Global Journal of Medical Research: B
Pharma, Drug Discovery, Toxicology and Medicine
Volume 14 Issue 3 Version 1.0 Year 2014
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Collection, Detection, Assessment, Monitoring and Prevention of Adverse Drug Reactions in the Nephrology Department of Gauhati Medical College and Hospital, Assam, India

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Objective: To identify the ADR by chart review method, to determine the causality of the ADR by Naranjo's algorithm, to analyze the severity of the ADR by modified Hartwig method and to motivate the health care professionals to report ADRs in Nephrology ward of Gauhatu Medical College and Hospital (GMCH), Guwahati. Preventability of ADR is done by Schumock &Thortonpreventibility scale.

Materials and methods: A prospective observational and hospital based case control study(June 2011-May 2012)was carried out in the Nephrology ward of GHMC, including both out-patient and in- patient departments. All the values are statistically determined using parametric t-test and non-parametric fisher's exact test or chi-square tests.

Keywords: *nephrology, renal dysfunction, moon face, hypersensitivity, hepatotoxicity.*

GJMR-B Classification : *NLMC Code: QV 37.5, QV 752*

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Results: Out of 850 patient records, thecommonly occurring ADRs were moon face (n=16, 18.6%) followed by hypersensitivity (n=9, 10.4%) and hepatotoxicity (n=4, 4.65%).Gastrointestinal ADRs were highest in number followed by the hypersensitivity. Prednisolone was found to be the most offending drug followed by Nimesulide and Diclofenac. It is very clear that 12.7% ADRs were preventable.

Conclusion: Renal dysfunction plays a significant role in occurrence of serious and multiple ADRs. Poly-pharmacy, co-morbidity and number of diagnosis were found to be risk factors for ADRs.

Keywords: nephrology, renal dysfunction, moon face, hypersensitivity, hepatotoxicity.

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I. Introduction

An adverse drug reaction (ADR) as defined by World Health Organization (WHO) is a noxious, unintended effect of a drug, occurring at normal doses in humans for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function(1). ADRs are considered as the fourth to sixth leading cause of death among hospitalized patients. About 2.9-5.6% of all admissions are caused by adverse related events, and approximately 35% hospitalized patients experience an ADR. ADRs are associated with significant morbidity, permanent disability and are a huge economic burden on patients due to prolonged hospitalization(2).

Kidney is the primary route of elimination for drugs and their metabolites. Hydrophilic drugs are mainly cleared by the kidney(3). ADRs are most commonly observed in elderly patients(4). Aging is associated with decreased renal and liver reserve and with the risk of delayed renal and hepatic clearance of drugs. Renal function can be readily estimated by the serum creatinine level(3).

The Gauhati Medical College and hospital (GMCH) has enjoyed a prestigious status in the country for its academic pursuites and patients care, and thereby being a referral centre for speciality and superspeciality treatment having a bed strength of 1,587 and 17 operation theaters It provide promotive, preventive and curative, through out-patient department (OPD), indoor, emergency and extension Services. An ADR reporting program exists in the hospital since 1970 and the same was coordinated by the department of pharmacy practice, National Institute of Pharmaceutical Education and Research (NIPER), Gauhati. The present study was undertaken to characterize the ADRs reported in Nephrology department(5).

II. Materials and Methods

The study was carried out in the Nephrology ward of GHMC from June 2010 to May 2011 including both out-patient (OP) and in-patient (IP) departments.

The study was a prospective observational, hospital based case control study.It was based only on those patients who experience an adverse reaction to medicine use, either during their stay in hospital or outside the hospital and visiting the outpatient and inpatient departments of Nephrology.

The degree of association of an adverse effect with a drug is done (table 1)with the help of Naranjo's algorithm where it involves a number of questionnaires, to each of which score has been provided (ranging from -1 to +2). Total score for a particular drug-ADR combination is calculated and the association is termed as>9: Highly probable; 5-8: Probable; 1-4: Possible; 0: Doubtful(6).

