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Research Article

STUDY OF DRUG-DRUG INTERACTION IN THE INPATIENTS OF A TERTIARY CARE HOSPITAL AT CALICUT

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ABSTRACT

Objective: The study was conducted to monitor the potential drug-drug interactions in the prescriptions of inpatients in a tertiary care hospital based on the mechanism and severity.

Methods: This prospective observational study was conducted by collecting the prescriptions containing two or more drugs. The interactions were checked using an interaction checker and were categorized into pharmacokinetic and pharmacodynamic interactions on the basis of mechanism of action and severity based on the risks or consequences of the interactions.

Result: Among 150 randomly collected prescriptions, 123 (82%) prescriptions had 396 drug-drug interactions. The pharmacodynamic drug interactions (77.27%) were more common when compared to pharmacokinetic drug interactions (22.73%). There was high prevalence of drug-drug interactions among the patients above the age of 60 years (56.09%). The moderate drug-drug interactions (81.81%) were found to be more when compared to the major (10.61%) and minor (7.58%) interactions. The neurology department prescriptions were observed to have more number of drug-drug interactions (26.01%).

Conclusion: A systematic approach and close monitoring of the medication chart is necessary to identify the potential drug-drug interactions. The clinicians and other health-care professionals at the study site require an awareness program in regard to identification and management of drug-drug interactions. Clinical pharmacist can play an important role in the monitoring and management of drug-drug interactions.

Keywords: Prescription review, Drug-drug interaction, Mechanism, Severity.

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INTRODUCTION

A drug-drug interaction (DDI) is said to occur when the effects of one drug are changed by the presence of another drug or when two or more medications are simultaneously administered and one medication increases or decreases the effectiveness of the other [1,2]. The pharmacological response to the administration of the drug combinations is different from the known effects of the two agents when given alone [5]. Approximately 37–60% of patients admitted to the hospital may have one or more potentially interacting drug combinations at admission [2]. Recognizing drug interaction is a daily challenge for family physicians and remembering all potential interaction has become virtually impossible [4]. The clinical result of a DDI may manifest as antagonism, synergism, or idiosyncratic and is common causes of adverse drug reactions and therapeutic failure [5]. The mechanism of DDIs can be sub-divided to pharmacokinetics and pharmacodynamics. In pharmacokinetic interactions can affect the processes by which drugs are absorbed, distributed, metabolized, and excreted. Pharmacodynamic interactions are those where the effects of one drug are changed by the presence of another drug at its site of action. Drug interactions may lead to adverse drug reactions that can be severe enough to necessitate hospitalization and increased health-care costs. About 5% of all the adverse drug reactions in the hospitals are caused by DDIs [2]. Numerous studies have demonstrated that many patients receive multiple drug therapy with agents of recognized potential for interaction [5]. In our study, site this is the first time a study related to drug-drug interaction was done since any prescription having two or more drugs are prone to interactions and awareness of its severity and management would be useful in-patient care.

The study was conducted to categorize DDIs in the prescriptions of the inpatients based on mechanism involved and assess the severity of DDIs.

METHODS

This observational study was carried out from October 2016 to March 2017 in PVS Hospital (P) Ltd., Calicut, a 350-bedded tertiary care hospital. The study was conducted after getting the approval from Institutional Ethics Committee of the hospital.

Patient case sheets, patient medical records, and a DDI documentation form were used for the study. DDIs were checked using drug interaction checker at www.drugs.com database which is powered by four independent leading medical information suppliers: Wolters Kluwer Health, American Society of Health-System Pharmacists, Cerner Multum, and Thomson Reuters Micromedex. According to this tool, drug interactions were categorized as minor, moderate, or major which indicate the possible risks of occurrence of DDIs which can occur in patients.

The initial part of the study was designed to provide awareness about DDIs and their impact to the health-care professionals such as doctors, nurses, pharmacists, laboratory technicians, nursing students, and pharmacy students. A DDI documentation form was prepared according to the data requirement for the study which included information such as patient details, diagnosis, drugs prescribed, drug interaction mechanism categorization, consequences and severity, and required management.

