Assessment of Drug Related Problems in Patients with Cardiovascular Diseases in a Tertiary Care Teaching Hospital

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A R T I C L E   I N F O

A B S T R A C T

Backgrounds: Drug related problems can be defined as any event (or) circumstance involving the drug treatment, which interferes or potentially interferes with the patient in achieving an optimum outcome of medical care. The aim of the study was to identify drug therapy problems and to assess the pharmacist interventions in patients with cardiovascular diseases.

Methods: The inpatient case records including drug history and other relevant details of the admitted patients under the cardiology department were collected and reviewed by the clinical pharmacist for drug related problems. In case if any drug related problem was identified, was discussed with the concerned physician and suitable interventions was provided and documented.

Results: A total of 112 patient case sheets were reviewed during the study period, out of which 53 drug related problems were identified from 44 patients. The most common drug related problem was found to be drug Interactions (49.05%) followed by Adverse Drug Reaction (18.86%), and failure to receive drugs (9.43%). The most frequent suggestions provided by the intervening pharmacist were cessation of drug (24.52%), followed by Change in frequency of administration (22.64%), change in drug dose (20.75%). The majority of level of significance of drug related problems was seen to have moderate significance in grade. The acceptance rate of recommendations and change in drug therapy was found to be high (96.21%).

Conclusion: The current study highlights the importance of a pharmacist in a multidisciplinary team of routinely reviewing the drug therapy for identification and resolution of drug related problems which helps in achieving better therapeutic outcomes and improved patient care.

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Introduction

Cardiovascular disease is a major public health problem and one of the leading causes of premature death throughout the world, and contributes substantially to increased health care costs. The most common underlying pathology expected to cause cardiovascular diseases is atherosclerosis. It is potentially a serious condition and

one of the most common causes of cardiovascular diseases develops over many years and they are often fatal before any medical care can be given. The early identification and modification of risk factors has been shown to reduce mortality and morbidity in people with diagnosed or undiagnosed cardiovascular disease. People with established cardiovascular disease have to give special care as they are at very high risk of recurrent events (1, 2).

Cardiovascular disease is usually seen in middle-aged or elderly men and women and it is expected that atherosclerosis is the main under pathology leading to coronary artery disease, cerebral artery disease and

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peripheral artery disease. Though several forms of therapy exist to prevent the coronary, cerebral and peripheral vascular events, decisions about whether to initiate specific preventive action, and with the degree of intensity, should be guided by estimation of the risk of any such vascular event. Management of major cardiovascular risk factors can be done through changes in the sedentary lifestyle and prophylactic drug therapies (3, 4).

The presence of cardiovascular risk factors such as tobacco use, an unhealthy diet and physical inactivity (which together result in obesity), elevated blood pressure (hypertension), abnormal blood lipids (dyslipidaemia) and elevated blood glucose (diabetes) and continuous exposure to them influences the progression of atherosclerosis. This may result in unstable atherosclerotic plaques, narrowing of blood vessels and obstruction of blood flow to vital organs, such as the heart and the brain. The clinical manifestations of these diseases include angina, myocardial infarction, transient cerebral ischemic attacks and strokes (5).

Drug related problems may arise at all stages of the medication process from prescription to follow-up of treatment. Most of the problem usually occurs on administration, dispensing and during the patient's use of a medicinal product, but lack of proper follow-up and reassessment of medical treatment by the physician is also a major problem (6).

Increased number of medications, complexity of drug regimens and availability of new drug therapies potentially increase the risks of patient for iatrogenic adverse drug events in hospitals. This can lead to prolonged hospital stay and increased health care costs. So the injury or death that may occur as a result of drug related problems has to be evaluated so as to reduce the occurrence of similar events in future (7).

