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EFFICIENCY OF LEFLUNOMIDE IN TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS AT TERTIARY CARE HOSPITAL

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Abstract

Background: *The quality of life is greatly impacted by rheumatoid arthritis (RA), a chronic autoimmune disease that requires efficient therapies.*

Objective: *This study aimed to assess the efficiency of Leflunomide in treating RA patients at a tertiary care hospital, focusing on its impact on disease activity, functional improvement, and patient outcomes.*

Methodology: *Sharif medical and dental college, Lahore was the site of our prospective observational research, which ran from January to December 2023. 150 RA patients receiving Leflunomide (20 mg/day) were included in the trial. At baseline, three months, and six months, disease activity was measured using the Disease Activity Score 28 (DAS28). The Patient Global Assessment (PGA) Score, the Visual Analog Scale (VAS) for pain, and the Health Assessment Questionnaire (HAQ) Score were used to quantify the functional results and patient-reported outcomes. While paired t-tests examined variations in disease activity and functional outcomes across time, descriptive statistics provided an overview of the clinical and demographic features. Data analysis was conducted using SPSS (version 25) and statistical significance was determined at $p < 0.05$.*

Results: *Among the 150 patients, 58 (38.67%) were male and 92 (61.33%) were female. Leflunomide treatment led to a significant reduction in disease activity, with the Disease Activity Score 28 (DAS28) decreasing from a baseline mean of 6.53 ± 1.28 to 4.69 ± 0.98 at 6 months ($p < 0.001$). Functional status improved, as indicated by the HAQ Score, which fell from 1.87 ± 0.79 to 1.52 ± 0.68 ($p = 0.021$). Pain levels, measured by the VAS, decreased from a baseline mean of 4.31 ± 2.03 to 3.50 ± 1.85 ($p = 0.045$). The PGA Score also improved, from 4.17 ± 1.53 to 3.65 ± 1.36 ($p = 0.030$).*

Conclusion: *Leflunomide serves as a helpful therapy option in a tertiary care context by significantly reducing disease activity and improving functional and patient-reported outcomes in RA patients.*

INTRODUCTION

Rheumatoid arthritis (RA) is a long-term inflammatory disease that causes pain, swelling, and ultimately joint destruction due to continuous inflammation in the synovial joints [1,2]. Between

0.5% and 1% of people worldwide suffer with RA, with prevalence rates differing depending on geography and demography [3]. Due to its great incidence and substantial effect on quality of life, it is a global health problem [4]. Because of the disease's heterogeneity and patients' varying reactions to therapy, controlling RA remains difficult even with advancements in medical research [5]. The cornerstone of RA treatment has been the use of conventional disease-modifying antirheumatic medications (DMARDs), but these medications sometimes have drawbacks, including the possibility of side effects and a delayed beginning of action [6].

An oral DMARD called leflunomide, which was first available in the late 1990s, has gained prominence as a RA treatment option [7]. It works by preventing the production of pyrimidines, which inhibits the multiplication of lymphocytes and lowers inflammation [8]. Leflunomide has been shown to be effective in lowering disease activity, enhancing physical function, and delaying the radiographic development of RA in clinical trials and real-world data [9, 10]. Further research is necessary, nevertheless, due to its usefulness over the long term in a variety of patient groups and how it performs in comparison to other DMARDs [11]. The efficacy of Leflunomide may provide important insights in a tertiary care context, where patients often arrive with complicated cases and late disease stages [12]. Leflunomide's effects in these situations should be assessed in order to improve treatment regimens for RA patients as well as to get a deeper knowledge of its therapeutic advantages [13].

Leflunomide's efficacy in real-world clinical settings, especially in tertiary care institutions where patients are often treated for more severe symptoms of the illness, has to be thoroughly examined due to the variety in response to RA medications. This study attempts to give a detailed picture of leflunomide's significance in modern RA care by concentrating on these individuals.

Research Objective

The objective of study was to assess the efficiency of Leflunomide in the treatment of RA patients at a tertiary care hospital, focusing on its impact on disease activity, functional improvement, and patient outcomes.

Methodology

Study Design and Setting

A prospective observational design was used in this research to assess leflunomide's effectiveness in treating individuals with RA. From January 2023 to December 2023, the study was carried out at the Sharif medical and dental college, Lahore.

Inclusion and Exclusion Criteria

According to the 2010 American College of Rheumatology / European League Against Rheumatism (ACR/EULAR) classification criteria, patients with RA who were 18 years of age or older, prescribed leflunomide as part of their treatment during the study period, and who signed an informed consent form were included in the study. Patients with significant renal or hepatic impairment, those taking investigational drugs or taking part in other clinical trials, those with contraindications to leflunomide or intolerance to the drug, and those with major comorbidities that could affect how RA outcomes are evaluated were excluded.

