Original Research Article

Distinguishing adverse drug reactions, the noxious effects of medicines at a tertiary care hospital

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Abstract

Introduction: Adverse drug reactions (ADRs) are unavoidable and are considered as the fourth-to-sixth leading causes of death. It makes it essential to detect and monitor the ADRs. Hence, this study was aimed to identify the agents involved in the occurrence of ADRs and to identify and monitor the ADRs occurred in inpatients of a tertiary care hospital.

Materials and Methods: It was a descriptive, prospective, observational study conducted for 2 years at a tertiary care hospital in Bengaluru, India. The ADRs were detected and monitored by interviewing the patients and reviewing the laboratory tests and medical charts. All the collected data were tabulated in Microsoft Excel 2016 and analyzed for possible results. Using Naranjo scale and Hartwig and Seigel's severity assessment scale, the probability and severity of the reactions have been identified.

Results: In this study, it was observed that majority of ADRs occurred in females. Patients belonging to the age group of 21–50 years old experienced higher number of ADRs than the patients in other age groups. The most commonly reported ADRs were associated with antimicrobial and cardiovascular agents. The most commonly reported ADRs were elevated liver function test (LFT) (12.2%) followed by diarrhea (9.5%). The gastrointestinal system was the most commonly affected organ system followed by fluid and electrolytes. Majority of the ADRs (55.1%) were found to be probable. In addition, the majority of the reported ADRs (84.2%) were mild.

Conclusion: The results of this study provide a database of ADRs, which aids clinicians in optimized and safer use of medicines and this, in turn, might lead to an enhanced level of patient care.

Keywords: Adverse drug reactions, Hartwig and Seigel's scale, Naranjo scale, pharmacovigilance

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INTRODUCTION

Drugs are considered as the double-edged weapons. Besides their merits, they can have some disadvantages as well. Despite drugs are considered to be the most common medical interventions and are essentially used to relieve sufferings, it has been perceived long ago that drugs themselves can be fatal through inducing adverse drug reactions (ADRs).[1]

Since the past 50 years, after the thalidomide tragedy happened, ADRs started creating headlines. From the time the US Institute of Medicine has published the report of "To Err is human: building a safer health system," international attention to patient safety has grown substantially. ADR does not have a standard definition. Early studies recruited their own definitions which

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were obscure and could be interpreted to subsume the intentional and unintentional overdose, as well as some administration errors.[2]

According to the World Health Organization, ADR is defined as "A response to a drug which is noxious and unintended, and which occurs in doses normally used in human for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological functions."[3]

An ADR is considered to be a type of adverse drug event (ADE) whose etiology can be directly attributed to the drug and its physiologic properties. ADRs can be differentiated from ADEs as the ADRs can happen despite appropriate prescribing and dosing, while ADEs can be attributed to the inappropriate use of the drugs or some other confounders that can happen during the drug therapy but are not essentially related to the pharmacology of the drug itself.[4]

Historically, ADRs have been classified as Type A or Type B. Type A reactions are associated with high morbidity and low mortality and are predictable from the known pharmacology of a drug. Type B reactions are associated with low morbidity and high mortality and are the novel responses that cannot be predicted from the known pharmacology of a drug. All ADRs do not fit into Type A and Type B categories; as a result, additional categories have been developed including Type C (continuing), Type D (delayed use), and Type E (end of use) reactions.[5]

ADRs have considerable economic as well as clinical costs as they often lead to hospital admission, prolonged hospitalization, and emergency department visits. The risk of ADRs is essentially an inherent risk of all drug therapies and is modulated by numerous factors, including dose and frequency of administration, genotype, and pharmacokinetic characteristics of special populations, such as pediatric and geriatric patients and those with hepatic or renal impairment.[6]

The prevalence rate of ADRs is estimated to be 6.5% in the community. In addition, it has been reported that 10%–20% of hospitalized patients deal with ADRs. Among hospitalized patients, older adults are at higher risk of development of ADRs due to increased drug consumption and age-related alterations in pharmacokinetics and pharmacodynamics.[7,8]

According to the recent epidemiological studies, ADRs are the fourth-to-sixth leading causes of death. Hence, it is essential to detect the ADRs and also it is very crucial to monitor both known and unknown adverse effects of medicines. Moreover, ADR monitoring and reporting activity is in its infancy in India mainly due to lack of awareness and lack of interest of health-care professionals in ADR reporting and documentation.[8,9]

This study was mainly designed to identify and monitor the ADRs occurred in inpatients of a tertiary care hospital and to identify the most common therapeutic agents involved in the occurrence of ADRs.

MATERIALS AND METHODS

Study setting

The study was conducted at a tertiary care hospital in Bengaluru, India, which is a 250-bed hospital with 18 specialists, 46 physicians, 15 pharmacists, and 105 nurses, who attend an average of 550 patients/month. In this study, the required data were collected from three departments including the department of general medicine, department of surgery, and Intensive Care Unit (ICU).

