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A study on adverse drug reactions in a tertiary care hospital in Bangalore

Basavaraj Bhandare[1], Shabeer D[2,*], Satyanarayana V[3]

[1]Professor & HOD, [2]PG Student, [3]Professor, Dept. of Pharmacology, Rajarajeswari Medical College & Hospital, Bangalore

***Corresponding Author:**
Email: drshabeerd@gmail.com

Abstract

Objectives: The study was conducted to assess the frequency of incidence of ADRs in our hospital, its causality with the suspected drug, severity of the ADR, preventability of ADRs and its relation to the duration of stay.

Method: A prospective study was conducted in a tertiary care hospital in Bangalore for a period of 12 months. Standard procedure was followed in reporting the ADRs by all healthcare personnel. Naranjo and Hartwig scales were used to assess the causality and severity of ADRs reported. Further analysis was made to evaluate the preventability and effect of duration of hospitalization on occurrence of ADRs.

Results: A total of 160 ADRs were reported during the study period from various specialties. Males comprised of 102(63.75%) and females were 58(36.25%). The assessment by Naranjo scale showed that relationship of ADR and the suspected drug was definite in 12 cases, probable in 45 cases, possible in 88 cases and doubtful in 15 cases. Hartwig scale classified 84 cases to be mild, 44 to be of moderate in severity and 20 to be severe. Preventability assessment was made that showed that 44 cases of ADR were definitely preventable, 12 probably preventable and 104 ADRs not preventable. Length of stay in the hospital showed a positive correlation with the occurrence of ADRs.

Conclusion: Adverse drug reactions are a significant health issue in India due to noncompliance and advent of polypharmacy. But majority of the ADRs can be avoided by the knowledge and awareness among all health care professionals. Standardized training of health professionals and reporting of ADRs not only helps in the prevention of ADRs in the hospitals, but also reduces the number of admissions related to ADRs.

Keywords: Adverse drug reactions, Causality, Severity, Preventability.

Introduction

Any drug that is capable of producing a therapeutic effect is capable of producing an unwanted or an adverse effect in human beings.

According to WHO, an ADR is defined as "A response to a drug that is noxious and unintended and occurs at doses normally used in a man for prophylaxis, diagnosis or therapy of disease or for modification of physiological function".(1)

A recent study showed that more than 50% of the drugs approved for human use in the United States were associated with some type of adverse effect in general population which was not detected prior to approval.(2)

Pharmacovigilance was launched by WHO in the 1960s for monitoring the ADRs caused by drugs. The aims of which was to monitor the occurrence of ADRs and coordinate between countries on information which is useful in bringing the number of adverse drug reactions to the minimum.

It has been reported that during the year 1966 to 1996 in USA, a staggering percentage of 6.7% ADRs were caused by over the counter drugs with deaths amounting to 3.2%.(3) Although such figures are not available in India but it is reasonable to infer that the figures would be much higher in view of high levels of indiscriminate and unmoitores drug use which is widely prevalent in the country.

Most of the developed countries have set up an adverse drug reaction reporting system at national level. ADR monitoring and reporting activity in India although established has a lot of room for improvement. Lack of well-structured and effective ADR reporting and monitoring program is a major problem in India along with lack of drug safety in Indian population.

Therefore, there is a greater and urgent need to create and enhance awareness about detection, reporting, management, prevention and of ADR among healthcare providers.

ADR monitoring is crucial in that it gives valuable information that a clinical trial just can't provide. The reasons being trials are conducted in a controlled environment which is not comparable to the real life. It is done in highly selected and limited number of individuals in a finite time which might not be suitable for chronic and delayed ADRs.

Objectives

- Identify suspected ADR and establish their frequency of development.
- Establish a causal relationship with suspected drugs.
- Assess the severity, preventability of ADRs and its relationship with the duration of hospitalization.

