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Adverse Drug Reaction Monitoring and Causality Assessment in a Teritary Care Hospital, Baptist Hospital, Bangalore

Sara Dabbaghi Varnousfaderani *, Balakeshwa Ramaiah

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Abstract

Background**:** Adverse drug reactions, or ADRs. which are officially described as: "A response to a drug which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. ADRs also might be results of polypharmacy, Pathogenesis, paradoxical reaction and other serious adverse events. This study aimed to recognize adverse drug reaction in the in-patient department and hence to find the predisposing factors associated with ADR.Result: Throughout the 6 months' study period, 70 ADR's were confirmed and reported in 69 patients. There were 3000 patient admission (which is taken for this study) at the hospital and the overall incidence of ADR's during hospitalization in this patient group was 2.33%. Mean age of the patient were 48.93 year. Among the study population 19(27.14%) were geriatric patients ,45(64.28%) were adults and 6(8.57%) were children and teenagers.Conclusion**:** provides the evidence that the incidence of ADR is relatively common in older patients and 50% of these cases could potentially be prevented if certain measures are taken. Additionally, there is also data confirming that the rate of ADR is increased in older patients although the rate remains relatively constant 35 patients gets much older i.e. above 80 years. The recognition of ADR is quite challenging in the patients, the prospective nature of identifying cases and classification of suspected events by independent reviewers increases the reliability of the Endings. Further effort to develop and design a preventative strategy should be imbued as there is a constant need to provide better health care especially in the Population.

Key words: Adverse Drug Reaction, WHO Scale, Naranjo Scale, Causality Scale

Introduction

Adverse drug reactions, or ADRs. which are officially described as: "A response to a drug which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. ADRs also might be results of polypharmacy, iatrogenesis, pradoxical reaction and other serious adverse events. (World Health Organization,1966) an adverse drug reaction (ADR) is defined by the World Health Organization (WHO) as any noxious, unintended, or undesired effect of a drug that occurs at doses used in humans for prophylaxis, diagnosis, or therapy (World Health Organization,1966). ADRs are a major cause of morbidity and place a substantial burden on limited healthcare resources (Juntti-Patinen & Neuvoren, 2002). Multiple factors influence ADR susceptibility, including multiple drug therapy, disease severity, age, and the type and number of drugs prescribed. (Lobstein et al., 1997; May, 1997; Passarelli, 2005; Tatro, 1996; Wong, 2003) Several studies have shown that the proportion of patients admitted with ADRs ranges from approximately 2.0 to 21.4%, whereas between 1.7 and 25.1% of inpatients are reported to have developed an ADR during their hospital stay.(Brandão & Vasconcelos, 2000; Einarson, 1993; [1], Lazarou et al., 1998) There are marked differences in disease prevalence, access to medicines, drug use patterns, and drug management systems between developed and developing countries, and such differences impact the frequency and nature of ADRs.(Sobravime, 2005) Reports of ADRs have become an important component of monitoring and evaluation activities performed in hospitals. 1 This information may be useful for identifying and minimising preventable ADRs while generally enhancing the ability of prescribers to manage ADRs more effectively. (WHO, 2004)

The word pharmacovigilance has derived from the Greek word pharmacon means 'drug'' and the Latin word vigil are means for to keep awake or alert, to keep watch.' Pharmacovigilance is the pharmacological science relating to the detection, assessment, understanding

Sara Dabbaghi Varnousfaderani*, Balakeshwa Ramaiah
Doctors of pharmacy, Department of pharmacy practice, Karnataka College of pharmacy, Bengaluru, India

***Email:**Sara6236@yahoo.com

[1] http://www.cvs.saude.sp.gov.br/farde_hos.html.

and prevention of adverse effects, particularly long term and short term side effects of medicines.(Ahmet & Sule, 2007; Oshikoya et al., 2007; Passarell, 2005).

These adverse drug reactions (ADRs) not only add to the suffering of patients but also increase morbidity and mortality along with a financial burden on society. The overall incidence of ADRs in hospitalized patients is estimated to be 6.7 %(range 1.2-24.1%) and that of fatal ADRs 0.32% (0.1-. 85%).Data indicates that in patients who experience ADRs death rates are 19.18% higher and the length of hospital stay is 8.25% higher. Total medical costs for patients with ADRs are increased by an average of 19.86%.

