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Research Article

ASSESSMENT OF ADVERSE DRUG REACTIONS ON CARDIOVASCULAR DRUGS IN HOSPITALIZED PATIENTS OF A TERTIARY CARE HOSPITAL – A PROSPECTIVE ANALYSIS

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ABSTRACT

Objective: The present study was taken up to assess the adverse drug reactions (ADRs) based on the spontaneous reactions among the inpatients who were hospitalized for the treatment of cardiac ailments.

Methods: A prospective and observational study was done in the department of cardiology for a period of 6 months. Patients on cardiac drug therapy were evaluated to detect unwanted effects and were given treatment for the developed complications. The ADRs were identified, followed up, and documented.

Results: In the present study, 255 inpatients were assessed to pinpoint the negative effects and about 80 (n=80) sufferers were recognized with 28 types of ADRs. The highest percentage of ADRs was in adults of age group 60–70 years. Type A accounted for most of the reports which was based on severity. The number of ADRs in heart muscle disorders was found to be 44% (n=35) followed by coronary artery disease 40% (n=32), then heart valve disorders and patients underwent surgery were affiliated to 8% (n=6) each. The highest number of ADRs was reported in patients suffered from disorders pertained to heart muscle. Majority of ADRs were rated as possible, preventable, and moderate according to causality, preventability, and severity parameters, respectively. The data were tabulated, analyzed, and subjected to statistics using Graph Pad Prism 8.

Conclusion: It was concluded that proper management and monitoring of drug therapy are the key to prevent ADRs.

Keywords: Adverse drug reaction, Severity, Treatment, Inpatients, Preventability.

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INTRODUCTION

Pharmacovigilance is the study in connection with the recognition, assessment, interpretation, and prevention of negative effects of a drug [1]. The WHO defined an adverse drug reaction (ADRs) as any response to a drug which is harmful and undesired and occurs at normal doses used in human, but may not possess a causal relationship escorted by treatment [2]. Patients on exposure for longer periods of time are more vulnerable to develop ADRs. The basic principle of the unexpected reaction is any drug that is capable of providing a therapeutic effect could be a major cause of adverse reaction [3]. This is the major challenge faced by the health-care professionals. A significant proportion of the inpatients frequently experiences ADRs that may worsen and enhance their hospital stay. There are few causes of ADR such as overdosing of drug, improper dosage of medicament at a correct time, drug interactions, allergic reaction to the component, taking over the counter drugs, and taking an unnecessary drug. ADRs are mostly reported during the ward round by interviewing the patient and reviewing the patient's medical chart [3]. A few steps involved in the ADRs are identification of ADR at appropriate time, causality assessment using various methodologies and documentation of ADRs in patient's medical records and reporting the same to ADR regulating authorities [4].

Globally, cardiovascular diseases (CVDs) account for majority of deaths, with an approximated value of 17.9 million deaths annually. About 1/3rd of the deaths have been observed in people below 70 years of age. Factors such as age, gender, comorbid condition, number of drugs used, and length of hospital stay are responsible for the development of significant ADRs [5]. The present study was taken up to assess the ADRs of cardiovascular agents in a tertiary care hospital. In fact, every drug given for any type of treatment produces ADRs. Cardiovascular medications need to be monitored occasionally to scrutinize the medication errors and misuse of drugs by patients. This is because of huge number of patients who suffer from CVDs are prescribed with more number of drugs and the ADRs might not be preventable perfectly; certainly several factors matters. There exists a causal relationship between the ADRs and the drug administered [6]. The causality, severity, and preventability assessment scales was used to improvise the accuracy of results. Individual ADR assessment were undertaken using the Naranjo's causality assessment scale, Hartwig and Siegel ADR severity assessment scale, and Schumock and Thornton preventability scale. The present study highlighted a clarity in ADR assessment in hospitalized patients of cardio department.

METHODS

Study area, period, and design

The study was observational and prospective which was conducted in New Life Thumbay hospital, Hyderabad. It was carried out for a period of 6 months from December 2020 to May 2021.

Determination of sample size

A total of 80 patients (n=80) were included in the present study.

Study criteria

Inclusion criteria

Patients with ADR reports by health-care professionals and few by themselves identified with ADR were included in the study. Few of the patients detected with the knowledge they had about the drug reactions were also recognized and incorporated in the study. Few more

were identified with their interviews taken. All the patients were of age group between 18 and 80 years.

Exclusion criteria

Patients who were drug abusers and overdose of drug were excluded from the study. Pediatric age group with or without cardiac abnormalities, with age below 18 years and also other departments were excluded from the study.

Study procedure

In the cardiac department, the maximum number of incidences who underwent the treatment with cardiovascular drugs for different CVDs was recorded.

