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Adverse Drug Reactions of Cardiovascular Drugs In Intensive Cardiac Care Unit In A Tertiary Care Hospital: A Prospective Study

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Cardiovascular diseases are prevalent in developing countries like India. Patients with cardiovascular diseases are prescribed multiple drugs, hence polypharmacy may attribute to higher incidence of adverse drug reactions in these patients. To monitor and to analyze the pattern of occurrence of adverse drug reactions reported with cardiovascular drugs in intensive cardiac care unit of a tertiary care hospital, Chennai. This was a prospective surveillance study carried out for a period of 6 months. Analysis of various adverse drug reactions reported were done using various assessment scales. Descriptive statistics was used and values were expressed in numbers and percentage. During the study period, 282 adverse reactions were reported from 389 patients that includes 232 males and 157 females. The average age of the patients included in this study was 58.1± 16.8 years . The most common ADRs observed were electrolyte imbalance (14.89%), headache (13.12%) and gastritis (12.41%). Assessment using WHO Causality assessment scale revealed 60.28% were possible, 18.43% probable, 12.76% certain and 8.51% unlikely. According to Schumock and Thornton scale 65.9% of ADRs were preventable and 34% non preventable. Analysis with Hartwig and Seigel's scale 62.05% of ADRs were moderate in severity, 27.95% mild and 10.99% severe. Drugs attributing to highest ADRs were Digoxin and Furosemide. The common ADRs due to cardiovascular drugs can be reduced by improving the prescription pattern. Intense monitoring and reporting of ADRs could help in minimizing the preventable ADRs, among the health care professionals.

Keyword: Adverse drug reaction, Cardiovascular drugs, Causality, Preventability, Severity

Death due to cardiovascular diseases (CVDs) were estimated to be 17.3 million per year globally, and was expected to increase to 23.6 million approximately by 2030[1] . Prevalence and mortality of cardiovascular diseases seems to be declining in developed nations, but in developing country like India the above does not hold true. There is an alarming incidence in the prevalence of cardiovascular diseases and cardiovascular mortality in India[2] . Over 30% of deaths are attributed to cardiovascular diseases every year[3].

Currently, there are plenty of pharmacological measures available for preventing and treating cardiovascular diseases. Pharmacotherapy of cardiovascular diseases include Inotropic agents (Digoxin), Diuretics (Furosemide), fibrinolytic agents (Streptokinase), â blockers (Metoprolol, Carvedilol), Ca channel blockers (Verapamil), antiplatelet drugs (Aspirin) and anticoagulants (Heparin)[4].

The major contributors of morbidity, mortality and hospitalization, even death of patients are due to adverse drug reactions (ADR)[5]. In Indian population the incidence of ADRs ranges between 1.7 -25.1% with 8% of them resulting in hospitalization, but their reporting seems to be poor and inadequate[6].

Since there is increase in the prevalence of cardiovascular diseases, the number of cardiovascular drugs prescribed is also escalating. Added to this, the patients with cardiovascular diseases are prescribed multiple drugs compared to other diseases. Hence, polypharmacy accentuates the number of ADRs. There were compelling evidences suggesting that ADRs due to cardiovascular drugs are the most common cause of hospitalization of patients[7]. Considering, the limitations on drug safety evaluation in pre-marketing trials and post marketing surveillance and increased usage of cardiovascular drugs made the need for the present study. Hence this study was conducted to monitor and to analyze the pattern of occurrence of adverse drug reactions reported with cardiovascular drugs in intensive cardiac care unit of a tertiary care hospital, Chennai.

MATERIALS AND METHODS

This was a prospective observational study carried out at the intensive cardiac care unit, medicine department, Sree Balaji Medical College and Hospital, Chennai. Institutional Research Committee and Human Ethics Committee clearance were obtained. This study was carried out for a period of 6 months from January to June 2017. Patients who were admitted and treated in ICCU with cardiovascular drugs were included as active participants of this study. Informed consent was obtained from all patients who participated in this study.

