Original Article

Profile of adverse drug reactions in a rural tertiary care hospital

Naser Ashraf Tadvi[1], *Mabu Shareef S[2], Dinesh M Naidu C[3], Karuna Sree P[2], Venkata Rao Y[4]

[1]Associate professor, [2]Assistant professor, [3]Professor, [4]Professor and Head, Department of Pharmacology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda District, Telangana State, India.

ABSTRACT

Background: Adverse drug reactions are the fourth leading cause of mortality and a great concern in therapeutics. Atleast one adverse drug reaction has been reported to occur in 10 to 20% of hospitalized patients. The present study was conducted with the aim of analyzing the pattern of adverse drug reactions occurring in our institution and to identify the common drugs, their manifestations and severity.

Methods: An observational prospective study was conducted over a year. The red boxes for dropping the filled yellow adverse drug reactions forms were installed in all the wards and outpatient departments. Additional information and missing data was obtained personally by either consulting the physician or through case sheets.

Results: The most common class of drugs implicated in causation of adverse drug reactions was antimicrobials (52%), followed by drugs acting on central nervous system. The most commonly observed adverse drug reactions were dermatological (66.67%) and type B reactions. Majority of the adverse drug reactions belonged to possible (60%) or probable (33.33%) category.

Conclusion: Dermatological reactions are the most common adverse drug reactions occurring in our hospital and antimicrobials are the most common causative drugs. There is a need for increasing the awareness and knowledge about adverse drug reactions reporting system for promoting the safe use of drugs.

Key words: Adverse drug reactions, Pharmacovigilance.

Introduction:

Adverse Drug Reaction (ADR) is defined as any noxious, unintended or undesirable effect of a drug which occurs at dose normally used in man for prophylaxis, diagnosis or treatment of a disease or for modification of physiological function.[1]

***Corresponding author :**

Dr S Mabu Shareef

Department of Pharmacology,

Kamineni Institute of Medical Sciences, Narketpally, Nalgonda district, Telangana state – 508254,

drsharifshaik@gmail.com

Adverse drug reactions (ADRs) are the fourth leading cause of mortality and a great concern in therapeutics.[2] Atleast one ADR has been reported to occur in 10 to 20 % of hospitalized patients.[3,4] ADRs have an immense economic burden on the patients as well as health care establishment.[5] A study conducted in South India estimated the cost for management of ADRs in hospital as rupees 481/- per day.[6] Pharmacovigilance or ADR monitoring is an integral part of drug therapy but in Indian hospitals it is not well practiced.[7] Pharmacovigilance is defined as the science and activities relating to detection, assessment, understanding and prevention of adverse drug reactions or any other drug related

problem.[6] The importance of pharmacovigilance can be understood by the fact that spontaneous reporting system has led to withdrawal of some popular drugs like rofecoxib, rosiglitazone and terfenadine.[5] The Central Drugs Standard Control Organization (CDSCO) under the aegis of Ministry of Health and Family welfare, Government of India in collaboration with Indian Pharmacopoeia Commission, Ghaziabad has initiated nationwide Pharmacovigilance Programme of India (PvPI). One of the targets of PvPI is to enroll all medical colleges in India as ADR monitoring centres by year 2014.[8]

The present study was conducted with the aim of analyzing the pattern of Adverse Drug Reactions occurring in our institution and to identify the common drugs implicated in causation of ADRs and to report the most common manifestations associated with these ADRs and their severity.

Materials and Methods

An observational prospective study was conducted over a period of one year from October 2012 to September 2013. Before the start of study introductory awareness lectures were organized by pharmacovigilance cell for all health care professionals i.e. clinicians, postgraduate students, interns and nursing staff. They were informed about the spontaneous ADR reporting system and importance of pharmacovigilance to motivate the voluntary reporting of adverse drug reactions. They were requested to report all observed adverse events and were also imparted training for filling the yellow ADR reporting forms. The yellow ADR reporting forms were made available at all nursing stations in the hospital for easy access of all the health care professionals. The red boxes for dropping the filled yellow ADR reporting forms were installed in all wards, emergency units and outpatient departments in accordance with the guidelines of PvPI. The yellow ADR reporting form included the information like patient initials, age, sex, diagnosis, name of suspected drug with route and frequency of administration and the signature of the reporter etc. The red ADR boxes were checked daily for ADR forms. On receiving the ADR reporting form they were checked for completeness and the missing data was obtained by personally visiting the patient and going through the case sheets in case of doubt or for any clarification, the treating physicians were consulted. Demographic analysis of the patients with respect to age and gender was done.