Collection of data

ADR form was designed with the suitable data of patients which included: Age, sex, body weight, height, ward, IP number, date of administration, diagnosis, patients allergy status to drugs and food, laboratory data, medication history, description of reaction, and on set of action. Prescribing details such as: Generic name, strength, manufacturer, batch number, dose, route of administration, frequency, drug therapy, risk factors, serious interactions, drug-drug interaction, management, outcome of management, details of reporter, and details of clinician.

The data were collected from patient's case sheets, medical records, ADRs documentation, causality, severity, and preventability scales.

Ethics

Ethical committee approval was obtained from MRM College of Pharmacy, Chintapallyguda, Ibrahimpatnam, Ranga Reddy District.

Analysis of data

The data collected were double-checked, structured, and entered in excel. The data were expressed in the form of frequency and %, also analyzed and presented using tables and figures. Chi-squared test was used to determine the significance of the values. $p \leq 0.001$ was considered as statistically significant.

Table 1: Incidence of adverse drug reactions among different age groups with gender

Age group (years)	No of ADRs (n=80) (%)	Sex distribution n (%)	
		Male	Female
10–20	1 (1)	1 (1)	0 (0)
20–30	1 (1)	0 (0)	1 (1)
30–40	1 (1)	1 (1)	0 (0)
40–50	19 (24)	8 (10)	11 (14)
50–60	22 (28)	13 (16)	9 (12)
60–70	29 (36)	22 (27)	7 (9)
70–80	5 (6)	3 (4)	2 (2)
80–90	2 (3)	1 (2)	1 (1)
	Total=80	49 (61)	31 (39)

Table 2: Distribution of ADRs based on heart diseases

Heart diseases	Number of ADRs	% of ADRs
Congenital heart disease	0	0
Heart valve disorders	6	8
Rhythm disorders	1	1
Heart muscle disorders	35	44
Coronary artery disease	32	40
Undergone surgery	6	8
Total	80	100
[b]p=0.001; Chi square – 94.136; df=5; α < 0.05	Mean – 13.33 SD–14.46	

All data were expressed in Mean±SD, [b]p<0.001 considered as significant

RESULTS

In the 6 months' period, out of 255 patients evaluated, 80 patients had developed ADRs, among which males were 49 and females were 31. Patients with age group between 60 and 70 y showed more number of ADRs 36% than any other groups followed by age group between 50 and 60 y which was 28%.

In the distribution of ADRs based on copious heart diseases, the incidence of ADRs varied. Based on different illnesses related to heart, the prevalence of diseases/disorders was categorized. The number of ADRs in heart muscle disorders was found to be 44% (n=35) followed by coronary artery disease 40% (n=32), then heart valve disorders and patients underwent surgery were affiliated to 8% (n=6) each. The highest number of ADRs was reported in patients suffered from disorders pertained to heart muscle.

Table 3 illustrated the length of hospitalization in people who developed ADRs, this showed that the hospital stay might be the one of the reason for increase in ADR occurrence. The patients who stayed for 8–10 days' period developed ADRs with 42% (n=33) followed by 26.25% (n=21) in those patients whose hospital stay was about 10–12 days from the date of admission.

Table 4 showed the types of ADRs according to Wills and Brown classification. The study emphasized that most prevalent ADRs were Type A 36% (n=29), followed by Type C and Type U 16% (n=13), Type B 14% (n=11), followed by Type D and E.

In the distribution of ADRs based on suspected drug during therapy, (Table 5) depicted that out of the different cardiovascular drugs used, patients with nitroglycerin usage were of 13% followed by diltiazem and metoprolol each (10%), and furosemide which was 8%.

Fig. 1 represented that a total number of 28 different ADRs reported with their frequency of occurrence and %. The episodes of headache 16% (n=13) were the most common adverse drug reaction followed by constipation the other most common ADR.

All the ADRs reported were assessed for their causality using Naranjo assessment scale and the results are tabulated in Table 6 [7].

Table 3: Distribution of ADRs based on length of hospitalization

Number of days stayed in hospital	Number of ADRs	% of ADRs
(0–2)	0	0
(2–4)	3	4
(4–8)	19	24
(8–10)	33	42
(10–12)	21	26.25
(12–14)	2	2.50
(14–16)	1	1.25
Total	80	100

Table 4: Distribution of ADRs based on Wills and Brown classification in hospital in-patients

Type of ADR	Number of ADRs	% of ADRs
Type A	29	36
Type B	11	14
Type C	13	16
Type D	6	6
Type E	7	9
Type F	1	3
Type U	13	16
Total	80	100
[b]p=0.001; Chi-square – 41.33; df=6; α<0.05	Mean – 11.42 SD – 8.20	

