MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2016.6.760.764

OPEN ACCESS

Key Words
Cardiac patients, drug-drug interactions, polypharmacy

Corresponding Author
Dr. K.N. Saivisveswar,
Srinivas Institute of Medical Sciences and Research Centre Surathkal, Mangalore, India
saivisveswar@yahoo.com

Author Designation
[1]Assistant Professor

Received: 20th October 2016
Accepted: 15th December 2016
Published: 30th December 2016

Citation: Dr. K.N. Saivisveswar, 2016. Evaluation of Clinically Significant Drug-Drug Interactions in Cardiovascular Therapy Among Hospitalized Patients: A Cross-Sectional Study. Res. J. Med. Sci., 10: 760-764, doi: 10.36478/ makrjms.2015.6.760.764

Evaluation of Clinically Significant Drug-Drug Interactions in Cardiovascular Therapy Among Hospitalized Patients: A Cross-Sectional Study

Dr. K.N. Saivisveswar
Srinivas Institute of Medical Sciences and Research Centre Surathkal, Mangalore, India

Abstract
Drug-drug interactions (DDIs) appear to be the most common issue that can alter the overall therapeutic response while increasing hospital stays and medical costs. They are more common in patients with cardiovascular disease (CVD) than in people with other disease states, according to studies. This prospective observational study was conducted in 2016 on hospitalized cardiac patients at a tertiary care hospital. Of 687 screened patients, 500 met the inclusion criteria, excluding those <18 years, with medical handicap, or on alternative medicine. Data were collected via direct patient interviews and review of case sheets, recording demographics, clinical profile, and prescribed medications. Potential drug-drug interactions (pDDIs), including routine and PRN drugs, were identified using Micromedex® and www.drugs.com, and classified by type (pharmacodynamic or pharmacokinetic) and severity (major, moderate, minor) based on clinical relevance. Frequencies of pDDIs were summarized with respect to patient demographics, diagnosis, number of medications, hospital stay, and drugs involved. Of 500 cardiac patients, pDDIs were identified in 415 cases. Males had a slightly higher prevalence (290; 57.68%) than females (125; 56.87%). Most interactions occurred in patients with hospital stays of 4-6 days (380 cases) and were more common in those aged 60-70 years. A higher incidence (68.72%) was observed in patients prescribed more than seven medications. Hypertension was the most frequent comorbidity (266; 64%), followed by angina with diabetes mellitus (149; 36%). Each patient had one or two diagnoses on average. Aspirin + clopidogrel was the most common interacting drug pair, producing major pharmacodynamic interactions in 118 cases (28.43%).This study showed a high incidence of pDDIs in cardiac patients, associated with longer hospital stays, male gender, older age, and polypharmacy. Proper medication management and discontinuation of non-essential drugs are recommended to reduce pDDIs. Assessing the severity of each DDI is crucial for guiding clinical decisions.

INTRODUCTION

When a patient's reaction to a medication is altered by diet, nutritional supplements, formulation excipients, environmental variables, other medications, or illness, this is known as a drug interaction. These days, drug interactions are a serious problem. It is anticipated that research on genetic variables influencing pharmacokinetics and pharmacodynamics, as well as interactions between drugs, foods, and diseases, would enhance medication safety and make customized drug therapy possible. Many serious adverse drug reactions that result in hospitalizations and ED visits are thought to be caused by drug-drug interactions. By identifying possible drug interactions (pDIs), many adverse effects can be avoided. However, a number of factors, including polypharmacy, chronic illnesses, and numerous disorders, may make a drug-drug interaction more likely.

Drug-drug interactions (DDIs) seem to be the most common problem that can change the overall therapeutic response and raise hospital stays and medical expenses. Research indicates that individuals with cardiovascular disease (CVD) experience Drug-drug interactions more frequently than people with other disease states. This is likely because of risk factors like age, polypharmacy, and the pharmacokinetic and pharmacodynamic characteristics of the medications[1]. According to the literature, Drug-drug interactions are the cause of up to 1% of hospital admissions and 16% of hospitalizations brought on by adverse drug reactions (ADRs)[2]. In individuals with CVD, the reported prevalence rate of potential DDIs (pDDIs) ranges from 65% to 99.2%[3]. Drug-drug interactions are more common in CVD patients than in other illness groups, according to studies[4].

