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ORIGINAL ARTICLE

A comparison of Methotrexate and hydroxychloroquine with leflunomide in active rheumatoid arthritis

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ABSTRACT:

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that primarily affects the joints but can also impact other organs and systems in the body. The present study was conducted to compare methotrexate and hydroxychloroquine with leflunomide in active rheumatoid arthritis. **Materials & Methods:** 120 rheumatoid arthritis patients of both genderswere divided into 2 groups of 60 each. Group I received a combination of drugs, namely 7.5 mg/week tablet methotrexate and 200 mg tablet hydroxychloroquine daily. Group II received 10 mg tablet leflunomide daily. Parameters were compared in both groups. **Results:** Group I had 25 males and 35 females and group II had 32 males and 28 females. The mean total joint count was 19.4 in group I and 19.8 in group II. Swollen joint count was 8.2 in group I and 10.4 in group II. VAS was 84.2 in group I and 89.7 in group II. Disease activity score was 6.3 in group I and 6.9 in group II. The difference was significant (P< 0.05).Disease activity score in group I and group II, at baseline was 6.3 and 6.9, at 6th week was 5.2 and 5.8, and at 12th week was 3.4 and 3.9 respectively. The difference was significant (P< 0.05). **Conclusion:** For the initial treatment of severe rheumatoid arthritis, the combination of methotrexate and hydroxychloroquine is as effective in lowering disease activity as leflunomide.

Keywords: Rheumatoid arthritis, hydroxychloroquine, methotrexate

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease that primarily affects the joints but can also impact other organs and systems in the body. It is characterized by inflammation of the synovium (the lining of the joints), which can lead to pain, stiffness, swelling, and joint deformity.[1] RA typically affects multiple joints symmetrically and can cause significant disability if left untreated.Rheumatoid arthritis occurs when the immune system mistakenly attacks the body's own tissues, particularly the synovium, leading to chronic inflammation.[2]Family history of RA increases the risk of developing the condition, suggesting a genetic predisposition.Certain environmental triggers, such as smoking, hormonal changes, infections, or exposure to pollutants, may contribute to the development or progression of RA.Women are more likely to develop RA than men.Rheumatoid arthritis can develop at any age, but onset is most common between the ages of 30 and 60.[3]

Methotrexate and hydroxychloroquine are both commonly used medications in the treatment of rheumatoid arthritis (RA). They belong to different classes of drugs and can be used alone or in combination to help manage symptoms and slow the progression of the disease.[4]Leflunomide is another disease-modifying antirheumatic drug (DMARD) used in the treatment of active rheumatoid arthritis (RA), particularly in individuals who have not responded adequately to conventional therapies such as methotrexate or who cannot tolerate methotrexate.[5]The present study was conducted to compare methotrexate and hydroxychloroquine with leflunomide in active rheumatoid arthritis.

MATERIALS & METHODS

The present study consisted of 120 rheumatoid arthritis patients of both genders. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 60 each. Group I received a combination of drugs, namely 7.5 mg/week tablet methotrexate and 200 mg tablet hydroxychloroquine daily. Group II received 10 mg tablet leflunomide daily. Parameters were compared in both groups. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Groups	Group I	Group II
Drug	MTX + HCQ	LEF
M:F	25:35	32:28

Table I shows that group I had 25 males and 35 females and group II had 32 males and 28 females.

Table II Comparison of parameters

Parameters	Group I	Group II	P value
Total joint count	19.4	19.8	0.81
Swollen joint count	8.2	10.4	0.15
VAS	84.2	89.7	0.27
Disease activity score	6.3	6.9	0.84

Table II, graph I shows that mean total joint count was 19.4 in group I and 19.8 in group II. Swollen joint count was 8.2 in group I and 10.4 in group II. VAS was 84.2 in group I and 89.7 in group II. Disease activity score was 6.3 in group I and 6.9 in group II. The difference was significant (P< 0.05).

