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Research Article

Prospective Study on Monitoring and Reporting of Adverse Drug Reactions at Tertiary Care Teaching Hospital Bagalkot

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Abstract

Aim: To conduct a prospective study on monitoring and reporting of adverse drug reactions at tertiary care teaching hospital.

Materials and Methods: The study was conducted at H S K hospital and research center, Bagalkot. The study was approved by Human Ethics Committee and clearance was obtained from institutional ethics committee of HSK College of Pharmacy, Bagalkot. This study was carried out for a period of one year. This was a prospective study based only on those patients who experienced adverse reactions to medicine use, during their stay in H.S.K hospital. The reported ADRs discussed with doctors, involved the use of different forms for data collection, documentation, causality assessment and analysis of the data.

Results: In this study from 68 patients 90 ADRs were reported. The elderly adults were most affected and males (53.3%) were predominant over females (43.3%). Majority of them were type-A reactions with 82.8%. As per WHO causality assessment scale 75.5% ADRs were probable, Naranjo scale 95.5% were probable, as per Hartwig and Siegel severity scale 88.8% were moderately severe and only 7.7% were definitely preventableas per Schumock and Thornton preventability scale. Most of ADRs were managed by withdrawing suspected drug and most of the patients were recovered.

Conclusion: ADRs to drugs happen commonly irrespective of their therapeutic effects and their reporting is important for the early recognition and prevention of ADRs and will also help in generating signals. ADR monitoring not only acts as an alerting mechanism for physicians, but also helps the regulatory authorities in making the policy decision.

Keywords: *Adverse Drug Reaction; WHO Causality Scale; Naranjo Scale; Hartwig and Siegel Severity Scale*

Abbreviations

ADR: Adverse Drug Reaction; CDSCO: Central Drug Standard Control Organization; WHO: World Health Organization; FDA: Food and Drug Administration; ASHP: American Society of Health-System Pharmacist; NSAID: Non-Steroidal Anti Inflammatory Drugs; UMC: Uppsala Monitoring Center; HCPs: Health Care Professionals; AGEP: Acute Generalized Exanthematous Pustulosis

Introduction

Drugs are the most common medical interventions, primarily used to relieve sufferings. But it has been recognized long ago that drug themselves can prove fatal by causing one or the other adverse drug reactions; as the saying rightly goes "Drugs are Double Edged Weapons" [1]. Adverse drug reactions (ADRs) are considered as one among the leading causes of morbidity and mortality [2]. It has been reported that ADRs account for 5% of all hospital admissions and occur in 10 - 20% of hospitalized patients [3]. An overall incidence of serious and fatal ADRs among hospitalized patients is 6.7% and 0.32%, respectively [4].

Pharmacovigilance is the branch of pharmacology which deals with detection, assessment, understanding and prevention of ADRs [5]. It is vital to detect ADRs in a timely manner. Uppsala monitoring center (UMC) in Sweden is the WHO collaborating center internationally for ADR monitoring [6]. UMC developed and maintains a global individual case safety report database known as Vigibase on behalf of WHO [7].

Reporting of ADRs has become an important component of monitoring and evaluation activities performed in hospitals [8]. Spontaneous reporting program, a common method of drug surveillance is capable of recognizing ADRs in the daily medical practice, even though under reporting and absence of information on number of people actually exposed to the drug are its disadvantages [9,10].

Aim of the Study

The present study was conducted with the aim of analyzing the pattern of Adverse Drug Reactions occurring in and to identify the common drugs implicated in causation of ADRs and to report the most common manifestations associated with these ADRs and their severity.

Materials and Methodology

Study design

This was a prospective study.

Sample size [11]

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From the above study, most of the ADRs were definitely Preventable (69.7%) and were predictable in nature.

Absolute Precision: 10%

By using Open Epi Software, we got n = 90.

Equation

Sample size n = [DEFF*Np(1-p)]/ [$(d^2/Z^2_{1-\alpha/2}$*(N-1)+p*(1-p)]

Sample size = 90.

