Research Article

Drug-Drug Interactions in Cardiac Patients in A Tertiary Care Hospital - A Prospective Observational Study

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ABSTRACT

The main objective of this study was to identify the drug-drug interaction between cardiac drugs that occurred in the cardiology department in ICU and in wards in this tertiary care hospital. This study also aimed to identify the clinical pharmacist role in identification and management drug-drug interactions in the cardiology department. A prospective observational study was conducted in the PCTVS, ACTVS, CCU, and wards in cardiac patients in a tertiary care hospital during March-June 2019, for three consecutive months. During the study period a total of 150 patient prescriptions were randomly collected from cardiology department among which 100(66.67%) prescriptions were found with 166 DDIS. In 166 DDIs moderate interactions were more 92(39.75%) followed by major 66(55.42%) and minor interactions were only 8(4.81). Among 166 drug- drug interactions most frequently occurring was Aspirin+ramipril/Lisinopril/enalapril. In 166 DDIs there were 89(53.61%) Significant drug interactions and 77 (46.38%) were Non-Significant drug interactions. Among the DDIs observed majority of interactions, 25 (15.06%) could be managed by monitoring signs and symptoms and monitoring renal functions 22 (13.25%). This study concluded that the drug interactions were more in hospitalized cardiac patients as they were on poly pharmacy and were having more co-morbid conditions. This study showed the need of monitoring of drug- drug interactions by the clinicians, clinical pharmacist and other health care providers so that any adverse reactions can be minimized.

Keywords: Cardiology, Drug-Drug Interactions, Medscape, Poly Pharmacy.

INTRODUCTION

Drug therapy is becoming more complex, thus the selection of appropriate drug therapy is more challenging. Drug-related problems such as adverse drug reactions, drug-drug interactions, idiosyncratic reactions, and hypersensitivity reactions remained a major challenge in clinical practice.[1] Drug interactions are most important in this context and proper handling of drug-drug interactions may prevent harmful events.[2] Potential drug-drug interaction is observed to be one of the most frequently appearing challenges that may alter pharmacokinetic and pharmacodynamic of drugs thus alter the overall therapeutic response.[1] Although their response can be both positive and negative, Drug interactions are often unpredictable and undesirable in pharmacotherapy. [2] Despite advances in technology and information provided by health authorities to prevent clinically significant Drug interactions, hundreds of millions of these events occur annually, affecting millions of patients. [3]

Due to the intricacy of the pharmacotherapy involved in critically ill patients in the simultaneous use of several drugs and various therapeutic classes, there is an increased risk for drug interactions.[4] Hospitalized cardiac patients need more attention regarding drug-drug interaction due to the complexity of their diseases and therapeutic regimen.[1]The possible reasons behind higher potential drug-drug interactions rate in cardiovascular disease may include age, multiple drug regimen and pharmacokinetic or pharmacodynamic nature of drugs used in cardiology. [1]

Patients presenting for invasive cardiovascular procedures are frequently taking a variety of medications, during the procedure, antithrombotic, sedative, and analgesic medications are commonly needed, and after interventional procedures, new medications are often added for primary and secondary prevention of ischemic events and this might result in drug-drug interactions that affect the balance of thrombotic and bleeding events during the procedure and long-term treatment. Interventional providers need to be attentive to the potential for a drug-drug interaction, the associated harm, and the appropriate action, if any, to minimize the potential for medication-related adverse events. [5]

The study of drug interaction becomes an important tool to optimize the therapeutic regimen, which may contribute to the safety, effectiveness, and quality of pharmacotherapy in the ICU.[2] Thus, it is essential that health professionals, such as pharmacists, can clinically assess possible Drug interactions, collaborating with the health staff and developing strategies for the management of patients.[2]

In this study, the identified drug-drug interactions were classified according to the severity of interaction that is major, moderate and minor and also based on significant and non-significant interaction.

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METHODOLOGY

Study setting and period

The study was conducted in the PCTVS, ACTVS, CCU, and wards in cardiac patients in a tertiary care hospital during March-June 2019, for three consecutive months.

Study Design

A 3-month Prospective Observational Study.

Inclusion Criteria

All the patients who were admitted with cardiac disease were taken into this study.

Exclusion Criteria

All other patients not having cardiac diseases were excluded from the study.

Data Collection

Data were collected by using a designed data collection form from the patient's case notes, and treatment charts. The data included were a patient demographics identification number, diagnosis, Comorbidities, number of drugs in prescription, from which department the cases were collected, name of the drugs, dose, route, and frequency.