Graph I Comparison of parameters

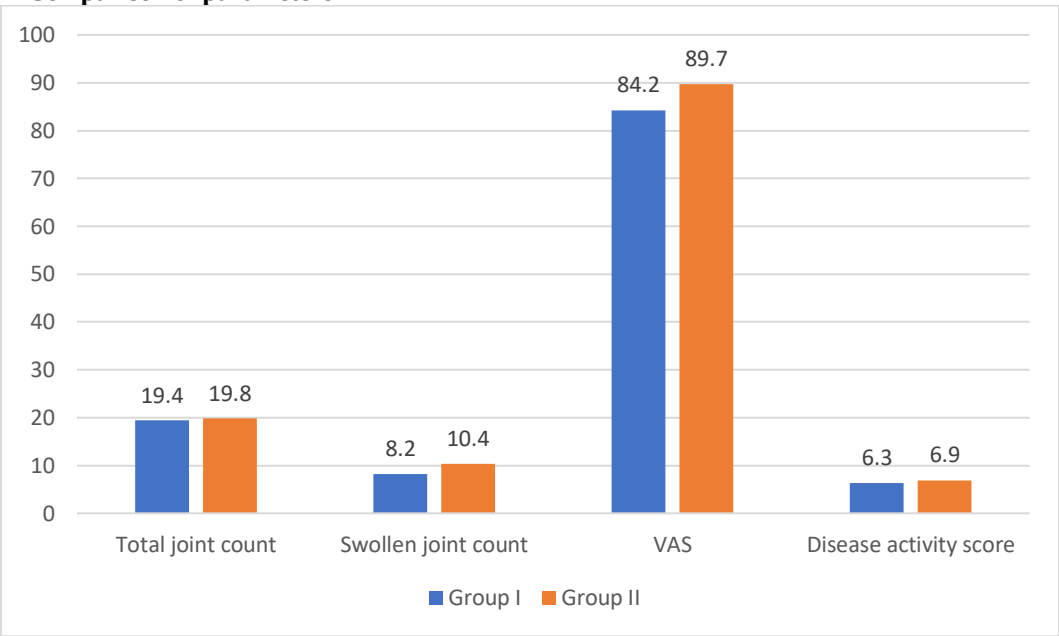

Table III Comparison of disease activity score

Disease activity score	Group I	Group II	P value
Baseline	6.3	6.9	0.81
6th week	5.2	5.8	0.54
12th week	3.4	3.9	0.71

Table III shows that disease activity score in group I and group II, at baseline was 6.3 and 6.9, at 6th week was 5.2 and 5.8, and at 12th week was 3.4 and 3.9 respectively. The difference was significant (P< 0.05).

DISCUSSION

Methotrexate and hydroxychloroquine are often used together as combination therapy in the treatment of RA, particularly in individuals with moderate to severe disease or inadequate response to monotherapy.[6]Combining these medications can provide additive or synergistic effects, allowing for better control of symptoms and potentially reducing the need for higher doses of individual medications. However, combination therapy may also increase the risk of side effects, so careful monitoring and dose adjustments are necessary.[7]

Leflunomide works by inhibiting dihydroorotate dehydrogenase, an enzyme involved in the synthesis of pyrimidine, which is necessary for the proliferation of activated lymphocytes. By suppressing the proliferation of lymphocytes, leflunomide helps reduce inflammation and slow the progression of joint damage in RA.[8]Leflunomide has been shown to be effective in reducing the signs and symptoms of RA, including joint pain, swelling, stiffness, and fatigue.It can also improve physical function and quality of life in individuals with active RA.Leflunomide is often used as monotherapy or in combination with other

DMARDs, such as methotrexate, to achieve better disease control and improve treatment outcomes.[9]The present study was conducted to compare methotrexate and hydroxychloroquine with leflunomide in active rheumatoid arthritis.

We found that group I had 25 males and 35 females and group II had 32 males and 28 females. Shashikumaret al[10]evaluated the efficacy of combination of methotrexate and hydroxychloroquine with leflunomide, a new disease modifying antirheumatoid drug. Analysis was of intent to treat group. Patients who have diagnosed with rheumatoid arthritis as per American College of Rheumatology aged between 18 and 60 years were recruited and randomized to receive leflunomide (10 mg/day p.o.) or a combination of methotrexate and hydroxychloroquine (7.5 mg/week p.o. and 200 mg/day p.o., respectively) along with folate supplementation for 12 weeks. The European League Against Rheumatism criteria of improvement according to disease activity score 28 was considered as the primary efficacy variable. Baseline and end of study values were evaluated. After 12 weeks, improvement noted in patients treated with leflunomide was similar to those treated with a combination of methotrexate and hydroxychloroquine. There was no statistical significance in improvement in disease activity between the two groups (P = 0.377).

We found that mean total joint count was 19.4 in group I and 19.8 in group II. Swollen joint count was 8.2 in group I and 10.4 in group II. VAS was 84.2 in group I and 89.7 in group II. Disease activity score was 6.3 in group I and 6.9 in group II. We found that disease activity score in group I and group II, at baseline was 6.3 and 6.9, at 6th week was 5.2 and 5.8, and at 12th week was 3.4 and 3.9 respectively. Mladenovic V et al[11]assessed the safety and effectiveness of leflunomide versus placebo in patients with active rheumatoid arthritis (RA) treated for 6 months.Four hundred two patients were randomly assigned to receive placebo or leflunomide at 5 mg, 10 mg, or 25 mg daily. Statistically significant improvement in primary and secondary outcome measures, as well as by responder analyses, occurred in the 10-mg and 25-mg dosage groups compared to placebo. Twenty-one patients (7.0%) in the active treatment groups withdrew due to adverse events (AEs). The incidence of AEs was higher with leflunomide than with placebo. Gastrointestinal symptoms, weight loss, allergic reactions, skin rash, and reversible alopecia were more common in the 10-mg and 25-mg dosage groups. The incidence of infections was similar between the treatment and placebo groups; no opportunistic infections were seen. Transient elevations in liver function studies were noted in a small number of patients.

The limitation of the study is the small sample size.

CONCLUSION

Authors found that for the initial treatment of severe rheumatoid arthritis, the combination of methotrexate and hydroxychloroquine is as effective in lowering disease activity as leflunomide.

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