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Research Article

Incidence of adverse drug reactions with commonly prescribed drugs in tertiary care teaching hospital in India

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ABSTRACT

Adverse drug reactions Is a worldwide public health problem and an important cause of death and hospitalizations in developed countries. An adverse drug reaction is a major cause of patient morbidity and mortality, Increase in hospital stay and unnecessary economic burden to the patient. To study the incidence of ADRs in tertiary care teaching hospital, in Tamil Nadu at Southern part of India. An analytical cross sectional, observational study was carried over a period of 6 months. A total of 40 cases were reported to have ADRs from 500 patients. ADRs were monitored by using standard developed and designed by CDSCO, India. Data thus obtained were analyzed by using casualty assessment. The WHO scale and Naranjo Algorithm score were used to evaluate ADRs. In this study overall Incidence of ADR found to be 8% and male to female ratio was 3.6 and 4.4% respectively. Maximum number of ADRs were reported from the GIT 37.5% followed by Skin 25% and CNS 12.5%. Different types of ADRs were studied in which rashes (35.13%) the most commonly ADR. Then reported followed by vomiting (13.51%), dizziness (10.81%) and with respect to outcome attributed to ADRs 15 patient got hospitalized due to ADRs. When causality of ADRs was assessed by Naranjo algorithm scale and it is found to be 42.5% probable, 37.5% possible, 7.5% definite and doubtful 12.5% and WHO scale certain 15%, probable 30%, possible 32.5%, unlikely 10%, conditional 7.5% and unassessable 5%. The result of our study is similar to other studies. All ADRs were not toxic reactions and they were unpredictable.

Keywords: Incidence; Naranjo Score; Casualty Assessment; ADR; Pharmacovigilance

INTRODUCTION

Medicines which are used in the treatment of various ailments will have ability to alter body function. Using such substances always carries a certain risk of unwanted or unintended effects (Parthasarathi G. 2007). But in clinical trials up to phase III it is done only with a very small population, following that the drug candidate become eligible to file for new drug application (NDA) and gets marketing permission (Tripathi KD 2008). Clinical trial data is not providing sufficient information about ADR and safety on prolong use, so after launching the new drug moiety in the market is necessary to watch continuously the adverse effects of the drug. Drug therapy has been recognized as a significant cause of harm since the earliest times. Around 400 BC the father of medicine (Hippocrates) warned about the dangers of drugs, recommending that they should never be prescribed unless the patient had been thoroughly examined (Walker Roger 2008).

Adverse drug reactions have been creating headlines over the last forty years since the thalidomide tragedy. More recent issues, such as cardiovascular attack in users of rosiglitazone, it is a antidiabetic drug, re-examination of the risks and benefits of hormone replacement therapy and psychiatric reactions associated with selective serotonin re-uptake inhibitors, have attracted significant media and public attention. Many drugs were withdrawn from the Indian market past recently few of them are sibutramine, rosiglitazone and gatifloxacin, tegaserod and Nimesulide formulations for human use in children below 12 years of age, due to serious adverse effects (CDSCO 2011). Pharmacovigilance is an integral part of drug therapy. Still, it is not widely practiced in Indian hospitals but now, the Government of India, Central Drugs Standard Control Organization (CDSCO) is initiating a nationwide Pharmacovigilance program for protecting the health of the patients by assuring drug safety. The program shall be coordinated by the Indian Pharmacopeia commission, Ghaziabad as a National Coordinating Centre (NCC). The long term objective of the PvPI is to establish a 'Centre of Excellence' for Pharmacovigilance in India. To achieve this objective, the PvPI National Coordinating Centre will collaborate with the WHO Collaborating Centre - Uppsala Monitoring Centre (UMC) based in Sweden (CDSCO 2011). In various studies, adverse drug reactions have been implicated as a leading cause of considerable morbidity and mortality (Beijer HJM

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2002). Adverse drug reactions (ADRs) are a common problem, which affect patients in the hospital and community setting. Early studies used their own definitions (Ogilvie R, 1967) which were vague and could be interpreted to encompass intentional and unintentional overdose, as well as some administration errors. The World Health Organization's definition from 1972 stated that an ADR is "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function" (WHO 1972). The definition has been widely used (Classen. DC 1997, Vargas E.2003) and is intended to include all doses prescribed clinically, but to exclude deliberate overdose. The incidence of adverse drug reactions (ADRs) varies with studies which show incidences ranging from as low as 0.15% to as high as 30% (Beijer HJM 2002, Jose J- Rao PG 2006, Lazarou J 1998).