Methodology

This was a prospective observational study conducted at a tertiary care hospital in Bangalore between November 2014 and October 2015 for a duration of 12 months. The study was a multidisciplinary voluntary reporting of suspected

adverse drug reactions. The approval by the institutional ethics committee was taken before starting the study.

Source of study: All new admissions diagnosed as ADR and inpatients of various clinical departments of the hospital.

Study criteria:

Inclusion criteria:

- All the patients with recognizable symptoms that can be ascribed to the group of ADRs which present at the admission or after the initiation of treatment for which he or she is admitted.

Exclusion criteria:

- Allergic reactions due to pollen dust and insects were excluded.
- Cases that developed ADR following poisoning or intoxication
- ADRs due to blood and blood products were excluded.

Demographic data: The demographic data, patient's history of presenting illness and relevant past history including the drug history, medical conditions and allergies were noted. Previous exposure to the suspected drug and any related risk factors that might play a role in the development of the ADR is enquired.

Reporting of ADRs: Adverse drug reaction reports were collected from all the healthcare professionals of different departments. Various modes of reporting were used including the use of ADR forms, telephonic reporting, referral of patients.

Once report of the suspected ADR was received, relevant data like the details about the present ADR (onset, duration and nature and severity of reaction) and suspected Drug (nature of drug, dosage, route, frequency, duration of treatment) are collected from patient's medical records and patient's treating physician. All the relevant data are fed into the ADR form. Further analysis was done to find out the causation using the Naranjo scale and severity using the Hartwig scale.

The ADRs are recorded in the specified proforma designed by the CDSCO for this purpose. Laboratory investigations are done in appropriate cases.

All reported ADRs are evaluated for the following parameters using appropriate scale.

1. Causality(Naranjo's algorithm)[4]
2. Severity (Hartwig et al scale)[5]

Causality assessment is done using the Naranjo's Scale. This scale evaluates the degree of association of an adverse effect with the suspected drug by a method that involves a set of questionnaire directed towards the suspected ADR, which are ascribed a certain score (ranging from -1 to +2). Total score for a particular ADR is calculated and the association is termed as highly probable, probable, possible or doubtful-depending on the score.

In hartwig's severity assessment scale, patients are classified under 7 levels, and categorized into mild, moderate and severe groups.

The preventability was determined using modified criteria adopted from Schumock and Thornton.[6] Seriousness of reaction were categorized according to FDA criteria,[7] while predictability was determined by classifying the ADRs.[8]

Criteria for preventability correspond directly to the questions published by Schumock and Thornton. An answer of "yes" to any question suggests that the ADR might have been preventable. In addition to this, effect of length of stay on the occurrence of an ADR and impact of hospitalized ADR and ADR related hospitalization with preventability was assessed. ADRs that were both preventable and nonpreventable were compared in the view of types of ADR and age group.

Management of an ADRs: Withdrawal of the suspected drug is the first step taken. Consideration should be given to the adjustment of dose in possible dose related reactions. Treatment for the reaction in the form of symptomatic treatment should be started in cases where specific treatment cannot be started. Patients were reviewed and follow up was carried out as necessary.

Statistical analysis: Statistical analysis is performed and the results are presented either as medians and inter-quartile ranges or percentage frequencies and 95% confidence intervals, as appropriate. A P value< 0.05 is regarded as being significant.

Results

A total of 160 patients were included in the study of which the age group of 45 to 60 years formed the majority, signifying that the frequency of ADR development id more frequent in elderly. The study population comprised almost 2/3rd males and 1/3rd females.