Materials and Methods

This prospective observational studies were done for monitoring ADRs and analyse its causality at Bangalore Baptist Hospital. Visiting the respective ward or the department and collected the necessary details. When an ADRs were suspected, the data from the patient profile form such as patient details, patient medication details including nonprescription drugs, alternative treatments and recently ceased medications, comprehensive adverse reaction details including description of the reaction, lime of onset and duration of the reaction and treatment given with relevant investigation reports were collected.

The patient's case sheets, prescriptions, nurses note will randomly be selected on daily basis and will be reviewed for usage pattern and adverse drug reactions. The overall process is done to ensure safety of drugs, minimize ADRs by setting up a pharmacovigilance center. Causality and severity assessment: The causality was assessed by using Naranjo causality assessment scale and the seventy was assessed by using the seventy assessment scale according to the recommendation by the WHO Uppsala Monitoring Center.

The inpatient case sheds and prescriptions will be screened for adverse drug reactions on daily basis. All the prescribed medications along with other medications and relevant information will be noted in a customized data collection form to find out the adverse drug reaction and other allergies. the study patients will be followed daily until their discharge. The Micromedex. Medscape article and relevant references books will be used as tools to review the collected data. The prescribed medication will be checked for their existence in the hospital and also the relevant dosing calculation and drug concentration.

The data from customized data collection form will be transferred to VigiFlow and will be subjected to further analysis as required. The global guidelines of PvPI will be used as reference to study the ADRs in our hospital. Inspecting Nurses note, patient counseling and also by visual inspection the ADRs can be noted. The system in our hospital will be compared with the global guidelines and will recommend for any modifications.

Also the ADRs forms will be allotted to the candidates to find out and collect new adverse drug reaction and along with the supporting proofs. This ADRs forms are documented in the Pharmacovigilance center which is implementing and update through VigiFlow.

global guidelines of PvPI will be used as standard criteria for developing a pharmacovigilance center.

Result and Discussion

Throughout the 6 months' study period, 70 ADR's were confirmed and reported in 69 patients. There were 3000 patient admission (which is taken for this study) at the hospital and the overall incidence of ADR's during hospitalization in this patient group was 2.33%. Mean age of the patient were 48.93 year. Among the study population 19(27.14%) were geriatric patients ,45(64.28%) were adults and 6(8.57%) were children and teenagers.

The most frequent causative drugs and drug classes » shown in Table6. 13(18.57%, of the total 70 ADRs identified in this study were caused by both analgesics (including non-steroidal anti-inflammatory drugs and opioid analgesics). This is followed by antibiotics which accounted for 6(8.57%)of the implicated drug classes causing ADRs.

Focusing on individual medications rather than drug classes. Diclofenac .as found to be most frequent causative medication, caus.ng 13(18.570/.) ADR. This was Mowed by Ceftriaxone (n-6), betamethazone (n=6), ciprofloxacin (n=5), acenocoumarol (n=5), heparin (n=4), and ondansetron (n=4). However, there were only three cases of ADR associated with analegsic, two with antiemetic, and one with ARBs in this study. Surprisingly there was. only one ADR caused by metronidazole in this study, a drug which has previously been associated with gastrointestinal bleeding in many cases. table 1

Table 1: Therapeutic drug class implicated in ADRs

Drug Class	Drug	No Of Adrs(%)
Nsaids	Diclofenac	13(18.57)

Cephalosporin	Ceftriaxone	6(8.57)
	Cefotaxine	
	Cefazolin	
Corticosteroids	Beta Methadone	4(5.71)
	Hydrocortisone	
	Dexamethasone	
Fluroquinoi.One	Ciprofloxacin	
Anticoagulant	Acenocoumarol Heparin	4(5.71)
PPI	Ondansetron	3(4.28)
	Pantoprazoi.E	
	Omeprazole	
Penicillin Antibiotic	Penicillin	3(4.28)
	Amoxicillin And	
	+Clavulanic	
	Acid	
	Amoxilin	
Lincosamide	Clindamycin	3(4.28)
Antispasmodics	Iiyoscine Bltylbro.Mide	3(4.28)
Arbs	Telmisartan	2(2.85)
Analegsic	Acetaminophen Tramadol	2(2.85)
Beta Lactamase Inhibitor	Cefoperazone Sodium In Jection	2(2.85)
Nitroimidazoles	Metronidazole	2(2.85)
Antiemetic	Do.Meprido.Ne	2(2.85)
Antidiabetic	Glimeperide	2(2.85)
Others		13(18.57)

Cutaneous problem accounted for 13(18.57%) of all of the overall ADR identified. This was closely followed by digestive 21(30%), cardiovascular (n=4, 5.71%), neuropsychology (n=4, 571%), endocrinology (n=9,12.85%), metabolic and renal (12%), hemorrhage (11.42%), altered transaminases (3%), hematological (n=8 11.42%).