Study location

This study was carried out in H.S.K Hospital and Research center, Bagalkot. It is a tertiary care teaching hospital associated to S.N. Medical College. It is an 1110 bedded general hospital run by the BVV Sangha. It is one of the premier institutes in Karnataka with around 15 specialties, serving to the health care needs of a huge population.

Study setting

This study was based only on those patients who experienced an adverse reaction to medication use, during their stay in H.S.K hospital and were ultimately reported.

Study criteria

Inclusion criteria

ADRs of drugs used in all departments in any age of either sex from in-patients.

Exclusion criteria

The ADR that occurred due to Medication errors, over prescribing, over dosing/excess consumption, Drug-Drug interaction, Drug-Food interaction, Drug interaction with the use of alternative system of medicine, ADR from outpatients.

Age criteria

The study considered the age groups for study as newborn infants (0 to 27 days), infants and toddlers (28 days to 23 months), children (2 to 11 years), adolescents (12 to 16 - 18 years dependent on region), patients of age group 18 - 30 years are considered as young adults, patients of age 31 - 45 years as adults, patients of age 46 - 60 years as older adults and patients of age 61 - 75 years as elderly adults and patients of age group above 75 years considered as very elderly adults were considered as geriatrics [11].

Study duration

Study was carried out for a period of one year. From 01st July 2019 to 30th June 2020.

Study approval

This study was approved by Institutional Ethics Committee of HSK college of pharmacy Bagalkot (Certificate Ref. No: HSKCOP/IEC/19/1).

Collection of data

Notification of a suspected ADR and ADR reporting and documentation forms used for data collection, documentation and analysis of adverse drug reactions. Collection of "Notification of a suspected adverse drug reaction forms" and duly filled ADR reporting forms were collected from the clinicians/reporting persons during ward rounds.

Motivation for spontaneous reporting of ADR

To motivate the spontaneous reporting of ADR from nurses, doctors and patients on everyday basis, a personal meeting with head of SNMC hospital was held, with a request to report the suspected cases of ADRs. Forms of "Notification of suspected Adverse drug reaction" were made available at nursing station and the all departments of hospital and informed them to report suspected ADR spontaneously to department of clinical pharmacy, located at 1st floor of HSK hospital (Near female orthopedic ward) or to Drug Information Center (3rd floor near female medical ward).

Documentation of reports

This data was documented after receiving the ADR notification forms, only those cases which fulfilled the criteria were included in the study. The details of cases were documented in "Adverse drug reaction reporting and documentation form". Complete history of the patient was takenfrom case reports, medication charts and personal interviews with patient and patient's attendants. Disease states of the patients and other comorbid conditions are properly enquired and noted down. Medication history of the patient is obtained from the patient medication slips, prescriptions and also from in-depth patient interview regarding medication use. Sometimes the screening of the remaining medication of the patients that he had used prior to the reaction, which helps in disclosing the facts of medication use and details of the drug products like brand name, manufacturer, Lot no, Expiry dates, and other information. Efforts were made to collect as much information as possible.

Assessment of preventability/unpredictability

As per WHO and AHFS ADRs can be classified as Type A and Type B reactions according to the drug administered to the patient. Type A reactions (Insulin induced hypoglycemia) are predictable and Type B reactions (Itraconazole induced AGEP).

Assessment of causality, severity and preventability

In order to improve the accuracy of our assessments, individual causality assessments were undertaken using "Naranjo causality assessment scale" and WHO- UMC scale, which classifies drug reactions into definite, probable, possible, doubtful and certain, probable, possible, unlikely, conditional, unassessable respectively. Severity of the reaction was assessed using Severity assessment scale Hartwig and Siegel scale, which classifies ADR into mild, moderate and severe. Preventability assessment was done by using Schumock and Thornton scale which classifies ADR into definitely preventable, probably preventable ant not preventable.

Follow up and feedback

The documented cases were followed up daily for documentation and to note the prognosis of the patient. Patients or patient's attendants were interviewed daily so as to excavate any unnoticed and unseen details of history of the patients and events prior to the reaction. Discussion with reporters/clinicians to give feedback on the reaction and management of the patient condition by providing reports and needed drug information service.

