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Research Article

Prescribing pattern and adverse drug reactions monitoring in patients with rheumatoid arthritis in a tertiary care hospital

Lakshmi Prabha M*, Geetha Rani A, Meenakshi Balasubramanian, Ezhil Ramya J

Department of Pharmacology, Tirunelveli medical college, Tirunelveli, Tamilnadu, India

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***Correspondence to:**
Dr. Lakshmi Prabha M,
Email: drprabhachandar @gmail.com

ABSTRACT

Background: Rheumatoid arthritis is a chronic inflammatory arthritis which requires lifelong treatment to prevent the damage to joints and to maintain day to day functioning of patients. All the drugs used in the treatment of rheumatoid arthritis show significant toxicity and hence it is very important that their use require regular monitoring for adverse reactions. The present study is designed to estimate the prescribing pattern and the occurrence of adverse drug reactions in patients with rheumatoid arthritis.
Methods: This prospective observational study was conducted from July 2014 to September 2014 in rheumatology outpatient department.75 patients who fulfilled the study criteria were observed for 3 months. Their prescriptions were collected and analysed. The CSDCO reporting forms were used for the collection of adverse drug reactions. Causality assessment was done by using WHO-UMC scoring system and severity assessment by modified Hartwig and Siegel scale.
Results: The study group consists of 85.6 % female. Majority of them were in age group 40-49 years. Average number of drugs per prescription was 4.97.Out of 75 patients, 57.33% were on single DMARD, and 33.33% required 2 DMARDs and 9.33% were prescribed 3 DMARDs. A total of 64 adverse drug reactions were reported out of which 29.6% was due to glucocorticoids, 25% was due to the use of NSAIDS and steroids. Chloroquine maculopathy occurred in 2 patients and elevated liver enzymes occurred in 6 patients due to methotrexate which necessitated DMARD withdrawal. Eight percent of the ADRs were severe.
Conclusions: Treatment of rheumatoid arthritis is based on DMARDs and glucocorticoids where it is difficult to prevent the occurrence of ADRs. Consistent monitoring of therapy is needed for early recognition of ADRs and prompt action.

Keywords: Rheumatoid arthritis, Prescribing pattern, Adverse reactions

INTRODUCTION

Rheumatoid arthritis is an autoimmune disease which is characterised by chronic inflammatory synovitis and joint erosion.[1] It affects around 1% of the population worldwide. It can occur at any age.[2] But the peak age of onset is more common in 4-5th decade. It is more common in female than male and the ratio of female to male is 3:1.[3] The patients with rheumatoid arthritis suffer from significant disability, morbidity and mortality.[4]

The primary goal of treatment of rheumatoid arthritis should aim to reach clinical remission, to prevent structural damage and to provide improved quality of life in patients.[5] Disease modifying anti rheumatic drugs (DMARDS) are the first line agents used in the treatment for patients with established rheumatoid arthritis.[6] DMARDs should be initiated within 3 months of diagnosis of rheumatoid arthritis to prevent bone destruction. They may be classified into biologic and non-biologic or synthetic DMARDs. The non-biologic agents include drugs like methotrexate, chloroquine,

hydroxychloroquine, azathioprine, cyclophosphamide, sulfasalazine, gold salts, cyclosporine, leflunomide, mycophenolate mofetil. Biologic DMARDs used in the treatment of rheumatoid arthritis include abatacept, rituximab, tocilizumab and TNF-alpha blocking agents.[7]

Non-steroidal anti-inflammatory drugs are used in the treatment of rheumatoid arthritis to decrease the pain and inflammation of joints but they don't prevent the joint damage or the progression of disease activity.[8] Glucocorticoids in rheumatoid arthritis will retard the disease progression and joint damage in addition to the anti-inflammatory effects.[1] Glucocorticoids are mainly used to control the short term acute flare ups while waiting for the DMARDs to act.[9] However chronic use of glucocorticoids is associated with increased frequency of significant adverse drug reactions.[10]

All the drugs used in the treatment of rheumatoid arthritis show significant toxicity and hence it is very important that their use require regular monitoring for adverse reactions.[11] The present study is designed to estimate the prescribing pattern and the occurrence of adverse drug reactions in patients with rheumatoid arthritis.