RESULTS

During the study period a total of 150 patient prescriptions were randomly collected from cardiology department among which 100(66.67%) prescriptions were found with 166 DDIS. There were 105 (70%) males and 45(30%) were females which is illustrated in table 1.

Table 1: Gender Distribution

Gender	Frequency	Percentage (%)
Male	105	70
Female	45	30
Total	150	100

Among the 150 cases, 53(35.3%) patients were in the age above 60 years followed by 29(19.3%) patients within 46–59 years, 15(10%) patients within age group of 31–45 years, 4 (4.07%) patients within age group of 15–30 years and 49(32.67) patients within age group of range 0-14 years which the study found that there was a higher prevalence of DDIs among the patients above the age of 50 years (56.62%). The age could be one of the factors responsible for poly pharmacy and co morbid conditions.

In 150 cases there were 95 (63.3%) patients with Nil co morbidities, 4(2.7%) patients with CAD, DM, HTN and TVD, 4(2.7%) patients with COPD and DM,8(5.3%) patients with DM and HTN, 8(5.3%) patients with DM and 8(5.3%) patients with HTN and 23 (15.3) patients with other comorbidities.

Among 150 cases 66(44%) patients admitted with CAD, 18(12%) with VSD, 14(9.3%) with CHD, 9(6%) with ACS and 43(28.67%) with other diagnosis which is illustrated in table 2.

Table 2: Diagnosis

Diagnosis	Frequency	Percentage
ACS	9	6
CAD	66	44
CHD	14	9.3
VSD	18	12
OTHERS	43	28.67
TOTAL	150	100

Among 150 cases there were 6-10 range of drugs in 63(42%) prescriptions, 11-15 drugs in 50(33.3%) prescriptions, 0-5 drugs in 20(13.3%) prescriptions,16-20 range of drugs 12(8%) prescriptions and more than 20 drugs in 5(3.3%) prescriptions which is shown in graph 1.

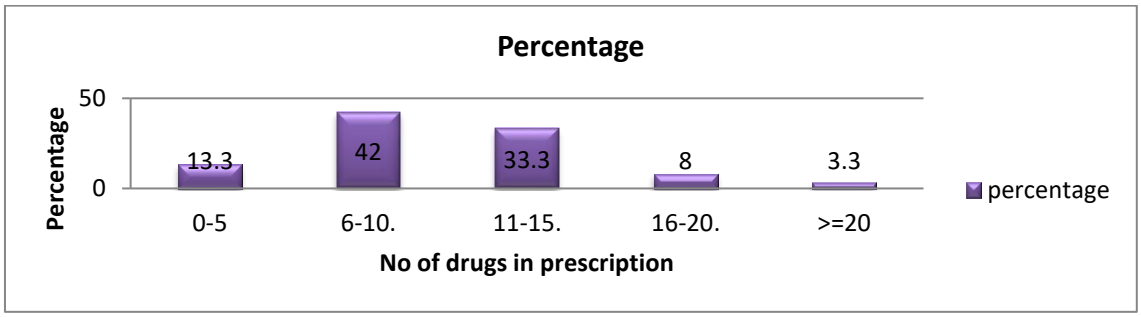
Among 166 DDIs moderate interactions were more 92(39.75%) followed by major 66(55.42%) and minor interactions were only 8(4.81) which is illustrated in graph 2.

Among 166 drug- drug interactions most frequently occurring was Aspirin+ramipril/Lisinopril/enalapril followed by furosemide + amikacin and then aspirin + clopidogrel which is shown in table 3.

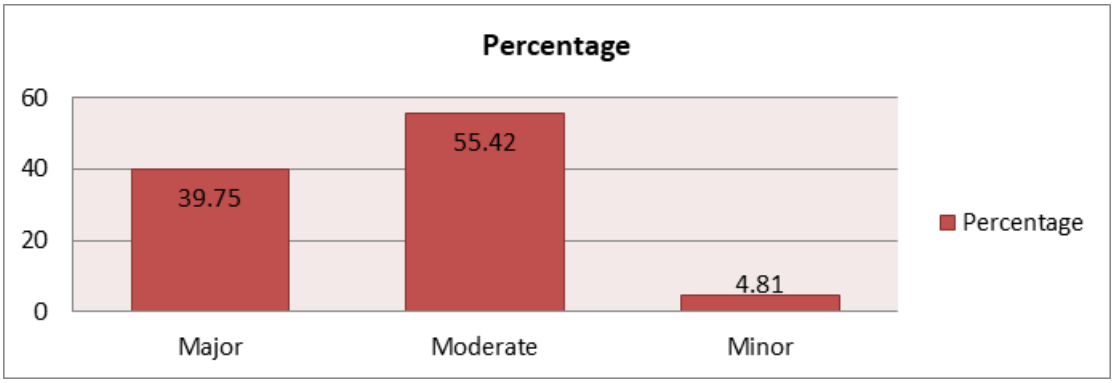
Table 3: Most Frequently Occurred Drug interactions

