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The Effect of Low Dose Methotrexate in Rheumatoid arthritis Bangladeshi Patients

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Abstract **Original Research Article**

Background*:** Rheumatoid arthritis is a painful, disabling joint condition characterized by synovium growth and progressive cartilage and bone loss. Methotrexate (MTX) has been used to treat Rheumatoid Arthritis (RA) for over three decades. Because it improves symptoms, signs, disease activity, and functions, it is one of the most effective and widely used Disease Modifying Antirheumatic Drugs (DMARDS). ***Objective*:** In this study our main goal is to evaluate the effect of low dose Methotrexate in Rheumatoid arthritis. ***Method*:** This cross-sectional study was carried out at tertiary medical hospital from June 2021 to June 2022. Where a total of 100 patients of Rheumatoid Arthritis were attended OPD were included as a sample size. Patients were prescribed low dose methotrexate 5-10mg/ week. Folate supplementation in the form of folic acid was also given to all patients. ***Results*:** During the study, majority were belonging to >60 years age group, 65% and most of them were male. 80% had high APR before treatment and 35% had low APR after treatment with MTX. 70% had swollen joints and 80% had tender joints before treatment. After treatment it reduced to 11% swollen joints and 45% tender joints. Moreover, At 0 week, 55% patients were in high disease activity (DAS 28>5.1), 43% patients were in moderate disease activity (DAS 28 between 3.2-5.1) and 2% patients were in low disease activity (DAS 28 <3.2). AT 4th week, 20% were in high disease activity, 65% were in moderate disease activity and 15% were in low disease activity. At 8th week, 70% were in moderate disease activity and 30% were in low disease activity. At 12th weeks, 60% were in moderate disease activity and 40% were in low disease activity. ***Conclusion: From our study, we found that low-dose MTX improves symptoms, signs, disease activity, and functions, and that early management with DMARDs in annual RA provides the least possibility for disease remission.

Keywords: Rheumatoid Arthritis (RA), methotrexate (MTX), Disease Modifying Antirheumatic Drugs (DMARDS).

INTRODUCTION

Rheumatoid Arthritis is a systemic autoimmune disease characterized by persistent polyarticular synovial inflammation caused by elevated cytokine release, which can result in irreparable joint destruction [1-3].

It has a frequency of around 0.5 to 1 percent. It mainly affects middle-aged people, with females being more impacted than males. The condition has a direct impact on physical function and movement, resulting in significant short- and long-term morbidity [4].

According to study, from mid 1980s MTX used as the DMARD after clinical trials proved its efficacy in RA. It interferes with an enzyme important to DNA replication and inhibits cell reproduction that's why it is called “immunosuppressive” drug. MTX is also referred as a “disease modifying antirheumatic drugs or DMARD” as it can modify the course of the incurable disease.

It inhibits the formation of polyamines that reduce production of rheumatoid factor and increase adenosine concentration and reduce cytokines [5, 6].

In this study our main goal is to evaluate the effect of low dose Methotrexate in Rheumatoid arthritis.

OBJECTIVE

- To evaluate the effect of low dose Methotrexate in Rheumatoid arthritis.

METHODOLOGY

This cross sectional study was carried out at tertiary medical hospital from June 2021 to June 2022. Where a total of 100 patients of Rheumatoid Arthritis were attended OPD were included as a sample size. Proper history was taken. Clinical examinations and baseline investigations were done to detect the cases after discussion of the nature of study.

Patients were prescribed low dose methotrexate 5-10mg/ week. Folate supplementation in the form of folic acid was also given to all patients. All relevant information from history, clinical examination and investigations were collected in a semi-structured data collection sheet. Collected data were processed and analyzed by using computer based software, statistical package for Social Science (SPSS).

RESULTS

In table-1 shows age distribution of the study group where majority were belonging to >60 years age group, 65%. Followed by 25% belong to 41-50 years group and 10% belong to 31-40 years age group. The following table is given below in detail:

Table-1: Age distribution of the patients

Age group	%
31-40 years	10%
41-50	25%
>60 years	65%

In Figure-1 shows gender distribution of the study group where majority were male, 69.44%. The following figure is given below in detail:

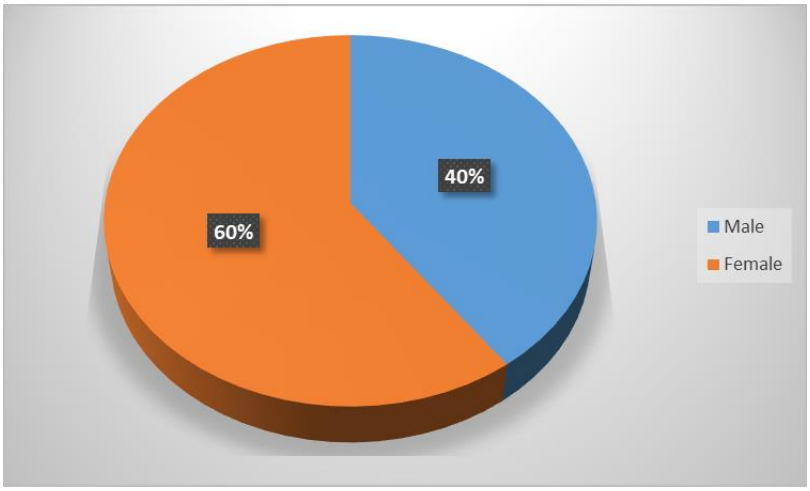

Figure-1: Gender distribution of the patients

In Table-2 shows response of acute phase reactant (APR) where 80% had high APR before treatment and 35% had low APR after treatment with MTX. The following table is given below in detail:

Table-2: Response of acute phase reactant (APR)