The ADRs were classified depending upon the organ system affected and also based upon the type of reaction as per Rawlins and Thomson criteria.[9] The severity of reaction was determined based on the classification system of Hartwig et.al.[10] Causality assessment for relationship between the drug and reaction was established using World Health Organization: Uppsala Monitoring Centre (WHO:UMC) scale for causality assessment.[11] The results were analyzed using descriptive statistics.

Results

Thirty ADR forms were received by the pharmacovigilance unit from various clinical departments. Out of these 25 were utilized for analysis and the rest were rejected due to their incompleteness in terms of reporters sign, patient initials, drug name and drug reactions. These 25 patients had 30 reported ADRs as few patients have multiple manifestations like vomiting, rash, pain abdomen and others.

Out of 25 ADRs received, 52% of the ADRs were reported by the postgraduate students, 44% by faculty members and 4% by interns. ADRs reported by nursing staff and medical students were nil.

The patients were categorized into four groups based on their age. In the present study, 64% of the patients were in age group of 21-40 years, followed by 16%, 12% and 8% in the age groups of 41- 60 years, 0-2 years and more than 60 years respectively. Out of 25 patients, 36% were males and 64% were females.

The reported ADRs were categorized according to the organ system involved. We observed higher percentage of reactions affected skin (66.67%)

and lowest percentage affected gastrointestinal and endocrine system of 3.33% each (Table 1).

Table 1 : ADR categorization according to system involved

S.No	System	No. of ADRs	% of ADRs
1.	Dermatological system	20	66.67
2.	Central Nervous System	06	20
3.	Gastro-intestinal system	01	3.33
4.	Endocrine System	01	3.33
5.	Others	02	6.67

Class of drugs implicated in the suspected ADRs is given in table 2 and the suspected ADRs associated with individual drugs given in table 3. The most common class of drugs involved in causation of ADRs was anti microbial drugs followed by central nervous system (CNS) drugs. Among the anti microbial drugs, anti bacterial drugs specifically cefotaxime resulted in higher number of ADRs. Among the CNS drugs, anti psychotics followed by anti epileptic drugs were associated with more ADRs.

Table 2 : Class of drugs implicated in suspect ADRs

S.No	Class of Drug	No of patients	% of patients
1	Antimicrobials		
	Antibiotics	9	36
	Antivirals	2	8
	Antitubercular	2	8
2	Drugs acting on CNS		
	Antipsychotics	5	20
	Antiepileptics	3	12
	NSAIDS	2	8
	Sedative hypnotics	1	4
	Gastro-intestinal drugs		
3	Antiemetic and anti ulcer drug	1	4

Out of 30 ADRs, 86.67% of the reactions were type B (bizarre reactions or unexpected reactions) and 13.33% were type A (Augmented pharmacological effects which are dose dependent and predictable) Among the ADRs assessed, serious ADRs (those requiring hospitalization or prolongation of hospital stay or fatality) constituted 16.67%. Non serious ADRs constituted 83.33% among which 13.33% were mild ADRs and 70.00% were moderate.

Table 3 : Suspected Adverse Drug Reactions and the implicated drugs

Drug reaction	Drug implicated	No. of patients	% of patients
Erythematous Rash	Inj cefotaxime	5	20
	Tab clonazepam	1	4
	Inj Augmentin / inj Gentamicin	1	4
	Tab Ciprofloxacin + Tinidazole	1	4
	Tab Norfloxacin + metronidazole	1	4
Itching and burning sensation all over body	Inj Ciprofloxacin	1	4
Stevenson Johnson Syndrome	Tab Nevirapine	2	8
	Inj Diclofenac	2	8
	Tab Phenobarbitone	1	4
Sialorrhoea	Tab. Clozapine	1	4
Drowsiness and weight gain	Tab Oxcarbamazepine	1	4
Extrapyramidal syndrome	Tab Risperidone	1	4
	Tab Fluphenazine	1	4
	Tab Trifluperazine	1	4
Visual hallucinations	Tab Zolpidem	1	4
Abdominal cramps and Seizures	Tab Esomeprazole + Tab. Domperidone	1	4
Galactorrhoea	Tab Risperidone	1	4
Hepatotoxicity	Isoniazid + Rifampicin + Pyrazinamide	1	4
Flu like symptoms	Tab Rifampicin	1	4

