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Original Research Article

An assessment of pattern of adverse drug reactions of cardiovascular drugs in a tertiary care institute

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ABSTRACT

Background: Cardiovascular disease is very prevalent in India. So, use of cardiovascular drugs is also more. So, it is very important to keep watch on adverse drug reactions. Aim of this study was to assess the pattern of adverse drug reactions (ADRs) reported with cardiovascular drugs in a tertiary care institute.
Methods: The study was carried out in medicine department of a tertiary care hospital over a period of one year. Each ADR was analysed for demographic data, causality, relationship between frequency of ADRs and the number of drugs used etc. In statistical analysis Microsoft excel 2013, SPSS software was used.
Results: A total of 136 patients, 58 (43%) men and 78 (57%) women, using cardiovascular medications reported ADRs during the entire study period. Total 168 ADRs were reported out of which, Amlodipine (causing headache and edema feet) was the most common drug with 51 (30.3%) ADR's followed by Enalapril, Aspirin and Isosorbide Dinitrate with 37 (22%), 24 (14.2%), 23 (13.6%) ADRs respectively. Most common ADR was headache (due to amlodipine and Isosorbide di nitrate) affecting 38 (22.62%) cases followed by dry cough 37 (22.02%) cases, edema feet 36 (21.43%), gastritis 24 (14.29%) and 10 (5.95%) of nausea.
Conclusions: Monitoring ADRs in patients using cardiovascular drugs is a matter of importance since this class of medicines are mostly used as multidrug therapy and always prone for ADRs.

Keywords: Adverse drug reaction, Cardiovascular drugs, Pharmacovigilance

INTRODUCTION

Worldwide, the number of deaths from cardiovascular diseases (CVDs) was estimated at 17.3 million per year, and it is expected to increase to approximately 23.6 million patients by 2030.[1] While the prevalence and mortality due to CHD is declining in the developed nations the same cannot be held true for developing countries. There has been an alarming increase over the past two decades in the prevalence of CHD and cardiovascular mortality in India and other south Asian countries.[2] The incidence of cardiovascular diseases has been increasing in recent decade. It is the most common cause of death in the developed as well as developing countries. Over 30% of all deaths every year attributed to cardiovascular disease.[3] Currently, important interventions to prevent and to treat CVD are available, e.g. pharmacological treatment of elevated low density lipoprotein (LDL) cholesterol levels elevated blood pressure and inhibiting platelet function with statins, anti-hypertensive agents (thiazides, beta blockers, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, or angiotensin II receptor blockers (ARBs), etc. and antiplatelet agents e.g. Low dose aspirin, respectively.[4-9] In this scenario, the large number of cardiovascular agents are used in population worldwide. Considering the increased use of cardiovascular drugs and its limitations in pre-marketing

trials for drug safety evaluation, post marketing evaluation of adverse drug reactions (ADRs) induced by this class of medicinal products seems very necessary and it's the need of the time.

Cardiovascular medications have been cited as one of the most common class of drugs associated with medication errors and ADRs, which need to be monitored from time to time.[10] Adverse drug reactions are the major contributors of morbidity, mortality and hospitalization of the patients and even death.[11] Though the incidence of ADR's in Indian population ranges between 1.7-25.1% with 8% resulting in hospitalization, the reporting of the same is poor and inadequate.[12] Since the prevalence of CVD is on the rise, the number of patients prescribed with cardiovascular drugs is also escalating. In addition, as patients with CVD are prescribed multiple drugs compared to other diseases, there is an accentuation of ADRs due to polypharmacy.[13] This has been further confirmed in a study, which found incidence and prevalence of cardiovascular drugs related adverse drug reaction (ADR) is 2.4 times that of other medicines.[14] Studies also show that ADR due to cardiovascular drugs are the most common cause of hospitalization of patients with ADR of which 4% are fatal ADRs.[15] India rates below 1% in pharmacovigilance as against the world rate of 5%, this is due to ignorance of the subject and lack of training.[16] Hence this study was conducted to assess the pattern of adverse drug reactions (ADRs) reported with cardiovascular drugs in a tertiary care institute.

