Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

Pharmacology

Adverse Drug Reactions Monitoring of Antimicrobials in ICU, Department of Medicine at a Tertiary Care Hospital, Rewa, MP

Raj Bhupendra[1], Pandey Vivek[2*], Singh Prabhakar[3], Singh Amita[4], DubeyVandana[5]
[1]Professor & HOD Pharmacology, SS. Medical College, Rewa, Madhya Pradesh, India
[2]Tutor, Pharmacology, SS. Medical College, Rewa, Madhya Pradesh, India
[3]Professor, Pharmacology, SS. Medical College, Rewa, Madhya Pradesh, India
[4]Associate Professor, Physiology, SS. Medical College, Rewa, Madhya Pradesh, India
[5]Sr. Biochemist, Pharmacology, SS. Medical College, Rewa, Madhya Pradesh, India

Original Research Article

***Corresponding author**
Pandey Vivek

Article History
Received: 26.09.2018
Accepted: 09.10.2018
Published: 30.10.2018

DOI:
10.36347/sjams.2018.v06i10.047

Abstract: Adverse drug reaction (ADR) contributes to the burden of drug related patient morbidity, mortality and adding to the cost of patient health care. The aims of study is to assess the frequency & pattern of ADRs and the group of drugs commonly involved to producing the suspected ADRs in intensive care unit of medicine department. This study was conducted between August 2015 to July 2016. All cases that have suspected ADRs conform to WHO definition, having of age 18 years or more were enrolled in the study. Total 164 cases with suspected ADRs were presented during study. The data were analyzed by Microsoft word - excel version 2007. All the multiple responses were presented in terms of number and percentage. Total 4860 patients were admitted in medicine ICU during study period, out of which 2714 were males and 2146 were females. Maximum 49 (29.13%) patients with suspected ADRs were belong to ≥60 years of age and minimum 13 (6.08%) were belong to 30-39 years of age group. Gastrointestinal system is the most commonly (35.21%) involved organ system and nausea is most commonly (19.13%) reported ADR, followed by vomiting, diarrhea and skin rashes. Among antimicrobials Ceftriaxone was maximally (17.73%) associated with ADRs, followed by Levofloxacin (9.92%), Quinine and Metronidazole (7.8%). In our study the majority of patients were females. The gastrointestinal system is the most common affected organ system and the antimicrobials are the drugs having highest incidence of suspected ADRs, among AMAs Ceftriaxone is maximally associated with suspected ADRs.

Keywords: Pharmacovigilance, Antimicrobials, Adverse drug reaction (ADR), Adverse drug event (ADE).

INTRODUCTION

Adverse drug reaction (ADR) contributes to the burden of drug related patient morbidity, mortality and adding to the cost of patient health care. They are common and often preventable cause of hospital admission. The detection and monitoring of ADRs is of vital importance for patient safety, as more than 50% of approved drugs are associated with some types of adverse effects that are not detected prior to their approval for clinical use [1]. An adverse drug reaction as defined by WHO is a "response to a medicinal product which is noxious, unintended and occurs at doses normally used in men for the prophylaxis, diagnosis or treatment of disease or for the restoration, correction or modification of physiological function [2]. ADRs constitute an enormous burden for the society and it is one among the leading cause of death. Many physicians are unaware that any suspected ADRs should be reported to the ADR reporting and monitoring centers, as a result, ADRs are often not detected or documented. There is greater and urgent need to create and enhance the physician's awareness about detection, management, prevention and reporting of ADR. The incidence of ADR in Indian population ranges between 1.8-25.1%, with 8% resulting in hospitalization [3]. Data on ADRs are poor and inadequate and up to 57% of ADRs are unrecognized by attending physicians[4], though they are implicated as 7th common cause of death[5] Advancing age is not an independent risk factor for adverse drug reactions [6] but **c**o-morbidity with advancing age becomes a risk factor. Awareness of those co-morbid conditions which predict adverse drug reactions can help clinicians to identify which older adults are at greater risk, therefore, who might benefit from closer monitoring [7]. So studying the adverse drug reactions/events becomes important to give better patient care. There might be many factors responsible for this scanty reporting such as heavy patient load on prescribers, irrational prescribing drugs that are dispensed without

prescriptions, polypharmacy, use of many alternative system of medicines, and unavailability of sufficiently trained and motivated doctors and other paramedical staff for ADR reporting [8].

