of DHODH, which impairs T cell function with, as secondary effect, inhibition of monocyte/macrophage function. This is supported by the inhibition which occurs at concentrations of active metabolite present in patients with RA .

2.Leflunomide has also been shown to interfere with IFN-alpha induced inducible nitric oxide synthase activation and nitric oxide production in fibroblast.T cells are inhibited by leflunomide in the G1-S phase. the inhibitory effects of leflunomide are due to a combination of both inhibition of pyrimidine biosynthesis and interference with signalling events.

Radiological progression of rheumatoidarthritis (Pispati, 2003)

Stage I - Juxtaarticular osteoporosis
Stage II - Reduction and loss of joint space
Stage III - Juxtaarticular erosion
Stage IV - Deformities, sublaxation, ankylosis

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. The study design was open, Dexamethasone . controlled, randomized, prospective 24 weeks trial. The subjects selected for study were grouped as follows viz.

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 Methotrexate 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 methotrexate 7.5 mg/week.

ACR criteria for the classification of RA:

1. **Morning stiffness:** stiffness in an around the joints lasting 1 hour before maximal improvement.
2. **Arthritis of three or more joint areas :** at least three joint areas, observed by a physician simultaneously, having soft tissue swelling or joint effusions, not just bony over growth. The 14 possible joint areas involved are right or left PIP, MCP, wrist, elbow, knee, ankle and MTP joints.
3. **Arthritis of hand joints :** arthritis of wrist, MCP, PIP joints.
4. **Symmetric arthritis :** simultaneous involvement of same joint areas on both sides of the body.
5. **Rheumatoid nodules :** Subcutaneous nodules over bony prominences, extensor surfaces or juxtaarticular lesions observed by a physician.
6. **Serum Rheumatoid factor :** Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in less than 5% of normal control subjects.
7. **Radiographic changes :** Typical changes of RA on posteroanterior hand and wrist radiographs which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints.

Four of seven criteria are required to classify a patient as having rheumatoid arthritis. Patients with two or more clinical diagnosis are not excluded. Criteria 1-4 must be present for at least 6 week; criteria 2-5 must be observed by physician.

1. PATIENT GLOBAL ASSESSMENT(PGA) OF DISEASE ACTIVITY IN SUBJECTS STUDIED

Group	PGA in mm (VAS) (Mean± S.D.) Time in week				Mean Change	P value baseline v/s endpoin
	0 baseline	4	8	12end point		
Dexamethasone	48.91±14.20	50.89±13.03	50.27±13.09	45.18±14.11	-3.73±0.09	> 0.05 N.S .
Methotrexate	52.16±13.62	52±13.95	52.48±12.58	47.91±12.68	-4.25±0.94	< 0.001

2. PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN SUBJECTS STUDIED

Group	Physician ASSESSMENT (VAS) (Mean±S.D.) Time in weeks				Mean Change	P value baseline vis end point
	0 baseline	4	8	12 end point		
Dexamethasone	45.40± 13.45	45.83±14.08	44.37±13.06	44.91±12.78	0.49±0.67	> 0.05 N.S.
Methotrexate	46.37±14.01	48.86±13.87	49.94±13.55	48.43±13.30	2.06±0.69	< 0:001

3. MORNING STIFFNESS IN SUBJECTS STUDIED

Group	Morning stiffness (Mean±S.D) in min utes Time in week				Mean Change	P value baseline vis end point
	0 Baseline	4	8	12 end point		
Dexamethasone	88.27±38.95	79.64±43.22	88.43±44.34	80.40±42.32	-7.87±3.37	> 0.1 N.S.
Methotrexate	73.97±35.08	59.64±30.01	57.18±30.91	65.86±30.40	8.11±4.68	<0.1

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), and B (Methotrexate) are identical in all the aspects like age,sex .
- In group A (DEXAMETHASONE GROUP) 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 (Methotrexate group) (36patients,more effective and can be given for longer duration , and is well tolerated by the patients without any serious side effects,) Their functional capacity class was improved , and the in 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.
- While methotrexate is highly effective in low tender joint count and lowering the incidence of morning stiffness.
- Hence the routine use of Methotrexate therapy is recommen ded 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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