Statistical analysis

The data analysis was done by using statistical methods like Percentages, Chi-Square test and student's *t* test for arrive at a conclusion for finding the significant differences. The minimum level of significance was considered as $p < 0.05$.

Results

A total 90 adverse drug reactions from 68 patients were reported during one year study period from July 2019 to June 2020. A total number of patients admitted during study period were 11932 from which 90 ADRs were reported. The overall incidence of ARDs during hospitalization in this patient group was 0.0075%.

Demographics

From total 90 ADRs, 1.4% for 28 days-32 months of age, 2.9% for 2 - 11 years, 10.2% for 12 - 18 years, 16.1% for 19 - 30 years, 13.1% for 31 - 45 years, 19% for 46 - 60 years, 30.8% for 61 - 75 years and 5.8% for more than 76 years were observed. Results were summarized in figure 1.

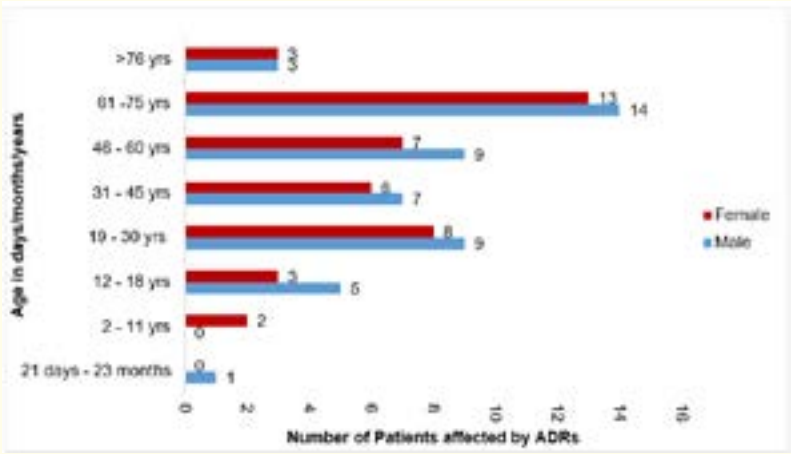

Figure 1: *Demographic data of patient characteristics.*

Organ system affected by ADRs

The most common organ system affected by ADRs was haematological system 15 (16.65%) followed by CNS 13 (14.4%). Twelve (13.3%) ADRs were associated with hepatic system. Results were summarized in figure 2.

Therapeutic drug classes implicated to cause ADRs

In this study we observed the most common therapeutic drug classes implicated to cause ADRs were analgesics 14 (15.5%), anti-tuberculosis 13 (14%) and antibiotics 10 (11.1%), anti-diabetics 10 (11.1%). Results were summarized in figure 3.