Drug-related problems occur more frequently in hospitalized patients where multiple changes are being made in patient's medication regimens and lack of continuity of care may be accompanied (8). The most common problems associated with drug use are many and includes inappropriate medication prescribing, discrepancies between prescribed and actual regimens, poor adherence, drug interactions, inappropriate use, patients monitoring and inadequate surveillance for adverse effects etc. Drug related problems lead to substantial morbidity, mortality as well as increased health care expenditure which in turn affects the patient's quality of life (9).

The goal of pharmaceutical care is to improve an individual patient's quality of life through the achievement of definite (predefined), medication-related therapeutic outcomes (10, 11).

The outcomes sought are
1. Cure of a patient's disease.

2. Elimination or reduction of a patient's symptomatology.
3. Arresting or slowing of a disease process.
4. Prevention of a disease or symptomatology (12).

This, in turn, involves three major functions: (1) Identifying potential and actual medication-related problems, (2) resolving actual medication-related problems, and (3) preventing potential medication-related problems. A medication-related problem is an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient. There are at least the following categories of medication-related problems (12).

Untreated indications
The patient has a medical problem that requires medication therapy (an indication for medication use) but is not receiving a medication for that indication.

Improper drug selection
The patient has a medication indication but is taking the wrong medication.

Sub therapeutic dosage
The patient has a medical problem that is being treated with too little of the correct medication.

Failure to receive medication
The patient has a medical problem that is the result of not receiving a medication (e.g., for pharmaceutical, psychological, sociological, or economic reasons).

Over dosage
The patient has a medical problem that is being treated with too much of the correct medication (toxicity).

Adverse drug reactions: The patient has a medical problem that is the result of an adverse drug reaction or adverse effect.

Drug interactions: The patient has a medical problem that is the result of a drug–drug, drug–food, or drug–laboratory test interaction.

Medication use without indication
The patient is taking a medication for no medically valid indication (13).

Many studies have been conducted in various countries as well as in India about the clinical pharmacist interventions (11-16). All these studies have shown that clinical pharmacist with the concept of pharmaceutical care concept empowers with greater responsibility and accountability in patient care and enlightens the need of clinical pharmacists in a multidisciplinary health care team for more identifying and prevention of drug related

problems. Thus, considering the results and conclusions of all the studies, the clinical pharmacist interventions in ward rounds should be considered as the most essential aspect for optimizing patient care.

Cardiovascular patients usually get exposed to multiple comorbid conditions and are prescribed with multiple drugs. So the chances of occurring drug related problems are more in such kind of patients. So in order to identify the drug related problems in such patients with cardiovascular diseases, the study has been carried out.

Methods

It was a prospective, observational, interventional study carried out for a period of 7 months in hospitalized cardiovascular patients admitted in the cardiology department of Justice "KS Hegde" charitable hospital, which is a 1000-bed hospital with various speciality departments located in Mangalore, Karnataka, India. The study proposal was approved by the hospital human ethics committee. All the patients with cardiovascular diseases admitted in the cardiology department of either sex and above 18 years old have been included in the study. The exclusion criteria were patients receiving treatment on an outpatient basis. All the cases were reviewed by the clinical pharmacist and those who met the study criteria were followed after getting the informed consent and the drug therapy details including the drug history, laboratory parameters and demographic details of those patients were recorded in the suitable designed data collection form as per the need of the study. The clinical pharmacist routinely monitored the patient's drug therapy for any drug related problems and interviewed with physicians as well as with patients when necessary. The identified drug therapy problems were discussed with the concerned physicians with interventions and have been documented as per the Hepler and Strand Classification. The classification includes drug use without indication, improper drug selection, sub therapeutic dose, adverse drug reaction, overdose, drug interactions, failure to receive drugs and untreated indication. The intervening pharmacist was a post graduate pharmacy practice student. All the interventions made by the intervening pharmacist were preceded by consultation with the academic clinical pharmacist. The intervening pharmacist assessed the clinical significance of each intervention. The acceptance level of physician for each intervention was also recorded as either accepted or nor accepted. Similarly whether or not any change in drug therapy was also noted.

