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

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20182679

Original Research Article

A retrospective study of Adverse Drug Reactions in a tertiary care centre

V. J. Ambika Abhishake[1], S. Basalingappa[1], Arun Gopi[2], More Pankaj Daulat[3]*

[1]Department of Pharmacology, [2]Department of Community Medicine, DMWIMS Medical College, Meppadi, Wayanad, Kerala, India
[3]Department of Pharmacology, SMBT IMS & RC, Dhamangaon, Nashik, Maharashtra, India

Received: 19 April 2018
Accepted: 23 May 2018

***Correspondence to:**
Dr. More Pankaj Daulat,
Email: pankajdoc19@gmail.com

ABSTRACT

Background: Adverse drug reactions (ADRs) are a major concern in present day clinical practice. They are inevitable consequences of drug therapy; as no pharmacotherapeutic agent is completely free from noxious and unintended effects. They are major contributors for morbidity, mortality and hospitalization of the patients increasing the economic burden on the society and uncertainty in clinical outcomes.
Methods: This was a retrospective observational study, extending over 6 months (September 2016 to February 2017). A total of 290 cases were studied, excluding the geriatric age group. The data was collected using CDSCO ADR reporting form. A comparison of ADR between males and females was made; based on the organ system affected and the category of drug using "proportion test".
Results: The study showed the ADR incidence was equal in both sexes (≈50%). It was observed that majority ADRs were from gastro intestinal system (39%) followed by CNS (20%) and skin and soft tissue (14%). Constipation was found to be the most common of the reported ADRs (18%) followed by vomiting (9%) and diarrhoea (8%).
Conclusions: ADRs are a major cause of morbidity worldwide. Several studies; including the present one, has shown GIT to be the most common system affected. Frequency of ADRs can be reduced by careful follow up and a robust hospital based pharmacovigilance setup.

Keywords: Adverse Drug Reactions, Clinical trials, CDSCO, Pharmacovigilance

INTRODUCTION

Adverse Drug Reactions are one of the leading cause of hospital admissions and death worldwide. Adverse drug events cause substantial morbidity and mortality, yet they remain underappreciated and misunderstood.[1] Expensive clinical trials are not sufficient to uncover all of the adverse reactions a drug may cause, necessitating systems for post-marketing surveillance, or pharmacovigilance. These systems have typically relied on voluntary reporting by health care professionals.[2] Spontaneous reporting is the most common method used in pharmacovigilance and the best one to generate signals on new or rare adverse drug reactions (ADRs). Under-reporting is a major drawback of this system.[3]

The issue of drug-related harm is currently one of the most important public health problems all over the world, although public and scientific attention has focused on adverse drug reactions (ADRs) since the thalidomide tragedy in the early 1960s.[4] Premarketing studies of drugs, although large enough to demonstrate efficacy and detect common adverse events, cannot reliably detect an increased incidence of rare adverse events or events with significant latency. For most drugs, only about 500 to 3000 participants are studied, for relatively short durations, before a drug is marketed.[5] ADR contributes to the burden

of drug related patient morbidity and mortality adding to the cost of patient health care. They are common and often preventable cause of hospital admission. Detection and monitoring of ADRs is of vital importance for patient safety, as more than 50% of approved drugs are associated with some type of adverse effects that are not detected prior to their approval for clinical use.[6]

The uses of the medications mainly depend on the extent of the expected benefit of the remedy and the possible unwanted effects. Every time the patient is exposed to a new medication, the risk of ADRs may be high, as we cannot predict the incidence. Thus, no drug is absolutely safe, even when prescribed in therapeutic doses.[7] Present study aimed at describing the frequency and pattern of adverse drug reactions among In Patients visiting the hospital and earmark the commonest adverse reactions amongst them and the drugs associated with each one.

METHODS

The study was conducted at DM Wayanad Institute of Medical Sciences, Kerala. This was a retrospective observational study. The study period extended for 6 months - September 2016 to February 2017. The data was collected using CDSCO ADR reporting form, which was distributed to the hospital pharmacovigilance team of clinical pharmacists and pharmacologist for assessment and reporting.

Inclusion criteria

- In patients of either sex in wards and ICU up to age 60 years who had any form of adverse drug reaction.
- Availability for follow up if required

Exclusion criteria

- Adverse Drug reaction occurring due to prescribing and dispensing error.
- ADR due to medicines of alternate systems like Ayurveda, Unani, Homeopathy.
- Transfusion related adverse reactions.

Sample size

A total of 10094 subjects were admitted during the study period, of these subjects a total of 290 ADR cases were reported by the pharmacovigilance team (3%).

