Section: Pharmacology

Original Research Article

REAL-WORLD EVIDENCE ON TOFACITINIB: ASSESSING DISEASE ACTIVITY AND PAIN REDUCTION IN RHEUMATOID ARTHRITIS PATIENTS

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Abstract

Background: Tofacitinib is a potent and orally active Janus kinase inhibitor that is effective in patients with RA by reducing their disease activity and pain. The current study evaluates the efficacy and safety profile of this molecule when given to RA patients over six months. **Material and Methods:** This was an observational prospective clinical study on 40 RA patients at Varun Arjun Medical College and Rohilkhand Hospital. All subjects received tofacitinib, 5 mg orally, twice daily. The scores of DAS28 and VAS were evaluated at baseline, three months, and six months. ADRs were also reported at all follow-up periods. One-way ANOVA analysis for DAS28 and VAS scores and Chi-Square test were applied to analyze data. **Results:** Significant improvement was observed in DAS28 and VAS scores over 6 months. DAS28 decreased from 5.6 ± 1.1 at baseline to 4.2 ± 1.0 at six months, $p = 0.004$. VAS score significantly reduced from 70.4 ± 15.3 at baseline to 42.7 ± 13.8 at six months, $p = 0.002$. The most common ADRs were headache (22.5%), upper respiratory tract infection (20%), and high cholesterol levels (17.5%). **Conclusion:** Using tofacitinib, JAK inhibitor, for a period of six months dramatically and significantly reduces the disease activity as well as the pain of RA patients, with an overall manageable safety profile. These ADRs should be actively monitored. The outcome can vouchsafe its usage as an effective treatment for RA. Further studies on larger samples that include randomized controlled trials will help validate these results.

INTRODUCTION

Rheumatoid arthritis is a long-term inflammatory disorder that predominantly affects joints and often leads to severe disability if unmanaged. The therapeutic landscape of RA has improved dramatically with the introduction of biologic and targeted synthetic disease-modifying antirheumatic drugs (DMARDs), offering more effective methods to assist patients in controlling disease activity, along with improving quality of life.[1] Among these, a JAK inhibitor that has gained importance for oral administration is tofacitinib. The 5-mg twice-daily dose of tofacitinib reduced the signs and symptoms of RA and improved physical function and remission based on clinical trial evidence.[2] There is keen interest in tofacitinib because of its unique mechanism of action against intracellular signaling pathways at the center of the pathogenetic chain in RA.[3] This interest has been the driver of numerous research studies investigating its effectiveness and safety profile within various groups of patients. The idea behind this study was the dire need to gather real-world information on the long-term efficacy of Tofacitinib and its safety profile. While clinical trials can provide beneficial data, they are commonly under restrictive inclusion criteria, thus limiting the generalization of their findings. Other potential results of observational studies complementing clinical trials are insights into how the drug could be performing under routine clinical practice and among patients with other comorbidities and backgrounds. In fact, the most recent work emphasizes the need for constant monitoring of patients on tofacitinib with respect to the occurrence of adverse events, such as infections and laboratory abnormalities.[5] However, longitudinal data is quite limited for Tofacitinib, especially from a real-world context and setting over the long term. This would further suggest the need for more in-depth observational studies in this domain. This study's justification will bridge the gap between information gathered through clinical trials

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and practice in the real world. This is a prospective observational study that could yield a very detailed assessment of the performance of a drug with time because each patient is followed prospectively at baseline and then at 3 and 6 months. Data from studies like this are instrumental in guiding clinical decisions on the best treatment strategies for more excellent patient outcomes. We conducted this prospective observational study to evaluate the effectiveness and safety of Tofacitinib 5 mg in patients with RA over six months. By following up and documenting the clinical responses and adverse events, in specified intervals, this study will try to contribute valuable data in proving the real-world evidence in the body of knowledge already existing concerning Tofacitinib.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was carried out among patients with rheumatoid arthritis attending the Outpatient Department of General Medicine and Pharmacology at Varun Arjun Medical College and Rohilkhand Hospital. It was designed to evaluate the effectiveness and safety of tofacitinib 5 mg administered twice daily in patients with rheumatoid arthritis over six months. All patients will be followed up at the end of three and six months from baseline for review.