At the end of the study, all the documented data were quantified and analysed by using mean ± standard deviation.

Results

A total of 112 cases were followed and reviewed in the cardiology department during the seven month study period. Of the cases reviewed, 53 drug related problems were identified from 44 patients. Out of 44 patients 32 (72.72%) were male and 12 (27.28%) were female. The majority of the drug related problems occurred in the age group of 41-60 years. The gender and age wise distribution of the study patients are summarized in Table 1.

Among the study population, 9.09% patients were diagnosed without any co-morbidity, 25.0% were diagnosed to have one co-morbidity, 31.81% patients were diagnosed with two co-morbidities, 20.45% were diagnosed with having three co-morbidities, greater than four co-morbidities were found in 13.63% patients which has been mentioned in the Table 2.

The most common drug related problem was found to be drug Interaction, which accounted for 49.05% (n=26) followed by adverse drug reaction 18.86 %(n= 10), Failure to Receive Drug 9.43% (n=5), Drug use without indication 5.66% (n=3) and Untreated Indication 3.77%. The types of drug related problems are summarized in Table 3.

The most frequent interventions provided by the intervening pharmacist was cessation of the drug 13 (24.52%) followed by change in frequency of administration 12 (22.64%), change in drug dose 11 (20.75%). Various suggestions provided by the intervening pharmacist are summarized in Table 4.

Of the total drug related problems, the significance level 'moderate' was found to be high 58.50% (n=31) followed by significance level 'minor' 41.50% (n=22). The significance level of drug related problems is shown in the Table 5.

Outcomes of the recommendation concerning drug related problems are suggestion accepted and therapy changed 29 (54.71%), suggestion accepted and therapy not changed 22 (41.50%) and neither suggestion accepted nor therapy changed 2 (9.43%). The result of clinical pharmacist recommendations is shown in Table 6.

Discussion

Among 112 patients followed during the study period, a total of 53 DRPs were identified in 44 patients. Out of 44 patients, 72.72% were found to be males and 27.28% were females. This might be due to increased medication use because of their multiple comorbid conditions and also possible of various risk factors like smoking, alcoholism and a sedentary life style etc. compared to the female population. This result was similar to the study carried out by the Ganachari et al., (16),which showed male predominance over females .Similar results has also been obtained in studies conducted by Alagiriswami et al., (17) and Sathish kumar et al., (18) which showed an increase in number of male population than females..

The incidence of DRPs was high (55.35%) in patients aged between 41-60 years. Among the number of drugs, patients receiving more than 6-10 drugs were found to

Table 1. Gender wise distribution of patient population in the study (n=112).

Characteristics		Number (%) (n=112)
Sex	Male	32 (72.72)
	Female	12 (27.28)
Age group	**Number**	**Percentage (%)**
21-40	12	27.27
41 - 60	23	52.27
61 - 80	9	20.45

Table 2. Number of co-morbidities.

No of Co-morbidities	Number	Percentage (%)
None	4	9.09
1	11	25.0
2	14	31.81
3	9	20.45
≥ 4	6	13.63

Table 3. Types of drug related problems (n= 53).

TYPES OF DRPs	Number (%) (n=53)
Untreated Indication	2 (3.77)
Improper Drug Selection	0 (0)
Sub Therapeutic Dosage	7 (13.20)
Failure to Receive Drugs	5 (9.43)
Over Dose	0 (0)
Adverse Drug Reaction	10 (18.86)
Drug Interaction	26 (49.05)
Drug use Without Indication	3 (5.66)

have more drug related problems (52.30%) (17). This observation was supported by a 2002 national survey indicated that 50% of the overall population took 5 or more medications and developed DRPs (8). In another study conducted by. Vinks et al., (19), it was found that DRPs may frequently occur in adults over 65 years of age using six or more drugs concomitantly. This also indicates that special attention should be done in such group of patients were regular review of drug therapy might help potentially to decrease the drug related problem.