After the causality assessment has been done, the severity of the ADR is analyzed using adapted Hart wig severity scale(7).The scale was classified as mild:a reaction that does not required treatment or prolongation of hospital stay; moderate: a reaction that requires treatment and or prolongs hospitalization by at least one day; severe: a reaction that was potentially life threatening or contributes to the death of patient was permanently disabling requires intensive medical care or results in a congenital anomaly cancer or unintentional overdose.

Preventability of ADR is done by Schumock & Thorton preventibility scale. Preventable adverse drug reaction was defined according to Schumock and Thornton (1992) as ADR which was preventable or avoidable. There were seven questions. Answering "YES" to one or more of the questions that an ADR was preventable (8).

To study the onset of ADR, acute: those which are observed within 60 minutes after the administration of medication; sub-acute: those occur within 1-24 hours from the time of administration of medication; and latent: those take 2 or more days to become apparent, parameters were used.

III. Statistical Analysis

Data were recorded on a pre-designed proforma and managed on an MS Office Excel spread sheet. The descriptive statistics are represented by mean ± standard deviation and percentages. The differences between the groups were determined by the parametric t-test and non-parametric fisher's exact test or chi-square tests wherever appropriate. Graph Pad InStat version 3.12 statistical software was used for the data analysis. The Odds ratio and its 95% confidence interval were calculated for certain risk factor of ADRs in renal failure patients. Statistical significance was defined as $p<0.05$. All P values were two tailed.

IV. Results

The results were based on 850 patient records taken from the Nephrology department of GHMC. Out of them 72 (8.47%) patients resulted in one or more ADRs. Thecommonly occurring ADRs were moon face (n=16, 18.6%) followed by hypersensitivity (n=9, 10.4%) and hepatotoxicity (n=4, 4.65%)(Table2).

V. Types of Adrs by System

Gastrointestinal ADRs were highest in number followed by the hypersensitivity ADRs. Gastrointestinal ADRs mainly include hepatotoxicity, ulcers, melaena, nausea, vomiting diarrhea and constipation (table 2).

Table 2 : List of ADRs reported during study period

S.No	ADRs			
	Description	Frequency (%)	System wise	Frequency (%)
1	Moon face	16(18.6)	Gastrointestinal disturbances	18(20.9)
2	Allergic reactions	9(10.4)	Hypersensitivity	9(10.4)
3	Fluid electrolyte imbalance	4(4.65)	Ophthalmic	8(9.3)
4	Hepatotoxicity	4(4.65)	Cardiovascular	7(8.13)
5	Tachycardia	3(3.40)	Dermatological	5(5.81)
6	Melaena	3(3.40)	Respiratory	4(4.65)
7	Tremor	3(3.40)	Electrolytic	4(4.65)
8	Constipation	3(3.40)	Central nervous system	3(3.4)
9	Cataract	3(3.40)	Hematological	3(3.4)
10	Blurred vision	3(3.40)	Endocrinal	1(1.16)
11	Others	33(45.83)	Others	24(27.9)

The causality assessment was done using Naranjo's scale and it shows that majority of the ADRs were probable (n= 87, 91.57%). As the ADRs had been identified, their severity level was also assessed. This was done using Hartwig criteria and majority of the patients had mild ADR (n = 44, 51.16%). Mostly ADRs have latent onset. It was very clear that 12.7% ADRs were preventable.The other 87.2% were not preventable because the susceptibility of these ADRs is still not defined and is a matter of research.This assessment is based on Schumoch and Thornton preventability criteria.In this study maximum number of ADRs found in one patient are 3.They are fluid electrolyte imbalance, blurred vision, hyperglycemia.

The incidence and certainty of ADRs in male and female were also studied. It was found that female populations showed a higher incidence of ADRs than in male populations (table 3).The percentage of ADRs was found out by dividing number of patients with ADRs of a particular gender by total number of patients of the same gender.

For gender, the p-value is 0.042 (<0.05). It shows that there is significant difference between occurrences of ADRs in different gender. In this study females were found to be more prone to ADR when compared to the male patients, similar to more other studies in the literature.