Acute phase reactant	Before treatment, %	After treatment, %
High	80%	-
Low	-	35%

In table-3 shows pre and post treatment response of MTX on joints before and after treatment. Where 70% had swollen joints and 80% had tender joints before treatment. After treatment it reduced to 11% swollen joints and 45% tender joints. The following table is given below in detail:

Table-3: Pre and post treatment response of MTX on joints before and after treatment

Variable	Before treatment, %	After treatment, %
Swollen joint	70%	11%
Tender joint	80%	45%

In figure-2 shows sero positivity where s rheumatoid factor positive in 80% cases and Anti CCP (anti citrulinated pyrophosphate) positive in 20% cases. The following figure is given below in detail:

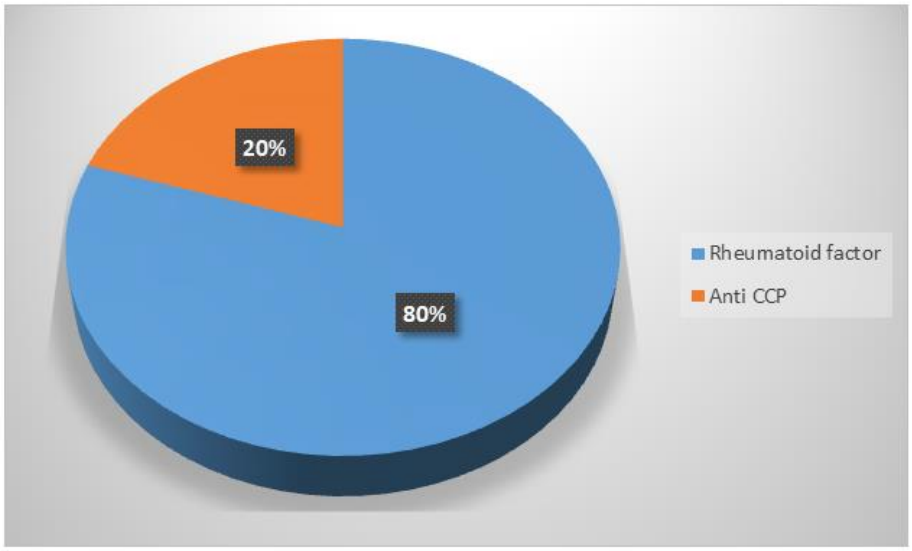

Figure-2: Sero positivity

In table-4 shows pre and post treatment disease activity. Where At 0 week, 55% patients were in high disease activity (DAS 28>5.1), 43% patients were in moderate disease activity (DAS 28 between 3.2-5.1) and 2% patients were in low disease activity (DAS 28 <3.2). AT 4th week, 20% were in high disease activity, 65% were in moderate disease activity and 15% were in low disease activity. At 8th week, 70% were in moderate disease activity and 30% were in low disease activity. At 12th weeks, 60% were in moderate disease activity and 40% were in low disease activity. The following table is given below in detail:

Table-4: Pre and post treatment disease activity

Variable	0 week, %	4th week, %	8th week, %	12th week, %
High disease activity DAS 28->5.1	55%	20%		
Moderate disease activity DAS 28 ≥ 3.2-5.1	43%	65%	70%	60%
Low disease activity DAS 28 ≤ 3.2	2%	15%	30%	40%

DISCUSSION

In 2009 one study showed MTX improved signs, symptoms, disease activity and functions to a similar degree as the TNF alpha blockers in monotherapy [7].

Whereas a study on 1160 patients of rheumatoid arthritis who was treated with DMARD-methotrexate, hydroxychloroquine, and injectable gold [8].

Methotrexate the most effective DMARD among three because of the length of therapeutic segment [9].

Another study examined small group of patients and commented who received MTX showed rapid and greater improvement [10].

In this study before treatment high ESR were found in 80% cases. But it reduced to 35 % after treated with MTX. In a study where ESR & CRP measured after administration of MTX and showed decrease level of ESR and CRP indicates rapid clinical effect of drug in RA [11].

Here in this study we prescribe MTX at a dose 5-25 mg every weekly. In one study on 32 patients of RA with low dose MTX range 7.5 to 10 mg weekly and showed improvement in 75% patients [12].

Another study showed improvement of 45 of the 78 (58%) RA patients within 4 weeks after treatment with MTX [13].

Other study showed response of RA among twenty nine patients. 11of them had major clinical improvement and 14 had moderate improvement [14]. But when the dose of MTX reduced below 10mg every week or when discontinued, a flare of arthritis occurred in more than 80 % of the patients [15].

In this study response of MTX on joints showed 70% had swollen joints and 80% had tender joints before treatment. After treatment it reduced to 11% swollen joints and 45% tender joints.

A randomized trial on 133 patients of RA with oral MTX. After two years of therapy he found marked improvement in acute phase reactant, joint pain, tenderness index and joint swelling Index [11].

In this study at 0 week, 55% patients were in high disease activity (DAS 28>5.1), 43% patients were in moderate disease activity (DAS 28 between 3.2-5.1) and 2% patients were in low disease activity (DAS 28 <3.2). AT 4th week, 20% were in high disease activity, 65% were in moderate disease activity and 15% were in low disease activity. At 8th week, 70% were in moderate disease activity and 30% were in low disease activity. At 12th weeks, 60% were in moderate disease activity and 40% were in low disease activity.

Whereas other study concluded that there where reduction in disease activity during one year follow up. DAS was 5.8± 0.8 (high disease activity) at early and 3.9 ± 1.3 (moderate disease activity) at one year later [9].

CONCLUSION

From our study, we found that low-dose MTX improves symptoms, signs, disease activity, and functions, and that early management with DMARDs in annual RA provides the least possibility for disease remission.

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