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Original Research Article.

Prevalence of Risk Factor Casualties and Causative Factors of ADRs in Rheumatoid Arthritis in a Tertiary Care Hospital Rajasthan

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of the joints with predominant symptoms of pain, swelling and stiffness. The pattern of disease activity often varies in patients and can include periods of high disease activity (flares) interspersed with periods of low disease activity (remission). Currently, there is no cure for RA and so the goal of treatment is to suppress disease activity, reduce disease progression and adequately treat co- morbidities. Drugs are double edged weapons they can save life but also can cause adverse drug reactions and are major cause of morbidity and mortality worldwide.

Material and Methods: After obtaining approval and clearance from institutional ethics committee, Data of ADRs was collected from the inpatients and outpatients admitted in the Medicine (Rheumatology) Department in P.B.M. hospital and associated group of hospital, Bikaner. Patient was included in the study after getting their written informed consent.

Results: The most common organ system affected by ADR were gastrointestinal system (39.50%) followed by heaptobilliary system (19.75%) in this study. Severity of the ADRs was determined by applying the Hartwig's Severity Assessment Scale. The results of assessment of the severity revealed that 63 ADRs (77.78%) were mild in severity followed by 18 moderate (22.23%) and no severe reaction was reported according to the scale.

Conclusion: The clinical spectrum of ADRs were like gastritis, elevated liver enzymes, nausea, diarrohea, skin hyperpigmentation, myalgia, headache and rashes etc.Most commonly affected organ system was gastrointestinal system.

Keywords: Rheumatoid Arthritis, ADR, Nausea, Diarrohea.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of the joints with predominant symptoms of pain, swelling and stiffness. The pattern of disease activity often varies in patients and can include periods of high disease activity (flares) interspersed with periods of low disease activity (remission). Poor control of disease activity can result in erosive bone damage which can then lead to joint destruction and physical disability.[1] RA affects approximately 1% of adult population globally.[2]

The prevalence of RA in the adult population in India is approximately 0.75%.[3] Patients with RA have a high mortality rate when compared to the general population, with cardiovascular disease contributing up to 50% of all deaths.[4] Currently, there is no cure for RA and so the goal of treatment is to suppress disease activity, reduce disease progression and adequately treat co-morbidities.

Drugs are double edged weapons they can save life but also can cause adverse drug reactions and are major cause of morbidity and mortality worldwide10. Heightened interest in ADRs was stimulated by the thalidomide tragedy in the 1960s.[5]

The safe use of medicine is an important issue and an ongoing ADR monitoring and reporting program can provide benefits to the organization, pharmacists, other health care professionals and more importantly to patients.[6]

The definition and scope of pharmacovigilance have evolved to recognize the importance of a systems approach for monitoring and improving the safe use of medicines.[7]

MATERIALS AND METHODS

After obtaining approval and clearance from institutional ethics committee, Data of ADRs was collected from the inpatients and outpatients admitted in the Medicine (Rheumatology) Department in P.B.M. hospital and associated group of hospital, Bikaner. Patient was included in the study after getting their written informed consent. The present study was a prospective study. Enrolment of patient was done from July 2016 to December 2016. For each patient a detailed history taking was noted on which includes drug history, personal history, family history, present and past medical history, and history of allergy details of drugs, presenting complaint were documented and any untoward event was labeled as adverse drug reaction. Baseline laboratory investigations such as hemoglobin (Hb), total counts, differential counts, renal function test, serum electrolytes and liver function test were carried out in each patient. Data collected was entered in a specially designed Performa (Case Recording Form) for study. The study involves various aspects of ADR like types, grades, drugs causing them, onset and duration and outcome.

Data analysis: Data thus collected were entered into excel and were then analyzed with help of SPSS software through tables, diagrams and appropriate statistical test wherever required.

Table 1: Organ System Affected

Organ system	Male		Female		Total	
	No.	%	No.	%	No.	%
Gastrointestinal	05	27.78	34	53.96	39	48.14
Dermatological	02	11.11	11	17.46	13	16.04
Central Nervous system	04	22.22	08	12.69	12	14.81
Hepatobilliary system	01	05.55	08	12.69	09	11.12
Muskuloskeletal system	03	16.66	02	3.17	05	7.69
Endocrine	03	16.66	00	00	03	4.93
Total	18	100	63	100	81	100

Table 2: Suspected Therapeutic Drugs

Suspected Drug	Male		Female		Total	
	No.	%	No	%	No.	%
NSAIDs	02	11.1	20	31.7	22	27.1
Methotrexate	03	16.6	15	23.8	18	22.2
Leflunomide	01	5.5	13	20.6	14	17.2
Hydroxychloroquine	02	11.1	09	14.2	11	13.5
Prednisolone	06	33.3	03	4.7	09	11.1
Tramadol	04	22.2	03	4.7	07	8.6
Total	18	100	63	100	81	100

RESULTS

Organ system Involvement: In our study ADRs detected in patients affected different organ systems according to the class of drug. Table 1 shows the organ system affected due to ADRs with gender distribution. The most common organ system affected by ADR were gastrointestinal system (39.50%) followed by heaptobilliary system (19.75%) in this study.