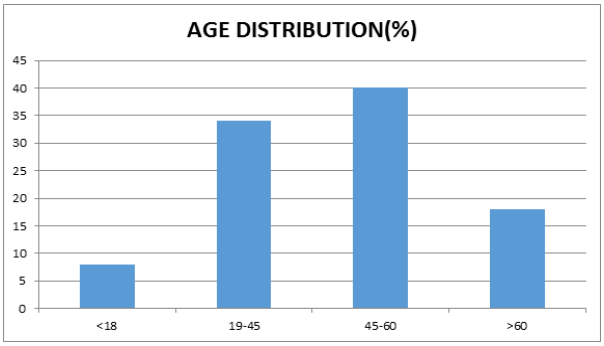

Fig. 1: Age distribution graph

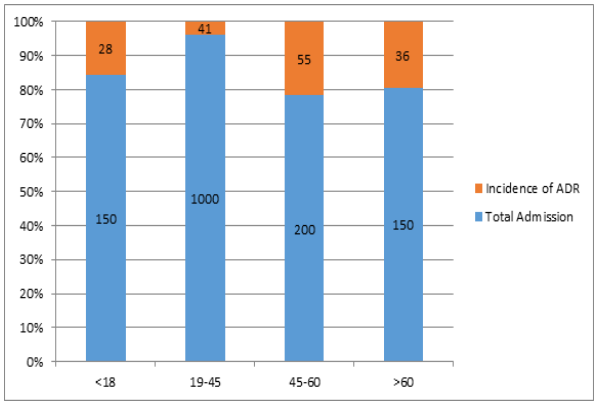

Fig. 2: Density of ADR based on age

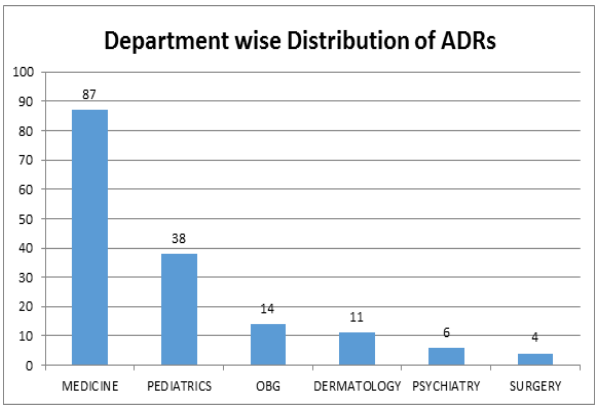

Fig. 3: Dept. wise distribution graph

Density of ADR among the different age group implies the number of ADR developed in that age group, which again showed an increased number in the age group 45 to 60 years. Antibiotics were most commonly associated with ADRs, followed by NSAIDs and antidiabetics(Table 1).

Table 1: Classification of drugs associated with ADRs (n=160)

S. No	Type or class of drug	No. of ADRs
1	Antibiotics	56
2	NSAIDs	36
3	Antidiabetics	14
4	Antileprotic and	03
5	Sulpha drugs	03
6	Cardiovascular Drugs	04
7	Antidiabetics	14
8	Corticosteroids	03
9	Anticonvulsant	01
9	Antimalarial drugs	02
10	Antiemetic drugs	04
11	Opiod analgesic	05
12	Lipid lowering agent	16
13	Diuretics	04
14	Anticoagulants	06
15	Antiparkinson drugs	01
16	Herbal drug	02

Systems most commonly affected was GIT in 38% of patients, followed by Skin in 24% of patients, central nervous system in 13% of patients and cardiovascular in 10% of patients.

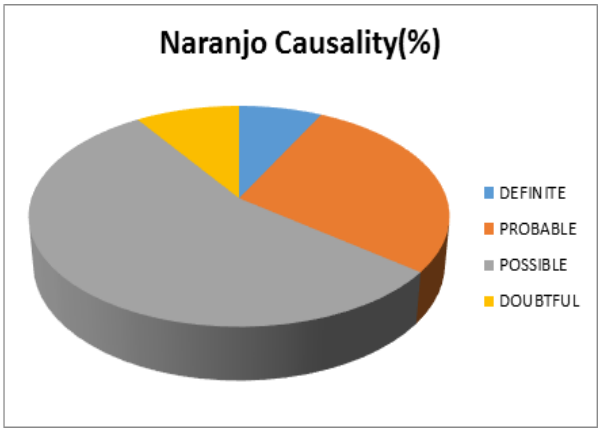

Fig. 4: Naranjo causality scale

Causality assessment was done by using Naranjo scale. Assessment by Naranjo scale showed that 55% of ADRs were possibly drug-related, whereas 28% were classified as probably and 7% definitely related to the drug.