ADEs have been defined as "injury resulting from medical intervention relating to the drug" (Bates. DW 1997) Therefore, all ADRs are ADEs but the reverse is not necessarily true. Indeed, the terms are not interchangeable as ADE studies can encompass errors of administration, prescription and ordering of medication, and ADEs are not necessarily due to the drug itself (Emma C Davies 2007).

OBJECTIVE

To study the incidence of ADRs in tertiary care teaching hospital, Annamalai University, in Tamil Nadu at Southern part of India.

MATERIALS AND METHODS

Study Design: The study was analytical cross sectional, noninvasive, observational, prospective and retrospective study.

Study Place: The study was carried out in a 1625 bedded tertiary care teaching based hospital attached to a medical college, situated in Tamil Nadu, southern India.

Study Period: In that hospital 2600 patients per day was enrolled as outpatient departments during the period October 2010 to March 2011 (average patient enrollment per day was 2612) and in the same period around 36, 000 patients was admitted as inpatient in various departments.

Inclusion Criteria: Special attention was given for patients of 1–24 months old (pediatrics) with a hospitalization period of at least 24 hours. Repeat admission of the same patient was counted as two admissions when separated by an interval of at least 1 month.

Exclusion criteria: Cancer patients and those with HIV infection were excluded from our study.

Patient collection form : The collected data were validated through the information on patient characteristics (sex, age, medical histopathology of diseases, etc.), drug treatment (suspected drug, dosage, route of administration, indication, date of beginning and stopping therapy, date of reaction, date of reporting and clinical details, concomitant drugs, etc.) and outcomes of the adverse event (like life threatening attributes, hospitalizations, disability, death, congenital anomaly and other etc.).

Causality assessment methods: Once the case was validated, an immutability score was obtained from the Naranjo Algorhythm score and WHO scale, based on the successive evaluation of different criteria where each possesses several degrees, and which provides grades for the causality and severity association between drug and adverse event. The evaluation followed a two-scale scheme: the Naranjo Algorithm score and WHO scale. Microsoft Excel 2007 and SPSS software were used to analyze the data. Data related to any patient showing an adverse drug reaction was analyzed as per the structured questionnaires designed by national Pharmacovigilance program, India.

RESULTS

Current study, total of 5000 patients prescription were selected randomly for study out of which 500 prescription was considered for the further follow-ups.

Table 1: Demographic Details and Percentage of ADRs

Sex	ADR		No. of Patients	% Population
	No.	%		
Females	22	55	280	56
Males	18	45	220	44
Total	40	100	500	100

Table 2: Different life stages, ADRs and Percentage of incidence

Life stages	No. of ADRs	% of ADRs	% of Incidence
Pediatrics	13	32.5	2.6
Neonates	2	5	0.4
Infants	4	10	0.8
Children	7	17.5	1.4
Adults	17	42.5	3.4
Geriatrics	10	25	2
Total	40	100	8

Table 3: ADRs in Pediatrics age group with ADRS

Pediatric	Age	No. of ADRs	% of ADRs	% of Incidence
Neonate	1st 4 week of life	2	5	0.4
Infant	4 week to 1 year	4	10	0.8
Child	1 – 12 year	7	17.5	1.4
Total		13	32.5	2.6