MATERIALS & METHODS

This study was conducted after getting approval from institutional ethics committee, in the department of Pharmacology and department of Medicine, Sanjay Gandhi Memorial Hospital, Rewa (M.P.) between Aug.2015 to July 2016, total 12 months of duration, to assess the incidence and pattern of ADRs and the group of drugs mostly associated with suspected ADRs among patients admitted in the department of medicine. Patients with suspected ADRs were enrolled after taking their informed written consent with willingness to available for follow up. All cases that have suspected ADRs conforms to WHO's definition, having of age 18 years or more of either gender with suspected ADRs and patient with suspected ADRs developed after being admitted to the hospital or having suspected ADRs prior to being admitted in hospital were enrolled in study. All the patients having unclear drug intake history or patient those not willing to complete the procedure or ADRs occur due to alternative medicines like Ayurveda, Homeopathy & Unani system and patients having psychiatric illness were excluded from study. Before conducting the study resident doctors, nursing staff and paramedical staff were motivated to report the suspected ADRs. Data of spontaneously reported suspected ADRs were collected by healthcare professionals. For each patient with suspected ADR, a detailed history including drug history, personal history, family history, present and past medical history, and history of previous drug allergy were documented and any untoward event was labeled as suspected adverse drug reaction after discussion with the treating physician. The data were analyzed by using Microsoft word excel version 2007. All the multiple responses were presented in terms of number and percentage.

RESULTS

In this study total 4860 patients were admitted in medicine ICU during study period, out of which 2714 were males and 2146 were females.(*Table*1) Among which the maximum number 49 (29.13%) of patients were belong to ≥60 years of age group followed by 47 (26.52%) patients 18-29 years; 26 (20.0%) patients 50-59 years; 29 (18.26%) patients 40-49 years and minimum 13 (6.08%) patients 30-39 years of age group. (*Table2)* Total 230 suspected ADRs were reported during study in total of 164 patients, of which 106 (46.08%) were reported in 71 males and 124 (53.91%) in 93 female patients. The overall incidence of suspected ADRs is 3.37%. *(Table1)* Among organ system, the gastrointestinal system is the commonest (35.21%) affected organ system with suspected ADRs followed by skin and mucous membrane (24.78%), central nervous system (8.26%), cardiovascular system (6.08%), hepatobiliary system (4.34%) and respiratory system (3.04%) in decreasing order. Others 18.26% suspected ADRs were related to the genitourinary, musculoskeletal and endocrine system. (*Graph1)* Among the suspected ADRs, nausea is the most commonly(19.13%) reported ADR, followed by vomiting, diarrhea, skin rashes and pruritus (12.60%), Gastritis/GI upset and burning sensation (11.30 %), Rigor and chills(8.26%), Fever (5.21%), Breathlessness and oral ulcer (3.91%), Headache, deranged liver function and dryness of mouth (3.47%), Weakness & sweating (hypoglycemia) 3.04%, pedal edema and constipation (2.60%). Oral candidiasis, dizziness, drowsiness and disorientation (2.17 %), anxiety and swelling of lips (1.73%) whereas SJS, Gum hypertrophy and palpitation (1.30%) and altered sensorium and Bullous eruption were seen with minimum (0.86 %) incidence.*(Table 3)* Among the antimicrobials; Ceftriaxone was the drug which is associated with maximum (17.73%) suspected ADRs followed by Levofloxacin (9.92%), Quinine and Metronidazole (7.8%), Piperacillin+Tazobactam were associated with 5.67%, Vacomycin 4.96%. Ciprofloxacin, Amoxicillin+Clavulanic acid, Meropenam, Linezolid and Clindamycin were associated with 4.25% of ADRs, Ofloxacin and Lumefantrine+Artemether 3.54%. HRZE, Norfloxacin and Artemether were associated with 2.83%, Cefixime, Albendazole and Fluconazole 2.12% and Ampicillin and Moxifloxacin were associated with 1.41% of suspected ADRs *(Table 4).*