Lifestyle choices and diet can occasionally have a big influence on drug use. These could be the result of careless abuse or ignorance of the active components in the pertinent drugs. Food-drug interactions may unintentionally lessen or intensify the effects of the medications. Changes in the absorption of fatty, high-protein, and fiber diets are among the main adverse effects of certain diets (foods) on medications. Patients exposed to pDDIs had a higher risk of hospitalization, according to 16 cohort and case-control studies[5]. Drug therapy management requires an understanding of drug-drug interactions, food-drug interactions, and disease-drug interactions. Studies on the pDDIs in the departments have been carried out, according to the thorough literature research. Hence, the aim of our study is to evaluate the clinically significant drug-drug interactions in cardiovascular therapy among hospitalized patients.

MATERIALS AND METHODS

This study was carried out on hospitalized cardiac patients in our tertiary care hospital over the course of a year in 2016. Among 687 screened cardiac patients, 500 cardiac patients were recruited in the study finally. Patients under the age of 18, those with a medical handicap, and those following Ayurveda, Siddha, or another alternative medical system were excluded. A written informed consent was obtained from all the patients included in the study. Direct patient interviews from the cardiology department and case sheets of hospitalized patients were used to collect the data. Clinical records were used to gather data on the patient's age, sex, length of hospital stay, primary diagnosis, number of medications, and comorbidities associated.

Prescribed drugs were checked for pDDIs, including both routine and pro re nata (meaning as needed) drugs. The Drug Interactions Checker in Micromedex®-2.7 and www.drugs.com was used to find pDDIs. Based on their clinical relevance and cross-checked manually for the presence of sufficient published medical evidence for the identified interacting advertisers, the observed DDIs were categorized as major, moderate, and minor. Primarily, the DDIs were identified and categorized in accordance with www.drugs.com and Micromedex®-2.5 based on the profile of prescribed medications. According to the types, pDDIs are divided into two categories: pharmacodynamics, which includes additive, synergism, and antagonism, and pharmacokinetics, which includes absorption, distribution, metabolism, and excretion. pDDIs were classified according to severity: Major: the consequences are likely to be life-threatening or capable of causing permanent harm; moderate: the consequences may also lead to a decline in the patient's scientific reputation and the need for further treatment or an extension of hospital stay; and minor: the consequences are usually moderate. Although the effects may be uncomfortable or undetectable, they must not significantly impact the healing process. Sex, diagnosis, number of medications distributed, frequency of pDDIs, pharmaceuticals related to pDDIs, length of hospital stay, kinds, and severity of pDDIs were summarized using frequencies stated as possibilities.

RESULTS AND DISCUSSIONS

Among 500 cardiac patients, 415 cardiac patients had pDDIs identified. In our study, males had greater pDDIs than females of these, 290 (57.68%) were males and 125 (56.87%) were females (Figure 1).

According to the length of hospital stay (4-6 days), the incidence of interactions was in 380 patients, and the incidence of pDDIs was greater in patients aged 60-

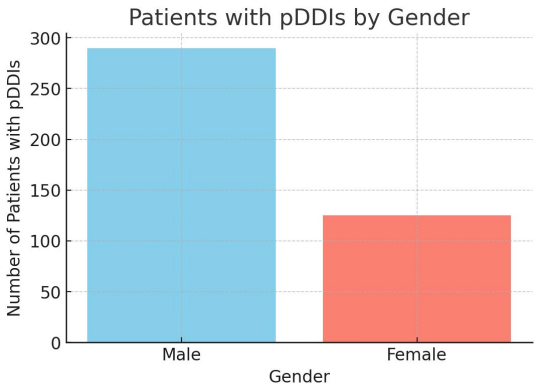

Fig. 1: Patients with pDDIs Gender

Table 1: Shows conditions associated with percentage

Condition	Percentage (%)
N=415	
Hypertension	266 (64%)
Angina with Diabetes Mellitus	149 (36%)

Table 2 shows most potential drug-drug interactions among cardiac patients

pDDI combination	Type	Severity	Frequency n=415 (%)
T. Aspirin + T. Clopidogrel	PD	Major	118 (28.43)
T. Aspirin + T. enalapril	PD	Moderate	34 (8.19)
T. Atorvastatin + T. Clopidogrel	PK	Moderate	40 (9.64)
T. Aspirin + T. Atenolol	PD	Moderate	12 (2.89)
T. Clopidogrel + T. Amlodipine	PK	Moderate	38 (9.16)
T. Atenolol + T. Metformin	PK	Major	13 (3.13)
T. Spironolactone + T. Enalapril	PD	Moderate	9 (2.17)
T. Enalapril + T. Metformin	Unknown	Major	7 (1.69)
T. Enalapril + T. Furosemide	PD	Moderate	6 (1.45)
T. Aspirin + T. Spironolactone	PD	Major	19 (4.58)

70 years. A greater number of pDDIs was discovered in 68.72% of patients who were prescribed more than seven medications. Among all 415 patients, hypertension was the most prevalent ailment (266, 64%), followed by angina with diabetes mellitus (149, 36%) (Table 1). On average, each patient had one or two classified diagnoses.