DDIs	Frequency	Percentage
Aspirin+Ramipril/ Lisinopril/Enalapril	19	11.44
Furosemide + Amikacin	16	9.6
Aspirin+Clopidogrel	12	7.22

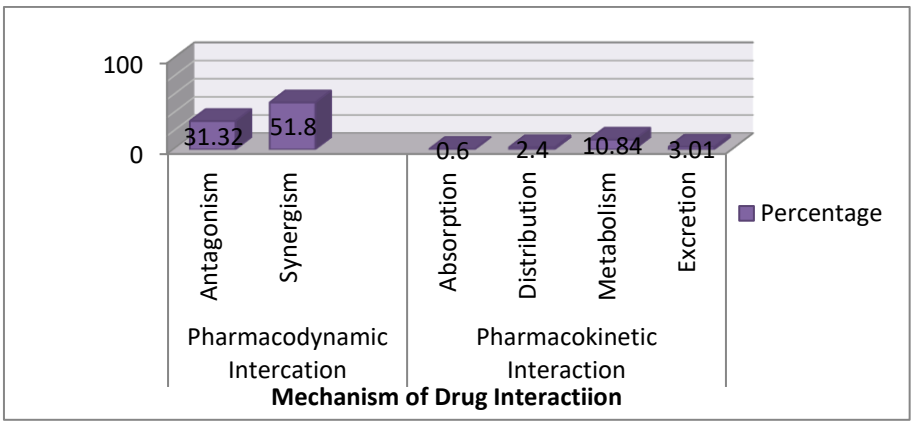
Out of 166 DDIs, there were 28(16.86%) pharmacokinetic DDIs and 138 (83.13%) pharmacodynamic DDIs within the different pharmacokinetic DDIs, where drug interactions due to altered metabolism were found most often 18 (10.84%) followed by absorption-related drug interactions 1(0.6%), interactions-related excretion 5(3.01%), and altered distribution 4 (2.4%). Pharmacodynamic DDIs had synergistic drug interactions 86(51.8%) and antagonistic drug interactions 52 (31.32%) which is illustrated in graph 3.



Graph 1: No of drugs in Prescription



Graph 2: Drug - Drug Interactions



Graph 3: Mechanism of Drug-Drug Interaction

Among 166 DDIs there were 89(53.61%) Significant drug interactions and 77 (46.38%) were Non-Significant drug interactions which was illustrated in table 4. [6]

Table 4: Level of Significance

Level of significance	Frequency	Percentage
Significant	89	53.61
Non-Significant	77	46.38
Total	166	100

Among the DDIs observed majority of interactions, 25 (15.06%) could be managed by monitoring signs and symptoms, monitoring renal functions 22 (13.25%). The management plan for the DDIs observed is represented in Table 5.

Table 5: Management of Drug – Drug Interactions

Management of Interaction	Frequency	Percentage
Monitoring of signs and symptoms	25	15.06
Monitoring of electrolytes	8	4.81
Monitoring renal function	22	13.25
Monitoring hematological parameters	17	10.24
Changing of dosing interval	15	9.03
No management need	79	47.59
Total	166	100

DISCUSSION

Drug – Drug interactions is a major concern in the treatment of patients presenting with cardiovascular diseases as most of the cardiac patients present with co morbid conditions and are having multiple drugs. It has been observed that cardiac patients are more prone to drug interactions as compared to other patients according to *Bernhard S et al.* [7] A study conducted by *Askari M et al*[8] has demonstrated that patients admitted in ICU had a number of clinically relevant DDI requiring intervention. A number of different software programs are available which help to identify and assess the pattern of DDI. One of them which was used in the present study was the Medscape drug interaction checker. [9]

Most of the patients involved in this study were of the age of above 60 years (35.3%) similar as the study Shipra *Jain et al.* [10] Male patients were more 70% when compared to female patients 30% which is similar with a study conducted in *Sharma S et al* Western Nepal. [11]