Table-1: Gender wise distribution of reported suspected ADR and its incidence

S.no.	Gender wise distribution of patients	Numbers and percentage (%) of reported suspected ADRs	Number of patients with ADR/total number of patients admitted during the study period	Incidence of suspected ADR (%)
1	Male	106 (46.08%)	71/2714	2.61%
2	Female	124 (53.91%)	93/2146	4.33%
	Total	230 (100%)	164/4860	3.37%

Table-2: Age wise distribution of patients and reported suspected ADR

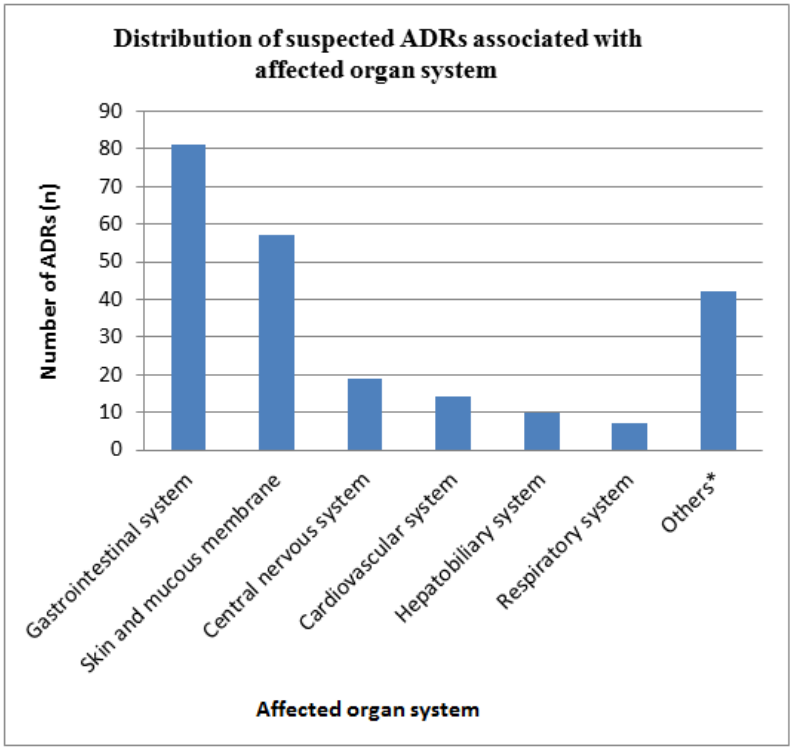
S.no.	Age group (in years)	Number of patients enrolled during study period			Age wise distribution of suspected ADRs	
		Number of male patients	Number of female patients	Number of total patients	Number of suspected ADRs	Percentage of suspected ADRs (%)
1	18-29	18	29	47	61	26.52%
2	30-39	4	9	13	14	6.08%
3	40-49	12	17	29	42	18.26%
4	50-59	13	13	26	46	20.00%
5	≥60	24	25	49	67	29.13%
	Total	71	93	164	230	100%

Table-3: Frequency distribution of pattern of suspected ADRs reported during study period

S.no.	Pattern of Suspected ADRs reported during study period	Number and Percentage of suspected ADRs	
		Number	Percentage
1	Nausea,vomiting&Diarrhoea	44	19.13%
2	Skin rashes /Pruritis	29	12.6%
3	Gastritis/GI upset/burning sensation	26	11.3%
4	Rigour& chills	19	8.26%
5	Fever	12	5.21%
6	Breathlessness	9	3.91%
7	Oral ulcers	9	3.91%
8	Dryness of mouth	8	3.47%
9	Headache	8	3.47%
10	Deranged Liver function	8	3.47%
11	Weakness & sweating (hypoglycemia)	7	3.04%
12	Constipation	6	2.60%
13	Pedal odema	6	2.60%
14	Dizziness/drowsiness/disorientation	5	2.17%
15	Oral candidiasis	5	2.17%
17	Tinnitus	5	2.17%
18	Anxiety	4	1.73%
19	Swelling of lips	4	1.73%
20	Gum hypertrophy	3	1.30%
22	Hypotension	3	1.30%
23	Palpatation	3	1.30%
24	SJS	3	1.30%
25	Altered sensorium	2	0.86%
26	Bullous eruption	2	0.86%
	Total	230	100%