Demographic characters such as age/gender were represented using mean, SD and %. ADRs and the possible reasons were represented in percentage. A comparison of ADR between males and females was made using "proportion test". The data was entered in Excel format and the analysis was carried out using "R" software.

The data collected was divided into 8 systems and analyzed system wise for the relative frequencies of ADR and the drugs involved.

RESULTS

In this study period extending over a period of 6 months – (September 2016 to February 2017) a total of 290 ADRs were studied. Our study showed nearly equal distribution of ADRs amongst both sexes, of the 290 ADR cases studied; 146 (51%) were females and 144 (49%) were males (Figure 1). Mean age of female patients was 40.32 and of males was found to be 40.65 years with a standard deviation (SD) of 15.78 and 19.23 respectively.

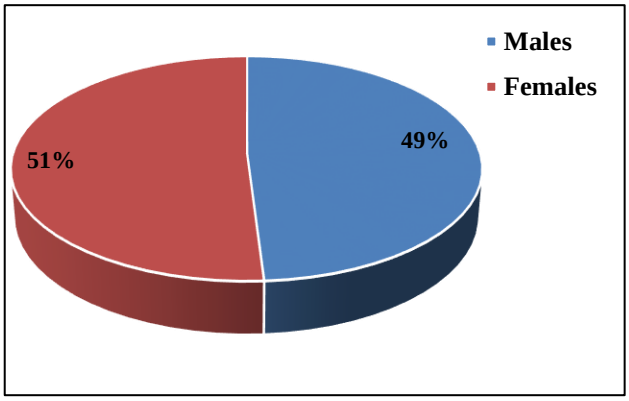
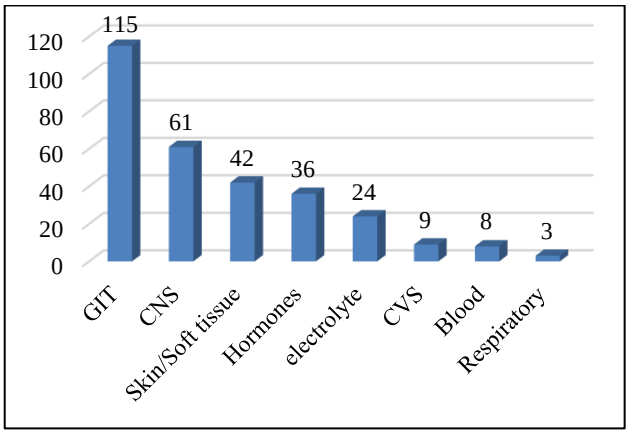


Figure 1: Gender distribution.

Of the systems studied, majority ADRs were from GIT (39%) followed by CNS (20%), skin/soft tissues (14%), Hormones/Genito urinary (12%), Electrolyte (8%), CVS (3%), Blood (3%), Respiratory (1%) (Figure2).



Total number of ADRs are 298 as some patients had ADRs involving more than one organ system

Figure 2: System wise ADRs.

Amongst GIT ADRs (n 115), constipation was the most frequent ADR observed (47%), followed by vomiting (23%) and diarrhoea (21%), tramadol was found to be the most common drug causing constipation followed by i.v pantoprazole. Tramadol was also the drug involved in majority cases of vomiting which was the next most common git ADR observed in our study (Table 1). Amongst CNS ADRs (n 61), headache (24%) was the most common followed by blurred vision (15%) and sedation (13%) (Table 2).

In this study there was no single drug found to be the most common one causing headache but it was rather observed to be a non specific complaint from different drug classes like antihypertensives, antimicrobials, drugs for peptic ulcer etc. Visual blurring was rather a rare ADR reported mostly with CNS drugs e.g Lithium, tramadol, clonidine. Phenytoin used as an antiepileptic was implicated in most cases of sedation which was observed to be the 3rd most common CNS adverse event.

Skin and soft tissue ADRs studied (n 42) showed majority cases of pruritus (38%) followed by rash (33%) (Table 3).

Injection ciprofloxacin i.v was the most common cause for pruritus observed followed by i.v ceftriaxone. Ceftriaxone i.v was also linked with most cases of rashes, which was the next most common cutaneous ADR reported in our study followed by oral moxclav which was given mostly to cases of upper respiratory infections.

ADRs reported from other systems are depicted in (Table 4). Amongst CVS ADRs tachycardia caused by salbutamol was most commonly reported. Our study showed few dyspnea cases reported from Diclofenac use. Hypokalemia was the most common electrolyte anomaly detected in our study; salbutamol again being the drug most commonly involved. Warfarin induced bleeding was the most common hematological ADR. Insulin induced hypoglycemia was most common hormonal ADR observed.

