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DETECTION OF POTENTIAL DRUG-DRUG INTERACTIONS IN PRESCRIPTIONS DISPENSED IN HOSPITAL PHARMACY

LIYA SIBY[1], ATHIRRA SUKUMARAN[1], ESWARAN MAHESWARI*[2]

[1]Department of Pharmacy Practice, M.S. Ramaiah College of Pharmacy, Bangalore, Karnataka, India.
[2] Department of Pharmacy Practice, Faculty of Pharmacy, M.S. Ramaiah University of Applied Sciences, Bangalore, Karnataka, India.

ABSTRACT

This prospective observational study examined the severity, type and frequency of potential drug-drug interactions (PDDIs) in prescriptions dispensed in the hospital pharmacies of M.S. Ramaiah Memorial Hospital and M.S. Ramaiah Hospital, Bangalore, Karnataka. A total of 500 prescriptions were collected over a period of 5 months. PDDIs were identified and analysed using Micromedex database. The frequency of PDDIs was 71.8%, with at least one interacting combination with major (14.20%), moderate (72.70%) and minor (13.09%) interactions. Out of the total PDDIs identified, 60% were pharmacodynamic interactions, 38% were pharmacokinetic interactions and 2% had interaction of unknown mechanism. The largest number of active drugs prescribed with major PDDIs were related to the cardiovascular system (32.63%), central nervous system (22.28%), gastrointestinal tract and drug metabolism (13.37%).The results of the present study showed a high frequency of PDDIs in prescriptions received at hospital pharmacies.

KEYWORDS: **Drug-drug interaction, Prescription, Severity, Frequency**

ESWARAN MAHESWARI
Department of Pharmacy Practice, Faculty of Pharmacy, M.S. Ramaiah University of Applied Sciences, Bangalore, Karnataka, India

INTRODUCTION

In modern health care, drugs are considered as essential tool for attaining desired therapeutic outcomes. But, these drugs may cause significant morbidity and mortality which may lead to increase in treatment cost.[1]Drug-drug interactions (DDIs) may occur due to alteration of activity of a drug with concomitant use of other drugs or by the presence of some other substance.[2]The factors leading to potential drug interactions are polypharmacy, drugs with narrow therapeutic index, Polypharmacy and health care system in which multiple physicians manage each patient. The common patient related factors are age, genetics, co-morbidities and patient non-compliance.Drug interactions may occur based on pharmacodynamics or pharmacokinetic nature of drugs. Pharmacodynamic interactions are due to receptor effects of different agents which interact to produce synergy or antagonism and pharmacokinetic interactions are due to altered plasma concentrations.[3] The medications such as beta-blockers, calcium channel blockers, diuretics, anti-arrhythmics, anti-epileptics, anti-psychotics, oral contraceptives, fluoroquinolones etc. are mainly involved in causing drug-drug interactions.[4-5] The number of drug interactions increases exponentially with the number of drugs used.[6] Incidence of DDIs are high although it is widely recognized to cause harm to the patients.[7] Most of the DDIs can be avoided or controlled safely through careful screening and proper interventions. Since DDIs are distressing problem for our society, health care providers have an important role in preventing them.[8] Pharmacists are in a privileged position to recognize PDDIs because medical prescriptions from multiple prescribers, dental prescriptions and persons approaching pharmacist for self-medications converge in the pharmacy. The pharmacist's role becomes vital in analysing and finding the appropriate strategies to minimize and prevent morbidity and mortality due to DDIs.The study was designed to evaluate the severity, type and frequencies of PDDIs in prescriptions dispensed at hospital pharmacy.

MATERIALS AND METHODS

A prospective observational study was carried out in pharmacies of M.S. Ramaiah Memorial Hospital and M.S. Ramaiah Hospital, Bangalore with the motive of identifying PDDIs in the prescriptions over a period of five months from January 2015 to May 2015. The study was initiated after obtaining approval from Institutional Ethics Committee. All prescriptions were reviewed and the patient's demographic data such as age, gender, frequency and number of drugs prescribed were entered into a suitably designed data collection form. All the prescriptions containing two or more drugs were included in the study and incomplete prescriptions were excluded. The selected prescriptions were reviewed for DDIs by using Micromedex database and standard textbooks. The identified DDIs were classified based on the type and severity of interaction as major, moderate and minor. All these data were gathered, analysed and presented in the form of tables and graphs as frequencies and percentages using Microsoft Excel 2010.