DISCUSSION

In the present study maximum number of patients (29.13%) with suspected ADRs were belong to ≥60 years of age group. This was similar to the spontaneous study conducted by Jose J *et al.* [9], in which significantly higher percentage of suspected ADRs were occurs among geriatric patients compare to adults. This may occur because geriatric patients have higher incidence of admission in the intensive care unit (ICU) with multi-organ dysfunction as well as altered pharmacokinetic parameters. Hence they are more susceptible to appear adverse drug reactions [10, 11]. In the present study the overall incidence of ADRs were very low (3.37%) compare to two other meta-analysis conducted by Lazarou *et al.* [12] and Murphy BM *et al.*[13] in which the incidence of ADRs were 15.1% and 35% respectively. This discrepancy could be due to relatively small sample size, inclusion of only the medicine ICU patients and also due to the under reporting of cases. The reasons for under reporting are more likely due to lack of initiative, fear of personal liability etc. The higher incidence of ADRs was seen in female population (4.33%) compare to male population (2.61%) in our study, this is similar to the study conducted by Camargo AL *et al.* [14].



Graph 1

Table-4: Frequency distribution of specific Antimicrobial Agents associated with suspected ADRs

S.no.	Antimicrobial Agents associated with suspected ADRs	Number and Percentage of suspected ADRs	
		Number	Percentage (%)
1	Ceftriaxone	25	17.73%
2	Levofloxacin	14	9.92%
3	Quinine	11	7.8%
4	Metronidazole	11	7.8%
5	Piperacillin+tazobactam	8	5.67%
6	Vancomycin	7	4.96%
7	Ciprofloxacin	6	4.25%
8	Amoxicillin+Clavulanic acid	6	4.25%
9	Meropenam	6	4.25%
10	Linezolid	6	4.25%
11	Clindamycin	6	4.25%
12	Ofloxacin	5	3.54%
13	Lumefantrine+Artemether	5	3.54%
14	HRZE	4	2.83%
15	Norfloxacin	4	2.83%
16	Artemether	4	2.83%
17	Cefixime	3	2.12%
18	Albendazole	3	2.12%
19	Fluconazole	3	2.12%
20	Ampicillin	2	1.41%
21	Moxifloxacin	2	1.41%
	Total	141	100%

There are various reasons have been proposed to explain the higher incidence of ADRs in females like difference in pharmacodynamic response, difference in drug metabolism through CYP 3A4 whose activity is higher in females than males. Camargo AL *et al*. [14]. Female gender may have enhanced tissue sensitivity, lower weight, sex related differences in pharmacokinetic parameters and pharmacological, immunological and hormonal differences are also responsible for the higher incidences of ADRs [15-17]. In the present study the gastrointestinal system was commonest (35.21%) affected organ system, followed

by Skin and mucous membrane (24.78%), this was similar to the study conducted by Chatterjee S *et al*.[18], in which gastrointestinal system was the main organ system affected by the ADRs with the incidence of 31.63%, this result was also similar to the study conducted by Kathiria J M *et al*. [19], in which gastrointestinal system was most commonly affected organ system (26.67%) followed by skin and mucous membrane (20%), central nervous system (15.56%) and the least affected organ system was respiratory system which having only 2.22% of incidence of ADRs. In our study the maximum reported ADR is nausea, vomiting and diarrhea (19.13 %) followed by skin rashes and pruritus (12.60%). This result was dissimilar to the earlier study conducted by Jose J *et al*. [9], in which the highest incidence of reported ADR was diarrhea (12.24%) and another study conducted by Saravanan SS *et al*.[20], in which diarrhea was the commonest (28.57%) reported ADR followed by skin rashes (14.28%). In our study, antimicrobials were associated with highest incidence of ADRs; among antimicrobials Ceftriaxone was associated with highest number (17.73%) of suspected ADRs, followed by Levofloxacin (9.92%), Quinine and Metronidazole (7.8%) and minimum 1.41% suspected ADRs were associated with Ampicillin and Moxifloxacin. This pattern of suspected ADRs was similar to the result of the study conducted by Kathiria JM *et al*.[19], in which Ceftriaxone and Levofloxacin were associated with 16.66% and 12.55% of ADRs respectively. Result our study was also similar to another study conducted by Harsha R *et al*. [21], in which Ceftriaxone was responsible for most (18.0%) of suspected ADRs among antimicrobials.