Table 1: GIT ADRs.

GIT ADRs	Drug	Number of ADRs 'n'	Percentage %
Constipation	Tramadol	7	13
	Pantoprazole In*	5	10
	Amitriptyline	4	7
	Ondansetron In	4	7
	Diclofenac	3	6
	Others	31	57
	Total	54	100
Diarrhea	Moxclav	7	29
	Ceftriaxone In	4	17
	Moxclav In	2	8
	Diclofenac	1	4
	Pantoprazole	1	4
	Others	9	38
	Total	24	100
Vomiting	Tramadol	8	31
	Metronidazole In	5	19
	Metronidazole	4	15
	Tramadol In	3	11
	Others	20	24
	Total	26	100

OTHERS GIT ADRS n 11- Gastritis, nausea, malena. *In - Injection

Table 2: CNS ADRs.

CNS ADRs	Drug	Number of ADRs 'n'	Percentage %
Sedation	Phenytoin	5	64
	Chlorpheniramine Maleate	1	12
	Lorazepam	1	12
	Lupitus	1	12
	Total	8	100
Fever	Cefuroxime in	2	50
	Cefuroxime	1	25
	Isoniazid+Rifampicin	1	25
	Total	4	100
Headache	Glyceryl Trinitrate In	1	7
	Ofloxacin	1	7
	Pantoprazole	1	
	Azithromycin	1	7
	Others	11	72
	total	15	100
Blurring of vision	Lithium	1	11
	Prednisolone	1	11
	Tramadol	1	11
	Clonidine	1	11
	Others	5	56
	Total	9	100

OTHER CNS ADRSn25 - shivering, vertigo, somnolence, febrile seizure, asthenia, anisocoria, delirium

Table 3: Skin and soft tissue ADRs.

Skin soft tissue ADRs	Drug	Number OF ADRs'n'	Percentage %
Pruritus	Ciprofloxacin In	3	19
	Ceftriaxone In	2	13
	Moxclav In	2	13
	Ranitidine In	1	5
	Others	8	50
	Total	16	100
Rash	Ceftriaxone In	4	29
	Moxclav	2	14
	Diclofenac In	1	7
	Piptaz	1	7
	Others	6	43
	Total	14	100
Oral candidiasis	Budesonide	1	100
Angioedema	Ranitidine In	1	100

Other skin soft tissue ADRs n 10 - Apthous ulcer, gingivitis, erythema.

ADR variations based on gender are shown in (Table 5), in this study using the proportion test; it was observed that different systems showed no statistically significant gender variations in ADRs.

It was observed that GIT ADRs were most common in both sexes; with a slight female preponderance this was followed by CNS ADRs which were observed more amongst male patients. Skin and soft tissue ADR showed no gender specific variations in this study.

DISCUSSION

In the present study, the mean age of the study subject is 40.77 years, this is quite similar to study conducted by Anita G et al.[8] A slight male preponderance was observed in this study; which is in conformity with previous studies.[9-11]

In this study; GIT constituted the most common system affected, accounting for (39%) of total ADRs reported. This is in congruence with studies conducted earlier by Chan S et al.[12] CNS was the next most common system affected, total reported ADRs were (20%), of which headache was the most frequent complaint (24%).

Table 4: Most common ADRs system wise.

System	ADRS	ADRs n and %	Drugs causing	Most common ADR	Most common drug
CVS	Hypotension, Pedal EDEMA, tachycardia	n 9 (3%)	Amikacin IN, Amlodipine, Enalapril, Risperidone Adrenaline NEB, Salbutamol, Theophylline IN	Tachycardia	Salbutamol
Respiratory	Dyspnea	n 3 (1%)	Cefoperazone IN, Diclofenac, Diclofenac IN		
Electrolyte	Acidosis, AKI, Creatinine high, K High, K low, LFT altered	n 24 (8%)	Acetazolamide, Mefenamic, Amikacin, Tramadol IN, Spironolactone, Cefoperazone IN, Insulin, Lasix, Lasix IN, Piptaz, Salbutamol, Salbutamol N, Thiazide, Clozapine	K low	Salbutamol N
Blood	Anemia, bleed, Pancytopenia, Petechi, Platelet low, Purpura	n 8 (3%)	Methotrexate, Phenytoin, Warfarin, Piperazine in, Clopidogrel, Heparin, Cefoperazone	Bleed	Warfarin
Hormones/ GU	Hematuria, hyperglycemia, Hypoglycemia, Hypothyroidism, Urinary Retnention	n 36 (12%)	Enoxaparin, Heparin, Betamethasone, Betamethasone in, Hydrocortisone in, Insulin, Methylprednisolone, Glimepride, insulin, Metformin, LI, Trihexyphenidyl	Hypoglycemia	Insulin

Cutaneous ADRs were the next most common, pruritus (38%) was the most frequent one reported, followed by rash, this finding matches the result from a previous study conducted by Rohini Sharma et al.[13] Of the remaining systems studied, amongst CVS adverse effects, tachycardia induced by salbutamol was found to be the

commonest. Warfarin induced bleeding was the most frequent ADR in blood and haematinics, which usually was prescribed to patients with coagulopathies. Amongst hormonal ADRs, insulin induced hypoglycaemia was recorded to be the commonest one in this study.

