Assessment of Drug Related Problems in Patients with Cardiovascular Diseases in Tertiary Care Hospital: A Clinical Pharmacist Intervention

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Abstract Drug related problems in cardiovascular disease patients may lead to morbidity, mortality and the decreased quality of life. The main aim of the study is to assess, identify and resolve drug related problems in patients with Cardiovascular Diseases. A total of 150 cardiac patients were enrolled into the study. In our study, out of 150 we got 71 DRPs like Drug-Drug interactions 33(46.4%), ADRs 14(20%), indication without Drug 6(8.4%), drug use without indication 8(11.2%), sub therapeutic dose 10(14%). The association between risk factors like alcohol abuse, smoking, diabetes, hypertension increased risk of CVD. The P value was statistically significant in males than in females. In this study, for individuals with drug related problems of cardiovascular diseases, males were found to be more when compared with females due to risk factors such as smoking, alcoholism, life style etc. the drug related problems were high in patients aged between 40-60 years because of their multiple co-morbid conditions. Polypharmacy was the main predisposing factor for drug related problems.

Keywords Adverse Drug Interactions, Cardiovascular Diseases, Drug Related Problems, Drug-Drug interactions

1. Introduction

Cardiovascular disease is a major public health problem and one of the leading causes of premature death throughout the world. Cardiovascular disease encompasses coronary heart disease (CHD), stroke, peripheral vascular disease, congenital heart disease, endocarditis, and many conditions like angina pectoris, cardiac arrhythmias, heart failure, cardiomyopathy, valvulitis, rheumatic heart disease, myocardial infarction(MI), peripheral artery disease, aneurysm, stroke, congenital heart disease, pericarditis. Cardiovascular disease is a global health problem reaching epidemic proportions in both developed and developing countries and it is the principal cause of morbidity and mortality universal (Karim MA et al. 2015).

According to world health organization report 2011, approximately 17.1 million people die due to cardiovascular disease each year, representing 30% of all deaths. Of these deaths, approximately 7.3 million people die of coronary heart disease and 6.2 million people die mainly from heart diseases and stroke, which are projected to remain the single leading cause of death. (Gelchu T et al. 2019).

Even though, drugs play a major role in the cure, palliation and inhibition of disease, they also expose patients to drug related problems. In many instances, drug related problems are a major safety issue for hospitalized patients and it may lead to reduced quality of life, increased hospital stay, and increases risk of morbidity and mortality. (Gashaw binega meknoman et al. 2016). Drug related problems may be defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcome. (Mannu Meria wincent et al. 2017). Drug related problems may occur in any phases of medication usage; it may start from the prescribing phase and may last till the drug dispensing phase. Lack of follow-ups and reassessment of therapeutic outcomes may also contribute to drug related problems. (Adusumilli PK, Adepu R 2014).
Clinical pharmacists play an important role in identifying these drug related problems through careful pharmaceutical practices. There is increased evidence that participation and interventions of clinical pharmacists in health care have a positive influence on clinical practice. (Maxwell O Adibe et al. 2016).

The objective of this study is to identify the type of drug related problems and assess the outcomes of drug related problems among cardiovascular disease patients.

2. Research Methodology

**Study Site:**

The study was conducted at government general hospital with 500 bed Inpatient capacity Anantapuramu. An average of 300-400 patients were treated in the hospital per day on an outpatient basis by different departments like general medicine, paediatric, surgery, dermatology, ENT, ophthalmology, gynecology.

**Study Design:** A Prospective Interventional study design was conducted in cardiac Inpatients of general medicine for identification of drug related problems.

**Study period:** The study was conducted for the period of 6 months.

**Ethical Approval:** The complete project work was carried out after obtaining ethical clearance by the ethical committee.

**Study sample:** All the cardiac patients who follow up within the study period and who fulfilled the inclusion criteria were 150 patients.