REFERENCES

1. Rabbour RSM, Emmerton L. An introduction to adverse drug reporting system in different countries. 2005; 13 (1):91-100.
2. Edward IR, Aronson JK. Adverse drug reaction: definition, diagnosis and management Lancet. 2000; 356 (9237):1255-1259.
3. Sriram S, Ghasemi A, Ramaswamy R, Devi M, Balasuramanian R, Ravi TK, Sabzghabaee AM. Prevalence of adverse drug reaction at a private tertiary care hospital in south India. JRMS 2011; 16 (1):16-25.
4. Fracas A, Bojita M. Adverse drug reaction in clinical practice: a causality assessment of a case of drug-induced pancreatitis. J Gastrointestin Liver Dis. 2009; 18 (3): 353-58.
5. Padmaja U, Adhikari P, Pereira P. A prospective analysis of adverse drug reaction in a south Indian hospital. Online J Health Allied Scs. 2009; 8(3):12.
6. Carbonin P, Pahor M, Bernabei R, Sgadari A. Is age an independent risk factor of adverse drug reactions in hospitalized medical patients? J Am Geriatr Soc 1991 Nov; 39(11):1093-9.
7. Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. Bmj. 2009 Jan 7;338:a2752.
8. Uppsala reports, URI-31, October 2005 www.whoumc.org/defs.html.
9. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. Pharmacological research. 2006 Sep 1;54(3):226-33.
10. Sharma B, Bhattacharya A, Gandhi R, Sood J, Rao BK. Pharmacovigilance in Intensive Care Unit-An Overview. Indian Journal of Anaesthesia. 2008 Jul 1;52(4):373.
11. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. Annals of Pharmacotherapy. 2008 Jul;42(7-8):1017-25.
12. Lazarou J, Pomeranz BH and Corey PN. Incidence of Adverse Drug Reactions in Hospitalized Patients. A Meta analysis of Prospective Studies. Journal of American medical Association. 1998; 279(15):1200-1205.
13. Murphy BM, Frigo LC. Development, implementation, and results of a successful multidisciplinary adverse drug reaction reporting program in a university teaching hospital. Hospital pharmacy. 1993 Dec;28(12):1199-204.
14. Camargo AL, Ferreira MB, Heineck I. Adverse drug reactions: a cohort study in internal medicine units at a university hospital. European journal of clinical pharmacology. 2006 Feb 1;62(2):143-9.
15. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. Bmj. 2004 Jul 1;329(7456):15-9.
16. Rademaker M. Do women have more adverse drug reactions?. American journal of clinical dermatology. 2001 Dec 1;2(6):349-51.
17. Palaian S, Mishra P, Shankar PR, Dubey AK, Bista D, Almeida R. Safety monitoring of drugs--where do we stand?. Kathmandu University medical journal (KUMJ). 2006;4(1):119-27.
18. Chatterjee S, Ghosh AP, Barbhuiya J, Dey SK. Adverse cutaneous drug reactions: A one year survey at a dermatology outpatient clinic of a tertiary care hospital. Indian J Pharmacology 2006; 38:429-431.
19. Kathiria JM, Sattigeri BM, Desai PM, Patel SP. A study of adverse drug reactions in patients admitted to intensive care unit of a tertiary care teaching rural hospital. Int J Pharm Pharm Sci. 2013;5(1):160-3.
20. Saravanan S Selva, Kavitha P, Ponnuswamy T.K. Patterns of Adverse Drug Reactions in the Medical Intensive Care Unit of an Indian Tertiary Care Hospital, International Journal of Pharmaceutical & Biological Archives; 5(3): 64 –68, 2014.

21. Harsha R. A prospective study of adverse drug reactions in outpatients and in patients of medicine department in a tertiary care hospital, Kempegowda institute of medical sciences. A Thesis, at department of pharmacology kempegowa institute of medical sciences Bangalore, 2013.