Table 5: Gender wise distribution of ADRs.

System	Male		Female		P value
	N	%	n	%	
GIT	51	17	64	22	0.177
CNS	32	11	29	10	0.681
Skin/Soft tissues	21	7	21	7	1
Hormones/Genito urinary	18	6	18	6	1
Electrolyte	12	4	12	4	1
CVS	5	2	4	1	0.727
Blood	4	1	4	1	1
Respiratory	3	1	0	0	0.081

It was observed that constipation induced by tramadol (13%), was the commonest GIT adverse effect. Tramadol was commonly prescribed for musculoskeletal indications like arthralgia, lumbago etc., this probably is because of the fact that it is relatively free of gastric irritation when compared to traditional NSAIDs, constipation by tramadol is attributed to its action on μ opioid receptors. Opioid Induced Constipation (OIC) was defined as a change, after initiating opioid therapy, from baseline bowel habits that were characterized by any of the following: reduced frequency of spontaneous bowel movements; development or worsening of straining to pass bowel movements; a sense of incomplete rectal evacuation; or harder stool consistency.[14] It remains challenging to determine whether constipation in the setting of opioid use is caused exclusively by the opioid (i.e. OIC) or reflects a combination of OIC and other constipating factors. In general, management is enhanced by addressing all possible factors contributing to the development of constipation.[15]

Headache was not implicated specifically to any particular drug class. Non-serious adverse reactions, such as headache, are not quantified and described as accurately as serious, life threatening ones. However, non-serious reactions can also be extremely troublesome, above all when they are chronic: they can affect patients quality of life and contribute to non-compliance.[16] The incidence of ACDR in developed countries range from 1 to 3% among in patients, whereas in developing countries such as India, some studies peg it to 2-5% of the in patients.[17-22]

In asthmatics salbutamol is generally given for bronchodilation as nebulisation or tablets, it was found to be the drug causing majority cases of tachycardia, which was the most common ADR in CVS cases, another known ADR of salbutamol is muscle tremor which was not reported as often. Salbutamol was also found to be the drug involved in most cases of hypokalemia, which happened to be the most common electrolyte abnormality recorded.

In this study GIT was found to be the commonest system involved and constipation was the most common symptom. Tramadol; an opioid analgesic was found to be the drug associated with majority cases of constipation. Lack of awareness and knowledge on what, when, and to whom to report ADRs is the common factor followed by lack of commitments of Health Care Providers and unavailable format.[23] Results of the study clearly show that ADRs are in fact a matter of serious concern. Attending clinicians often find difficulty in reporting and attending to all possible ADRs. This necessitates the presence of a dedicated, well established pharmacovigilance team in all hospitals to attend promptly all ADRs and manage them appropriately. Sensitisation programmes on pharmacovigilance to HCP and training staff nurses in all wards on identifying ADRs and reporting it to the pharmaco vigilance team can greatly help in expediting the whole process. Automating the data entry to minimise manual errors in reporting is also highly recommended.

CONCLUSION

ADRs are a rising concern in present day medical practice. The study conducted showed the pattern of ADRs; most of which were related to GIT. Drugs causing the ADRs were the ones prescribed for some other organ system involved. It's concluded that educating the health care providers and timely reporting all adverse events by a prompt pharmacovigilance team is vital in controlling these unfortunate occurrences.

ACKNOWLEDGEMENTS

Authors would like to thank Mr. Praveen Jose, clinical pharmacist and his hospital pharmacovigilance team for all their support. We would also like to thank Dr. Madhusudan, Assistant professor in Community medicine; for his guidance through the project.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee (IEC/DM WIMS/May/2017/006)

REFERENCES

1. Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting Ann Intern Med. 2004 May 18;140(10):795-801.
2. Robert L, Laura W, Ryan S, Annie S, Jian Y, Graciela G. Towards Internet-Age Pharmacovigilance: Extracting Adverse Drug Reactions from User Posts in Health-Related Social Networks Workshop on Biomedical Natural Language Processing. 2010:117-124.