Participants

A total of 40 patients fulfilling the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for diagnosing RA were recruited into this study. Inclusion criteria: adults aged between 18 and 75, with active RA despite conventional DMARD treatment. Exclusion criteria: history of malignancies or serious infections; current biologic DMARD use. Written informed consent was obtained from all participants before their inclusion in the study.

Study Groups

All 40 subjects received tofacitinib 5 mg b.i.d. as part of their treatment regimen. No control or placebo group was included in this observational study.

Drug Administration

Tofacitinib 5 mg tablets were given orally twice a day. The dose was calculated using standard prescribing information and personalized to the clinical response and tolerance of the patient.

Data Collection Procedure:

The data was recorded at three different points in time, which were baseline, three months, and six months.

Parameters

The parameters taken for data collection comprise Age, Sex, BMI: noted at baseline. Duration of RA: obtained from patient history.

- VAS Score: Analogue Visual Scale—assessment for pain at baseline, three months, and six months.
- DAS28 Score: Disease Activity Score on 28 joints—calculated on each visit.
- Adverse Effects: The patient was monitored for the appearance of adverse drug reactions such as upper respiratory tract infections, nasopharyngitis, diarrhea, gastroenteritis, nausea, headache, hyperlipidemia, elevated blood creatine phosphokinase, rash, hypertension, and anemia. Adverse drug reaction assessments were obtained based on patient self-reports and clinical evaluation at the follow-up visits.

Ethical Considerations

A prior approval from the Institutional Ethics Committee of Varun Arjun Medical College and Rohilkhand Hospital was taken for the study. Ethics approval and consent to participate: All procedures performed in the study were by the ethical standards of the institutional and/or national research committee, including the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical Methods

For statistics processing, the data package of SPSS software version 26.0 (IBM Corp., Armonk, NY, USA) was used. The continuous variables were presented as mean ± standard deviation (SD), whereas categorical variables were expressed as frequencies and percentages. Paired t-tests were done to compare baseline data with both the 3-month and 6-month data. A p-value of <0.05 was considered to be significant.

Equipment and Instruments

All laboratory analyses were done at the laboratory within the hospital. The equipment that was availed for these studies was what was used during regular reporting times. These included hemograms, blood analysis for lipid profile, and creatine phosphokinase concentrations.

Instruments

The following instruments were used in the collection of data:

- Visual Analog Scale (VAS): A 10 cm line was used for scoring pain intensity.
- DAS28 Calculator: A software tool for calculating DAS28 scores according to counts of tender and swollen joints, patient's global assessment on health, and erythrocyte sedimentation rate (ESR).

New Methods and Modifications

In this research, no new methods were introduced. All procedures were according to standard clinical practices and guidelines as referenced.

RESULTS

A total of 40 subjects with rheumatoid arthritis were included in the study. The demographic and baseline characteristics of the subjects are summarized below.

The demographic and baseline characteristics show that the average age of the participants was 52.5 years, with a mean BMI of 27.8 kg/m². The duration

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of rheumatoid arthritis among the subjects averaged 10.2 years. [Table 1]

The DAS28 scores decreased significantly from baseline to 6 months, indicating an improvement in disease activity over time. [Table 2]

The VAS scores also showed a significant reduction from baseline to 6 months, reflecting a decrease in pain levels over the study period. [Table 3]

The frequencies and prevalence percentages of various adverse drug reactions indicate the most common ADRs were headache, upper respiratory tract infection, and elevated cholesterol levels. [Table 4]