**Study Criteria:**

**Inclusion Criteria:**
- The Patients admitted in the hospital with cardiovascular diseases of above the age of 18 years.
- The patients on multiple drug therapy of which at least taking two cardiac medicines.
- The patients of both sexes.

**Exclusion criteria:**
- Outpatient basis and self-medication patients was excluded from the study
- Patient below 18 years of age and Patients with more than four co morbidities was excluded from study
- Pregnant and lactating women

**Source of data:** Patient interview, Case record file – Demographic data (name, age, sex), Clinical condition, therapy given.

3. Results

In the present study a total of 150 Cardiac patients were admitted in department of general medicine during the six month period.

**Gender wise distribution:** Of these 150 patients it was observed that females were 66(44%) and males were 84(66%).

**Age wise distribution**

Majority of the subjects were 36(24%) belonging to age group of 41-50 years and 51-60 years, followed by 24(16%) years between 61-70 years, 21(14%) between 31-40 years, 18(12%) between 71-80 years, 12(8%) between 21-30 years and 3(2%) in greater than 80 years as shown in Table 1.

| Age Group(years) | Total (n=150) |
|------------------|--------------|
| 21-30            | 12(8%)       |
| 31-40            | 21(14%)      |
| 41-50            | 36(24%)      |
| 51-60            | 36(24%)      |
| 61-70            | 24(16%)      |
| 71-80            | 18(12%)      |
| >80              | 3(2%)        |

**Length of Stay in Hospital**

It is observed that, of 150 patients 81(54%) stayed in the hospital for 1-3 days, 51(34%) for 4-6 days, 18(12%) for more than six days as shown in Table 2.

**Correlation of Drugs with Cases**

Majority of patients 81(54%) were taking more than 9 drugs, 39(26%) were taking 7-8 drugs, 27(18%) were taking 5-6 drugs and 3(2%) were taking 3-4 drugs as shown in Table 2.
Table 2. Correlation of drugs with classes

| DRUGS | N=150 |
|-------|-------|
| 3-4   | 3(2%) |
| 5-6   | 27(18%) |
| 7-8   | 39(26%) |
| >9    | 81(54%) |

Correlation of Co Morbidities with Cases

It is observed here that, of the 150 subjects 45(30%) were having one diagnosis, 57(38%) were having two diagnosis, 36(24%) were having three diagnosis, 12(8%) were having four diagnosis as shown in Table 3.

Table 3. Correlation of co- morbidities

| Co morbidities | Number (n=150) | Percentage |
|----------------|----------------|------------|
| 1              | 45             | 30%        |
| 2              | 57             | 38%        |
| 3              | 36             | 24%        |
| 4              | 12             | 8%         |

Drug Related Problems Identified

Table 4. Drug related problems identified

| DRP’S                          | Males | Females | Total (n=71) | p-value   |
|--------------------------------|-------|---------|--------------|-----------|
| Drug-drug interactions         | 18    | 15      | 33           | <0.0001   |
| Adverse drug reactions         | 8     | 6       | 14           | <0.0001   |
| Indication without drug        | 4     | 2       | 6            | <0.0001   |
| Drug without indication        | 5     | 3       | 8            | <0.0001   |
| Sub therapeutic dose           | 6     | 4       | 10           | <0.0001   |

A total of 150 cases were screened for Drug related problems, out of which 71 Drug related problems were identified like 33(46.4%) were drug- drug interactions, 14(20%) were adverse drug reactions, 6(8.4%) were indication without drug, 8(11.2%) were drug use without indication, 10(14%) were sub therapeutic dose as shown in Table 4.

Type of Drug Interactions

Total 33 interactions had observed in 150 patient medication chart given to Cardiac disease patients for their therapy. They may give for the synergistic beneficiary effect for the patient to relieve from the illness, but there may have the possible occurrence of interactions by their combinations.

Severity of Interactions

These represents 8(24%) were major interactions, 18(55%) were moderate interactions, 7(21%) were minor interactions.