The causality assessment using the WHO scale revealed that 60% of ADRs were categorized as possible and 33.33% as probable, whereas 6.67% were classified as conditional as the details of rechallenge (recurrence of ADR with reintroduction of drug), dechallenge (cessation of ADR on withdrawal of drug) and recovery were missing in these patients.

Majority of the patients (68%) recovered from the adverse drug reaction and in 28% of patients details regarding the recovery were not known. In one patient the reaction was fatal (4%) and the action taken on the drug responsible for ADR was given in table 4.

Table 4 : Action taken on causative drug

Treatment	No. of Patients	% of Patients
Stopped the medication	21	84
Continued the same	01	4
Reduce the dose	02	8
Substituted another drug	01	4

Discussion

Adverse Drug Reactions are one of the commonest causes of morbidity and mortality worldwide, but they are overlooked by the clinicians most of the times. In India also ADRs have emerged as leading killers.12 The purpose of Pharmacovigilance Programme of India is to facilitate and improve the reporting of ADRs in India and increasing the safe use of medications. Establishment of Pharmacovigilance units in the hospitals has facilitated the spontaneous reporting of ADRs to a greater extent.

The present study was conducted in order to identify the most frequent ADRs occurring in the hospital, their nature, causality, severity and drugs commonly causing these ADRs. The functional ADR monitoring system in a hospital can help to measure ADR incidence rates over a period of time and increase the knowledge of health care professionals about the drug effects and improve risk management activities of ADRs. In this study ADRs were reported in 30 patients voluntarily over a period of one year by the health care professionals. Five cases were excluded from analysis due to insufficient data. When compared to the studies done by Swamy S et al5 (2013, 75 ADRs reported/ year), Arulmani R et al6 (2008, 120 ADRs reported/ year) the number of spontaneous ADRs reported was low. Many reasons can be identified for under reporting of ADRs, busy schedule of the clinicians, lack of incentive and lack of awareness etc were some of them.

The demographic analysis of the ADRs showed predominance among adults over geriatric and paediatric age group. This was in accordance with the previous studies by Murphy et al (1993),[13] Patidar et al (2013),[12] and Lobo et al (2013)[14] but differed from studies carried out by Lin and Lin (1991).[15] The reason may be higher number of adults visiting the hospital OPD or being hospitalized and dose adjustments made in paediatric or geriatric groups. The incidence of ADRs was more in females. This may be due to high medication use in females or metabolic or hormonal reasons.[14] This was in accordance with study by Arulmani et al (2008),[6] but contradicted the study by Lobo et al (2013).[14]

The most commonly observed ADRs were dermatological type B reactions. The reactions had a broad variety ranging from mild erythematous rash to life threatening conditions like Steven-Johnsons Syndrome. This finding was consistent with many other studies which have reported higher percentage of dermatological manifestations.[7,12,14,16] The probable reason for this is the visibility of these ADRs which makes the diagnosis easier. Antimicrobials were the most common drugs implicated in the ADR causation, cefotaxime being most common antibiotic to produce adverse drug reaction indicating wider usage of higher antimicrobials. Antipsychotics and antiepileptic drugs were the next leading cause of ADRs. This may be explained on the basis of their need of long term use. These findings are consistent with the previous studies by Patidar et al (2013),[12] Murphy et al (1993),[13] and Carnos et al (1974).[17] Most of the ADRs reported were from the post graduate students and faculty members and the undergraduate students and nursing staff have no participation in reporting ADRs. This may be due to lack of awareness or knowledge regarding the reporting of ADRs among the nursing staff.