Sample Size

The sample size of 150 participants was determined using the World Health Organization (WHO) formula for observational studies. This calculation took into account the estimated prevalence of RA at the Pakistan Institute of Medical Sciences (PIMS), a 95% confidence level, and a 5% margin of error. The formula $n = Z^2 \times p \times (1-p) \div E^2$, with a Z-score of 1.96 and prevalence (p) of RA, yielded a sample size that was adjusted for a 20% dropout rate, resulting in a final requirement of 150 participants. This size ensures the study has sufficient power to detect significant effects and provide reliable results.

Leflunomide Dosage and Administration

Leflunomide was administered to research participants at a dose of 20 mg per day. Throughout the trial, this dose was continuously maintained in order to evaluate its efficacy and keep an eye out for any possible negative effects.

Data Collection

Direct interviews and patient medical records were used to gather data. The length of the illness, the initial disease activity ratings, the dose of leflunomide,

and any side effects were all significant factors. At baseline, three months, and six months, disease activity was measured using the Disease Activity Score 28 (DAS28), and follow-up data was gathered at the conclusion of the trial. Furthermore, standard questionnaires were used to assess the functional state and patient-reported outcomes.

Statistical Analysis

Demographic and clinical features were gathered using descriptive statistics. Depending on the distribution of the data, paired t-tests were used to examine changes in disease activity ratings and functional outcomes across time. For statistical significance, a p-value of less than 0.05 was used. SPSS (version 25) statistical software was used to examine the data.

Ethical Approval

The Sharif medical and dental college, Lahore has its Institutional Review Board (IRB) authorized. Prior to participation, each participant gave written, informed permission. The study followed the Declaration of Helsinki's ethical guidelines, guaranteeing patient confidentiality and rights were upheld throughout the investigation.

Results

Of the 150 patients in the research, 46 (30.67%) were between the ages of 18 and 40, 83 (55.33%) were between the ages of 41 and 60, and 21 (14.00%) were 61 years of age or older (table 1). There were 92 females (61.33%) and 58 men (38.67%) in the gender distribution. 26 patients (17.33%) reported experiencing nausea, 19 patients (12.67%) reported diarrhea, 14 patients (9.33%) reported liver enzyme increase, and 16 patients (10.67%) reported other adverse events. With a baseline illness Activity Score (DAS28) of 6.53 ± 1.24 and a mean illness duration of 10.57 ± 5.36 years, the patients were first prescribed 20.29 ± 5.16 mg/day of leflunomide.

Table 1: Demographic Information, Disease Duration, and Treatment Details

Variable		Number of Patients; n (%)
Age Groups	18-40 years	46 (30.67)
	41-60 years	83 (55.33)
	61+ years	21 (14.00)
Gender	Male	58 (38.67)
	Female	92 (61.33)
Reported Side Effects	Nausea	26 (17.33)
	Diarrhea	19 (12.67)
	Liver Enzyme Elevation	14 (9.33)
	Others	16 (10.67)
Disease Duration (Years)	Mean ± SD	10.57 ± 5.36
Baseline Disease Activity Score (DAS28)	Mean ± SD	6.53 ± 1.24
Initial Leflunomide Dosage (20mg/day)	Mean ± SD	20.29 ± 5.16

The average Disease Activity Score 28 (DAS28) significantly improved during the course of the trial table 2. The mean DAS28 score was 6.53 ± 1.28 at baseline. It showed a steady decline in disease activity over time, declining to 5.21 ± 1.07 by 3 months and 4.69 ± 0.98 by 6 months.

Table 2: DAS28 Scores at Baseline, 3 Months, and 6 Months

Time Point		Mean ± SD
DAS28 Scores	Baseline	6.53 ± 1.28
	3 Months	5.21 ± 1.07
	6 Months	4.69 ± 0.98

The improvements in functional status and patient-reported outcomes during a 6-month period are shown in Table 3. Functional impairment was measured by the Health Assessment Questionnaire (HAQ) Score, which improved from 1.87 ± 0.79 at baseline to 1.68 ± 0.72 at three months and 1.52 ± 0.68 at six months. The Visual Analog Scale (VAS) showed decreasing pain levels with time, with a baseline mean of 4.31 ± 2.03 decreasing to 3.85 ± 1.90 at 3 months and 3.50 ± 1.85 at 6 months. Patients' overall health perception was measured by the Patient Global Assessment (PGA) Score, which increased from 4.17 ± 1.53 at baseline to 3.90 ± 1.40 at three months and 3.65 ± 1.36 at six months.