Table 1: Prescribing intention of interacting drugs versus severity

Prescribing	Severity			Total (%)
	Major (%)	Moderate (%)	Minor (%)	
Intentional	2 (0.51)	14 (3.53)	0	16 (4.04)
Non-intentional	40 (10.1)	310 (78.28)	30 (7.58)	380 (95.96)
Total	42 (10.61)	324 (81.81)	30 (7.58)	396

Table 2: Management of DDIs

Management	Number of DDIs (%)
Monitoring of signs and symptoms	127 (32.07)
Dose adjustment	48 (12.12)
Monitoring of blood glucose level	45 (11.36)
No management need	30 (7.57)
Monitoring of electrolytes	26 (6.57)
Changing of dosing interval	24 (6.06)
Avoid combination	19 (4.79)
Change the medication	16 (4.04)
Monitoring patients therapeutic response	15 (3.79)
Monitoring renal function	12 (3.03)
Monitoring ECG	8 (2.02)
Monitoring signs and symptoms plus biochemical parameter	7 (1.77)
Monitoring pulmonary function	7 (1.77)
Monitoring hematological parameters	6 (1.52)
Monitoring liver function	6 (1.52)

DDIs: Drug-drug interactions

The case sheets that had two or more drugs in the day to day prescriptions were randomly selected by the clinical pharmacist. After the prescription selection, the relevant data from the prescription was entered into the DDI documentation form. The DDIs were classified into pharmacokinetic and pharmacodynamic DDIs based on their mechanisms involved. Further, the severities of the interactions were assessed and categorized as major (can cause permanent damage or life risk), moderate (can cause harm and treatment is required), or minor (can cause small or no clinical effect, with no treatment required).

SPSS 20 was used to run statistical analysis. Mean difference (significant at 0.05 level) was used to predict the relationship between the number of drugs and DDIs. Probability (p value) of 0.001 was considered statistically significant.

RESULTS

During the study period, a total of 150 patient prescriptions were randomly collected among which 123 (82%) prescriptions were found with 396 DDIs. There were 65 (52.85%) males and 58 (47.15%) females. Among the 123 cases, 69 (56.1%) patients were in the age above 60 years followed by 38 (30.89%) patients within 46–60 years, 11 (8.94%) patients within age group of 31–45 years, and 5 (4.07%) patients within age group of range 18–30 years.

The study found that there was a higher prevalence of DDIs among the patients above the age of 60 years (56.09%). The age could be one of the factors responsible for polypharmacy due to comorbidities, and there was more admission of geriatrics when compared to the adults.

Classification of DDIs

Out of 396 DDIs, there were 90 (22.73%) pharmacokinetic DDIs and 306 (77.27%) pharmacodynamic DDIs. Statistical analysis showed a significant difference ($p<0.001$) within the different pharmacokinetic DDIs, where drug interactions due to altered metabolism were found most often 48 (53.33%) followed by absorption-related drug interactions 22 (24.44%), interactions-related excretion 16 (17.77%), and altered distribution 4 (4.44%). Pharmacodynamic DDIs had synergistic drug interactions 209 (68.30%) and antagonistic drug interactions 97 (31.69%) (Fig. 1).

Severity of DDIs

Among the DDIs, there were 324 (81.81%) moderate DDIs followed by 42 (10.61%) major DDIs and 30 (7.58%) minor DDIs.

DDI based on prescriber's intention

The results showed that out of 396 DDIs, 380 (95.96%) were unintentionally prescribed and 16 (4.04%) were intentionally prescribed (Table 1).

Management of DDIs

Among the DDIs observed majority of interactions, 127 (32.07%) could be managed by monitoring signs and symptoms followed by dose adjustment 48 (12.12%). The management plan for the DDIs observed is represented in Table 2.

Department wise findings of DDIs

Among 123 prescriptions, 32 (26.01%) DDIs occurred in Neurology Department, 25 (20.32%) in Cardiology Department, 14 (11.38%) in Endocrinology Department, 14 (11.38%) in Pulmonology Department, 12 (9.75%) in Infectious Department, 9 (7.31%) in Gastroenterology Department 9 (7.31%) in Urology Department, 4 (3.25%) in Dermatology Department, and 4 (3.25%) in Hematology Department.

