Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20160129

Research Article

Study of adverse drug reactions in a tertiary care teaching hospital

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Received: 16 December 2015
Accepted: 07 January 2016

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ABSTRACT

Background: Adverse drug reactions (ADRs) are the recognized dangers of drug treatment and can arise with several groups of drugs. The purpose of this study was to identify and assess ADRs in inpatients of a tertiary care teaching hospital in Potheri.
Methods: A prospective spontaneous reporting was carried out in a tertiary care teaching hospital, Potheri for a period of eight months. The causality assessment of the reported ADRs was done using the Naranjo causality assessment scale. The severity of ADRs was classified as mild, moderate or severe according to the modified Hartwig and Siegel scale.
Results: A total of 62 ADRs were reported with male preponderance (51.6%). Majority of ADRs was from General Medicine and General Surgical departments in which the most affected organ systems were the skin (69.4%) and the gastrointestinal system (8.1%). The most frequent drugs causing ADRs were antibiotics (53.2%) in which type B reactions were more compared to type A. The severity assessment showed that most of them were mild reactions (51.6%). Causality assessment revealed that 61.3% of the reactions were probable, possible (30.6%), definite (8.1%) and no reactions were unlikely.
Conclusions: The study accomplished that ADRs are widespread and a few of them raised the healthcare expenditure due to the increased hospital stay. The reporting of ADRs to regional pharmacovigilance centres should be encouraged to ensure drug safety.

Keywords: Adverse drug reactions, Drug safety, Pharmacovigilance

INTRODUCTION

An adverse drug reaction is 'a response to a drug that is noxious and unintended and which occurs in doses normally used for the treatment, prophylaxis, or diagnosis of disease, or the modification of physiological function' (World Health Organization).[1] Adverse drug reactions affect patients' convalescence as well as the finances of health care. They are important causes of mortality and morbidity in both ambulatory and hospitalized patients. So there is a need to analyse ADRs to create awareness among patients and to motivate healthcare personnel to report ADRs. Early recognition, evaluation and monitoring of ADR are essential to improve public health.

In the United States, it has been reported that ADRs due to over the counter and prescription drugs from 1966 to 1996 affected 6.7% of patients with 3.2% death.[2] While similar figures are not available for India, it is logical to assume that the figures would be much higher considering high levels of unmonitored and indiscriminate drug use widespread in the country.[3] India is a developing country with a large drug utilising population. It is the fourth largest producer of pharmaceuticals in the world with more than 6000 licensed drug manufacturing firms and over 60,000 branded formulations. It is also emerging as a focus for clinical trials exposing larger population to newer drug treatments. It is critical to identify ADRs at the earliest and to prevent them if possible, to ensure the welfare of the patient at a reasonable expenditure.

The Central Drugs Standard Control Organisation (CDSCO), New Delhi, under the guidance of Ministry of Health & Family Welfare, Government of India has initiated a countrywide pharmacovigilance programme (PvPI) in 2010, with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordinating Centre for monitoring ADRs in the nation. Our hospital is one of the centres for monitoring and reporting ADRs through this programme.

METHODS

After obtaining approval of the Institutional Ethics Committee, a prospective spontaneous reporting study involving active methods (pharmacist actively seeking suspected ADRs) and passive methods (stimulating clinicians to report suspected ADRs) was carried out in all departments of a tertiary care teaching hospital, Potheri for a period of eight months. [4] Patients of all age groups who developed Adverse Drug Reactions were included for the study. Informed consent was obtained from the patients. The data for the study were taken from case sheets, investigation reports, personal interviews with clinicians, and personal interviews with patient or patient's attendant, past history of medications and reports of Medical and surgical interventions.

The causality assessment of the reported ADRs was done using the Naranjo causality assessment scale into definite, probable, or possible.[5] The modified Hartwig and Siegel scale defines the severity of ADR as mild, moderate or severe according to factors like necessities for change in treatment, length of hospital stay, and the disability produced by the ADR.[6]

RESULTS

During the study period, 62 adverse drug reactions were reported. Of these, 32 (51.6%) were males and 30 (48.3%) were females (Figure 1). The male to female ratio according to occurrence of ADRs was 1.06. Pediatric patients (<18years) experienced 2 (3.22%) ADRs, followed by geriatric patients (>60years) 12 (19.35%) ADRs and adults 48 (77.42%) ADRs (Figure 2). Classification of ADRs showed that most of the reactions were type B (Bizarre) reactions.