All data were expressed in Mean±SD, [b]p<0.001 considered as significant

Table 5: Distribution of ADRs based on suspected drug

Individual drugs	No of ADRs	% of ADRs
Carvedilol	1	1.25
Metaprolol	10	12.5
Propranolol	4	5
Atenolol	1	1.25
Atorvastatin	7	9
Simvastatin	1	1.25
Aspirin	7	9
Clopidogrel	1	1.25
Heparin	1	1
Spironolactone	1	1.25
Furosemide	8	10
Nifedepine	4	5
Verapamil	1	1.25
Nitroglycerin	13	16.25
Diltiazem	10	12.5
Enalapril	8	10
Telmisartan	1	1.25
Adrenaline	1	1
Total	80	100
[b]p=0.001; Chi square – 63.133; df=17; α<0.05	Mean – 3.94 SD – 14.46	

All data were expressed in Mean±SD, [b]p<0.001 considered as significant

Table 6: Causality, severity, and preventability assessment of ADRs based on their respective assessment scales in hospital in-patients

	Frequency (number of ADRs)	% of ADRs
Causality assessment (types)		
Definite	10	13
Probable	28	34
Possible	32	40
Unlikely	10	13
Total	80	100
Severity assessment (types)		
Mild	28	35
Moderate	39	49
Severe	13	16
Total	80	100
Preventability assessment (types)		
Definitely preventable	47	58
Probably preventable	29	36
Not preventable	4	6
Total	80	100

According to the scale, 40% (n=32) of the reported ADRs fallen under the category of possible ADRs which was the highest and commonest type of ADR documented in the present study, followed by 34% was probable, with 13% definite and unlikely. Furthermore, the ADRs reported were assessed for their severity using Hartwig and Siegel assessment scale and the result was tabulated [8]. According to the scale, 49% (n=39) of all the reported ADRs were moderate. The severe ADRs were of 16% (n=13) with 35% (n=28) that were fallen into the category of mild ADRs. The results emphasized that reported ADRs were evaluated by using Schumock and Thornton preventability scale. A maximum number of ADRs reported were found to be definitely preventable 58% (n=47) of total reported ADRs, followed by probably preventable 36% (n=29) and only 4% were found to be not preventable.

The results in Fig. 2 elaborated the management of the ADRs observed during the study. It instantiated that 58.75% (n=47) of the patients were recovered, 36.25% (n=29) of patients were still under recovery followed by 5% (n=4) of patients were considered as unknown.

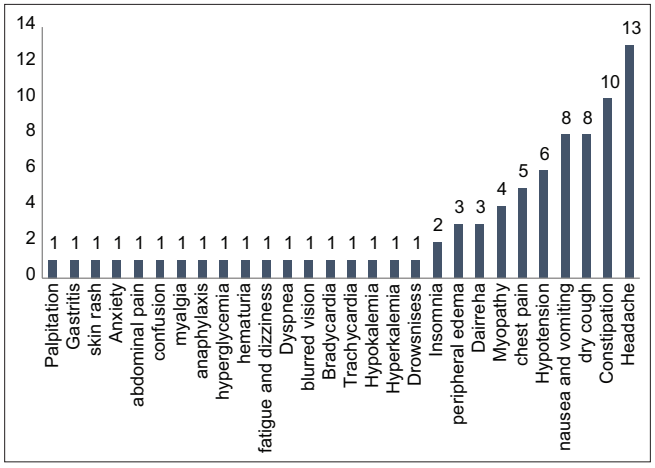

Fig. 1: Most commonly noticed ADRs with frequency of distribution

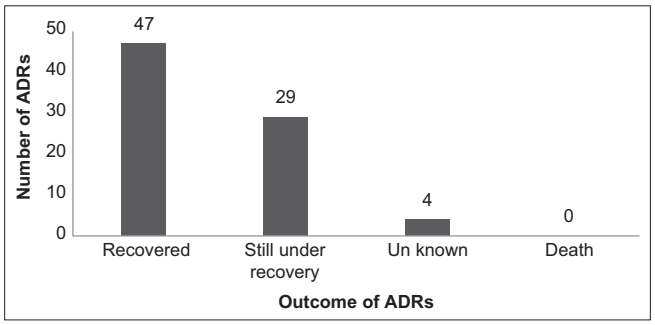

Fig. 2: Outcome on Management of ADRs in hospital in-patients

DISCUSSION

Pharmacovigilance in India is in budding state, though India stands in fourth place in production of pharmaceuticals in the world. This may be due to deficiency in training and education with regard to the monitoring of ADRs and reporting the same to the relevant authorities [9]. However, the importance of pharmacovigilance has gained gradually as Medical Council of India has proposed to set up pharmacovigilance center in every single teaching hospital. The incidence of ADRs which were reported in the present study was average. Indeed, there is every chance for variability in the ADRs with respect to the country and also to the various prescribing patters chosen [10].