Although the digestive system was identified as the system most commonly affected with ADR, itching all over the body. swelling. Redness of the skin and popped up was the most frequent ADR observed. This was followed by eleven cases of hypoglycemia, confusion and drowsiness M I), hypokalemia (n=5). hyperkalemia (n=l) and hyponatremia (n=l).

Electrolyte disturbances were the fourth most common type of ADR identified. Nausea and vomiting (n=6) and constipation (n=6) can be considered regular ADR among patients. Increasing age is identified risk factor for drug reactions. Hypoglycemia was also identified as quite a common ADR Allowed by confusion and drowsiness however neuropsychological symptoms are very difficult assess in the patient especially if the patient is impaired. table 2

Table 2: Organs affected in patients with multiple ADRs

Organs affected	Type of ADR	Total	
		N	%
Digestive	Headache, Vomiting, Watery Loose Stools, Diarrhea, Nausea, Abdominal Discomfort, Constipation.	21	30
Cardiovascular	HTN, Edema, Nose Blocked, Hypotension, Giddiness	04	5.71
Neuropsychological	Chills, Shivering, Sleeping Difficulty, Myopathy, Sjs, Excessive Sweating	04	5.71
Endocrinology	Hyperglycemia, Hypoglycemia, Hypothyroidism	09	12.85

Hematological	INR, PT, CR£, Bleeding. Malena, Gum Bleeding	08	11.42
Cutaneous	Rashes. Itching, Edema. Bluish Discoloration, Increase The Size Of Wheel, Discoloration Of The Skin	13	18.57
Respiratory	Breathing Difficulty. Breathlessness, Chest Discomfort	11	15.71
Total		70	100

Manegment and Outcomes of ADRs

there were "NO " fatal reactions. Complete recovery was achieved in 36 (51.42%) of patients with ADRs 28(40.00%) were in the recovery process, and 6(8.57%) were classified as having 'unknown outcomes (i.e., outcomes that could not be assessed due to a lack of recorded reports).

Treatment with the offending drug was interrupted in 43(25.59%) of patients. Another drug was substituted for the offending drugs in 0(0.00) of patients, and other drugs were added to relieve the symptoms in 09(12.85%) of patients; the drug dosage was reduced in 10(14.28%) patient. treatment was unchanged in 11(6.54%)of patients'. Others treatment' (that could not be assessed due to a lack of recorded reports) is 6(8.57%). Table 3

Table 3: Outcomes and Management

Outcomes	Male		female		Total	
	N	%	N	%	N	%
Fatal	0	0	0	0	0	0
Fully Recovered	19	27.14	17	24.28	36	51.42
Recovering	23	"32.85	5	7.14	28	40
Unknown	4	5.71	2	2.85	6	8.57
Total	46	65.71	24	34.28	70	100
Treatment						
Slopped The Medication	17	24.28	5	7.14	22	31.42
Reduce The Dose	7	10	3	4.28	10	14.28
Added Another Drug	5	7.14	4	5.71	9	12.85
Substituted Another Drug	00	00	00	00	00	00
No Change	4	5.71	4	5.71	8	11.42
Drug withhold	9	12.85	6	8.57	15	21.42
Others	4	5.71	2	2.85	6	8.57
Total	46	65.71	24	34.28	70	100

Co-morbidities for each patient were recorded. 24(34.28%) of the patients were not having previous history of admission 11(15.71%) of patients had a diagnosis of hypertension and diabetic. 7(4 16%) of patients reported lower respiratory tract infection. urinary tract or chest infection. 16(9.52%) of patients had a diagnosis of asthma COPD and breathless. 40% of the study population reported 4 or more co morbidities. These diseases are commonly seen in the older population.