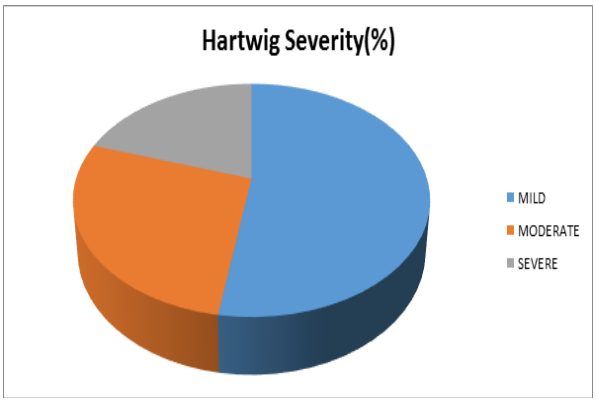

Fig. 5: Hartwig severity scale

Discussion

The incidence of the suspected ADRs among the total hospital admissions was found to be 1.06% and is similar to the findings of Rao e al.[9]

Age played an important role in the development of the ADRs as observed in the study, which showed

that the patients in age group 45 to 60 years experienced maximum ADRs 55 (34.37%), followed by 41 ADRs(25.62%) in the age group between 19 and 45, 36 (22.5%) in the above 60 years age group patients. According to Pirmohamed et al,[10] the geriatric population suffered from increased risk of adverse drug reactions which is consistent with the present study (Fig. 2).

The present findings of ADRs in the hospital patients were more documented in male population (Table 1) which is consistent with an earlier study conducted by Gupta et al.[11] Different ratio between the sexes during admission might be an intervening factor.

The drug class mostly associated with ADR was antibiotics (35%), followed by NSAIDs(22.5%) in our study. These findings were similar to a study by Murphy and Frigo.[12]

The study also revealed that the most common adverse drug reaction noted was nausea and vomiting, and antibiotics were the offending drug class in most of them. The results were also comparable with other studies like one done by Classen et al.[13]

Organ systems most commonly affected was GIT(38%) followed by Skin(24%), CNS(13%) and CVS(10%) which was consistent to a study by Suh et al.[14]

Department of medicine reported maximum number of ADRs (87 cases), followed by pediatrics department (38 cases). Other departments that reported ADRs were OBG, Dermatology, Psychiatry and Surgery.

Causality assessment was done by using Naranjo scale. Assessment by Naranjo scale showed that 55% of ADRs were possibly drug-related, whereas 28% were classified as probably and 7% definitely related to the drug. These results are in similar to a study by Davies et al[15] which assessed the impact of ADRs on inpatients.

Severity of the suspected ADRs assessed using Modified Hartwig and Siegel Scale, revealed that 14% of suspected ADRs were severe, 54% of ADRs were moderate and 32% of ADRs were mild in severity. These were comparable with the review conducted by Shuster[16] in reporting ADR in a 200-bedded community hospital which reported that 9% of the cases was categorized as severe, and 76% of the events were regarded as moderate.

Preventability of suspected ADRs were assessed by using Modified Schumock and Thornton scale, revealed that 27.5% of ADRs were definitely preventable while 7.5% of ADRs were probably preventable. This study showed an increased risk of ADRs in elderly patients, and that almost one-thirds of reactions were preventable. Knowledge of pharmacokinetics of a drug and how aging affects it is essential if we are to promote safe prescribing practices.[17]

Specific treatment was given to 55(91.67%) patients and symptomatic treatment was given to 4(6.67%) patients. There was no change in the treatment observed in one patient.