From 150 cases there were 6-10 range of drugs in 63(42%) prescription it was seen that there is a linear increase in the percentage incidence of drug interactions with an increase in the number of drugs prescribed to the patients according to studies *Virendra K Pet al.* [1]

From the 150 prescriptions 166 drug -drug interactions were found. Out of 166 DDIs there was more number of pharmacodynamic drug interactions when compared with pharmacokinetic drug interactions similar to study of *Greeshma K George et al.* [12] In this study most frequently occurring drug interactions were aspirin and Ramipril, furosemide and amikacin and then aspirin and clopidogrel which requires monitoring of renal function, monitoring of hematological parameters and monitoring of signs and symptoms.

The class of drugs most commonly involved the moderate (55.42%) DDIs were more than the major DDIs and minor DDIs. In 166 Drug-Drug Interactions 89 interactions were significant interactions and requires management. 25 significant interactions require management by monitoring signs and symptoms, 22 interactions require monitoring of renal function. This study affirms the fact that DDIs will be more with increase in age and with patient who are having co morbid conditions and taking multiple drugs.

CONCLUSION

This study concluded that the drug interactions were more in hospitalized cardiac patients as they were on poly pharmacy and were having more co-morbid conditions. This study also classified the drug interactions on the basis of its severity and level of significance. The study identified the most recurrently occurring drug interactions and its management in this tertiary care hospital. This study showed the need of monitoring of drug- drug interactions by the clinicians, clinical pharmacist and other health care providers so that any adverse reactions can be minimized.

REFERENCES

1. Patel VK, Acharya LD, Rajakannan T, Surulivelrajan M, Guddattu V, Padmakumar R, Potential drug interactions in patients admitted to cardiology wards of a south Indian teaching hospital, The Australasian medical journal, 4(1), 2011, 9.
2. Mateti UV, Rajakannan T, Nekkanti H, Rajesh V, Mallaysamy SR, Ramachandran P, Drug-drug interactions in hospitalized cardiac patients. Journal of Young Pharmacists, 3(4), 2011, 329-33
3. Murtaza G, Khan MY, Azhar S, Khan SA, Khan TM,Assessment of potential drug–drug interactions and its associated factors in the hospitalized cardiac patients, Saudi Pharmaceutical Journal, 24(2), 2016, 220-5.
4. Kaur S, Kapoor V, Mahajan R, Lal M, Gupta S. Monitoring of incidence, severity, and causality of adverse drug reactions in hospitalized patients with cardiovascular disease. *Indian J Pharmacol*. 43(1), 2011, 22-26.
5. Snaith A, Pugh L, Simpson CR, McLay JS, The potential for interaction between warfarin and coprescribed medication, American journal of cardiovascular drugs. 8(3), 2008 May 1, 207-12.
6. Ahmad A, Khan MU, Haque I, Ivan R, Dasari R, Revanker M, et al, Evaluation of potential drug-drug interactions in general medicine ward of teaching hospital in southern India, J Clin Diagn Res, 2015;9:FC 10- FC13.
7. Straubhaar B, Krähenbühl S, Schlienger RG, The prevalence of potential drug-drug interactions in patients with heart failure at hospital discharge, Drug safety, 29(1), 2006 Jan 1; 79-90
8. Askari M, Eslami S, Louws M, Wierenga PC, Dongelmans DA, Kuiper RA, Abu-Hanna A, Frequency and nature of drug-drug interactions in the intensive care unit, Pharmacoepidemiology and drug safety, 22(4), 2013 Apr; 430-7.
9. Multi-Drug Interaction Checker-Medscape Reference. Available on http://www. reference.medscape.com/drug-interactionchecker.
10. Jain S, Jain P, Sharma K, Saraswat P, A prospective analysis of drug interactions in patients of intensive cardiac care unit, Journal of Clinical and Diagnostic Research: JCDR, 11(3), 2017 Mar; FC01.
11. Sharma S, Chhetri HP, Alam K, A study of potential drug-drug interactions among hospitalized cardiac patients in a teaching hospital in Western Nepal, Indian journal of pharmacology, 46(2), 2014 Mar; 152
12. George, G. K., S. Sundaran, A. A. Cp, M. Km, T. Ph, B. G, and A, Gopalakrishnan, Study of Drug-Drug Interaction in The Inpatients of A Tertiary Care Hospital At Calicut, *Asian Journal of Pharmaceutical and Clinical Research*, Vol. 11, no. 9, Sept. 2018, pp. 162-4.

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