Aspirin and clopidogrel were shown to be the most often occurring interacting pair in the cardiac department, resulting in significant pharmacodynamic interactions with a frequency of 118(28.43%)(Table 2).

These days, DIs are an important concern for the efficient treatment of patient illness. Inaccurate estimation of the risk-benefit ratio of mixing interacting medications can pose a significant health risk to patients. Drug interactions have been estimated to have a range of effects, from modest morbidity to lethal consequences. It is anticipated that studies on the interactions between drugs, foods, and diseases as well as genetic variables influencing pharmacokinetics and pharmacodynamics would enhance medication safety and make customized drug therapy attainable. In the present study involving 500 cardiac patients, a high prevalence of potentially detectable drug–drug interactions (pDDIs) were observed, with 415 patients (83%) experiencing at least one interaction. Males demonstrated a slightly higher rate of pDDIs than females, with 290 males (57.68%) and 125 females (56.87%) affected, although the difference was not substantial. In a comparable study conducted by George et al, male patients (67%) had a higher rate of cardiovascular incidence than female patients (33%).6 Another study found that male patients had a greater, and pDDIs potential when compared to females in the current study, which could be the primary explanation[1]. Another factor may be that men are more likely than women to suffer from cardiovascular and pulmonary conditions, which necessitates the use of several medications and ultimately leads to drug interactions.

The incidence of pDDIs was greatest in the 60-70 year age group, which is in line with previous literature indicating that age-related pharmacokinetic and pharmacodynamic changes, combined with higher disease burden, contribute to greater susceptibility. According to a study by Fita *et al*., the majority of patients were between the ages of 70 and 747, while a study by Chelkeba *et al*. reported an age group of 59-69 years[8]. Due to a number of factors, older adults were more likely to experience an adverse drug reaction (ADR) from pDDIs. They probably take a lot of prescription and over-the-counter medications since

they have greater commodities. The older adults are over twice as likely as younger adults to experience adverse drug reactions. The body's water content falls with age, whereas the proportion of fat tissue to water increases. Additionally, the liver's capacity to metabolize many medications decreases with age, and the kidneys' capacity to eliminate drugs into the urine also declines.

The majority of pDDIs (n=380) occurred in patients with a hospital stay of 4-6 days, consistent with evidence that longer admissions increase exposure to multiple medications and prescribing changes, thereby elevating interaction risk. A study by Lubinga *et al*. revealed that most cases had hospital stays of fewer than six days[9]. Increasing the length of hospital stay raises the chance of receiving several medications, which in turn increases the risk of pDDIs.

Polypharmacy emerged as a significant driver, with 68.72% of patients prescribed more than seven medications having pDDIs, reflecting the well-established correlation between the number of drugs and the probability of interactions. According to the de Andrade *et al*. study, between 13 and 16 medications were recommended in 40.6% of cases[10]. More than seven medications were administered in 54% of instances, according to a study by Ismail et al.11 According to Mannesse *et al*., using three or more medicines at the same time elevated the risk of ADEs by 9.8 times[12]. The likelihood of unreasonable polypharmacy increases with the number of prescribed medications. The likelihood of strong cytochrome P450 (CYP 450) interactions in elderly hospitalized patients receiving more than five medications at once was assessed by Doan *et al*[13]. Eighty percent of those taking more than five medications at the same time had potential drug-drug interactions.

With a frequency of 118 (28.53%), aspirin and clopidogrel were the most frequently seen interacting pair in the cardiac department, resulting in significant pharmacodynamic interaction. Another study also found that aspirin–clopidogrel and clopidogrel–fondaparinux were the most often occurring interaction pairs[1]. While spironolactone and potassium chloride together may raise potassium levels, diltiazem may raise serum amlodipine levels by influencing CYP3A4.

Among the 415 patients with pDDIs, hypertension was the most prevalent condition (n=266, 64%), followed by angina with diabetes mellitus (n=149, 36%), and most patients had one or two classified diagnoses, indicating multimorbidity. These findings parallel reports from other studies that highlight the compounded risk of pDDIs in older, multimorbid patients with prolonged hospital stays and complex drug regimens, and they underscore the importance of careful medication review, clinical pharmacist involvement, and deprescribing strategies to mitigate adverse outcomes.