According to the Naranjo algorithm scale, 38 (61.3%) reactions were assessed to be probable, 19 (30.6%) as possible and 5 (8.1%) as definite. Severity assessment of the ADRs showed that the majority of the reactions were mild (32, 51.6%), followed by moderate (24, 38.7%) and severe (6, 9.7%). In 56 (90.3%) ADRs, complete recovery were achieved. Five (8.1%) ADRs were classified as 'unknown outcomes' since the outcomes could not be assessed as the patients wanted voluntary discharge from the hospital. In 45 (72.5%) patients, the offending drug was stopped. The offending drug was substituted with another drug in 2 (3.2%) patients and the dose was reduced to alleviate the symptoms in 4 (6.5%) patients. No change in treatment was endeavoured in 11 (17.7%) patients. Causality assessment was done according to Naranjo et al. Outcomes were assessed according to Hartwig et al (Table 1).

Table 1: Classification and assessment of ADRs.

Parameter	Number of ADRs (%)
Causality	
definite	5(8.1%)
probable	38(61.3%)
possible	19(30.6%)
Onset of ADRS	
Acute(<1hr)	4(6.5%)
Sub-acute(1-24 hrs)	37(59.6%)
Latent(>2days)	21(33.9%)
Severity	
mild	32(51.6%)
moderate	24(38.7%)
severe	6(9.7%)
Outcomes	
fatal	1(1.6%)
fully recovered	56(90.3%)
unknown	5(8.1%)
Treatment	
stopped the medication	45(72.5%)
reduced the dose	4(6.5%)
substituted another drug	2(3.2%)
no change	11(17.7%)

Antibiotics were associated with about half of all the ADRs reported (33, 53.2%) (Figure 3). Among the antibiotics, Ciprofloxacin was the most common drug to produce ADRs (9, 27.3%) followed by Cefotaxime (6, 18.2%) (Table 3). Itching (24, 38.7%) was the most common ADR reported followed by rashes (17, 27.4%) and vomiting (5, 8.1%). The most commonly affected organ system was found to be the skin (43, 69.35%) followed by gastrointestinal and cardiovascular systems (5, 8.1% each) (Table 2).

Table 2: Organ systems affected due to ADRs. The numbers represent the total number of ADRs that involved the corresponding organ system.

Organ system	Number of ADRs (%)
Skin	43(69.4%)
Gastrointestinal system	5(8.1%)
Cardiovascular system	5(8.1%)
Central nervous system	4(6.5%)
Respiratory	2(3.2%)
Genitourinary	2(3.2%)
Eyes, ears, nose and throat	1(1.6%)

Table 3: ADRs associated with antibiotics.

Drug	Route of administration	Number of ADRs (%)
Ciprofloxacin	IV/PO	9(27.3%)
Cefotaxime	IV	6(18.2%)
Metronidazole	IV/PO	3(9.1%)
Levofloxacin	PO	3(9.1%)
Penicillin	IM/PO	2(6.1%)
Cefixime	PO	1(3.1%)
Ofloxacin	IV	1(3.1%)
Cefoperazone-Sulbactam	IV	1(3.1%)
Ceftriaxone-Tazobactam	IV	1(3.1%)
Cephalexin	PO	1(3.1%)
Amoxicillin	PO	1(3.1%)
Cotrimoxazole	PO	1(3.1%)
Amikacin	IM	1(3.1%)
Amoxicillin-Clavulanic Acid	IV	1(3.1%)
Ampicillin	IM	1(3.1%)

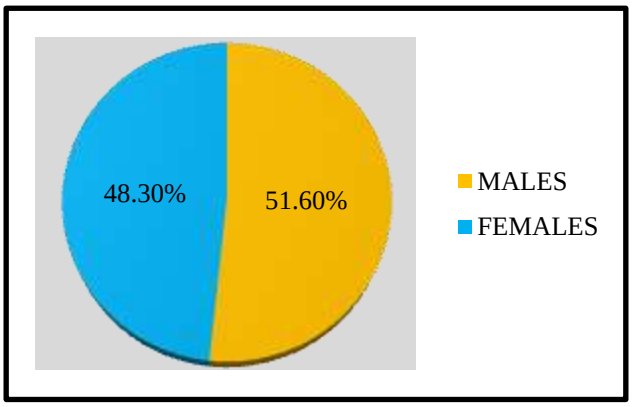

Figure 1: Division of ADRs based on the gender of the patients.

