

HOSPITALIZATION CAUSED BY ADVERSE DRUG REACTIONS(ADRS) IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA:A RETROSPECTIVE STUDY

Jamuna Rani.R¹, Priya.M²

ABSTRACT

Background: Adverse drug reactions (ADRs) are inevitable consequence of Pharmacotherapy. ADRs have been creating headlines over the last fifty years since the thalidomide tragedy. If we believe that the first principle in treating patients is '*primum non nocere*' i.e., 'above all do no harm' we should be aware of the possibility of ADRs.

Objective: To assess the nature, incidence, severity, causality and preventability of adverse drug events in a tertiary care hospital.

Materials and Methods: Patients presenting to the hospital with an adverse event due to medications were included in the study. Data on such adverse events collected for the year 2010-2011 were analyzed.

Results: The number of hospital admissions due to ADR was 23. Of these 10 were male, 13 were female. Elderly age group comprised of 30.4 %. Nearly 47.87 % of patients have taken these medicines as over the counter, 17.1 % of patients presented with severe life threatening reactions and 52.1% of patients seek hospital admissions >5-20 days which is statistically significant. More frequently implicated drugs causing ADRs were Antibiotics (47.8%) in which 36.3% allergic reactions were due to ofloxacin, followed by NSAIDs (39.1%) & the remaining adverse reactions were due to Anti Epileptics & hormonal drug.

Conclusions : The need for ADR monitoring in India is urgent in view of under reported Indian data, the genetic diversity of the Indian population and the many other factors that influence drug use behavior in the country. Prospective studies of similar nature could further help us to assess the burden of adverse drug reactions in patients and to develop better preventive measures.

INTRODUCTION

Adverse drug reactions have been creating headlines over the last fifty years since the Thalidomide tragedy. It is almost axiomatic that all drugs carry the potential to produce undesirable effects, in addition to the desired ones. This is often paraphrased by saying that all drugs are poisons, the dose alone making the difference. In various studies, adverse drug reactions have been implicated as a leading cause of considerable morbidity and mortality [1].

ADRs can arise from many sources, even if a drug is correctly selected and dosed. To the patient an unnecessary hospital admission caused by adverse drug reactions (ADRs) is an unnecessary loss of health as well as an unnecessary loss of quality of life [7]. Thus, prevention of unnecessary hospitalization by ADRs is an important goal in health policy decision-making.

Definition: According to the World Health Organization definition of ADR is, "Any response to a drug which is noxious, unintended, and undesired, which occurs at doses used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function". This definition excludes therapeutic failures, intentional and accidental poisoning (i.e, overdose), and drug abuse [8]. Also, this does not include adverse events due to errors in drug administration or noncompliance (taking more or less of a drug than the prescribed amount).

Recently, some authors prefer the term *adverse drug event* (ADE), is an injury resulting from administration of a drug. In contrast to the World Health Organization definition of ADR, the definition of ADE includes errors in administration [2]. We have chosen the World Health Organization definition for ADR because of its frequent use in the studies.

¹Professor & Head, ²Post Graduate, Department of Pharmacology, SRM Medical College, Kattankulathur-603203, Kanchipuram district, TamilNadu

Drug related hospital admission—Admission caused by any undesirable clinical manifestation that is consequent to and caused by the administration of a particular drug. The clinical manifestation may be a clinical sign, symptom, or abnormal laboratory test or it may be a cluster of abnormal signs, symptoms, or tests [9].

Incidence of ADRs: A study by Lazarou et al found ADRs to be the fourth to sixth leading cause of death in United States and serious ADRs accounted for 6.7% of hospitalized admissions [3].

A study by Ramesh et al in India carried out in a tertiary referral center in India showed that admissions due to ADRs accounted for 0.7% of total admissions and deaths due to ADRs accounted for 1.8% of total ADRs. [4].

Although numerous studies have done to evaluate the pattern and preventability of adverse drug reactions, only limited efforts have been made to systematically examine the problem of drug related injury in South India. Therefore we conducted this study in tertiary care hospital to evaluate the nature, incidence, severity, causality and preventability of adverse drug events among hospital admissions due to medications; to categorize adverse drug events by drug class, severity and clinical effects and over the counter medication leading to ADR.

METHODS

The study protocol was approved by the institutional ethics committee. This was a Retrospective study carried out in SRM Medical College Tertiary Care teaching hospitals, Kattankulathur, South India. All in patients who were admitted due to an adverse drug events related to medications from the period of January 2010 to December 2011 were included in the study. Data were obtained from Medical Records department. The information contained in these discharge summaries was reviewed for evidence of a drug-related incident that led to an admission to the hospital. Drug-related incidents occurring during the course of a hospitalization were not considered in the context of this study.

STATISTICAL ANALYSIS

Descriptive statistics using Microsoft excel software and data expressed as percentages and medians with 95% CIs.

RESULTS

ADR related admissions were 23 cases which accounted for about 0.3% of hospital admission. Those who develop an ADR during stay as inpatients were excluded. Table 1 gives the demographic characteristic of the patients. Females experienced a significantly higher incidence of ADRs (56.5%) than males (48.4%) $P < 0.05$. ADRs occurred in elderly age group (Age > 65 years) accounted for about 30.4%, which is consistent with the previous studies that ADRs are more common in elderly.

Details regarding classification and assessment of ADRs are given in Table 2. Most of the ADRs are reported on day 2 of the medication consumption. Severity assessment of the ADRs showed that the majority of the reactions reported were moderate (47.8%), followed by mild (30.4%) and severe (21.73%). Almost about half the patients (52%) of hospitalization due to ADR took the medicines as over the counter drug, as self medication.