METHODS

This was a prospective, observational study of adverse drug reactions occurring due to cardiovascular medicines. The study was carried out in Medicine Department of a tertiary healthcare and teaching hospital which includes cardiology special OPD, medicine wards and medicine ICU. Data was collected for a period of one and half year from January 2015 to May 2016. Approval from institutional ethics committee was obtained before conducting study. Patients with cardiac diseases receiving cardiovascular drugs of both the sexes who developed adverse drug reactions (ADRs) were included in this study. Patients with ADRs that occurred during hospitalization and ADRs that led to hospitalization were also included and those with cardiac disease but receiving any other drugs other than cardiovascular drugs were excluded from this study. During this period, all the ADRs reported to the pharmacovigilance centre of our institute pertaining to various cardiovascular drugs available in the hospital and routinely prescribed for various cardiovascular diseases were included in this study. The ADR profile in the patient was assessed by spontaneous reporting and intensive monitoring methods. In spontaneous reporting method, doctors directly informed the cases with ADRs to the pharmacovigilance centre of the institute through telephonic conversation with the representative of the centre. Then the patients were interviewed for all details about the reaction and findings were recorded on CDSCO ADR reporting form.[17]

In intensive monitoring method, representatives from pharmacovigilance centre intensely searched for the suspected ADR cases by thoroughly observing and interviewing the patients with cardiac disorders, attending the cardiac OPD or admitted in medicine wards. All patients with suspected ADRs were enrolled in this study. Additional information, pertaining to the system affected, vitals and alterations of biochemical characters was collected from patient's case sheets, if present. After getting all the necessary information, the data was filled in the ADR reporting form and was entered in the excel sheet for further evaluations and results.

Each ADR was analysed for causality, severity and lastly for relationship between frequency of adverse drug reactions and the numbers of drugs used. Causality assessment was done according to Naranjo scale which used the doubtful, possible, probable, and definite classification system.[18] The severity of ADRs was analysed by using modified Hartwig Siegel's severity assessment scale as mild, moderate and severe.[19] Data collected was analysed using Microsoft excel 2013 and SPSS software. Values were expressed in percentage (%).

RESULTS

Total 136 were obtained in this study with 168 adverse drug reactions (ADRs). Most patients (41) were above 60 years of age followed by 51-60 years age group. (38). In terms of sex distribution, more females were having ADRs (78) as compare to males (58). Out of which, more females were belonging to above 60 years of age group (32) and more males were belonging to age group of 51-60 years (32) (Table 1).

Table 1: Age and sex wise distribution of patients with ADRs.

Age	21-30	31-40	41-50	51-60	>60	Total
Male	2	8	14	25	9	58
Female	1	13	19	13	32	78
Total patients	3	21	33	38	41	136

Amlodipine was the most common drug with 51 ADR's followed by enalapril, aspirin and isosorbide dinitrate with 37, 23, 24 ADR's respectively. Digoxin, atenolol, atorvastatin, frusemide, prazosin propranolol and rosuvastatin showed 10%, 8%, 8%, 3%, 1% and 1% ADR's respectively (Figure 1).

Most commonly affected system was Central nervous system (25.6%) followed by gastrointestinal system (23.21%), Respiratory system (22.02%), other system (21.43%), cardiovascular system (4.17%) and musculoskeletal system (3.57%) (Figure 2).

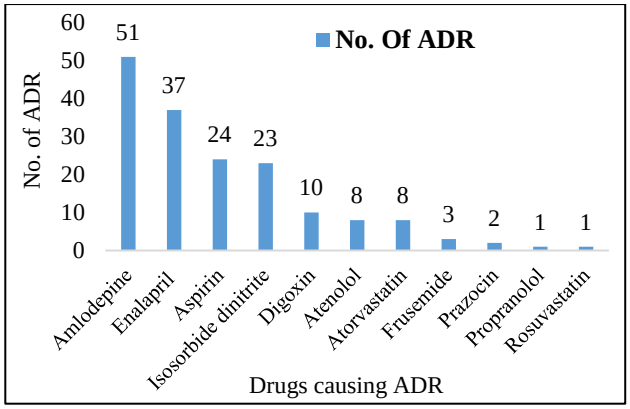

Figure 1. Suspected drugs causing ADRs in this study.