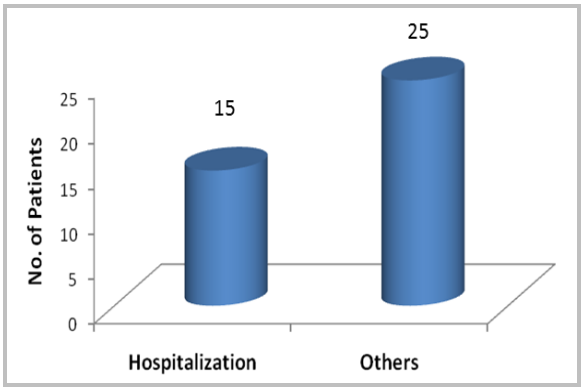

Figure 1: Outcomes of ADRs

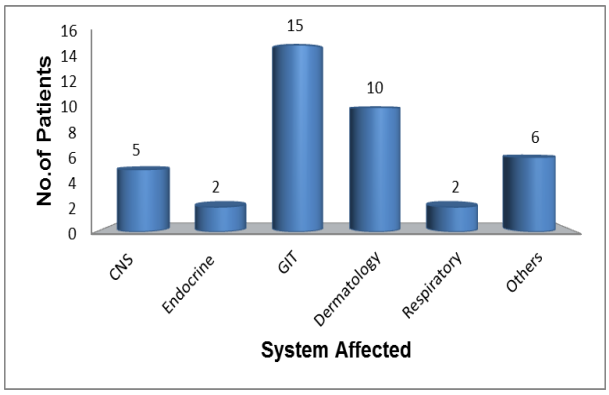

Figure 2: System affected by ADRs

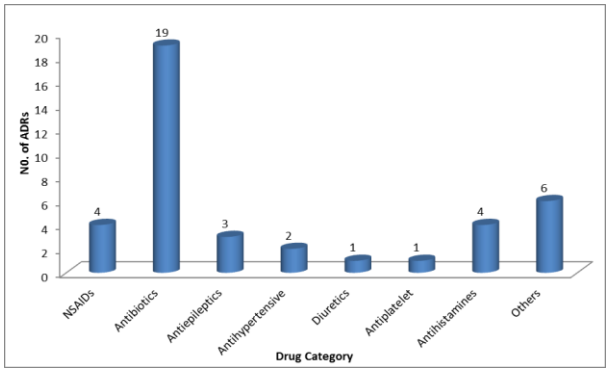

Figure 3: Drug categories causing ADRs

Table 4: Naranjo Algorhythm for ADR causality

S. No	Naranjo Scale	No. ADR	% of ADR
1	Definite	3	7.5 %
2	Probable	17	42.5 %
3	Possible	15	37.5 %
4	Doubtful	5	12.5 %

Table 5: WHO-UMC system for Standardized Case Causality Assessment

S. No	WHO UMC scale	No. ADR	Percentage of ADR
1	Certain	6	15 %
2	Probable	12	30 %
3	Possible	13	32.5 %
4	Unlikely	4	10 %
5	Conditional	3	7.5 %
6	Unassessable	2	5 %

Among the 500 prescription we found 40 were having ADR in this hospital with an incidence 8% and male incidence is 3.6% and female incidence was found to be 4.4%. In our study 280 females and 220 male subjects are included. Among the 40 ADR Prescription 22 (45%) are female and 18 (45%) are males subjects (Table 1). In the various life stages we found that maximum number of prescription having adults (42.5%) and followed by pediatrics (32.5%) and geriatrics (25%). The data were given were given Table 2. ADR in Pediatric patients (<12 years, neonates 1st four week of life, number of ADR 2 and 5 %, infants-four week to 1 year, number of ADR 4 and 10%, child 1 year to 12 year, number of ADR 7 and 17.5% and incidences 0.4, 0.8 and 1.4%) (Table 3). The highest percentage of ADRs was seen in adult patients however the difference was not statistically significant. Maximum number of ADRs were reported from the GIT 37.5% followed by Skin 25%, and then from CNS 12.5% (Figure 2). The most common drugs causing ADRs is shown in Figure 3, according to which, antibiotics were associated with maximum number of ADRs in which ampicillin produced the highest number of reactions, followed by quinolones. The other different drugs causing ADRs were antiepileptics, NSAIDs, antihypertensives, hormones, antihistaminics, diuretics, antiplatelet.