TABLE 1 Demographic characteristic of the patients. These include classification of patients admitted for ADR according to age and sex.

Characteristics	No of Patients hospitalized due to ADR
Male	10
Female	13
Pediatric	02
Adult	14
Elderly	07

DISCUSSION

In our study 0.3% of admissions were due to ADR. Our findings are similar to other reports generated in other study [10]. However ADR related hospitalization is lower in comparison with studies done in Western population. Determining the actual cause of ADR is most complex aspect of therapeutics. There is always difficulty to bridge the gap between 'clinical hunch' and 'scientific rigor'. Under-reporting by doctors is well known, and in India also, the spontaneous reporting system has produced lower rates of reporting [14]. The demographic details of our study showed female gender predominance over

TABLE 2: Classification and assessment of ADR outcomes

Parameter	No of Patients
Onset of ADRs	
Acute(<1 hr)	03
Sub -acute(1 -24 hrs)	10
Latent(> 2 days)	07
Unknown	03
Severity	
Mild	07
Moderate	11
Severe	05
Over The Counter Medication	
Taken as OTC drug	12
Prescribed elsewhere	11

Table 3 gives the effect of ADRs on length of stay. The financial burden of ADRs increases substantially with extent of hospitalization. Half of the patient (52%) admitted due to ADR had prolonged hospitalization (>1 week) and 21.7% of patients was admitted for more than 20 days. Increased length of stay may reflect the severity of ADRs.

TABLE 3: Days of Hospitalization due to ADR	
Hospitalized days	No of Cases
< 5 days	6
5 – 20 days	12
> 20 days	05

The most common drugs causing the ADRs and their reaction details are shown in Table 4 .Antibiotics were associated with about half of the ADRs (52.7%).Ofloxacin produced the highest number of reactions(36.3%) followed by Ampicillin(8.6%) and Amoxycillin(8.6%).The next common drugs causing ADRs were

Analgesics(39.1%),diclofenac,Paracetamol and Aceclofenac Paracetamol Combinations. The other drug classes reported with ADR were Antiepileptic (Phenytoin-1),Antispasmodic(dicyclomine-1) and hormonal pill(Progesterone-1).

TABLE 4: Drugs most commonly Involved in ADRs and their reaction details. Individual reactions reported for each drug and the total number of cases reported.

Drug	Reaction detail	No of Cases
Diclofenac	Drug hypersensitivity reaction	3
Paracetamol + Aceclofenac comb	Skin rashes, Gastritis, mucosal damage	3
Aceclofenac	Skin rashes, gastritis, DHR	3
Ofloxacin	DHR, Angioedema,SJS-2	4
Rifampin	Skin rashes, Periorbital swelling	2
Ampicillin	DHR, diarrhoea	
Amoxycillin	Skin rashes, giddiness	2
Azithromycin	Skin rashes	2
Grisofulvin	Drug eruption	1
Phenytoin	Ankle swelling, sore throat, rashes	1
Progesterone	Maculopapular skin rashes	1
DiCyclomine	Skin rashes, increased sweating	1

(Note - DHR: Drug Hypersensitivity Reaction
SJS: Steven Johnson Syndrome)

males, which was similar to that of other studies reported in the literature [4]. Previous studies have shown that a larger percentage of ADRs was reported from geriatric and pediatric population which was similar to our results [12]. In our study pediatric (8.6%) and geriatric patients (30.4%) experienced a higher percentage of ADRs than the adult population [13].

The most common systems associated with ADRs in our study were skin. This finding is consistent with many studies which have reported a higher percentage of dermatological manifestations than other system manifestation [16]. In our study, antibiotics (11) and analgesics (09) were the most commonly involved drug classes in ADRs. This finding is consistent with the studies reported by Murphy *et al* [16].The most common drugs involved in ADR were ofloxacin, Ampicillin, Amoxicillin, Aceclofenac, Diclofenac and Paracetamol.

Our Study showed that about 48.7% of the patients reported with ADR took the drugs as over the counter medications, which shows effective interventions should be made to bring awareness about ADR to the patients. About 58% of the patients in our study were hospitalized for more than one week, which shows the economic burden and sufferings of the patients due to drug related adverse events [17]. This can be prevented if ADR are minimized. It is likely that many of them particularly the avoidable and potentially avoidable ones can be minimized by patient and physician education and better prescribing practices and thus lead to considerable cost savings.

However this study has several limitations. Data has been collected from a tertiary care hospital, where on average, more serious patients are seen. We considered hospitalization due to ADR and not included Adverse events occurred during hospital stay of the patients. Secondly due to the retrospective nature of this study, we are unable to compute prevalence of AE based on inappropriate drug prescription due to lack of data on drug prescription which caused ADR. Third, the identification and reporting of an adverse event is dependent to a huge extent on information shared by the patient regarding drug usage.

CONCLUSION

To conclude, adverse drug reactions are important cause of hospital admissions. ADRs have proved a significant problem in healthcare sector, their occurrence is influenced by many factors and their severity and outcome may vary. There is a need to develop better preventive strategies like patient and physician education and good prescribing practices. Prospective studies of similar nature could further help us to assess the burden of ADRs.

ACKNOWLEDGEMENT

We thank Prof. Dr. James Pandian, Dean, SRM Medical College, Kattankulathur for support in the conduct of the study.

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