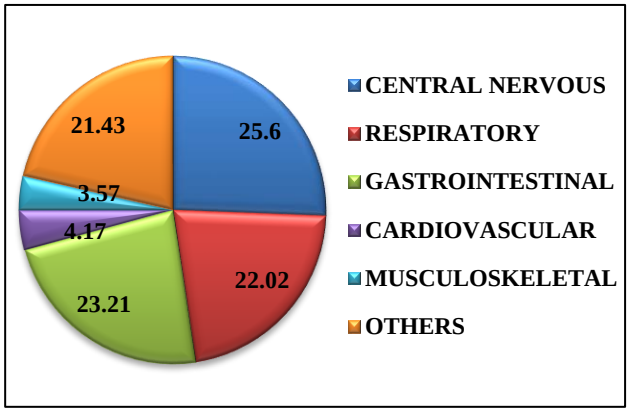

Figure 2: Systems affected by percentage of ADRs.

Causality assessment done by using Naranjo scale in which 96% (162) ADRs were found possible (Naranjo score 1-4) and only 4% were found probable (Naranjo score: 5-8). No ADR was in definite category (Naranjo score ≥9) (Figure 3).

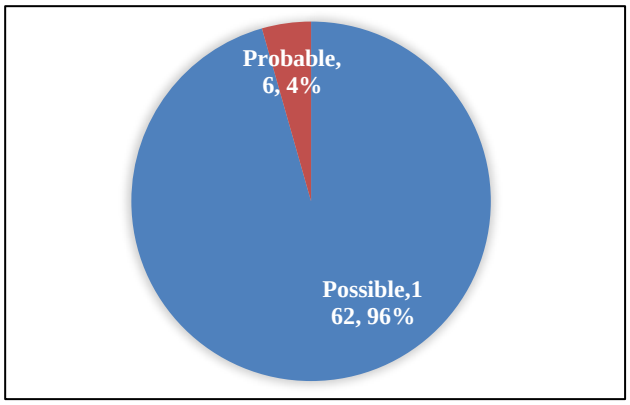

Figure 3: Causality assessment done by using Naranjo scale.

Distribution of cases was done by Modified HARTWIG scale, which categorized cases in Mild, Moderate and Severe. Present study showed 162 cases were of mild and 6 cases were of Moderate severity in nature. No case found to be of severe category (Figure 4).

In present study, ADR was 11.11% when patients were taking 2 drugs simultaneously. It was 28.3% when patients were taking 3 drugs simultaneously and it was 31.57% when patients were taking 4 drugs simultaneously (Figure 5).

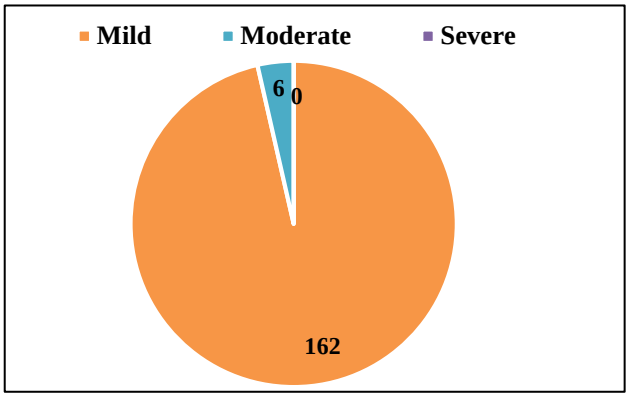

Figure 4: Severity assessment of ADR by modified Hartwig's scale.

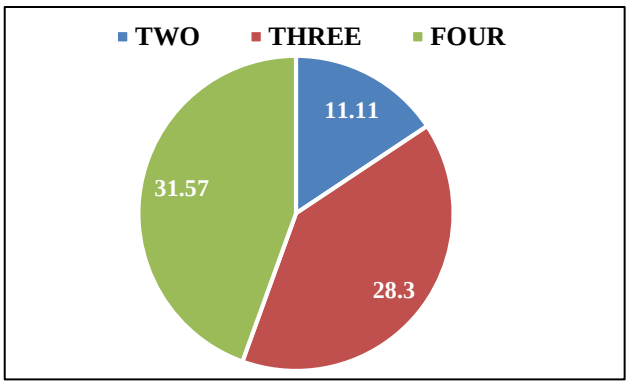

Figure 5: Relationship between frequencies of ADR obtained with number of drugs per patient.