Suspected therapeutic drugs Table 2 shows the suspected therapeutic drug causing ADR with gender distribution. The majority of the ADR were caused by the majority of the ADR were caused by NSAIDs (27.16%) followed by Methotrexate (22.22%) and Leflunomide (17.28%) in present study. List of adverse drug reaction and suspected drug Table 3 shows different type of ADRs and causative drug with frequency. It revealed that Gastritis is mainly caused by NSAIDs[8] and liver enzymes are elevated mainly due to ADR of Methotrexate.[9]

Causality assessment ADRs Table 4 show details of Probability assessment of ADR based on Naranjo's probability assessment scale. The result showed that majority of the ADR occurred in the study were probable 51 (62.96%) followed by possible 30 (37.04%). No ADR comes in definite or doubtful ADR category.

Severity of ADRs

Severity of the ADRs was determined by applying the Hartwig's Severity Assessment Scale. The results of assessment of the severity as shown in Table 5 revealed that 63 ADRs (77.78%) were mild in severity followed by 18 moderate (22.23%) and no severe reaction was reported according to the scale.

Table 3: Adverse Drug Reaction and Suspected Drug

S.No	ADRs	Suspected Drug
1.	Gastritis	NSAIDs (20)
		Leflunomide (01)
		Prednisolone (01)
2.	Elevated Liver Enzymes	Methotrexate (07)
		Leflunomide (02)
3.	Nausea	Methotrexate (03)
		Leflunomide (02)
		NSAIDs (02)
		Tramadol (01
4.	Myalgia	Prednisolone (05)
5.	Headache	Hydroxychloroquine (05)
6.	Rashes	Hydroxychloroquine (04)
7.	Apthous Ulcer	Methotrexate (04)
8.	Diarrohea	Methotrexate (04)
		Leflunomide (03)
9.	Skin hyperpigmentation	Hydroxychloroquine (03)
10.	Cushingoid features	Prednisolone (03)
11.	Insomnia	Leflunomide (03)
12.	Alopecia	Leflunomide (02)
13.	Constipation	Tramadol (02)
14.	Dizziness	Tramadol (02)
15.	Vertigo	Tramadol (01)

Table 4: NARANJO Scale of ADRs

Causality	Male		Female		Total	
	No.	%	No	%	No.	%
Definite	0	0	0	0	0	0
Probable	12	66.67	39	61.90	51	62.96
Possible	06	33.33	24	38.10	30	37.04
Doubtful	0	0	0	0	0	0
Total	18	100	63	100	81	100

Table 5: Modified HARTWIG Scale of ADRs

Severity	Male		Female		Total	
	No.	%	No.	%	No.	%
Mild	15	83.33	48	71.42	63	77.78
Moderate	03	16.67	15	23.81	18	22.23
Severe	00	00	00	00	00	00
Total	18	100	63	100	81	100

DISCUSSION

The present study was prospective observational study conducted for the duration of six months from July 2016 to December 2016 to analyze the occurrence of ADRs in RA patients at PBM and associated group of hospital with Sardar Patel Medical College, a tertiary care teaching institute in Bikaner, Rajasthan. The most commonly affected organ system was Gastrointestinal system (48.14%) Because the drug therapeutics used mainly was NSAIDs for the treatment of rheumatoid arthritis which have more adverse effects on gastrointestinal tract. Therefore, Gastritis was the most common ADR (27.16%) followed by Elevated liver enzymes (11.12%). This result is almost similar to study done by Prabha ML et al reported where Gastritis was 25% and elevated liver enzymes was 9.37%.

The drug therapy of rheumatoid arthritis causes various types of adverse reactions. Chronic pain is a common symptom of rheumatoid arthritis therefore NSAIDs are commonly prescribed to RA patients. In this study 27.16% ADRs are caused by NSAIDs. Therefore, it is the most common suspected drug responsible for adverse reactions in RA patients.[10]

Followed by NSAIDs, Methotrexate was associated with a total of 22.22% of ADR which Includes elevated liver enzymes (8.64%) followed by apthous ulcer (4.93%), diarrohea (4.93%) and Nausea (3.70%). The similar results were found in the study conducted by Prabha ML et al[11] in which 9.37% cases reported elevated liver enzymes followed by apthous ulcers (4.68%). Almost same results were found in the study conducted by Machado elba et al in which 15.48% cases reported elevated liver enzymes.

The drug Leflunomide also reported various adverse drug reactions like Diarrohea (3.70%), Insomnia (3.70%), Alopecia (2.46%), Nausea (2.46%), Elevated liver enzymes (2.46%) and Gastritis (1.81%). Results were similar with the study conducted by Razak AS et a[11] in which 4.11% patients reported diarrohea followed by Alopecia (2.74%), Nausea (2.74%).[12]

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 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.

Monitoring of ADRs is an ongoing ceaseless and continuing process. Though pharmacovigilance is still in its infancy in India, this is likely to expand in the times to come. This is because, as the newer and newer drugs hit the market, the need for pharmacovigilance grows more than ever before. Therefore, monitoring of the adverse effects of newer drugs particularly of serious nature is mandatory.

CONCLUSION

The clinical spectrum of ADRs were like gastritis, elevated liver enzymes, nausea, diarrohea, skin hyperpigmentation, myalgia, headache and rashes etc. Most commonly affected organ system was gastrointestinal system (48.14%). The predominant pattern of ADRs observed was gastritis. Most of the adverse drug reactions were caused by NSAIDs followed by Methotrexate. Most of the reactions were probable (62.9%) in causality assessment. Most of the reactions were mild in severity. No severe adverse drug reaction reported. However, ADRs associated with drugs used for treatment of rheumatoid arthritis can cause problems with patient therapies. 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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