Regarding the outcomes attributed to ADRs, no one patient died in our 6 months study in this hospital and 15 (40.54%) cases got hospitalized due to ADRs and 25 patients were reported as others outcomes attributed to ADRs which included disability, congenital malformation, and intervention required to prevent damage and permanent impairment, etc. The incidence of ADRs in different age group was not significant. Similarly there was no significant association between ADRs and sex. No significant difference was seen between the ADR cases in age group less than one year as compared to two or more years of age. Thus, it conforms that the hypothesis of this study was not proved. According to the Naranjo algorithm scale, 42.5%of reaction were assessed to be probable, 37.5% as possible and 7.5% were definite and doubtful 12.5% (Table 4). Due to unavailability of the necessary information for immutability of scoring, we could not carry causality assessment for 10% of the study population. Similarly, WHO Scale certain 15%, probable 30%, possible 32.5%, unlikely 10%, conditional 7.5% and unassessable 5% (Table 5). Different types of ADRs were studied in which rashes 35.13% the most common ADRs were reported followed by vomiting 13.51%, dizziness 10.81%. Similarly, other types of ADRs were hypoglycemia, diarrhoea, sedation, epigastric pain, agranulocytosis, headache, carpopedal spasm, apnoea, hypoacidity and hyperacidity etc.

DISCUSSION

The details of our study showed more ADR found in females then males, which was similar to that of other studies reported in the literature (Ramesh M. 2003).

Previous studies have shown that a larger percentage of ADRs were reported from pediatric and geriatric population which is not similar to our results (Green CF 1997, Murphy BM 1993). In our study we experienced a higher percentage of ADRs for adult population 17 (42.5%) and incidence of percentage is 3.4%, whereas pediatrics and geriatrics ADRs are found 13 (32.5%) and 10 (25%), incidence 2.6 and 2%, the total incidence is found in our study is 8 %. In the pediatrics (the age group 0 to 12 year) are divided into three category namely is neonates, infants and children. in our study total no of ADRs in pediatrics is found 13 and 2, 4 and 7 ADRs and percentage of ADRs is found 5 %, 10% and 17.5% and incidence is 0.4%, 0.8% and 1.4%. The most common systems associated with ADRs in our study were gastrointestinal tract (GIT), skin, central nervous system (CNS), respiratory system, endocrine system and some others. This finding is consistent with many studies which have reported a higher percentage of dermatological manifestations than others but in our study GIT. The gastrointestinal system has also been reported to be involved in the majority of ADRs (Jose J 2006, Suh DC 2000, Classen DC 1991, Prosser TR 1990).

In our study, antimicrobial drugs (19 ADRs out of 40 ADRs), NSAIDs (4 ADRs) and antihistamines (4 ADRs) were the most commonly involved drug classes for ADRs then followed by drugs affecting antiepileptics (3 ADRs), antihypertensive drugs (2 ADRs), diuretics (1 ADR) and antiplatelet (1 ADR). In our study out of 40 ADRs only 15 patients are hospitalized and 25 other, no death seen in our study due to ADRs. The incidence of ADRs in different age group was not significant. Similarly there was no significant association between ADRs the either of sex. No significance difference was seen between the ADR cases in age group less than one year as compared to two or more years of age. Pharmacovigilance is not properly developed before in our country but now National Pharmacovigilance Programme (NPvP) is running under the guidance of Central Drugs Standard Control Organization (CDSCO) New Delhi. It is largely based on the recommendations made in the WHO document titled “Safety Monitoring of Medicinal Products–Guidelines for Setting up and Running a Pharmacovigilance Centre”.

CONCLUSION

The incidence of ADR in this study was 8% which is similar to other studies in other countries. So, we concluded that all the adverse drug reactions were not toxic reactions and were unpredictable. In order to minimize the problem associated with ADRs it is suggested that every hospital should have Pharmacovigilance Centers involving medical staffs including nurse and pharmacist. Pharmacists are having a very important role in the ADRs monitoring programmed globally and preventing ADRs. We hope in India clinical pharmacist including PharmD graduates will be more beneficial than conventional pharmacist to involve in such program in India.

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