DISCUSSION

The present study was done to evaluate the pattern of adverse drug reactions among the patient with cardiovascular disease taking cardiovascular drugs in a tertiary care institute. This study found that central nervous system and cardiovascular system were most commonly affected systems by ADRs. In the studies carried out by Gholami et al and Singhal et al, central nervous system and gastrointestinal system were the commonly affected systems due to ADR which corresponds with the results of this study.[15,20] A study, found that the most commonly affected system with ADR were central and peripheral nervous system disorders (23.5%) and gastro-intestinal system disorders (16.5%), whereas in this study peripheral system is not involved.[21]

The most frequently reported ADRs were headache and dry cough and the cardiovascular drugs responsible for causing them were found to be amlodipine, isosorbide dinitrate and enalapril. These results matches with the

previous Indian studies.[20,22] As per Singhal et al study, which included 148 patients with 231 ADRs, concluded the most commonly reported ADRs were headache (24.2%) and dry cough (13.9%) and the common drugs causing ADRs were calcium channel blockers (23.4%) and nitrates (16.5%).[20] In Sharminder et al study, nitrates was the common offender (17.8%).[13,20] A study by Mohebbi et al, concluded, streptokinase (59.3%) and amiodarone (38.7%) as the drugs more frequently implicated with occurrence of ADR. These differences in variation of commonly occurring ADRs and drugs related to the ADRs may be due to drug availability and prescribing pattern of hospital, which is different at different setup.[21]

A study done by Palaniappam M et al was having cough and gastritis as common ADRs and GI (20.7%) and Respiratory system (18.4%) as most common system involved due to ADRs.[23] Results show that dry cough is common in this study like present study but not gastritis. The reason could be the prescribing pattern of our hospital, where enalapril was commonly prescribed. Another reason could be small sample size in this study, as exclusively patient taking only cardiovascular drugs were included in this study and all the other patient which were having cardiovascular disease, but they were taking other medications like drugs for diabetes or any other illness along with cardiovascular drug were excluded. Also, the incidence of ADRs may vary from place to place and even within a country because of differences in prescribing patterns.[24]

In this study, it was also found that, all the patients (n=136) were taking two or more drugs i.e., 45 patients were taking two drugs, 53 patients were taking three drugs and 38 patients were taking four drugs. Out of 136 patients, single adverse drug reaction was reported in 104 patients. ADR was 11.11% when patients were taking 2 drugs simultaneously.[5] It was 28.3% when patients were taking 3 drugs simultaneously and it was 31.57% when patients were taking 4 drugs simultaneously.[12,15] From this finding, one can conclude that as the number of drug increases, there are more chances of developing more ADRs in the patient. Similar results were found in the study done by Singhal et al.[20]

The present study revealed that advanced age and female gender were the independent risk factors for development of ADRs, which also matches with the results of previous study.[25,26] Age is an important risk factor for ADRs; and incidence of ADRs increases steadily with age. Another reason for increased incidence of ADRs in elderly is increased consumption of medicines.[27] Elderly patients with multiple medical problems who are taking multiple drugs, those who have a history of ADRs, and those with a reduced capacity to eliminate drugs are at high risk for ADRs.[28] Therefore, polypharmacy due to multiple diseases in elderly patient, could be an important factor for more number of ADR in this age group, considering the results obtained in this study. Relationship of female gender with more number of ADRs can be explained by the different rate of drug metabolism seen in the females as compared to males, according to Schwartz.[29]

Monitoring adverse drug reactions in patients using cardiovascular drugs is a matter of importance since this class of medicine is usually used by elderly patients with critical conditions and underlying diseases. The frequency of ADRs occurrence can be reduced by decreasing the number of drugs prescribed. ADRs of Cardiovascular drugs mostly occur in first days of treatment, therefore monitoring patients in first days of using cardiovascular drugs could help in preventing ADRs. As amlodipine was the most common drug causing ADR and it is most commonly prescribed drug for hypertension, one must cautiously monitor the patients taking amlodipine and also other commonly prescribe drugs to prevent ADRs. As this study was having less sample size and carried out in single centre, more studies are recommended in various populations to determine the rate and nature of adverse events induced by different subclasses of cardiovascular drugs.

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