Study design

It was a descriptive, prospective, observational study designed according to the objectives of the study to be conducted for 2 years from January 2016 to January 2018 at a tertiary care hospital.

Study inclusion/exclusion criteria

All the inpatients, of both genders and all age groups, who experienced an ADR after the commencement of treatment, were included in the study. All patients of obstetrics and gynecology department were excluded from the study.

Sampling and data collection

The research investigators had collected the data from the patients' case sheets, from the respective departments, from 9:00 am to 3:00 pm on a daily basis. The data collected include initials, age, sex, height, and weight of the patients; brief description; onset date and stop date of occurrence of the suspected ADR; name, indication, start and stop dates, dose, and frequency of the suspected medications; past and present medical history of the patients; concomitant medications; and relevant tests and laboratory data. The ADRs were detected and monitored by interviewing patients and reviewing laboratory tests and medical charts. Routinely, the physicians were consulted about the patients' clinical problems and ADRs were routinely recorded. For each detected ADR in the study, a yellow form, the form used for ADR reporting to National Pharmacovigilance Center, was filled and documented.

Ethical considerations

The study was ethically cleared by the Institutional Review Board of the hospital. In addition, for using each patient's information in this study, patients, caregivers, or parents were clearly explained about the study and signed informed consent form was obtained from him or her. Each patient, caregiver, or parent was assured that the information provided by him or her would be confidential and used only for the purpose of research.

Data analysis

All the collected data were tabulated in Microsoft Excel 2016 (ver. 2016, Microsoft, Redmond, WA, USA) and analyzed to identify the gender-wise prevalence of ADRs, incidence of ADRs in different age groups, department-wise incidence of ADRs, most common ADR-inducing classes of drugs, most common types of ADRs, most commonly affected organ systems, and probability and severity of the reactions. To appraise the probability and severity of the reactions, Naranjo Causality Assessment Scale and Hartwig and Seigel's Severity Assessment Scale were used.

RESULTS

During the study period of 2 years, a total of 390 ADRs were reported from 385 patients. Out of the 385 patients, 164 (42.6%) patients were male, while 221 (57.4%) patients were female. Of which, 380 patients had single ADR followed by five patients who were with two ADRs. The patients were from varying ages, ranging from 5 to 87 years old. Majority of the patients who experienced ADRs belonged to the age group of 21–50 years. The distribution of patients with respect to their age is presented in Table 1.

Majority of the ADRs occurred in patients who were admitted in the general medicine department followed by those admitted in the surgery department and ICU. The distribution of ADRs in different departments is presented in Table 2.

Out of the total ADRs, commonly reported ADRs were associated with antimicrobial agents and cardiovascular agents. The most common classes of medicines associated with ADRs are presented in Table 3.

Out of the total ADRs, the most commonly reported ADRs were elevated LFT (12.2%) followed by diarrhea (9.5%), itching (6.4%), hypokalemia (5.9%), hyponatremia (5.1%), hypoglycemia (4.9%), rashes (4.8%), drowsiness (4.3%), vomiting (4.1%), hyperglycemia (4%), edema (3.6%), bradycardia (3.5%), tachycardia (3.5%), constipation (3.5%), hematuria (3.3%), hyperkalemia (3.3%), cough (3%), nausea (2.8%), elevated creatinine (2.5%), headache (2.5%), insomnia (2.3%), and tremor (2%). Other ADRs such as weakness, gastritis, wheezing, urticaria, thrombocytopenia, abdominal pain, alopecia, and anaphylaxis were also observed but at lesser frequencies.

The gastrointestinal system was the most commonly affected organ system followed by fluid and electrolytes. Various organ systems affected by different ADRs are presented in Table 4.

Table 1: Distribution of patients with respect to age (*n*=385)

Age range (years)	Number of patients (%)
1-10	8 (2)
11-20	26 (6.8)
21-30	62 (16.1)
31-40	109 (28.3)
41-50	86 (22.3)
51-60	41 (10.7)
61-70	32 (8.3)
71-80	18 (4.7)
81-90	3 (0.8)

Table 2: Distribution of adverse drug reactions in different departments (*n*=390)

Department	Number of ADRs (%)
General medicine	245 (62.5)
Surgery	108 (28)
Intensive Care Unit	37 (9.5)

Table 3: Most common classes of medicines associated with adverse drug reactions (*n*=390)

Class of medicine	Number of ADRs (%)
Antimicrobial agents	156 (40)
Cardiovascular agents	109 (28)
Anti-asthmatic agents	28 (7.2)
Anticonvulsants	28 (7.2)
Steroids	21 (5.4)
Analgesics	14 (3.5)
Iron, folic acid, sodium, and mineral supplements	13 (3.3)
Anti-anxiety agents	9 (2.3)
Antithyroid agents	6 (1.5)
Antidepressants	3 (0.8)
Antacids	3 (0.8)