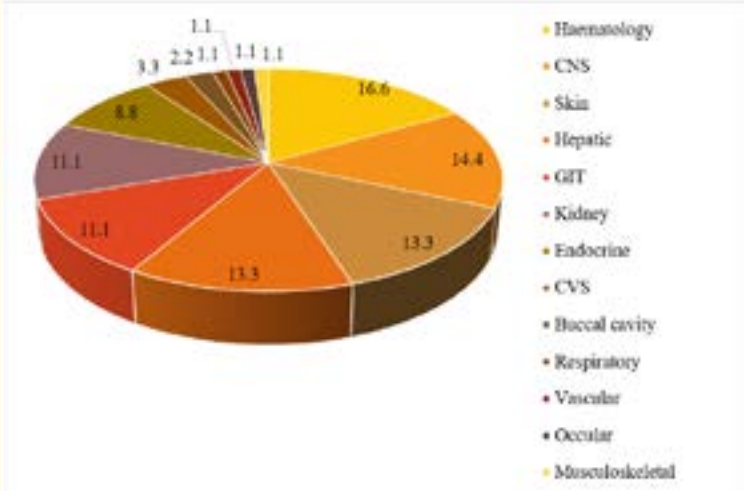

Figure 2: *Organ system affected with ADRs.*

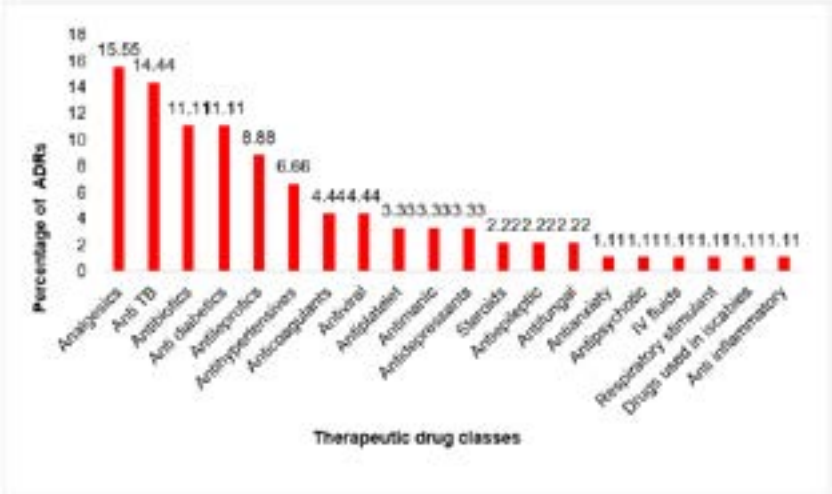

Figure 3: *Therapeutic drug classes implicated to cause ADRs.*

Classification of ADRs

ADRs were classified according to Rawlins and Thompson classification 82.2% ADRs were Type- A reactions and 17.7% ADRs were Type-B reactions. Out of 90 ADRs 74 (82.2%) ADRs were Type A and 16 (17.7%) were Type B reactions. Frequency of reactions includes, among 74 Type A reactions 37 (41.1%) were common, 24 (26.6%) were infrequent and 15 (16.6%) were rare whereas 2 (2.2%) were common, 4 (4.4%) were infrequent and 10 (11.1%) were rare among total 16 Type B reactions.

Assessment of ADRs with different scales

In total ADRs the WHO causality assessment of the reactions revealed that 66 (73.3%) were probable, 19 (21.1%) were possible and 4 (4.4%) were certain, according to Naranjo algorithm majority of ADRs 86 (95.5%) were probable and 4 (4.4%) were possible. As per Hartwig and Siegel's Severity of ADRs scale 86(88.8%) were moderate, 8 (8.8%) were mild, 2 (2.2%) were severe and 83 (90%) were not preventable, 7 (7.7%) definitely preventable ADRs according to Schumock and Thornton preventability scale. Results were summarized in table 1.

Scales for analysis of ADRs	Terms	Number of ADRs	% of ADRs
WHO-UMC causality scale	Certain	5	5.55
	Probable	68	75.55
	Possible	17	18.88
Naranjo probability scale	Probable	86	95.55
Hartwig and Siegel's severity scale	Mild	8	8.88
	Moderate	80	88.88
	Severe	2	2.22
Schumock and Thornton preventability scale	Definitely preventable	7	7.77
	Not preventable	83	92.22

Table 1: *Analysis of ADRs with different scales Analysis of ADRs with different scales.*

Management of ADRs

Out of 90 ADRs suspected drug was withdrawn in 61 (67.7%) cases, additional treatment was given in 13 (14.4%) cases, dose altered in 9 (10%) cases and there was no change in treatment in 7 (7.7%) cases. Among reported ADRs most of them were accepted by the doctors.

Outcome ADRs

After dechallenge, majority 49 (54.4%) of the patients who experienced ADRs were improved. 28 (31.1%) were unknown, 2 (2.2%) caused permanent harm and 3 (3.3%) were continued. After rechallenge, recurrence of symptoms were seen in 4 (4.4%) cases and the outcome of 4 (4.4%) were unknown. Results were summarized in figure 4.

