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A STUDY OF THE EFFICACY OF METHOTREXATE MONOTHERAPY V/S METHOTREXATE IN COMBINATION WITH INFLIXIMAB IN PATIENTS OF RHEUMATOID ARTHRITIS IN A RURAL SETUP.

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ABSTRACT

Aim : To study the efficacy of Methotrexate (MTX) monotherapy v/s Methotrexate in combination with a biological agent, Infliximab in the treatment of Rheumatoid Arthritis (RA).

Materials and Methods :- This was a randomized control trial and the study was conducted over 10 months in the patients attending the OPD and admitted in the wards of S.G.T. Medical College, Budhera, Gurgaon. 50 patients were studied and the inferences made. Out of these, 27 patients received monotherapy with MTX whereas 23 received combination therapy of MTX and the biological agent infliximab.

Results :- In our study the patients receiving the dual therapy with MTX and Infliximab fared better than the patient who received monotheraphy with MTX alone which was also shown by the highly significant p-value ($p < 0.01$) in the patients treated with the combination therapy.

Conclusion: - Our study showed that the patients who are treated with a combination of MTX and infliximab early in the disease fare better. So, the use of biological agents should be preferred early in the RA to prevent the complications an deformities of rheumatoid arthritis from occuring. One of the limiting factors in this regards may be the cost of the biological agent.

KEYWORDS

Rheumatoid Arthritis, Methotrexate, Infliximab.

Introduction:-

Rheumatoid Arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by symmetric peripheral polyarthritis. It is most common form of chronic inflammatory arthritis and results in joint damage and physical disability.[1]

The last 2 decades have witnessed a remarkable improvement in the outcomes of RA. The historic descriptions of crippling arthritis are currently encountered much less frequently. This progress can be traced to the expanded therapeutic armamentarium and the adoption of early treatment intervention.[1]

The clinical diagnosis of RA is largely based on signs and symptoms of a chronic inflammatory arthritis, with lab and radiographic results providing important supplemental information.

Disability as measured by the Health Assessment Questionannaire (HAQ) shows gradual worsening of disability over time or improvement with treatment. Previous studies have shown that more than half of patients with RA are unable to work 10 yrs after the outset of the disease; however increased employability and less work absenteeism has been reported recently with the use of newer therapies an earlier treatment investigations. Early in the course of the disease, the extent of the joint inflammation is the primary determinant of the disability.[2]

The ACR response criteria can be applied to patients to know the improvement in the patients with treatment.

ACR RESPONSE CRITERIA :-

It is a standard criteria to measure the effectiveness of various arthritis medications or treatments in clinical trials for Rheumatoid Arthritis.

The ACR criteria is used to maximally discriminate the effective treatment from placebo treatment in clinical trials. The ACR is reported as percentage improvement, comparing disease activity at two discrete time points (usually base line & post-baseline comparison).

- ACR 20 is > 20% improvement
- ACR 50 is > 50% improvement
- ACR 50 responders include ACR 20 responders
- ACR 70% is > 70% improvement
- ACR 70 responders include ACR 20 & ACR 50 responders

Definition :-

The ACR criteria is a dichotomous variable with a positive (responder) or negative (non-responder) outcome. The ACR criteria measures improvement in tender/swollen joint counts consisting of improvement in at least 3 of the following parameters :-

1) Patient assessment
2) Physician assessment
3) Pain scale
4) Disability / final questionnaire
5) Acute phase reactant (ESR, CRP)

ACR 20 has a positive outcome if 20% improvement in tender /swollen joint counts were achieved as well as a 20% improvement in at least 3 out of the 5 criteria.

ACR 50 has a positive outcome if 50% improvement in tender/swollen joint counts were achieved as well as a 50% improvement in at least 3 out of the 5 criteria.

ACR 70 has a positive outcome if 70% improvement in tender or swollen joint counts were achieved as well as 70 improvement in at least 3 out of the 5 criteria.

Several developments during the past decades have changed the therapeutic landscape in Rheumatoid Arthritis. They include :-

a) The emergence of methotrexate as the disease modifying anti-rheumatic drug (DMARD) of first choice for the treatment of early Rheumatoid Arthritis (RA).
b) The development of novel highly efficacious biologicals that can be used alone or the combination with methotrexate.[3]

Methotrexate is the DMARD of choice for the treatment of RA and is the anchor drug in most combination therapies. It was approved for treatment of RA in 1986 and remains the bench mark for efficacy and safety of new disease-modifying therapies. At the dosages used for treatment of RA, methotrexate has been shown to stimulate adenosine release from cell, producing an anti-inflammatory effects.[3]

Biologic DMARDs have revolutionized the treatment of RA over the past decade. They are protein therapeutics designed mostly to target cytokines and cell-surface molecules. The TNF-inhibitors were the first biologicals approved for treatment in RA.[4]

Infliximab is a chimeric monoclonal Ab Anti-TNF agent. It is typically used in combination with background methotrexate therapy. This combination regimen, which affords maximal benefits in may cases, is often the next step for treatment of patients with an inadequate response to methotrexate therapy.