Table 4: Most commonly affected organ systems by different adverse drug reactions (*n*=390)

Organ system	Number of ADRs (%)
Gastrointestinal	141 (36.2)
Fluid and electrolytes	57 (14.5)
Nervous	48 (12.3)
Dermatologic	44 (11.3)
Endocrine	28 (7.2)
Hematological	26 (6.7)
Cardiovascular	22 (5.6)
Respiratory	10 (2.7)
Renal	9 (2.3)
Musculoskeletal	3 (0.7)
Ophthalmic	2 (0.5)

ADRs: Adverse drug reactions

According to the Naranjo scale, 215 (55.1%) suspected ADRs were probable, 141 (36.2%) ADRs were possible, and 34 (8.7%) ADRs were doubtful. As per Hartwig and Seigel's Severity Assessment Scale, 327 (84.2%) ADRs were mild, 62 (15.5%) ADRs were moderate, and 1 (0.3%) ADR report was severe.

DISCUSSION

Majority of the drugs used in the pharmacotherapy of various diseases have a dual effect, beneficial effect as well as the adverse one. Hence, these adverse effects can be best regulated through having a pronged approach of prevention, treatment, and rehabilitation.[10]

In this descriptive, prospective, observational study, a total of 390 ADRs were reported from 385 patients. All the reported ADRs were analyzed to identify their prevalence in different genders, ages, drug classes involved, and organ systems affected. The causality assessment was done using Naranjo scale[11] and severity was appraised using Hartwig and Seigel's severity scale.[12]

In this study, similar to the studies carried out by Ahmad *et al*.[13] and Baniasadi *et al*.,[14] it was found that majority of ADRs occurred in women. Such a higher prevalence of ADRs among women compared to men might be due to the higher proportion of emotions in females which enhances their sensitivity to the pharmacological actions of the medicines, thus promoting the chances of development of ADRs. Rational dose titration may lead to the minimization of ADRs in females.[2]

Despite the vulnerable groups including pediatric and geriatric patients who are supposed to experience ADRs more often,[8] in this study, it can be observed that the frequency of ADRs was maximum in the age group of 21–50 years followed by the above 50 years' age group. This is on par with the results of a study conducted by Sharma *et al*.[15] It is likely that this population is attending hospital more frequently and is a major population receiving drug therapy.[8]

This study was conducted in one of the tertiary care hospitals of Bengaluru, India, and there is likely to be variation between different hospitals because of differences in the local population characteristics and the specialties within the hospitals.[8] In this study, similar to the study conducted by Baniasadi *et al*.,[14] the majority of the ADRs were reported from the general medicine department. A high incidence of ADRs in this department is possibly due to that generally more number of patients are admitted there and the patients in this department consume the highest number of medicines.

The major causative agents for ADRs were found to be antimicrobial agents. The same result has been found in the studies carried out by Gupta *et al*.,[10] Baniasadi *et al*.,[14] and Gajanan *et al*.[16] Such high number of ADRs caused by antimicrobial agents can be the result of high and irrational prescribing of antimicrobial agents in Indian hospital setups.[17] These agents should be initiated only if there is a clear potential clinical benefit and irrational use that enhances the chances of ADRs should be discouraged.[18]

In contrast to other studies conducted by Ahmad *et al*.[13] and Lobo *et al*.[19] in similar study settings where the most common ADR was rashes, in this study, the most common ADR was elevated LFT followed by fluid and electrolyte abnormalities. The reason for this difference is not clear but could be due to variation in the recording of such subjective symptoms.[20]

The most commonly reported ADRs were in agreement with the gastrointestinal system. In other words, this system was the most frequently affected organ system. In other studies conducted by Ahmad *et al*.,[13] Baniasadi *et al*.,[14] and Sharma *et al*.[15] also, similar result can be observed.

By using Naranjo scale,[11] causality assessment has been done in other studies conducted by Shrivastava *et al*.,[21] Arulmani *et al*.,[22] and Gupta *et al*.[23] in other hospital settings in South India, where the majority of the reported ADRs were classified as probable. A similar result can be observed in this study.

Using Hartwig and Seigel's Severity Assessment scale,[12] it was found that majority of the reported ADRs in this study were mild. It was followed by moderate and severe ADRs. Lihite *et al*.[8] and Gupta *et al*.[10] have conducted studies in which the same results can be observed.

CONCLUSION

The results of this study are comparable with the pattern of ADRs reported in other studies conducted in other hospital settings. This study delivers a database of ADRs caused by the most common drugs administered in our hospital. This database can be in turn facilitative for clinicians in the optimum and safe use of these drugs. As a result, effective execution of ADR monitoring leads to better and safer administration of the ADR-inducing drugs, which might ultimately result in an accelerated patient care.

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Conflicts of interest
There are no conflicts of interest.

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