Types and Severity of Adverse Drug Reactions

There were 14 adverse drug reactions found among 150 cases, in which 5(36%) were type-A, 9(64%) were Type-B reactions as shown in, whereas among severity, 2(14%) were certain, 11(79%) were possible, 1(7%) were probable as shown.

Predisposing Factor of Drug Related Problems

In the present study polypharmacy was responsible for 54%, which was more predisposing factor for drug related problems and 46% were responsible for co-morbid conditions.

Correlation of Category with Drugs

In the study, Most common categories of drugs showing were antibiotic and anti psychotics were 8(16%), antipyretic, antiplatelet, analgesics, ARB’S, anti diarrheal, calcium channel blocker were 2(4%), ACE inhibitors, anticholinergic, Bronchodilators, corticosteroids, laxatives, Nitrates and statin were 1(2%), antacids were 3(6%), anti diabetic, beta blockers and diuretics were 4(8%) as shown in Fig. 1.
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Correlation of Recommendations with DRP’S

Out of 71 recommendations of drug related problems, it was observed that change in dose were 18(25%), change in dosage form were 6(9%), addition of drug were 6(9%), cessation of drug were 10(14%), substitution of drug were 3(4%) and change in frequency were 28(39%) as shown in Table 5.

Table 5. Distribution of recommendation of DRP’S

| RECOMMENDATIONS       | N=71 |
|-----------------------|------|
| Change in drug dose   | 18(25%) |
| Change in dosage form | 6(9%) |
| Addition of drug      | 6(9%) |
| Cessation of drug     | 10(14%) |
| Substitution of drug  | 3(4%) |
| Change in frequency   | 28(39%) |

Correlation of Acceptance Rate with Recommendations

Out of 71 recommendations 39% were accepted and 61% were not accepted as shown in Table 6.

Table 6. Correlation of acceptance rate with recommendations

| Recommendations       | N=71 |
|-----------------------|------|
| Accepted              | 28(39%) |
| Not accepted          | 43(61%) |

4. Discussion

Among 150 patients followed during the study period, a total of 71 Drug related problems were identified in 150 patients. Out of 150 patients, 66% were found to be males and 44% were female. Males having possible risk factors like smoking, alcoholism, and a sedentary lifestyle etc. compared to the female population. This result was similar to the study carried out by the L. Sai Hamsini et al J, Drug Delivery 2019; 9(2-s), which showed male predominance over female. The study conducted by Soumya Shastry et al. Int. Res. J. Pharm. 2019, 10 (3) also shows an increase in number of male population than females.

The incidence of drug related problems was high in patients aged between 41-60 years (24%). Among the number of drugs, patients receiving greater than 9 drugs were found to have higher drug related problems (71). This result was lesser to the study conducted by Rani Reema Abraham IJBMSP Vol. 3 2013, who reported 394 Drug related problems in 80 patients. this may be due to increased drug use because of their multiple co-morbid conditions This indicates that special attention should be taken in patients were regular review of drug therapy might help to decrease the drug related problems.

Drug interactions were the most common drug related problems observed in our study (46.4%), followed by adverse drug reactions (20%), sub therapeutic dose (14%), drug use without indication (11.2%) and indication without drug (8.4%). This study is similar with the study conducted by Javeedh Shareef et al J Pharm Care 2014 in which drug interactions were found to be high (49.05%), followed by adverse drug reactions (18.86%).in the present study the therapeutic agents most commonly involved in drug interactions were antibiotics, antihypertensives, antidiabetic, antiplatelet, diuretics and GI drugs, which is similar with the study performed Yirga Legesse Niriayo et al J, Pone 2018 in that the average number of drug
interactions involving antihypertensives, antiplatelet and GI drugs increased number of medication use and the combination of various drug classes might have contributed to the high prevalence of significant potential drug interactions in this study patients. The most commonly occurring drug interactions among the cardiovascular drugs included aspirin, clopidogrel, amlodipine, and Telmisartan.