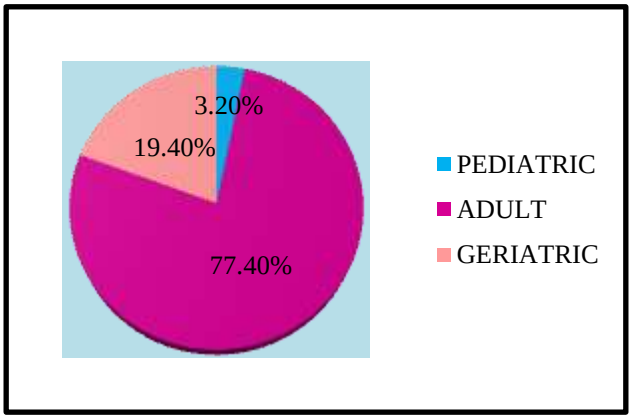

Figure 2: Distribution of ADRs based on age group of patients.

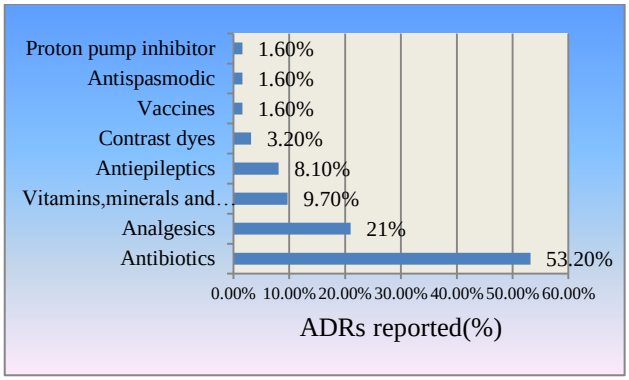

Figure 3: Most commonly involved groups of drugs in ADRs. The total number of reactions reported for each group is presented.

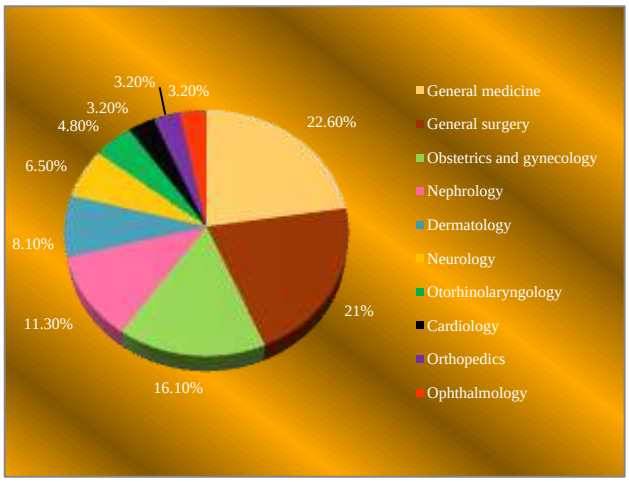

Figure 4: Number of ADRs received from different departments.

DISCUSSION

Majority of ADRs (77.4%) were seen in adult age group which was comparable with the previous study by Sharma et al. where it was 50.4%.[7] The most frequent ADRs were due to the antibiotics which could be associated with increased frequency of prescription of antibiotics. The number of ADRs were high in General Medicine and General Surgery departments due to amplified use of antibiotics in these departments for the treatment and prophylaxis of various diseases and also since the patients admitted were with multiple co-morbidities requiring polypharmacy. In accordance with previous studies by Misbah M et al, Oshikoya et al and Shareef et al, the present study showed the predominance of cutaneous manifestations.[8-10] Classification of reported ADRs according to Rawlin and Thompson scale revealed Type B predominance. This result is in line with the study by Suthar and Desai but on the contrary, studies conducted by Oshikoya et al. and Stavreva et al. showed a preponderance of Type A reactions.[9,11,12] On analysing the fate of the suspected drugs, it was found that the drug was withdrawn in most of the cases and the dose was

reduced in some while no change was made in others considering the risk benefit ratio in particular patients. Majority of the patients recovered completely from the ADR since most of the reactions were mild according to the modified Hartwig and Siegel scale. However, the study carried out by Shamna et al. reported that moderate reactions were more followed by mild and severe ones.[4] Only one ADR was fatal which was not preventable. The causality assessment of the reported ADRs according to the Naranjo scale revealed that no reactions were unlikely and most of them were probable with a lesser number of possible and definite ADRs. This data is in correlation with the study of Jimmy Jose et al.[12]

CONCLUSION

The results of this study provide awareness to the healthcare providers on the significance of monitoring and reporting adverse drug reactions. The study accomplished that ADRs are widespread and a few of them raised the healthcare expenditure due to the increased hospital stay. The reporting of ADRs to regional pharmacovigilance centres should be encouraged to ensure drug safety.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Ramya R, Jamuna Rani R, Varadarajan S. Study of adverse drug reactions in a tertiary care teaching hospital. Int J Basic Clin Pharmacol 2016;5:209-12.