Study of Demographic Occurrence of ADRs in Rheumatoid Arthritis Patients at a Tertiary Care Institute Bikaner

Arjun Vyas[1], Abhishek Acharya[2*], Amandeep Singh Hundal[3], R. P. Acharya[4],
R.P. Agarwal[5], Jitendra Acharya[6]

[1]M.Sc.(Medicine), Department of Pharmacology, S.P. Medical College, Bikaner, Rajasthan, India.
[2*]Senior Demonstrator, Department of Physiology, R.N.T Medical College, Udaipur, Rajasthan, India.
[3]Intern, Jodhpur Dental College and General Hospital, Jodhpur, Rajasthan, India.
[4]Senior Professor, Department of Pharmacology, S.P. Medical College, Bikaner, Rajasthan, India.
[5]Senior Professor, Department of Medicine, S.P. Medical College, Bikaner, Rajasthan, India.
[6]Senior Demonstrator, Department of Dentistry, S.P. Medical College, Bikaner, Rajasthan, India.

ABSTRACT

Background: Various Drugs like NSAIDs, disease modifying anti rheumatic drugs (DMARDs) and corticosteroids have been used in Rheumatoid Arthritis over the last 50 years to provide symptomatic relief, reduce disease activity and disability, and to prevent radiological progression. All of these drugs show significant toxicity, such that their use requires regular monitoring.

Materials and Methods: A prospective observational study was carried out in between July 2016 to December 2016. (6 months) at Department of Medicine (Rheumatology), P.B.M. hospital and associated group of hospital, Bikaner. Pre designed Pre structured Performa containing questions regarding Clinical History, Demographic data, drug history, personal history, family history, present and past medical history, and history of allergy details of drugs, presenting complaint, Baseline laboratory investigations such as hemoglobin (Hb), total counts, differential counts, renal function test, serum electrolytes and liver function test was used.

RESULTS: Females 76 (74.51) were more affected by RA as compared to male patients 26 (25.49). The ADR was more common in females 39 (63) as compared to males 09 (18). In female RA patients, out of 76, 39 (51.31%) patients developed ADRs while in male RA patients, out of 26, 09 (34.61%) patients developed ADRs. Age of the subjects ranged from 18 years to 65 year. The mean age was 43.40 years with standard error of mean is 12.82. 47.92% of the patients were illiterate while 20.51% were educated up to Primary level followed by 17.95% patients up to Secondary level and only 10.25 % patients reached to high school or above. In study there were 23.07% were such patients who can only write his/her name so we put them in literate category. Gastritis (27.16%) was the most common ADR followed by elevated liver enzymes (19.75%).

Conclusion: Proper monitoring of adverse drug reactions will help to identify the ADRs earlier for timely action to provide maximum benefit to the patient.

Keywords: ADRs, Rheumatoid Arthritis.

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). The continuous development of new medications is enhancing the effective treatment of this condition. Drug therapy in RA consists of non-steroidal anti-inflammatory drugs (NSAIDs) and/or disease modifying anti-rheumatic drugs (DMARDs) and/or corticosteroids for decreasing pain and/or slowing progression of joint damage.[1,2]
Various Drugs like NSAIDs, disease modifying anti rheumatic drugs (DMARDs) and corticosteroids have been used over the last 50 years to provide symptomatic relief, reduce disease activity and disability, and to prevent radiological progression.[3] All of these drugs show significant toxicity, such that their use requires regular monitoring.[4,5]
The WHO definition was criticized by Edwards and Aronson (2000). They define an ADR as "An appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product, which predicts hazards from future administration and warrants prevention of the dosage regimen, or withdrawal of product."[6]

MATERIALS AND METHODS

Study Design: A prospective observational study.

Study Period: The study was carried out in between July 2016 to December 2016. (6 months)

Study Place: Department of Medicine (Rheumatology), P.B.M. hospital and associated group of hospital, Bikaner.

Study Population: The study population involved inpatients and outpatients in the Medicine (Rheumatology) Department in P.B.M. hospital and associated group of hospital, Bikaner

Inclusion Criteria

1. Patient diagnosed of RA by rheumatologists.
2. Patients age between 18 to 65 years from both genders.
3. Patients or caregivers agreed to participate in the study.
4. Patient who received atleast one type of medications.

Exclusion Criteria

1. Patients with drug reaction due to deliberate or unintentional over dosage.
2. Drug reaction occurring due to prescribing and dispensing error.
3. Mentally retarded or unconscious patients. Patients already on other antipsychotic agents and drug abuse.
4. Non cooperative patients with age < 18 year and > 65 year.
5. Patients who are critically ill.
6. Pregnant and lactating females.
7. Drop outs will be excluded.