METHODS

It was a prospective observational study conducted from July 2014 to September 2014 in 75 patients attending Rheumatology OPD in Tirunelveli Medical College Hospital,Tamilnadu, India.

Inclusion criteria

- Age>18 years
- Sex-both male and female with established rheumatoid arthritis
- Disease duration >1 year
- Patients receiving stable therapy for at least 3 months.

Exclusion criteria

- Acute or chronic medical condition requiring hospitalization
- Preexisting hepatic or renal dysfunction
- Pregnancy and lactation

Methodology

The study was started after obtaining institutional ethical committee approval. Written informed consent in local vernacular language was obtained from every patient included in the study at the time of enrolment. Patients diagnosed with established rheumatoid arthritis were enrolled in the study. The patients satisfying the study criteria were followed up every week for a period of 3 months. Demographic details, medication details and relevant data of lab investigations were collected in a specially designed proforma. Prescriptions of the study patients were collected and analysed. The medication details collected from the patients included data like name of the prescribed drug or drug combinations, dosage form, daily dosage, frequency, drugs prescribed by generic or brand name and all the co-prescribed drugs. The central drug standard control organization (CDSCO) reporting forms were used for the collection of adverse drug reactions. The causal relationship of the adverse drug reaction reported by the patient was established by detailed clinical history, patient examination, relevant lab investigations and correlation between the drug intake and onset of adverse drug reactions. Collected data were analysed for the types of adverse drug reactions. Causality assessment was done by using WHO-UMC scoring system. The severity assessment was done by using modified Hartwig and Siegel scale.[12,13]

RESULTS

Out of 118 patients screened, 75 met the study criteria and were enrolled in the study. Out of the study population 85.4% were women and majority of the study population were in the age group of 40-49 years (Figure 1).

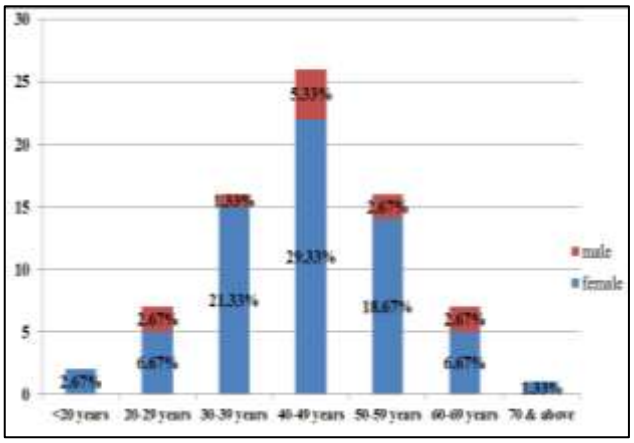

Figure 1: Age and gender distribution of rheumatoid arthritis patients.

Table 1: Prescription analysis of rheumatoid arthritis patients.

Prescribing indicators	Results
Average number of drugs per prescription	4.97
Percentage of drugs prescribed by generic name	100%
Percentage of drugs prescribed by brand name	0
Patients on single DMARD	43(57.33%)
Patients on two DMARDs	25(33.33%)
Patients on three DMARDs	7(9.33%)

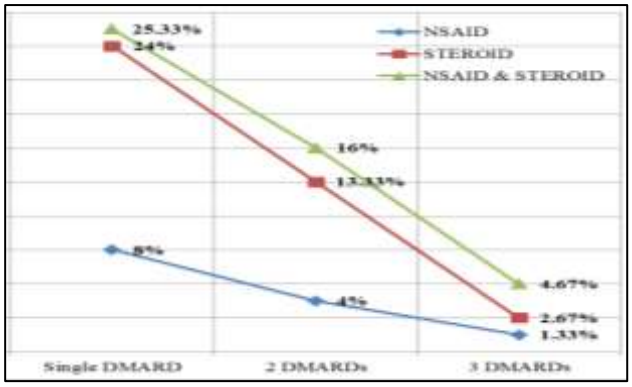

Figure 2: Prescribing pattern of DMARDs and other drugs in mono-therapy and combination therapy.