CONCLUSION

This study found that the overall incidence of pDDIs was significantly higher in the cardiac patients. It was discovered that longer hospital stays, male gender, older age, and the number of medications administered were all linked to the occurrence of pDDIs. In order to lower pDDIs, patients' medication intake must be appropriately managed, and it is advised to stop using any drugs that don't have a therapeutic value, purpose, or prescription. Since not all possible DDIs are equally detrimental, determining each one's level is essential to determining its clinical significance and the best course of action. Several instances of drug-disease interactions are reported in our study. Based on epidemiological knowledge of the commodities of individuals with the disease on which the guideline is focused, the authors of the guideline might think about taking a more methodical approach to the possibility of drug-disease interactions. They should specifically take into account whether cardiovascular diseases are prevalent in the target population. Their prompt detection and the avoidance of related morbidity depend on knowledge of such predictable or potential interactions.

Conflict of Interest: The authors declare that they have no conflicts of interest.

REFERENCES

1. Y. Albadr, Bohassan .A.K, Ming .L.C, Khan .T.M. An exploratory study investigating the potential drug-drug interactions in internal medicine department, Alahsa, Saudi Arabia. Journal of Pharmaceutical Health Services Research. 2014, 5:237-241.
2. T. Roblek, Trobec .K, Mrhar .A, Lainscak .M. Potential drug-drug interactions in hospitalized patients with chronic heart failure and chronic obstructive pulmonary disease. Archives of Medical Science. 2014, 10:920-932.
3. G. Sepehri, Khazaelli .P, Dahooie .F.A, Sepehri .E, Dehghani .M.R. Prevalence of potential drug interactions in an Iranian general hospital. Indian journal of pharmaceutical sciences. 2012, 74:75.
4. J.M. Cruciol-Souza, Thomson .J.C. Prevalence of potential drug-drug interactions and its associated factors in a Brazilian teaching hospital. J Pharm Pharm Sci. 2006, 9:427-433.
5. L.E. Hines, Murphy .J.E. Potentially harmful drug–drug interactions in the elderly: A review. The American journal of geriatric pharmacotherapy. 2011, 9:364-377.
6. J. George, Devi .P, Kamath .D.Y, Anthony .N, Kunnoor .N.S, Sanil .S.S. Patterns and

determinants of cardiovascular drug utilization in coronary care unit patients of a tertiary care hospital. Journal of cardiovascular disease research. 2013, 4:214-221.

7. F.I. Rahmawati, Hidayati .N.U, Rochmah .W.A, Sulaiman .S.A. Potentiality of drug-drug interactions in hospitalized geriatric patients in a private hospital, Yogyakarta, Indonesia. Asian J Pharm Clin Res. 2010, 3:191-194.
8. L. Chelkeba, Alemseged .F, Bedada .W. Assessment of potential drug-drug interactions among outpatients receiving cardiovascular medications at Jimma University specialized hospital, South West Ethiopia. Int J Basic Clin Pharmacol. 2013, 2:144-152.
9. S.J. Lubinga, Uwiduhaye .E. Potential drug-drug interactions on in-patient medication prescriptions at Mbarara Regional Referral Hospital (MRRH) in western Uganda: prevalence, clinical importance and associated factors. African health sciences. 2011, 11.
10. T.N. Andrade, Silvestre .C.C, Cunha .L.C, Silva .D.T, Marques .T.C, Oliveira Filho .A.D, Lyra Junior .D.P. Pharmaceutical intervention assessment in the identification and management of drug interactions in an intensive care unit. J Appl Pharm Sci 2015, 5:13-18.
11. M. Ismail, Iqbal .Z, Khattak .M.B, Javaid .A, Khan .T.M. Prevalence, types and predictors of potential drug-drug interactions in pulmonology ward of a tertiary care hospital. Afr J Pharm Pharmacol. 2011, 5:1303-1309.
12. C.K. Mannesse, Derkx .F.H, De Ridder .M.A, Man In't Veld .A.J, Van der Cammen .T.J. Contribution of adverse drug reactions to hospital admission of older patients. Age and ageing. 2000, 29:35-39.
13. J. Doan, Zakrzewski-Jakubiak .H, Roy .J, Turgeon .J, Tannenbaum .C. Prevalence and risk of potential cytochrome p450-mediated drug-drug interactions in older hospitalized patients with polypharmacy. Annals of Pharmacotherapy. 2013, 47:324-332.