Assessment Tool

Pre designed Pre structured Performa containing questions regarding Clinical History, Demographic data, drug history, personal history, family history, present and past medical history, and history of allergy details of drugs, presenting complaint, Baseline laboratory investigations such as hemoglobin (Hb), total counts, differential counts, renal function test, serum electrolytes and liver function test was used.

Table 1: Sex wise distribution

	Male		Female	
	No.	%	No.	%
Patients who had ADR	09	34.61	39	51.31
Patients who had no ADR	17	65.38	37	48.69
Total No. of RA patients	26	25.49	76	74.51

Table 2: Age Distribution of RA Patients

Age In Year	Male		Female		Total	
	No.	%	No	%	No.	%
11-20	00	00	01	1.31	01	0.98
21-30	02	7.69	16	21.05	18	17.64
31-40	06	23.07	19	25.0	25	24.50
41-50	06	23.07	13	17.10	19	18.62
51-60	09	34.61	20	26.31	29	28.43
61 and above	03	11.53	07	9.21	10	9.80
Total	26	100	76	100	102	100

RESULTS

Sex wise distribution

Table no.1 shows the gender distribution of patients who were suffering from RA and those who had encountered ADRs during the study period in present study. The results revealed that females 76 (74.51) were more affected by RA as compared to male patients 26 (25.49). The ADR was more common in females 39 (63) as compared to males 09 (18). In female RA patients, out of 76, 39 (51.31%) patients developed ADRs while in male RA patients, out of 26, 09 (34.61%) patients developed ADRs.

Age Group Wise Distribution

Table 2 shows age distribution of the patients who suffered from RA in present study. Age of the subjects ranged from 18 years to 65 year. The mean age was 43.40 years with standard error of mean is 12.82. The findings indicate that the majority of patients, suffering from RA during the study period were in the age group of 51-60 years (28.43%) followed by 31-40 years (24.50%) and 41-50 years (18.62%).

Level of Education

In present study 47.92% of the patients were illiterate while 20.51% were educated up to Primary level followed by 17.95% patients up to Secondary level and only 10.25 % patients reached to high school or above. In study there were 23.07% were such patients who can only write his/her name so we put them in literate category.

Spectrum of ADRs

Table 4 shows presenting complaints and adverse drug reaction caused by different drugs. After analyzing data we found that Gastritis (27.16%) was the most common ADR followed by elevated liver enzymes (19.75%).

Table 3: Level of Education and ADRs

Level of Education	Male	Female	Total
	n(%)	n(%)	n(%)
Illiterate	4(44.45%)	19(48.71%)	23(47.92%)
Literate	2(22.22)	5(12.82%)	7(23.07%)
Primary School	1(11.12)	7(17.95%)	8(20.51%)
Secondary School	1(11.12)	6(15.38%)	7(17.95%)
Higher Sec. & above	1(11.12)	2(5.12%)	3(10.25%)
Total	9(100)	39(100)	48(100)

Table 4: Spectrum of ADRs

ADRs	Male	Female	Total
	n(%)	n(%)	n(%)
Gastritis	1(5.55)	21(33.33)	22(27.16)
Elevated liver enzymes	1(5.55)	8(12.69)	9(11.12)
Nausea	2(11.11)	6(9.52)	8(9.87)
Diarrohea	1(5.55)	6(9.52)	7(8.64)
Myalgia	3(16.66)	2(3.17)	5(6.17)
Headache	1(5.55)	4(6.34)	5(6.17)
Rashes	0(00)	4(6.34)	4(4.93)
Apthous ulcer	1(5.55)	3(4.76)	4(4.93)
Skin hyperpigmentation	1(5.55)	2(3.17)	3(3.70)
Cushingoid features	3(16.66)	0(00)	3(3.70)
Insomnia	0(00)	3(4.76)	3(3.70)
Alopecia	0(00)	2(3.17)	2(2.46)
Constipation	1(5.55)	1(1.58)	2(2.46)
Dizziness	2(11.11)	0(00)	2(2.46)
Vertigo	1(5.55)	1(1.58)	2(2.46)
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.

When observing the results, the prevalence of rheumatoid arthritis was greater in female (74.59%) which is almost similar to the study conducted by H.M. Al-Malaq et al (88.5%), Gawde et al (87%)[7], Prabha ML et al (85.6%), Machado-Alba et al (87.4%), Bainddla S et al (87%).