Causality assessment was done to further strengthen the validity of findings by using WHO-UMC scale.[11] Majority of the ADRs belonged to possible or probable category but no reaction was categorized as definite. The severity assessment was done using Hartwig and Seigels severity assessment scale.[10] Majority of the ADRs were moderate in severity. These findings were in accordance with the study by Lobo et al (2013).[16] Timely intervention and stoppage of culprit drugs in 84% of patients may be the reason for decreased severity. Majority of the patients (68%) recovered from the ADRs but details regarding the recovery were not known for 28% of patients. This is in accordance with the study by Vijaya Kumar et al (2013).[7]

Most of the ADRs (83%) are non-severe and the reaction subsided with discontinuation of the causative drug. The drug was discontinued and symptomatic treatment was given in few cases. The causative drug was substituted with other drug in 4% of the cases.

Limitations of the study

The major limitation of this study was less number of ADRs. The preventability of the adverse drug reactions and cost incurred by ADRs was also not analyzed. The study was done using passive surveillance and not active method.

Conclusions

Dermatological reactions are the most common ADRs occurring in our hospital and antimicrobials are the most common causative drugs. Adverse drug reaction monitoring system is a new area for clinicians and spontaneous reporting can be increased by regular pharmacovigilance sensitization activities, which can help in promotion of safe use of drugs.

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References

1. World Health Organization: International drug monitoring: the role of the hospital. In Technical report series no. 425. Geneva, Switzerland: World Health Organization; 1969:1–24. Available at: http://whqlibdoc.who.int/trs/WHO_TRS_425.pdf
2. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA.1998;279(15): 1200-5.
3. Meyboom RH, Linquist M, Egberts AC, Edward IR. Signal selection and follow-up in pharmacovigilance. Drug Saf.2002; 25(6): 459–65.
4. Pirmohamed M, Breckenridge AM, Kitterinham NR, Park BK. Fortnightly review: adverse drug reactions.BMJ.1998; 316(7140): 1295–8.
5. Swamy S, Bhanuprakash, Nadig P, Muralimohan, Shetty M. Profile of Suspect Adverse Drug Reactions in a Teaching Tertiary Care Hospital. J Pharmacol Clin Toxicol. 2013; 1(1):1005.
6. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. Br J Clin Pharmacol. 2008; 65(2): 210-6.
7. Vijayakumar TM, Dhanaraju MD. Description of Adverse Drug Reactions in a multispeciality teaching hospital. Int.J.Integr.Med. 2013;1(26):1-6.
8. Pharmacovigilance programme of India 2010. CDSCO, Ministry of Health and Family Welfare, Government of India. 2010. Nov, [Last accessed on 2013 September 22]. Available from: http://www.cdsco.nic.in/pharmacovigilance_intro.htm.
9. Rawlins MD, Thomson JW. Mechanisms of adverse drug reactions. In Davies DM, editor. Textbook of Adverse Reactions. New York: Oxford University Press; 1991. p. 18–45.
10. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. American J Hosp Pharm.1992; 49(9):2229–32.
11. The use of the WHO-UMC system for standardised case causality assessment. [Last accessed on 2013 October 02]. Available from: http://www.who-umc.org/Graphics/24734.pdf
12. Patidar D, Rajput MS , Nirmal NP, Savitri W. Implementation and evaluation of adverse drug reaction monitoring system in a tertiary care teaching hospital in Mumbai, India. Interdiscip Toxicol. 2013; 6(1): 41–46.
13. Murphy BM, Frigo LC. Development, implementation and results of a successful multidisciplinary adverse drug reaction reporting program in university teaching hospital. Hosp Pharm.1993; 28(12): 1199–204.

14. Lobo MGA, Pinheiro SMB, Castro JGD, Momente VG, Pranchevicius MCS. Adverse drug reaction monitoring: support for Pharmacovigilance at a tertiary care hospital in Northern Brazil. BMC Pharmacology and Toxicology. 2013;14(5):1-7.

15. Lin SH, Lin MS. A survey on drug related hospitalization in a community teaching hospital. Int Clin Pharmacol Ther Toxicol.1991;31(2):66–9.

16. Chawla S, Kalra BS, Dharmshaktu P, Sahni P . Adverse drug reaction monitoring in a tertiary care teaching hospital. J Pharmacol Pharmacother. 2011; 2(3): 196–8.

17. Caranasos GJ, Stewart RB, Cluff LE. Drug induced illness leading to hospitalization. JAMA.1974; 228(6): 713–7.