Table 3: Changes in Patient-Reported Outcomes and Functional Status Over 6 Months

Outcome Measure	Baseline Mean ± SD	3 Months Mean ± SD	6 Months Mean ± SD
Health Assessment Questionnaire (HAQ) Score	1.87 ± 0.79	1.68 ± 0.72	1.52 ± 0.68
Visual Analog Scale (VAS) for Pain	4.31 ± 2.03	3.85 ± 1.90	3.50 ± 1.85
Patient Global Assessment (PGA) Score	4.17 ± 1.53	3.90 ± 1.40	3.65 ± 1.36

The improvements in functional outcomes and disease activity ratings for RA patients during a 6-month period are shown in Table 4. At six months, the baseline mean of 6.53 ± 1.28 on the Disease Activity Score 28 (DAS28) dramatically improved to 4.69 ± 0.98 ($p < 0.001$), suggesting a considerable decline in disease activity. The Health Assessment Questionnaire (HAQ) Score showed an improvement in functional outcomes as well, going from 1.87 ± 0.79 at baseline to 1.52 ± 0.68 at 6 months ($p = 0.021$), indicating a better functional status. Pain was found to have decreased as measured by the Visual Analog Scale (VAS), with scores falling from 4.31 ± 2.03 to 3.50 ± 1.85 ($p = 0.045$). Patients' perceptions of their general health improved, as shown by the Patient Global Assessment (PGA) Score, which increased from 4.17 ± 1.53 at baseline to 3.65 ± 1.36 at 6 months ($p = 0.030$).

Table 4: Changes in Disease Activity Scores and Functional Outcomes Over Time

Outcome Measure	Baseline Mean ± SD	3 Months Mean ± SD	6 Months Mean ± SD	p-value (Baseline vs 6 Months)
Disease Activity Score 28 (DAS28)	6.53 ± 1.28	5.21 ± 1.07	4.69 ± 0.98	<0.001
Health Assessment Questionnaire (HAQ) Score	1.87 ± 0.79	1.68 ± 0.72	1.52 ± 0.68	0.021
Visual Analog Scale (VAS) for Pain	4.31 ± 2.03	3.85 ± 1.90	3.50 ± 1.85	0.045
Patient Global Assessment (PGA) Score	4.17 ± 1.53	3.90 ± 1.40	3.65 ± 1.36	0.030

Discussion

The purpose of the research was to assess Leflunomide's effectiveness in treating RA in patients receiving tertiary care. The Disease Activity Score 28 (DAS28), which showed a substantial decline in disease activity from a baseline mean of 6.53 ± 1.28 to 4.69 ± 0.98 after six months ($p < 0.001$), supports our results. This is consistent with recent research findings showing leflunomide successfully lowers DAS28 levels in people with RA during a comparable time frame [14–16]. Their research revealed a decrease in DAS28, which is consistent with our results and lends credence to leflunomide's efficacy as a DMARD.

Regarding patient-reported outcomes, our research found that functional status and pain levels had improved. At baseline, the Health Assessment Questionnaire (HAQ) Score was 1.87 ± 0.79; after six months, it was 1.52 ± 0.68 ($p = 0.021$). This result is

in line with other studies that showed leflunomide therapy significantly improved HAQ scores [17]. They revealed a comparable drop in HAQ ratings, demonstrating how well the medication improves functional status.

The Visual Analog Scale (VAS), which measures pain, also showed a decline over time, going from 4.31 ± 2.03 at baseline to 3.50 ± 1.85 at six months ($p = 0.045$). This pain decrease is consistent with a prior study's findings that demonstrated substantial pain alleviation in RA patients receiving leflunomide [18]. Their research revealed a similar decline in VAS ratings, which confirms our conclusions on leflunomide's effectiveness in treating pain.

At six months ($p = 0.030$), the Patient Global Assessment (PGA) Score increased from 4.17 ± 1.53 at baseline to 3.65 ± 1.36. This increase in patients' perceptions of their general health is consistent with a recent research that showed Leflunomide to considerably improve patients' ratings of their overall health [19]. Their results support the findings of our research by demonstrating a similar pattern of enhanced health perception.

Although our research demonstrates the efficacy of leflunomide in lowering disease activity and enhancing patient outcomes, it is crucial to take into account the adverse effects that have been documented, which include nausea in 17.33% of patients and diarrhea in 12.67%. These negative effects align with those documented in earlier studies that have brought attention to comparable side effects related to leflunomide therapy [20].

Overall, the findings of our study support the body of knowledge on the efficacy of leflunomide in the management of RA. They also provide fresh perspectives on the drug's use in tertiary care settings.

Study Limitations

The observational design that makes it more difficult to determine causation. Despite being substantial, the sample size could not adequately represent the variety of RA patients or their long-term results. Furthermore, the outcomes of the research may not be as generalizable to different demographics or healthcare settings due to its single-center design. Lastly, the use of regular clinical measurements and self-reported outcomes may restrict the depth of clinical insights and increase reporting biases.

Conclusion

Our research shown that in RA patients in a tertiary care facility, leflunomide dramatically improves patient-reported outcomes and disease activity. Leflunomide is a useful medication for treating disease-modifying antirheumatic arthritis, as shown by the observed decreases in DAS28 scores, increases in functional status and pain levels, and improvements in overall health perception. These results corroborate earlier studies and support the ongoing use of leflunomide in the therapy of RA, despite some reported adverse effects such nausea and diarrhea. They also emphasize the drug's potential to optimize treatment regimens in complicated patient groups.

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