In the study, the average number of drugs per prescription was 4.97.About 57.33% was taking single DMARD, 33.33% (25) were taking 2 DMARDs and 9.33% were on 3 DMARDs. None of them were on biologic DMARDs. Chloroquine was commonly prescribed as monotherapy in about 55.88% of single DMARD users followed by methotrexate which was prescribed in about 44.1% of the patients. Sulfasalazine was commonly prescribed only in combination with other DMARDs (Table 1).

Table 2: Pattern of combined therapy of DMARDs.

Combination therapy	Number (%)
Methotrexate and chloroquine	21 (28%)
Sulfasalazine and chloroquine	2 (2.67%)
Sulfasalazine and methotrexate	2 (2.67%)
Methotrexate, chloroquine and sulfasalazine	7 (9.33%)
Total	32 (42.67%)

NSAIDs and steroids were commonly prescribed with DMARDs both in monotherapy as well as in combination therapy (Figure 2).

The most common combination used was methotrexate and chloroquine. About 9.33% of patients were prescribed methotrexate, chloroquine and sulfasalazine (Table 2).

Table 3: Analysis of adverse drug reactions.

ADR	Number	Percentage (%)	Causative drug	Causality assessment
Cushingoid features	19	29.6	Steroid	Probable
Gastritis	16	25	Steroids, NSAIDS	Probable
Elevated liver enzymes	6	9.37	Methotrexate	Probable
Hyperglycemia	3	4.68	Steroid	Probable
Hypertension	3	4.68	Steroids	Probable
Asthma exaceberation	3	4.68	NSAIDS	Possible
Hyperpigmentation	3	4.68	Chloroquine	Possible
Aphthous ulcers	3	4.68	NSAIDS, DMARD	Possible
Presenile cataract	3	4.68	Steroid	Possible
Maculopathy	2	3.12	Chloroquine	Probable
Skin rashes	1	1.56	DMARD	Possible
Insomnia	1	1.56	Steroid	Possible
Palpitation	1	1.56	Steroid	Possible

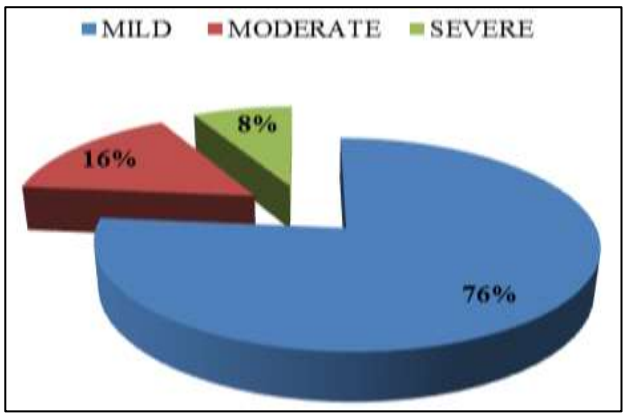

Figure 3: Severity of adverse drug reactions.

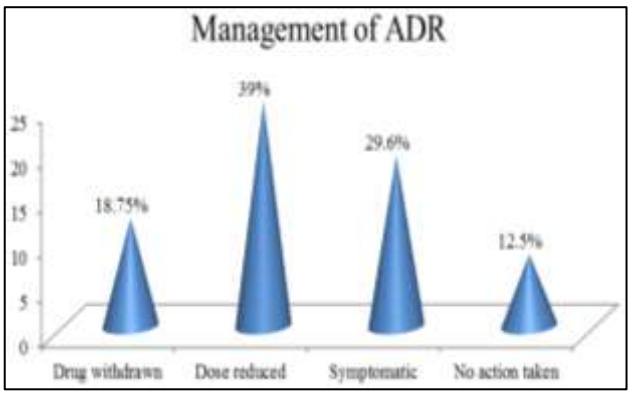

Figure 4: Actions taken in response to occurrence of adverse drug reaction.