Anti-TNF agents should be avoided in patients with active infection or a history of hypersensitivity to these agents and are contraindicated in patients with chronic hepatitis B infection or class III/IV congestive heart failure. All patients are screened for latent TB according to the national guidelines prior to starting anti-TNF therapy.

AIM :-

To study the efficacy of Methotrexate monotherapy v/s Methotrexate in combination with Infliximab in patients of Rheumatoid Arthritis in a rural set-up.

Inclusion criteria :- All patients attending the medicine OPD and admitted in the wards of Medicine department, having arthritis and positive RA factor were included in the study.

Exclusion criteria :-

All the patients who had common medical problems like diabetes mellitus, coronary artery disease (CAD), tuberculosis, kidney disease were excluded from the study.

Materials and methods :-

This was a randomized control study (RCT) done at S.G.T. Medical College, Budhera, Gurgaon, in the department of Medicine. The study period was from 01 March 2014 to 31st December 2014. i.e. 10 months. Approval for the study from the institutional ethics committee was taken.

Data was collected from the patient records in the OPD cards of the patients attending the OPD and from the records of the patients in the wards for admitted patients. Demographic details and the pre-existing medical problems were also noted. Patients were randomly assigned to the two treatment groups.

Data regarding the kidney function tests, blood sugar, previous history of tuberculosis, cardiac problems were gathered. Patients having derangements in these were excluded from the study. Tuberculosis was ruled out in the patients receiving Infliximab.

62 patients were enrolled in the study out of which 12 were excluded due to to the patients having the exclusion criteria.

So, 50 patients were studied and the inferences made. These were the patients who had clinical features of Rheumatoid Arthritis and had positive RA factor test. These patients had treatment with methotrexate alone or methotrexate in combination with infliximab.

Out of the 50 patients studies 27 patients had received treatment with methotrexate alone. 23 patients had received treatment with methotrexate in combination with infliximab.

Table –I Table showing the demographic profiles of the patients

Age group	No. of Cases	%
20-30 Yrs	5	10
30-40 yrs	7	14
40-50 yrs	28	56
50-60	10	20

Table II Table showing the distribution of the treatment groups

Treatment	No. of Cases	%
Methotrexate	27	54
Mtx + Infliximab	23	46

Table III

Treatment	Improvement in No. of cases by ACR criteria	%	p-value
Methotrexate	10	37.04	> 0.05
Mtx + Infliximab	15	65.22	< 0.01

Inferences regarding the improvements occurring in the patients were made based on the relief from the symptoms of joint pains and also the clinical improvement occurring in the patients as observed by decreased joint swelling by applying the ACR 50 criteria.

Discussion :-

Most of the patients in the study were between the age of 40-50 yrs. This also represents the most common age of the occurence of RA. Out the 50 cases which were enrolled in the study 27 were treated with methotrexate alone, and 23 patients were treated with the combination of MTX and Infliximab. Both the groups showed improvement with treatment. The group treated with a combination of methotrexate and infliximab had a better outcomes as compared to the group in which the treatment was given with methotrexate alone. This indicates that when biologicals are used in combination with methotrexate very early in the disease, the outcome and relief from the symptoms for the patients is better. It prevents the crippling arthritis from occuring. This is shown by the p-value in our study which was highly significant in the patients receiving the combination therapy of Methotrexate with Infliximab.[4]

Conclusion :-

Our study indicates that out of the large number of modalities available for the treatment of RA, whenever possible biological agents like infliximab should be added early to the patients to achieve a better outcome. The only drawback is the cost of the therapy but the benefits of the treatment outweigh the drawbacks.

References :-

1) LM Pedersen, H Nordin, B Svensson, H Bliddal. Microalbuminuria in patients with rheumatoid arthritis: Ann Rheum Dis. 1995 Mar; 54(3): 189-192.
2) Megan L Krasue, Cynthia S Crowson, Tim Bongarta, Eric L Matteson, Clement J Michet, Thomas G Mason. Determinants of disability in Rheumatoid Arthritis: A community based cohort study. Open Rheumatol J. 2015; 9: 88-93.
3) Jurgen Braun : Optimizing the Efficacy in Rheumatoid Arthritis. Ther Adv Musculokelet Dis. 2011 Jun; 3(3) : 151-158.
4) Jeffery R Curtis, Jasvinder A Singh. The use of Biologics in Rheumatoid Arthritis : Current and emerging paradigms of care; Clin Ther. 2011 Jun; 33(6): 679-707.