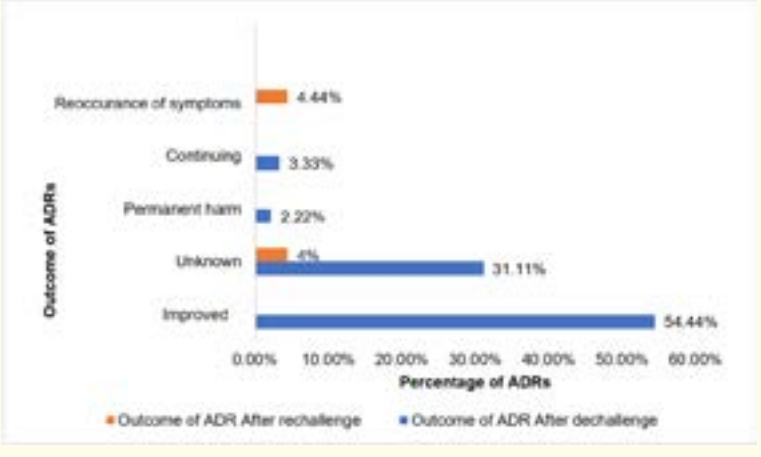

Figure 4: *Outcome of ADRs.*

Discussion

In present study we reported 90 ADRs from 68 patients during the study period. The majority of ADRs (30%) were seen in elderly adults in the age group of 61 - 75 years. This was coincides with a study conducted by Hurwitz [12] which includes most of the ADRs were found in the age group of 60 years and above. The reason being attributed to increased incidence of diseases like diabetes, hypertension leading to increased usage of medicines, increased visit to the hospital for regular checkup associated with increased complaints of drug related adverse events furthermore males predominance was noted in 53.3% of cases than females in 43.3% cases. There was no statistical significance difference observed in ADRs between male and female. This result coincides with the study conducted by Marcia GAAL., *et al* [13].

The most common organ system associated with ADRs was haematological system (16.6%) followed by CNS (14.4%) and skin and hepatic were identically (13.3%) affected, a finding was in contrast with a study conducted by Chandrashekhar VM., *et al* [11].

In our study, the suspected therapeutic drug classes implicated to cause ADRs were analgesics (15.5%) probably because they are available as OTC which was consistent with previous study conducted by Marcia GAAL., *et al.* [13] followed by anti TB (14.4%) and antibiotics (11.1%). Among analgesics diclofenac was leading causative drug of adverse effect (AKI, acute on chronic kidney disease, nephrotic syndrome) and mostly affected in the age group of elderly adults (60 - 75 years).

Analysis of the type of reported ADRs according to Rawlin and Thompson showed that type A more than type B, a finding similar to the one observed by Jamuna R., *et al* [14].

Upon causality assessment using WHO-UMC scale most of ADRs were probable (73.3%), followed by possible (18.8%) and certain (5.5%). Naranjo causality assessment scale involved most of ADRs were probable (95.5%) and possible (4.4%) which was consistent with previous studies conducted by Chandrashekhar VM., *et al*.

Severity was assessed by Hartwig and Siegel severity scale which includes majority of ADRs were moderate (88.8%) followed by mild (8.8%) and severe (2.2%), a finding similar to the one observed by Pankaj DM., *et al*. Preventability was assessed by using Schumock and Thornton preventability scale which includes majority of ADRs were not preventable (92.2%) followed by definitely preventable (8%), which was similar to a study conducted by Pankaj DM., *et al* [15].

In majority (54.4%) of ADRs there was definite improvement on dechallenging the suspected drug(s) which is the best way to get control over an ADR. However, in 31.1% of cases, the outcome of dehallenge was not known as these patients were discharged against medical advice or got transferred to the other units for further management hence they lost to follow up. Rechallenge was done in very few cases (8.8%) and reoccurance of symptoms was observed in 4% of cases.

Withdrawal of the suspected drug(s) (67.7%) was played an important role in management of ADRs in the present study. This is the ideal method for managing an ADR especially if the patient can do without that drug (s) at that particular movement. In 14.4% cases clinical treatments were implemented using antihistamines, corticoids and antidotes were given to relieve symptoms. In 7.7% of cases there was no change in the suspected drug (s) due to the presence of mild ADR [16-18].

Conclusion

Among HCPs pharmacists as medication experts, are a vital part of the treatment team, especially when an ADR occurs. Treating an ADR consists mainly of supportive therapy with symptom management. The major barriers to reporting are not knowing how to report,

what information to report, and where this information should be reported. As such, education and training interventions would help improve reporting practices.

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