Inclusion criteria

1) Patients admitted with or without previous history of Cardiac diseases to Intensive Cardiac Care Unit

2) Admitted for Pre and Post Cardiac Interventions care

3) Age group between 16 years to 80 years

Exclusion criteria

1) Patients with Pre and Post Surgical (CABG) Interventions

2) Pediatric age group with or without cardiac anomalies

A case report form (CRF) was prepared to document details regarding patient's personal data, presenting complaint, past history, drug history, investigations, treatment plan and modification of treatment due to any ADR. Adverse drug reactions reported were also recorded in CDSCO ADR reporting form.

Assessment of all ADRs collected using CRF were done by WHO causality assessment scale and Naranjo algorithm for causality , Schumock and Thorton scale for preventability and Hartwig and Seigel's scale for severity.[8,9,10,11].

Statistical analysis: Descriptive statistics was used and values were expressed in numbers and percentage.

RESULTS

Out of 523 patients who were admitted in ICCU during that 6 month period, 389 patients were considered for study after excluding 134 on the basis of physician's advice, poor medical status. Among the 389 patients, 207 patients had adverse

Table 1. Primary Admission Diagnosis Data

Diagnosis	n (%)
Ischemic Heart Disease	237 (60.92%)
Congestive Cardiac Failure	51 (13.11%)
Valvular Pathology	26 (6.68%)
Arrthymias	22 (5.65%)
Cardiomyopathy	7 (1.79%)
Pericardial diseases	6 (1.54%)
Post Angiography	18 (4.62%)
Others	22 (5.65%)

Table 1 * represents the initial diagnosis for admission in ICU and "n" represents the number of patients admitted with that particular diagnosis and expressed in % within brackets.

events. 282 adverse reactions were reported from 207 patients (few of them had more than one adverse reaction). were included in the study, the average age of the patients was 58.1 ± 16.8 years and their average duration of stay was 6.16 ± 3.8 days in CCU.

Ischaemic heart disease was the most common diagnosis for admission in ICCU followed by congestive heart failure, valvular pathology, arrthymias, cardiomyopathy, pericardial diseases, post angiography [Table 1].

The most common ADRs observed were electrolyte imbalance 14.89%, headache 13.12% and gastritis 12.41% [Table 2]. Assessment using WHO Causality assessment scale revealed 60.28% were possible, 18.43% probable, 12.76% certain and 8.51% was unlikely and causality assessment using naranjo's algorithm was 52.48% possible, 21.98% probable, 14.53% definite and 10.99% doubtful. According to Schumock and Thornton scale 65.9% of ADRs were preventable and 34% non preventable. Analysis with Hartwig and Seigel's scale 62.05% of ADRs were moderate in severity, 27.95% mild and 10.99% severe. Drugs attributing to highest ADRs were Digoxin and Furosemide [Table 2].

DISCUSSION

The major public health concern contributing to increased health burden are Adverse Drug Reactions. All effective medicines have unwanted effects; it has been said that all medicines have two effects: the one you intend and one you don't want. The consequence is that there must always be a continuing assessment of the balance of the risks and benefits of all medicines. In USA, adverse drug reactions were claimed as the 4th leading cause of death[12]. In recent years, documentation and reporting of ADRs have gained strength all over the world. The present study was done to evaluate the pattern of ADRs among patients who received cardiovascular drugs.

The most frequently reported ADR's in the present study were electrolyte imbalance, headache, gastritis and the cardiovascular drugs implicated in causing the above events were nitrates, digoxin, metoprolol, aspirin. The observation of this study was in contrast with the previous indian studies conducted to evaluate the ADRs by cardiovascular drugs[13,14,15]. In the present study there was 282 adverse reactions reported from 207 patients and also had CNS and GI system as the most frequent systems affected by ADR. These findings were similar to the study conducted by Singhal *et al* which also concluded that CNS and GI systems are the most frequently affected ones[16].