Table 1: Participant Demographics and Baseline Characteristics

Parameter	Mean ± SD
Age (years)	52.5 ± 12.4
BMI (kg/m²)	27.8 ± 6.1
Duration of Rheumatoid Arthritis (years)	10.2 ± 6.9

Table 2: Changes in DAS28 Scores Over Time

Time Point	DAS28 Score (Mean ± SD)	P-Value
Baseline	5.6 ± 1.1	0.004
3 Months	4.8 ± 1.2	
6 Months	4.2 ± 1.0	

Table 3: VAS Scores at Different Time Points

Time Point	VAS Score (Mean ± SD)	P-value
Baseline	70.4 ± 15.3	0.002
3 Months	55.2 ± 14.6	
6 Months	42.7 ± 13.8	

Table 4: Frequencies and Prevalence Percentages of Adverse Drug Reactions

Adverse Reaction	Frequency	Prevalence (%)
Upper respiratory tract infection	8	20%
Nasopharyngitis	6	15%
Diarrhea	5	12.5%
Gastroenteritis	4	10%
Nausea	3	7.5%
Headache	9	22.5%
Elevated cholesterol levels	7	17.5%
Increased blood creatine phosphokinase	2	5%
Rash	4	10%
Hypertension	3	7.5%
Anemia	2	5%

DISCUSSION

The current study was directed at finding out the efficiency and safety of tofacitinib 5 mg in patients who were diagnosed with rheumatoid arthritis for the past six months of taking the medication. Such a significant decrease in DAS28 and VAS scores during the follow-up study period depicts effective disease activity and a reduction in pain in RA patients on tofacitinib medication. The data were consistent with previous clinical studies confirming the effectiveness of tofacitinib in alleviating symptoms in RA.[6,7]

The DAS28 scores reduced from 5.6 at baseline to 4.2 after six months of administration, thus signifying that tofacitinib gives good relief in RA disease activity; in support of the evidence, it was established that changes in DAS28 scores are the same as Singh JA et al. in their study of patients with the use of tofacitinib.[8] This analgesic action is further supported by the fact that it significantly reduces the VAS scores from 70.4 at baseline to 42.7 after six months. Similarly, previous reports also support these analgesic findings.[9,10]

ADRs reported in the current study align with the data presented in the literature. Some of the common ADRs included headaches, upper respiratory tract infections, and hypercholesteremia. Again, this finding agrees with the safety profile of tofacitinib reported earlier.[11,12] However, comparatively higher burdens of headaches (22.5%) and cholesterol (17.5%) also indicate that the decision of necessity in relation to the administration of tofacitinib should be made with increased monitoring to eliminate these effects.

In this regard, although the study is highly informative regarding the effectiveness and safety of tofacitinib, it has some limitations. Besides, the sample size is of moderate magnitude, and the study was performed at one center only, complicating the aspect of generalization. It means that a comparison group was lacking in this study, and it led to an already biased, inherently observational study design. Thus, we are waiting for further prospective studies with large multicenter cohorts using a

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randomized controlled design to validate these findings.

Another possible limitation is that the VAS type of scoring relies on patient reporting, and hence, it carries subjective bias. The use of objective measures, along with the patient's reporting outcome, needs to be added to find a more comprehensive efficacy of tofacitinib in pain and disease activity.

This study adds evidence to existing data regarding the use of tofacitinib in managing RA. The marked improvements in DAS28 and VAS scores have high prospects for the treatment. Close monitoring of ADRs should be recommended so that severe side effects are minimized.

CONCLUSION

This study showed that tofacitinib 5 mg reduces disease activity and pain, with a manageable safety profile over six months in RA patients. These data support a tofacitinib option as a potential choice of drug for RA with a continuous check for management toward ADRs. Hence, future research should be more established by larger, multicentered, randomized controlled trials conducted under long durations to find evidence on the effectiveness and safety of tofacitinib in diverse patient populations.

Conflict of Interest

The authors declare that they have no conflict of interest.

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