This study shows the incidence of ADRs with respect to age in which elderly patients(age >60) had a higher incidence of ADRs (15.00%). The patients in between the age of 0-18 yrs were found to have 9.37% and the age between 19-60 yrs had 7.98%(table 3). For age, the p-value is 0.001(<0.05). It shows that there is significant difference between occurrences of ADRs in different age groups. In this study patients above 60 years were found to be more prone to ADR when compared to other age groups.

Table 3 : Total interpretation of results

S. No	Variable		Total (n)	Patients with ADR	Patients without ADR	Prevalence of ADR	OR* (95% CI**)
			850	72	778	8.47%	
1	Age (yrs)	0-18	96	9	89	9.37%	1 (reference)
		19-60	714	57	657	7.98%	0.85(0.41-1.8)
		≥ 60	40	6	34	15%	1.74(0.57-5.27)
2	Sex	Female	360	32	328	8.88%	1 (reference)
		Male	490	40	450	8.16%	0.91(0.56-1.48)
3	Number of medications	≤ 5	200	18	182	9%	1 (reference)
		6-10	280	19	261	6.77%	0.73(0.41-1.3)
		≥11	370	35	335	9.45%	1.06(0.4-1.5)
4	Number of diagnosis	1	198	9	189	4.54%	1 (reference)
		2	300	28	272	9.33%	2.16(0.99-4.61)
		≥3	352	35	317	9.94%	2.31(1.1-4.9)

OR – odds ratio, CI- confidence interval.

The prescription pattern in case of each patient with ADR was studied and accordingly the patients were divided into 3 groups namely, those receiving 1-5 numbers of drugs;those receiving 6-10 numbers of drugs; and those receiving more than 10 drugs. It was seen that patients receiving more number of drugs (>10)had higher chances of developing ADRs(9.45%) (table3). A total of 450 medicines were prescribed in patients with adverse reactions. prednisolone was found to be the most offending drug followed by nimesulide and diclofenac (figure 1).

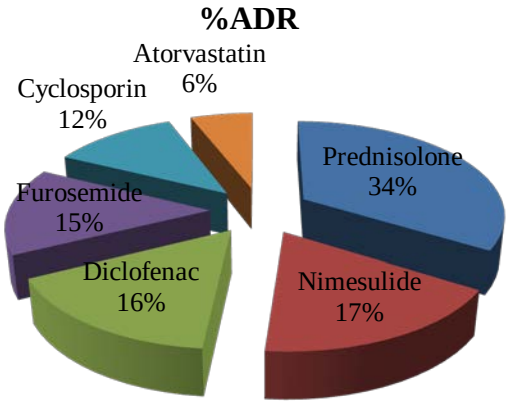

Figure 1 : Drugs causing ADRs

VI. Discussion

ADRs are the undesirable effects of the drug/ medicinal product beyond its intended therapeutic effect when used for clinical purposes. ADRs not only cause morbidity but also can be a reason for mortality in severe cases. They also contribute to greater extents in increasing health care costs to the patients and to the nation(9).

This was a prospective observational study carried out in the Nephrology department of GMCH. Out of the total 850 patient records collected in the Nephrology ward, 72patients resulted in one or more ADRs. Similar studies done in other countries reported a higher rate of incidence(10% to18%) than this study.

The commonly occurring ADRs in this study were moon face followed by Allergic reactions. This study finding was in accordance with the results of several other studies in literature(2, 4, 10).Where moon face was found to be the common ADR associated with prednisolone use.Causality assessment using Naranjo scale proved majority of the ADRs to be probably due to the drugs, while only 8.13%ADRs (table 1)were found to be possibly due to the drugs. Severity analysis using Hartwig scale showed majority of the patients had "mild" ADR (table 1).

Table 1 : Assessment of ADRs

Assessment	Criteria	No.of ADRs	% of ADRs
Naranjo's Score (causality)	Possible(1-4)	7	8.13
	Probable(5-8)	75	87.2
	Highly probable(>9)	4	4.65
Hartwig Criteria (severity)	Mild	44	51.16
	Moderate	38	44.18
	Severe	4	4.65

In this study females had a higher incidence of ADR as compared to the males. A higher incidence and more hospital admissions due to ADRs have been documented for women compared to men may be due to enhanced tissue sensitivity or the existence of sex-related differences in pharmacokinetics.