The potency of the interaction increases when these cardiovascular drugs 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. The higher incidence of drug interactions in the study suggests that regular review of the patient’s case sheets including the drug therapy helps in identifying and preventing drug related problems including the drug interactions.

In our study, almost half of the adverse drug reactions implicate antidiabetic drugs and anti-hypertensive’s which includes insulin and oral hypoglycemic agents. hypoglycemia due to anti diabetic drugs in diabetic patients was the most common ADR observed in our study followed by metaprolol causing Bradycardia, enalapril causing cough, aspirin causing GI irritation. This due to most of the cardiovascular patients admitted in our study might also have diabetic mellitus and hypertension as co morbid conditions where hypoglycemia can develop during the blood sugar management and hypotension can develop. Due to time constraints, many of time physicians may not be able to explain patients about the possible and desirable side effects of the drugs and management. As a part of health care team clinical pharmacist who is experts in the medicines helps in identification and management of adverse drug reactions. His timely involvement might help in decreasing drug interactions, adrs and reduce the hospital stay. He also counsels the patient what to do when such adrs occurs.

During the medication chart review it was found that (11.2%) of drug related problems accounts for drug use without indication. These study findings are slightly similar with the study carried out by Temene Gelchu J.SAGE V-7 2019, which shows that drug use without indication accounts for (12.2%). Few drugs often used without indication includes antibiotics, ranitidine, pantoprazole, antiemetic. many of times antibiotics were prescribed to patients when total count, urine analysis and chest x-ray was found to be normal in our study we have found that indication without drug was (8.4%) of the total drug related problems. these indicates that the drug has not been prescribed for which there is a valid indication. the untreated conditions include cough, hyperkalemia, anemia etc. This was found to be less when compared to the study conducted by Yirga Legesse Niriaya et al 2018 where (18.5%) of the untreated indications account for the total drug related problems because lack of knowledge regarding prescribing among house surgeons. Sub therapeutic dose was found to be (14%) in our study. This was found to be less when compared to the study conducted by Amith Sharma et al Pharma Aspire V-10 2018 the pharmacist suggestion was drug dose adjustment. There was no drug related problem attributed to over dose because all the drug therapy was prescribed as per the recommended dose by the concerned cardiologist.

Suggestions made in our study includes a change in frequency of administration, addition of drug, cessation of drug etc. addition of drug was suggested in case of untreated indications, change in drug dose has been suggested in case of sub therapeutic doses and adverse drug reactions. For example, the adverse reactions such as hypoglycemia caused by the insulin’s and oral hypoglycemia agents were corrected with the changes in the subsequent doses of insulin and oral hypoglycemia agents.

Of the total 71 drug related problems, the level of significance moderate was found to be high (55%) followed by the level of significance ‘minor’ (21%). These study findings were similar to the study done by Javeedh Shareef et al 2014 which reported that 58.50% 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 (39%). Of the 39% of interventions accepted, 255 of interventions led to change in drug therapy followed by 14% led to cessation of drug. This finding is in contrast with the study of Javeedh Shareef et al 2014 which showed a higher acceptance rate of clinical pharmacist interventions by the physicians. The reason may be that prescribing decisions are often governed by the clinical experience of the physicians. The overall findings from our study was that pharmacists could identify some drug related problems; prompt and proper intervention will helps achieving better patient care that can lead to improve the quality of life and drug therapy.

5. Conclusions

In this study, individuals with drug related problems of cardiovascular diseases, it was found that males were found to be more when compared with females due to risk factors such as smoking, alcoholism, life style etc. the drug related problems were high in patients aged between 40-60 years because of their multiple co morbid conditions.

Polypharmacy was the main predisposing factor for drug related problems. Predisposing factors contributing to drug related problems were multiple drug therapy and co morbid conditions. Drug related problems in the cardiovascular disease patients indicates all the cases were predictable and most of the cases preventable or probably preventable.
Clinical pharmacist who is experts in the medicines help in identification and management of drug related problems

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