DISCUSSION

The study found a high prevalence of DDIs among the patients above the age of 60 years. It may be due to the more number of admissions of geriatrics and multiple drugs for ailment when compared to the adults. The studies conducted by Jimmy *et al.* reported similar findings [2]. Out of 396 DDIs, there was more number of pharmacodynamic drug interactions when compared with pharmacokinetic drug interactions. These findings showed similarity to the study conducted by Jimmy *et al*. [2]. The moderate (81.81%) DDIs were more than the major DDIs and minor DDIs. The findings were similar to the studies carried out by Jimmy *et al.* [2], Umretiya *et al.* [5], and Nag *et al.* [13]. Out of 396 DDIs, 380 (95.96%) were unintentionally prescribed and 16 (4.04%) were intentionally prescribed. Studies related to these findings were not observed. During the monitoring of DDIs, it would be useful to separate out the intentional prescribing that has a therapeutic goal set by the prescriber. A general monitoring would be sufficient enough for the latter. Whereas in case of unintentional where prescribers are unaware or have little information on the consequences of combining two drugs more precautions are intended to be taken. 127 interactions were managed by monitoring of signs and symptoms followed by 48 interactions which were managed by dose adjustment. There were no studies showing such similar results. Out of 123 cases, DDIs were found more under neurology department followed by cardiology department. Hence, the prescriptions related to these departments should be closely monitored in future. No other study findings correlated with these findings.

CONCLUSION

A close monitoring of the medication chart is necessary to identify the potential DDIs which can lead to serious clinical problems in the patients. The study findings conclude that it is important to develop a systematic approach to minimize possible DDIs. The clinicians and other health-care professionals at the study site require an awareness program in regard to identification and management of DDIs, especially in case of unintentional prescribing of interacting drugs.

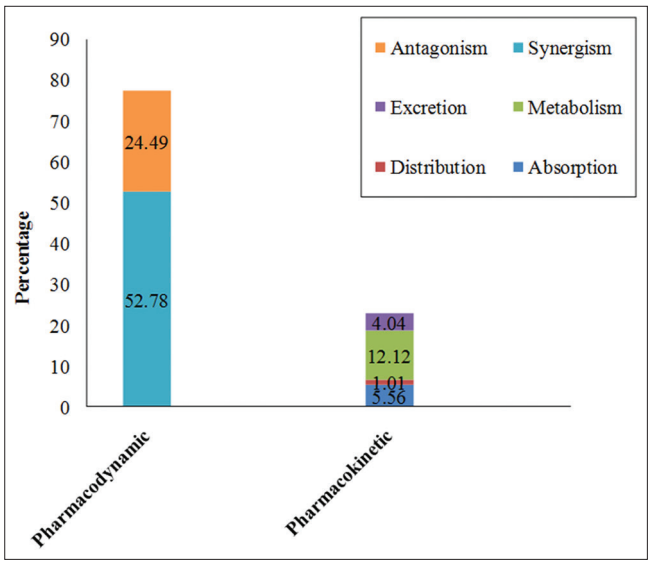

Fig. 1: Mechanism of drug-drug interaction

AUTHOR'S CONTRIBUTIONS

Dr. Siraj Sundaran has provided the design, intellectual content, innovations, and protocol for conducting the study along with mentorship. Ms. Greeshma K. George, Mr. Ashar Ali C. P, Mrs. Mubeena K. M., and Ms. Thansiya P. H. were involved with the adverse drug reaction reporting and data processing. Dr. Arun Gopalakrishnan was involved with the advisory of the study.

CONFLICTS OF INTEREST

The authors of this study declare that there is no conflict of interest regarding the publication of this article.