A reason for the underestimation or lower prevalence of certain co-morbid conditions in this inpatient population could be due to the poor documentation in the medical notes and an incomplete record of previous medical conditions in the patients notes. Patients" themselves were often unable to provide an accurate medical history due to acute and chronic confusion. This further contributed to the incomplete medical data obtained from medical inpatients. table 4

Table 4: list of Co-Morbidity of Patients Included in the Study

Co-Morbid Condition	No. Of Patients (%)	No. Of Adrs (%)
Previous His Toryand Admission	24	34.28
Hypertension And Dm	11	15.71

Asthma	6	5.35
Larti	7	4.16
Ckd	6	3.57
Cva	3	2.97
Acs	3	238
Carcinoma	2	238
Copd	2	1.78
Appendicitis	2	1.78
Delirium	1	0.59
Fever	1	0.59
Ccf	2	1.9
Total	70	100

Causality assessment: Naranjo scale

Causality assessment was undertaken for the total 70 ADR and was rated as certain in 6(8.57%) cases, probable in 33 cases (47.14%), and possible 29 (41.42%) cases and the remaining were 2(2.85) is doubtful according to" Naranjo scale". This study also included possible and doubtful ADR in the analysis although there are several studies systematically excluding patients in this category. Possible ADR cases were included in this study because there is still a marginal link or relationship between the suspected drug and reactions identified. For example, a possible reaction could be explained by the certain disease condition of the patient, contribution of a drug should not be totally excluded. This is particularly important in older patients where the complex relation between multiple disease conditions and multiple medications should not be neglected. table 5

Table 5: Causality assessment of Naranjo scale

PARA M ENTER	Total	
Naranjo scale	N	%
Certain	6	8.57
Probable	33	47.14
Possible	29	41.42
Doubtful	2	2.85
Total	70	100

Causality assessment: WHO scale

As WHO UMC scale certain defined 6(8.57%) cases. probable in33 cases (47 14%). and possible 29 (41 42%) cases and the remaining; were 2(2.85%) is unclassified according to WHO UMC scale. table 6

Table 6: Causality Assessment of WHO scale

WHO SCALE	Total	
Definite	6	8.57
Probable	33	47.14
Possible	29	41.42
Unclassified	2	2.85
Total	70	100

Causality Assessment : Severity Scale

Most of the identified ADR were of low level of seventy, although all required intervention to a varying degree. I he severity of ADR was classified into six main categories in this study. There were 3(1.28%) level 6 severity were identified ,8(11.42%) level 5 ,21 level 4.19(27.14) level 3,16(22.65) level 2 and 3(4.28) level I. table 7

Table:7: Causality assessment of Severity scale

Severity assessment	TOTAL	
Level 1	3	4.28
Level 2	16	22.85
Level 3	19	27.14
Level 4(a)	11	15.711
Level 4(b)	10	14.28
Level 5	8	11.42I
Level 6	3	1.281
Total	70	100

Conclusion

Hospital based monitoring of ADR and reporting is an important program to identify and quantify the risks associated with the use of drugs. This information may be useful in identifying and minimizing preventable ADRs while generally enhancing the knowledge of the prescribe to deal with ADRs more efficiently.

Under reporting the ADRs in the present study revealed that, more awareness about the importance of Pharmacovigilance have to be provided among the health care professionals by way of ADR bulletins, seminars and workshops, Serious ADRs account for hospital admissions, increased morbidity, prolonged treatment and in some cases death, as evidence in the present study. Hence, ADR monitoring is one of the important measures that can help reduce the burden of these ADRs and improve the benefit versus harm ratio of drugs.
Hence, it can be concluded from the present study that more intensive implementation of ADR monitoring and reporting by Pharmacovigilance Program is the need of the hour for patient so as to provide the optimum patient care.

This thesis provides the evidence that the incidence of ADR is relatively common in older patients and 50% of these cases could potentially be prevented if certain measures are taken. Additionally, there is also data confirming that the rate of ADR is increased in older patients although the rate remains relatively constant 35 patients gets much older i.e. above 80 years. The recognition of ADR is quite challenging in the patients, the prospective nature of identifying cases and classification of suspected events by independent reviewers increases the reliability of the Endings. Further effort to develop and design a preventative strategy should be imbued as there is a constant need to provide better health care especially in the Population.

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