A total of 64 adverse drug reactions were reported in the study and around 29.6% were the features due to chronic use of steroids. The second most common adverse drug reaction was gastritis which occurred in around 25% of the patients (Table 3).

Majority (76%) of the adverse drug reactions were mild according to Hartwig siegel scale. Around 16% of the patients had moderate ADRs and 8% had severe adverse drug reactions (Figure 3).

In 18.75% patients the causative drug had to be withdrawn to prevent deleritious effects. Around 39% of the patients required dose reduction while 29.7% required symptomatic treatment to control ADR and no action was needed in 12.5% patients (Figure 4).

DISCUSSION

Rheumatoid arthritis is a chronic inflammatory arthritis where the therapy with DMARDs is initiated at an early stage to prevent or delay the disability, mortality and morbidity. Chronic use of any drug can precipitate adverse drug reaction. The study of prescribing pattern and adverse drug reaction monitoring is very essential to provide suitable modifications in prescribing practice so that therapeutic benefits will be obtained to the maximum with minimal occurrence of adverse drug reactions. Drug prescribing studies always aim to provide the necessary feedback to the prescriber and awareness about the rational use of medicines so that the patient being treated obtains the maximum benefit.

In the present study the prevalence of rheumatoid arthritis was greater in female. Since rheumatoid arthritis is an auto immune disease, this female predominance is due to reasons like the influence of hormonal factors and X linked genes involved in pathogenesis of rheumatoid arthritis.[1]

The average number of drugs per prescription was 4.97.This is low when compared to the study done by Gawde et al in Mumbai.[14] As the study was done in a government institution all the drugs were prescribed by generic name and only non-biologic DMARDs were prescribed to the patients due to the non-availability of biologic DMARDs in the institution.

The overall drug usage describe that single DMARD was used in majority of the patients and when the disease was uncontrolled combination of DMARDs was used. This is comparable to the study by Shiny et al where majority of the patients were on single DMARD.[15] According to the ACR 2015 guidelines to treat rheumatoid arthritis recommend that regardless of the disease activity level, DMARD monotherapy should be started initially for treating the patients. Combination therapy can be started only when the disease activity remains high in spite of the monotherapy.[6]

Chloroquine was the commonest drug prescribed as monotherapy in the study followed by methotrexate. Glucocorticoids and NSAIDs were widely used in addition to DMARDs in the study. Drugs like ranitidine, omeprazole and calcium supplements were given in addition to the standard drugs to manage the adverse drug reactions.

Total of 64 adverse drug reactions were reported in our study. The most common adverse drug reaction was the cushingoid feature that developed due to use of steroids. It was followed by gastritis due to the use of NSAIDS and steroids. The most serious adverse reaction which was irreversible and required drug withdrawal was chloroquine maculopathy which occurred in 2 patients. The other reaction that required drug withdrawal was elevated liver enzymes (6 patients) due to methotrexate. These results were similar to adverse drug reaction study done by Machodo et al.

On assessing severity score, 76% of the reactions were only mild in nature, 16% reactions were moderate and 8% were severe.

Recommendations

Complete and timely recording and reporting of all adverse drug reactions in all rheumatoid arthritis patients.

CONCLUSIONS

Treatment of rheumatoid arthritis is based on DMARDs and glucocorticoids where it is difficult to prevent the occurrence of ADR. So proper monitoring of adverse drug reactions will help to identify the ADRs earlier for timely action to provide maximum benefit to the patient.

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