Drug interactions were the most common drug related problems observed in our study (49.05%) followed by Adverse drug reaction (18.86%) and Failure to receive drugs (9.43%). This observation was in contrast with the study conducted by Celin et al., (11) in which potential drug interaction was found to be high (43.42%) followed

by adverse drug reactions (25.0%) and drug use without indication (11.84%). Roberts et al., (7) study also showed similar results in which potential drug interactions accounted for a substantial amount of potential drug toxicity (34.8%). In the present study the therapeutic agents most commonly involved in drug interactions were antiplatelet agents, antihypertensive and GI drugs. This is consistent with the published study conducted by Roberts et al., (7), in that the average numbers of drug interactions involving antiplatelet agents were higher than other drug groups. In another study done by Abraham et al., (10) and Jimmy et al., (20) found that most of the interaction was found with antiplatelet agents and GI drugs. The high number of medications used and the combination of various drug classes might have contributed to the high prevalence of significant potential drug interactions in

Table 4. Suggestions provided by the intervening pharmacist.

Type of Interventions	Number (%) (n=53)
Cessation of the drug	13 (24.52%)
Addition of drug	2 (3.77%)
Change in drug dose	11 (20.75%)
Change in duration of therapy	0
Change in frequency of administration	12 (22.64%)
Substitution of drug	2 (3.77%)
Change in cost of therapy	5 (9.43%)
Change in route of administration	0
Change in dosage form	0
Pharmaceutical aid	0
Others*	8 (15.09%)

Need of the laboratory investigation (n=8).

Table 5. Level of significance of drug related problems.

Significance level	number (n=53)
Minor	22 (41.50%)
Moderate	31 (58.50%)
Major	0

Minor: Problems requiring small adjustments and optimization to therapy, which are not expected to significantly alter hospital stay, resource utilization or clinical outcome.
Moderate: Problems requiring adjustments, which are expected to enhance effectiveness of drug therapy producing minor reductions in patient morbidity or treatment costs.
Major: Problems requiring intervention, expected to prevent or address very serious drug related problems, with a minimum estimated effect on reducing hospital stay by no less than 24 hrs.

Table 6. Results of clinical pharmacist recommendations: (n=53).

Suggestion accepted and therapy changed.	29 (54.71%)
Suggestion accepted but drug therapy not changed.	22 (41.50%)
Neither suggestion accepted nor drug therapy changed.	2 (3.77%)

this study patients. The most commonly occurring drug interaction among the cardiovascular drugs includes aspirin, clopidogrel, calcium channel blocker such as amlodipine, simvastatin and anticoagulants like warfarin. The potency of the interaction increases when these cardiovascular drugs are co-prescribed with proton pump inhibitors such as pantoprazole. As drug interactions can affect patient's clinical outcomes, quality of life and contribute to increased length of hospital stay and health care costs. The higher incidence of drug interactions in the study suggests that regular review of the patient case sheets including the drug therapy helps in identifying

and preventing drug related problems including the drug interactions.

In our study, almost one third of the adverse drug reactions implicates antidiabetic drugs which include insulin's and oral hypoglycaemic agents. Besides the undesirable clinical consequences for the patients, adverse drug reaction can cause a significant financial burden to the health care system. Hypoglycaemia due to insulin and oral hypoglycaemic agents in diabetic patients was the most common ADR observed in our study followed by nitrates causing headache and hypotension, dopamine causing tachycardia, metoprolol causing

bradycardia, and ramipril causing cough. This may be because most of the cardiovascular patients admitted in our study might also had diabetes mellitus a as comorbid condition where hypoglycaemia can develop during the blood sugar management. Because of the time constraints many of time physicians may not be able explain to the patients about the possible undesirable side effects of the drugs and their management. But by Involving a clinical pharmacist in a multidisciplinary team who are expert in the medicines helps in identification and management of such adverse drug reactions. His timely involvement might help in reducing the hospital stay and the health care costs. He can also counsel the patient what to do when such adverse drug reactions occurs when they are in home settings.