In the contrary, study done by Schinerder[8] et al (65%) showing relatively lower incidence of RA in female over male patients. 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.[9]

The demographic characteristics for age of total 102 subjects enrolled in the study with age distribution showed that age of the subjects ranged from 18 years to 65 year and the mean age was 43.40 year with standard error of mean is 12.82. The majority of the study subjects come in the age group 51-60 years (28.43%) which is in accordance with previous studies done by Bainddla S. et al, H.M. Al-Malaq et al, Gawde et al.[10]

To determine the prevalence and characteristics of ADRs in RA patients, with assessment of its causality, severity and risk factors, obtained data have been analyzed. The result shows, in female RA patients, out of 76, 39 (51.31%) patients developed ADRs while in male RA patients, out of 26, 09 (34.61%) patients developed ADRs.[11]

The incidence of ADRs among age group 51-60 years (older group 32.09%) with mean age ($\pm$12.44) was significantly higher than other age groups. Compromised organ functions, decreased BMR (basal metabolic rate), concomitant disease conditions and multiple drug regimens might be assigned as likely reasons for higher incidence of ADRs in older patients.

Because of the adverse drug reactions caused by the Antirheumatoid drugs are higher the present study shows that 48 patients had developed 81 ADRs (79.4%) out of 102 study subjects. The result of the study corresponded closely to the study done by Prabha ML et al (85.33%) and similar with study done by Machado elba et al (69.57%). Result of present study shows that in 48 patients, Average ADR is 1.69 per patient which is similar to study done by Machado elba et al (Average = 2.26 ADR/Patient).

CONCLUSION

This prospective observational study was conducted for the duration of six months to analyze the occurrence of ADRs in rheumatoid arthritis patients. The demographic data shows the majority of the patients were female. The average age of study population was 43.40 $\pm$ 12.82 years. The majority of patients, suffering from RA during the study period were in the age group of 51-60 years. So proper monitoring of adverse drug reactions will help to identify the ADRs earlier for timely action to provide maximum benefit to the patient.

REFERENCES

1. Naranjo CA, Busto U, Sellars EM, Sandor P, Ruiz I, Roberts EA and Janecek E. Method for Estimating the Probability of Adverse Drug Reactions. Clin Pharmacol Ther. 1981;30:239–45.
2. Fries JF, Williams CA, Morfield D, Singh G, Sibley J. Reduction in long-term disability in patients with rheumatoid arthritis by disease-modifying antirheumatic drug-based treatment strategies. Arthritis Rheum. 1996 Apr;39(4):616-22
3. ACR Ad Hoc Committee on Clinical Guidelines. Guidelines for monitoring drug therapy in rheumatoid arthritis. Arthritis Rheum. 1996 May;39(5):723-31.
4. Davies E.C, Green CF, Mottram, Pirohamed M. Adverse drug reactions in hospitals: A narrative review. Current Drug Safety, 2007, 2, 79-87.
5. Lee TJ, Park BH, Son HY, Song R, Shin KC, Lee EB, Song YW. 2012. Cost of illness and quality of life of patients with rheumatoid arthritis in South Korea. Value in Health15: S43-S49
6. Clements JN. 2012. Treatment of rheumatoid arthritis: a review of recommendations and emerging therapy.Formulary 46: 532-45.
7. Schneider M, Manabile E, Tikly M. 2008. Social aspects of living with rheumatoid arthritis: a qualitative descriptive study in Soweto, South Africa-a low resource context. Health and Quality of Life Outcomes 6(54): 1-11
8. Symmons D, Mathers C, Pfleger B. 15 August 2006. World Health Organization.The global burden of Rheumatoid Arthritis in the year 2000.Global Burden of Disease 2000. Available: http://www.who.int/healthinfo/statistics/bod_rheumatoidarthritis.pdf [Accessed 14.02.2013]
9. Gawde SR, Shetty YC, Merchant S, Kulkarni UJ, Nadkar MY. Drug utilization pattern and cost analysis study in rheumatoid arthritis patients-a cross sectional study in a tertiary care hospital Mumbai in British Journal of Pharmaceutical Research. 2013;3(1):37-45.
10. Schinerder JK, Milon LC, Frengley JD. Adverse drug reaction in an elderly outpatient population.AmJ Hosp Pharm 1992;49:90-6
11. Shah A, William CE. Rheumatoid arthritis. In: Longo, Fauci, Kasper, Hauser, Jameson and Localzo's Harrison's principles of internal medicine, Mc Graw Hill, New york, 18th edition; 2012:2:27382752.