Previous studies done by Palaniappan *et al* and Wankhede *et al* was having cough as the most common ADR and respiratory system as the most common system involved[17, 18]. But in the present study the percentage of occurrence of cough was

Table 2. Types of ADR'S

ADR's	No (%)	Suspected drug /s
Electrolyte imbalance	42 (14.89%)	Digoxin, Frusemide
Headache	37 (13.12%)	Nitrates, Metoprolol
Epigastric pain/discomfort	35 (12.41%)	Digoxin, Aspirin
Nausea/vomiting	28 (9.92%)	Digoxin, Amiodarone,Streptokinase, Metoprolol
Dyspnoea	22 (7.87%)	Nifedipine, Metoprolol,Carvedilol, Streptokinase
Weakness	21 (7.44%)	Amiodarone, Digoxin, Carvedilol,
Palpitation	21 (7.44%)	Digoxin, Carvedilol
AV Block	18 (6.38%)	Digoxin
Hematoemesis	16 (5.67%)	Streptokinase, Heparin, Aspirin
Cough	16 (5.67%)	Enalapril, Captopril
Hematuria	10 (3.54%)	Streptokinase, Heparin
Atrial fibrillation	10 (3.54%)	Digoxin
Ventricular tachycardia	4 (1.41%)	Verapamil, Streptokinase
Ventricular fibrillation	2 (0.70%)	Verapamil, Frusemide, Streptokinase

Table 2 ** represents the number of adverse drug reactions attributed to the drugs. The number of ADRs were expressed in percentage.

only 5.67%. The reason could be the prescribing pattern of our hospital, where drugs like enalapril and captopril were not so commonly prescribed [Table 2]. Also the incidence of ADRs may vary due to the individual genetic differences and also from one place to another.

A study by Teweleit *et al*., found that arrhythmias (27.1%), syncope and variations in blood pressure were the most common ADRs. The drugs related to these ADR were angiotensin converting enzyme inhibitors and digitalis[19]. In contrast, the present study had the percentage of atrial fibrillation 3.54%, ventricular tachycardia 1.41% and ventricular fibrillation 0.70%. The contributing drugs being digoxin, verapamil and streptokinase [Table 2]. On comparing both the studies incidence of arrhythmias has reduced to a greater extent in the present study and apart from digitalis there are few more drugs like streptokinase and verapamil which might contribute this ADR.

On causality assessment, majority of ADRs were possible 60.28% in nature followed by probable 18.43%. These results are in compliance with the findings suggested by Karimzadeh *et al* -62.86%, Khurshid *et al* -57% and Wadhwa *et al* -73% which showed majority of reactions to be possible in nature[20,21,22].

Severity assessment of ADRs showed higher incidence of moderate reactions 62.05% in the present study. Similar findings were also reported by Davis *et al*, where 76.9% of ADRs were moderate in severity[23]. In contrast, studies conducted by Haile *et al* - 47.7% and Khurshid *et al* - 66.6% possessed reactions of mild severity[24, 21]. The discrepancies in the results could be attributed to the intensive approach for the high risk group patients and different healthcare settings.

Preventability assessment of ADRs showed 65.9% reactions were preventable as an earlier study by chan *et al* was 76.7%.[25]

The increase in the incidence of ADRs was due to increased consumption of medicines in elderly patients[26]. Geriatric patients taking multiple medicines and those who have reduced capacity to eliminate drugs are more prone for ADRs[27]. Polypharmacy was the major factor for more number of ADRs in this age group. However, the present study showed a significant reduction in the incidence of major life threatening ADRs like arrhythmias and almost 65.9% of ADRs reported were preventable.

CONCLUSION

Adverse drug reactions to cardiovascular drugs are matter of importance as they are used as the first line of treatment to cardiac diseases. Effective reporting might bring down the causalities. The most common drugs which cause ADRs can be meticulously used. Modification and redesigning of protocols from time to time based on the data's recorded will bring about the best for saving lives, improving quality and reduction in individual cost towards health.

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