ADRs may prolong hospital stay, but it is also important to understand that the patients who stay longer in the hospital are at an increased risk of developing an ADR. Therefore an association between an ADR and duration of stay does not necessarily reflect cause and effect relationship.[18,19] There is a definite association between ADRs and increased length of stay across several studies.[10] As mentioned above in Vora et al study,[20] In 62.84% cases ADRs prolonged the hospitalization of inpatients. Another study by Moore et al[21] found that patients admitted with ADRs did not stay in hospital significantly longer than patients without ADRs, whereas patients with ADRs in hospital did, which correlates that length of stay in hospital is directly proportional to the number of ADRs to the patient. Our findings showed that on the stay of 1 week, average number of ADRs was 1.57 but in case of stay of more than 2 weeks average number of ADRs increased from 1.57 to 2.87/patient. Patients with hospital stay more than 2 weeks had an average number of 3.17 ADRs per patient.

Factors associated with increased incidence of ADR were increasing age (especially > 70 years) increasing number of medicines and particular classes of medicine[22] polypharmacy, age, gender, race, genetics, multiple/ intercurrent diseases, inadequate knowledge of patients and allergy.

Polypharmacy is a recognized risk factor for ADRs particularly in the elderly and is likely to increase since therapeutic guidelines indicate use of multiple therapies to manage and control the diseases.[23]

Similarly, Patients with multiple diseases are at an increased risk of developing ADR due to multiple drug use of their multiple diseases. Similarly, patients with impaired hepatic or renal status are also at a high risk of developing an ADR to drugs which are eliminated by these organs.[24]

This study has the limitation of being a short term study, which yielded 160 ADR's, other limitations were the fact that the 'time of onset' and 'Rechallange' was not possible or performed. Polypharmacy was not assessed in this study.

Table 2: Classification of type of reactions observed from reported ADRs (n=160)

Sl. No	Type of Reactions	No. of ADR
1	Skin rashes	11
2	Nausea and Vomiting	32
3	Headache	8
4	Hypoglycemia	4
5	Postural Hypotension	8
6	Constipation	8
7	Gastric irritation	18
8	Diarrhea	20
9	Drycough	4

10	Arthritis	3
11	Swelling of lips	9
12	Itching	23
13	Myalgia	12

Table 3: Severity of reported ADRs by Modified hartwig

Sl. No	severity of adr	% of adr	Sex Distribution Male(%) & Female(%)
1	mild	84	56(66.7) & 28(33.3)
2	moderate	44	28(63.6) & 16(36.4)
3	severe	32	18(56.25) & 14(43.75)
4	lethal	-	-

Table 4: Preventability analysis with ref. to types of ADR and gender

	Definitely preventable	Probably preventable	Not preventable
Total ADR	44	12	104
Children(0-18 yrs)	4	1	8
Adults(19-59 yrs)	26	6	56
Geriatrics (>60 yrs)	14	5	40

Table 5: Effect of length of stay on ADR

Length of hospital stay(week)	Number of patients	Number of ADRs	Average number of ADR/patient
1-7 days	35	55	1.57
8-14 days	8	23	2.87
15-24 days	6	19	3.17

Conclusion

In India, although there are ADR monitoring centers, a lot of effort is needed to collect and process the data from such a vast nation. Many of the approved drugs in the market are tested in a controlled environment for a specified period of time which may not represent the conditions general population is exposed to. Therefore it is important to monitor these drugs for their safety in daily usage.

This study suggests that there is a strong need for a better hospital based ADR monitoring strategy that can be uniformly followed among various specialties. The study also suggests that active involvement of health care professionals not only reduces the ADRs that is missed, but also improves the quality of reporting.

Polypharmacy is increasing day by day as the patient care becomes more and more symptom based than disease based, which in turn increases the incidences of ADRs. So consideration should be taken in cases which have the potential to receive reduced number of medications wherever possible, with an extra effort towards the elderly patients.

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