REFERENCES

1. Baxter K, editor. Stockley's drug interactions. General Considerations and an Outline Survey of Some Basic Interaction Mechanisms. 7th ed. London: Pharmaceutical Press; 2006. p. 1.
2. Jimmy OD, Rani RH, Indira R, Ramjan S. Study of drug-drug interactions in the medication charts in medicine wards at a tertiary care hospital. Indian J Pharm Pract 2012;5:61-4.
3. Kulkarni V, Bora SS, Sirisha S, Saji M, Sundaran S. A study on drug-drug interactions through prescription analysis in a South Indian teaching hospital. Ther Adv Drug Saf 2013;4:141-6.
4. Vaidhun BH, Amirthalingam S. Physicians expectations to prevent the drug interactions in clinical practice. Int J Pharm Pham Sci 2010;2:172-3.
5. Umretiya T, Patil NR, Manjunath G, Kumar C. Assessment of potential drug-drug interactions in the department of medicine at Basaweshwara teaching and General Hospital Gulbarga. J Pharm Sci 2015;5:90-6.
6. Tripathi KD. Essentials of Medical Pharmacology. 6th ed. New Delhi: Jaypee Brothers Medical Publisher's Private Limited; 2008.
7. 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 J Pharmacol 2014;46:152-6.
8. Lubinga SJ, 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. Afr Health Sci 2011;11:499-507.
9. Devireddy P, Rekha PS, Kamala S, Venkateswarlu K. Evaluation and management of drug-drug interactions in ambulatory Patients. Int J Pharm Res Rev 2015;4:8-14.
10. 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.
11. Bhagavathula AS, Berhanie A, Tigistu H, Abraham Y, Getachew Y, Unakal C. Prevalence of potential drug-drug interactions among internal medicine ward in University of Gondar Teaching Hospital, Ethiopia. Asian Pac J Trop Biomed 2014;4 Suppl 1:S204-8.
12. Ismail M, Iqbal Z, Khan MI, Javaid A, Arsalan H, Farhadullah H, *et al.* Frequency, levels and predictors of potential drug-drug interactions in a paediatrics ward of a teaching hospital in Pakistan. Trop J Pharm Res 2013;12:401-6.
13. Nag KA, Umesh M, Churi S. Assessment of drug-drug interactions in hospitalized patients in India. Asian J Pharm Clin Res 2011;4:62-5.
14. 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. Australas Med J. 2011;14:9-14.
15. Rahmawati F, Hidayati N, Rochmah W, Sulaiman SA. Potentiality of drug-drug interactions in hospitalized geriatric patients in a private hospital, Yogyakarta, Indonesia. Asian J Pharm Clin Res 2010;3:191-4.
16. Bertoli R, Bissig M, Caronzolo D, Odorico M, Pons M, Bernasconi E. Assessment of potential drug- drug interactions at hospital discharge. Swiss Med Wkly Eur J Med Sci 2010;140:1-6.
17. Zwart-van Rijkom JE. Frequency and nature of drug-drug interactions in a Dutch University Hospital. Br J Clin Pharmacol 2009;68:187-93.
18. Nobili A, Pasina L, Tettamanti M, Lucca U, Riva E, Marzona I, *et al.* Potentially severe drug interactions in elderly outpatients: Results of an observational study of an administrative prescription database. J Clin Pharm. Ther 2009;34:377-86.
19. de Almeida SM, Gama CS, Akamine N. Prevalence and classification of drug-drug interactions in intensive care patients. Einstein 2007;5:347-51.
20. Doubova SV, Reyes-Morales H, del Pilar Torres-Arreola L, Suarez-Ortega M. Potential drug-drug and drug-disease interactions in prescriptions for ambulatory patients over 50 years of age in family medicine clinics in Mexico City. BMC Health Serv Res 2007;7:1-8.
21. Cruciol-Souza JM, Thomson JC. A pharmacoepidemiologic study of drug interactions in a Brazilian teaching hospital. Clinics 2006;61:515-20.
22. Johnell K, Klarin I. The relationship between number of drugs-drug interactions in the elderly. Drug Saf 2007;30:911-8.
23. George RM, James E, Vijayalakshmi S. Clinical pharmacist's interventions on drug related problems in a tertiary care hospital. Int J Pharm Pharm Sci 2015;7:401-4.