Patients above 60 years of age are more likely to develop ADRs and may even need hospitalization due to them. This study also showed a higher incidence of ADRs in the geriatric population when compared to the adults and pediatric age groups due to their modified pharmacokinetic and pharmacodynamics properties.

The number of patients visiting the IPD and OPD were recorded in this study. The incidence of ADR was found to be more frequently reported in the OPD setting than the IPD setting of the hospital.ADRs are very common in patients prescribed with poly therapy. In this study too it was observed that as the number of drugs prescribed increased, the cases of ADRs had also increased.

NSAIDs were implicated in a majority of ADRs (26.6%).Prednisolone was found to be the most offending drug followed by nimesulide and diclofenac. Previous Indian studies had documented non-opioid analgesics (18%) and Aminoglicosides(48%)(4).Mortality due to ADRs was 0.12% of the total admissions. The one death observed in the study was relatedto nimesulide induced melaena.The most common organ system associated with ADRs was GIT system followed by cutaneous reactions.

Some of the ADRs were preventable. For example, vancomycin injection caused finger necrosis due to a rapid injection. This ADR is avoidable by giving injection slowly.

VII. Conclusion

Some of the ADRs can be preventable by knowing clinical knowledge about drugs and their usage pattern. Elderly patients are at more risk of developing ADRs due to their modified pharmacokinetic and dynamic properties and renal dysfunction plays a major role in developing ADRs. Poly-pharmacy,age, co-morbidity and no. of diagnosis were found to be risk factors for ADRs.

So clinical pharmacists should be uptodate about their clinical knowledge and attend daily ward rounds with the Nephrologists in the hospital as part of the clinical services. All health care professionals should be encouraged to report the suspected Adverse Drug Events (ADE's) and have actively monitored those ADR's to ensure safe pharmacotherapy. A regular follow up of patients on drugs is required for the early detection and prevention of ADRs to increase patient's compliance to drug therapy and to provide a better drug therapy by prevention of related morbidity and mortality.

References Références Referencias

1. World health organization. International drug monitoring: The role of national centers. Technical report series 498. WHO: Geneva; 1972.
2. Concealed renal insufficiency and adverse drug reactions in elderly hospitalized patients. Corsonello A, Pedone C, Corica F, Mussi C, Carbonin P, Antonelli Incalzi R; Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA) Investigators.Istituto Nazionale di Ricovero e Cura per Anziani, Cosenza, Italy. andrea_ corsonello@tin.it

3. Roger Walker, Cate Whittlesea. Clinical Pharmacy and Therapeutics, Churchill Livingstone; 4 edn, 2007.
4. Adverse drug reactions in nephrology ward inpatients of a tertiary care hospital by Lisha Joshua, Padmini D Devi, Shoba Guido Pharmacovigilance Centre, Department of Pharmacology, St. John's Medical College, Bangalore, India.
5. Gauhati Medical College, Assam, India, accessed from http://gmchassam.gov.in/hospital.html
6. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reaction. Clin Pharmacolther 1981; 30(2):239-245.
7. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. American journal of hospital pharmacy 1992; 49:2229-2231.
8. Schumock and Thornton , Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the preventability of adverse drug reaction. Clin Pharmacolther 1992;30(2):239-45.
9. Montastruc JL, Sommeta A, Lacroixa,I, Oliviera P, Durrieua G, Damase-Michela C et al. Pharmacovigilance for evaluating adverse drug reactions:value, organization, and methods. Joint Bone Spine 2006; 73:629-632.
10. Hellden A, Bergman U, von Euler M, Hentschke M, Odar-Cederlöf I, Ohlen G. Adverse drug reactions and impaired renal function in elderly patients admitted to the emergency department: a retrospective study. Drugs Aging 2009; 26(7):595-606.