3. Alvarez A, Carvajal A, Bégaud B, Moride Y, Vega T, Arias LH. Under-reporting of adverse drug reactions. Estimate based on a spontaneous reporting scheme and a sentinel system. Eur J Clin Pharmacol. 1998 Aug;54(6):483-8.
4. Akici, Ahmet, Oktay, Sule. Rational Pharmacotherapy and Pharmacovigilance. Current drug safety. 2007;2:65-9.
5. Berlin JA, Glasser SC, Ellenberg SS. Adverse event detection in drug development: recommendations and obligations beyond phase 3. Am J Public Health. 2008 Aug;98(8):1366-71.
6. Rabbur R, Emmerton L. An introduction to adverse drug reporting system in different countries. Intl J Pharm Prac. 2005;13(1):91-100.
7. Parthasarathi G, Olson S. Adverse drug Reactions. A textbook of Clinical Pharmacy Practice by Parthasarathi G, Karin Nyfort-Hansen, and Nahata MC. Orient Longman. 2004;8:84-6.
8. Gupta A, Anjleen K, Shukla P, Chhabra H. Adverse Drug Reactions pattern in a tertiary level teaching hospital: A Retrospective Study. Indian J of Pharm Prac. 2017;10(1):27-31.
9. Fatima S, Noor S, Fatima A, Fatima H, Mohd AH, Khan MU. Study on Incidence of Adverse Drug Reaction in Hospitalized Patients in Teaching Hospital. Indo American J of Pharm Rese. 2013:3(10).
10. Vijendra R, Pundarikaksha HP, Gopal MG, Girish K, Vasundara K, Jyothi R. A Prospective study of cutaneous adverse drug reaction in a tertiary care hospital. Nat J of Bas Med Scie. 2013:3(1):44-51.
11. Acharya T, Mehta D, Shah H, Dave J. Pharmacovigilance study of adverse cutaneous drug reactions in a tertiary care hospital. Nat J Phys Pharm Pharma. 2013;3:75-81.
12. Chan SL, Ang X, Sani LL, Winther M, Liu J, Brunham LR, et al. Prevalence and characteristics of adverse drug reactions at admission to hospital: a retrospective observational study. Br J Clin Pharmacol. 2016 Dec;82(6):1636-46.
13. Sharma R, Dogra D, Dogra N. A study of cutaneous adverse drug reactions tertiary center in Jammu, India: Indian Dermatol Online J. 2015 May-Jun;6(3):168-71.
14. Nelson AD, Camilleri M. Opioid-induced constipation: advances and clinical guidance. Therapeutic Advances in Chronic Disease. 2016;7(2):121-34.
15. Nelson AD, Camilleri M. Chronic opioid induced constipation in patients with nonmalignant pain: challenges and opportunities. Therapeutic Advances in Gastroenterology. 2015;8(4):206-20.
16. Ferrari A, Spaccapelo L, Gallesi D, Sternieri E. Focus on headache as an adverse reaction to drugs. The J of Heada and Pain. 2009;10(4):235-9.
17. Shrivastava M, Uchit G, Chakravarti A, Joshi G, Mahatme M, Chaudhari H. Adverse drug reactions reported in Indira Gandhi government medical college and hospital, Nagpur. JAPI. 2011;59:1-4.
18. Bigby M. Rates of cutaneous reactions to drugs. Arch Dermatol. Jun 2001;137:765-70.
19. Craig KS, Edward WC, Anthony AG. Cutaneous drug reactions. Pharmacol Rev. 2001;53:357-79.
20. Noel MV, Sushma M, Guido S. Cutaneous adverse drug reactions in hospitalized patients in a tertiary care centre. Indian J Pharmacol. 2004;36:292-95.
21. Uppal R, Jhaj R, Malhotra S. Adverse drug reactions among in patients in a north Indian referral hospital. Natl Med J India. 2000;13:16-8.
22. Jhaj R, Uppal R, Malhotra S, Bhargava VK. Cutaneous adverse reactions in in-patients in a tertiary care hospital. Indian J Dermatol Venereol Leprol. 1999;65:14-7.
23. Gurmesa LT, Dedefo MG. Factors Affecting Adverse Drug Reaction Reporting of Healthcare Professionals and Their Knowledge, Attitude, and Practice towards ADR Reporting in Nekemte Town, West Ethiopia. Bio Med Resea Internat. 2016;2016:5728462.

Cite this article as: Ambika Abhishake VJ, Basalingappa S, Gopi A, Daulat MP. A retrospective study of Adverse Drug Reactions in a tertiary care centre. Int J Basic Clin Pharmacol 2018;7:1339-44.