During the medication chart review it was found that 5.66% of drug related problem accounts for drug used without indication. These study findings are in contrast with the study carried out by Alagiriswami et al., (17) and Celin et al., (11) which shows that drug use without indication accounts for 18% & 15% of total the DRPs respectively. Few drugs often used without indication includes ranitidine, pantoprazole, paracetamol, antibiotics and anti-emetics. Many of times antibiotics were prescribed to patients with infection even when total count, urinalysis and chest x-ray was found to be normal. In such where there is no valid indication to start the treatment. In some other cases were anti emetic has been prescribed for vomiting, but it has been continued even after the vomiting has stopped.

In our study we have found that untreated indication was to be 3.77% of the total drug related problems. This includes where a drug has not been prescribed for which there is a valid indication. These untreated conditions include anaemia, cough, dyslipidaemia, hypokalemia etc. This was found to be similar to the observation study conducted by Celin et al., (11) where 7% of the untreated indication account for the total drug related problems.

Sub therapeutic dose was found to be 13.20% in our study. This was found to be less when compared to the studies carried out by Binu et al., (15), Abraham et al., (10) and Alagiriswami et al., (17). The pharmacist's suggestion was to change in drug dose.

There was no drug related problem attributed to overdose because all the drug therapy was prescribed as per the recommended dose by the concerned cardiologist.

Failure to receive drug therapy was accounted for 9.43% of the total drug related problems. In most of the cases, it was due to the financial aspect of the patients that led to non-procurement of the prescribed medicines.

Cessation of the drug 24.52% were the suggestions most frequently provided by the clinical pharmacist. This study findings were consistent with the observation made by Alagiriswami et al.,(17) an Indian study in which cessation of the drug was reported as the most

common suggestion made. Other suggestions made in our study included a change in frequency of administration, addition of drug, etc. Addition of the drug was suggested in case of untreated indications. Change in drug dose has been suggested in the case of sub therapeutic doses and adverse drug reactions. For example the adverse reactions such as hypoglycaemia caused by the insulin's and oral hypoglycaemic agents were corrected with the changes in the subsequent doses of insulin's and oral hypoglycaemic agents.

Of the total 53 DRP's, the level of significance 'moderate' was found to be high (58.50%) followed by the level of significance 'minor' (41.50%). These study findings were similar to the study done by Parthasarthi et al., (14) which reported that 49% of drug related problems as 'moderate' significance. The moderate significance level was the level of problems requiring adjustments, which are expected to enhance effectiveness of drug therapy producing a minor reduction in patient morbidity.

The acceptance rate of intervening pharmacist suggestions was found to be high (96.21%).Of the 96.21% of interventions accepted, 54.71% of interventions led to changes in drug therapy. The remaining (41.50%) recommendation was accepted but the therapy was not changed to perhaps be due to lack of proper information which needs to strengthen the suggestions provided or the suggestions provide were thought to be insignificant. In (3.77%) cases, the suggestions were neither suggested nor drug therapy changed. This finding is in contrast with the study of Ganachari et al., (16), Kuchukarslan et al., (21) and Mangasuli et al., (22) which showed a higher acceptance rate of clinical pharmacist interventions by the physicians. Another reason may be that prescribing decisions are often governed by the clinical experience of physicians. This indicates that a clinical pharmacist can contribute to better patient care if involved in the health care team. The overall findings from our study was that pharmacists could identify some drug related problems, prompt and proper intervention will helps in achieving better patient care that can lead to improve the quality of care and drug therapy.

Conclusion

Review of the patient's drug therapy by a clinical pharmacist can positively influence the patient outcomes and quality of care. The present study highlights the fact that clinical pharmacist can play a very important role in the healthcare management by rationalising and optimising the drug therapy to achieving better quality of life.

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