In this study, 80 patients who were hospitalized and developed ADRs were evaluated, 36% of patients who were of age 60–70 year showed ADRs out of which most of them were males. ADR incidence was more in males than females. Among all the CVDs, heart muscle disorders, and coronary heart diseases accounted for more percentage (44 and 40%) than other heart related diseases. In the present study, on average inpatients who stayed for longer period of time in hospital were observed to get experienced with ADRs. There are several possible reasons for such prolongation of significant hospital stay such as the severity of the disease condition, infections, complications, and adverse reactions related to drugs [11]. In the elderly patients, age is considered as important risk factor in developing ADRs, due to the alterations in the pharmacodynamic and pharmacokinetic mechanisms, ultimately causing imbalance in the homeostasis. The consumption of medicines steadily increases with age, and this is responsible for developing ADRs in elderly.

In the present study, Wills and Brown classification was followed in categorization of different types of ADRs. Out of all types of ADRs, Type A was found to be in majority, occupied 36% in the patients. This

showed a clarity that at normal doses of drugs administered, there was an increase in the ADRs significantly ($p<0.001$). All the reactions of Type A were predictable, known expected but associated with morbidity and mortality. In this study, many cardiovascular drugs prescribed and used by inpatients were analyzed, with their observed ADRs [12]. Among all the drugs, nitroglycerin (Nitrates) was recorded as highest with 16.25% of the total ADRs evaluated. Metaprolol (β-blockers) and diltiazem (Calcium channel Blockers) were observed to produce 12.5% each of the total ADRs recorded. This might be due to the heavy usage of these drugs, in turn, depends on the diseased conditions, use of polypharmacy, and the individual body status [13]. In the present study, a number of 28 ADRs were reported by different category of drugs, of which headache was the most frequently identified adverse effect and the cardiovascular drug responsible was Nitroglycerin. Metaprolol and diltiazem produced constipation followed by enalapril and furosemide which were found to produce nausea, vomiting, and dry cough. One of the possible reason could be the prescribing pattern of that particular hospital, also the sample size included in the study [14].

The causality assessment of ADRs in the present study was evaluated. It was found that the maximum number of ADRs was possible (40%) followed by probable which was (34%). This is because of difference in the health-care system and varies from place to place [15].

The severity assessment of ADRs was done, in which an elevated occurrence of reactions was of moderate (49%) in the present study. It depends on the patients with several factors such as polypharmacy, drug-drug interactions, comorbid conditions, and length of hospital stay. In the preventability assessment of ADRs, the definitely preventable reactions were of 58% as comparable with the other studies [16]. This might be possible due to some alterations in the prescribing patterns, educating patients regarding the expected ADRs and alerting them to monitor and record if any. Patients who were acknowledged with ADRs were treated and evaluated. It was noticeable that 58.75% (n=47) of patients were treated properly on time and were subjected to recovery. In addition, it is the responsibility of every health-care professional to pursue for the benefit and comfort of patient [17].

An importance must be needed to monitor the patients experiencing with ADRs who consume cardiovascular drugs, particularly the elderly patients [18]. The drugs prescribed can be reduced to combat the frequency of occurrence of ADRs. With the aim of preventing the ADRs, usually patients experience ADRs in the beginning of their treatment, and a meticulous surveillance is mandatory to maneuver the ADRs. In the present study, nitroglycerin was shown to produce majority of ADRs, considered as the most commonly prescribed drug; hence, a close observance is entailed to conquer the ADRs.

The present study elaborated the observations made in inpatients of cardiovascular department only, with less sample size. However, this study strengthens the Indian data, more such studies are endorsed in a large population to ascertain the severity and type of ADRs related to cardiovascular drugs [19].

CONCLUSION

The present study concludes that the most widely prescribed drugs among the patients with CVDs were nitrates (Nitroglycerin). The prescribing patterns adopted play a key role in tackling the ADRs. The present study manifested with the preponderance of ADRs as "possible," because of use of concomitant medications. Principally, the ADRs were moderate and were definitely preventable. Therefore, this study illuminates to refine every physician about the essential use of multiple drugs rationally and sensibly along with the safety contemplations in their clinical practice.

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AUTHORS' CONTRIBUTIONS

Author Aishwarya D designed the study and guided. Sailaja Rao performed the statistical analysis of the data, drafted, and finalized the manuscript. QA Khanam and S Sultana managed the analysis of the study. U Fatima and M Azharuddin collected the data and managed the literature searches. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interests.

AUTHORS FUNDING

Nil.

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