Criteria for frequency

Formula to calculate the frequency of PDDIs:

$$\text{Frequency of PDDIs} = \text{Total number of PDDIs} \div \text{Total number of prescriptions} \times 100$$

Criteria for evaluation of severity

The severity criteria was used for evaluation of PDDIs (Table 1).

Table 1
Criteria for Severity[19]

Criteria	Description
Minor	The effects are usually mild, consequences may be bothersome or unnoticeable but should not significantly affect the therapeutic outcome. Additional treatment is usually not required.
Moderate	The effects may cause deterioration in a patient's clinical status. Additional treatment, hospitalization, or extension of hospital stay may be necessary.
Major	The effects are potentially life threatening or capable of causing permanent damage.

RESULTS

A total of 500 prescriptions were investigated for the identification of PDDIs. Out of 500 prescriptions, 291(58.2%) were males and 209(41.8%) were females. In the current study, majority of patients 265(53 %) fall under the age group of 50 and above (elderly), followed by 213(42.6 %) in the age group of 17-49 years (adults), and 22(4.4 %) patients were in the age group of 2-16 years (paediatrics).In 207 prescriptions (41.4%) a total of 359 PDDIs were observed with a mean of 2.0 ± 1.47 and frequency rate of 71.8%, with atleastone interacting combination with 14.20% major, 72.70% moderate and 13.09% minor interactions. (Figure 1)

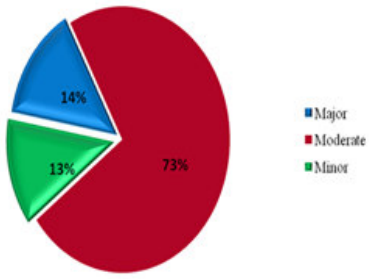

Figure 1
Severity of potential drug – drug interactions

Classification of drug- drug interactions based on severity
Out of 359 PDDIs identified, 60% was found to be pharmacodynamics (PD) interactions, 38% was observed as pharmacokinetic(PK) interactions and 2% was due to interaction of unknown mechanism. (Figure 2)

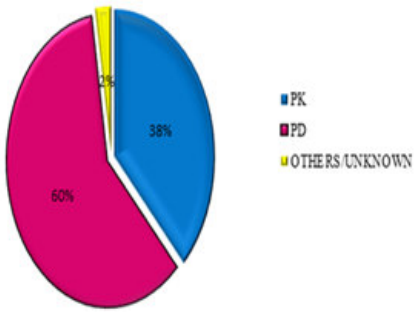

Figure 2
Type of potential drug-drug interactions

Out of 500 patients, majority (53%) of the patients belonged to above 50 years and the PDDIs were found to be maximum. (Figure 3)

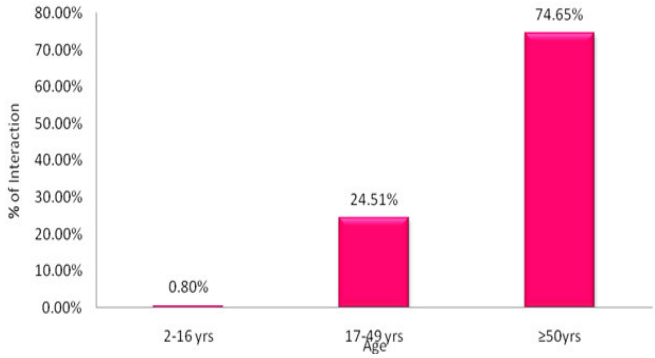

Figure 3
Correlation of age with potential drug - drug interactions

Prescriptions with one or more DDIs used a significantly large number of drugs with an average of 4.9 drugs (range 2-17 drugs).Approximately 47% of patients were prescribed with more than four drugs. Polypharmacy is highly prevalent in elderly population due to increased number of co-morbid disease states that accompany aging. (Figure 4)

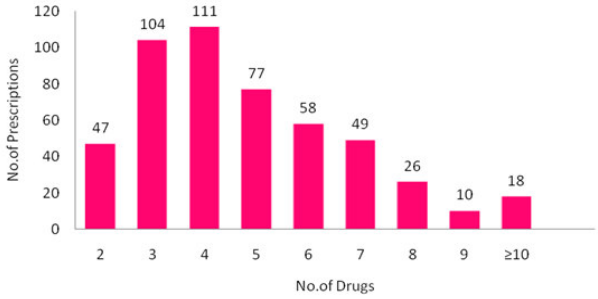

Figure 4
Number of drugs per prescription

In the current study, DDIs were classified based on the medication class involved. The drugs commonly producing interactions are cardiovascular drugs, antipsychotics and proton pump inhibitors (Figure 5).

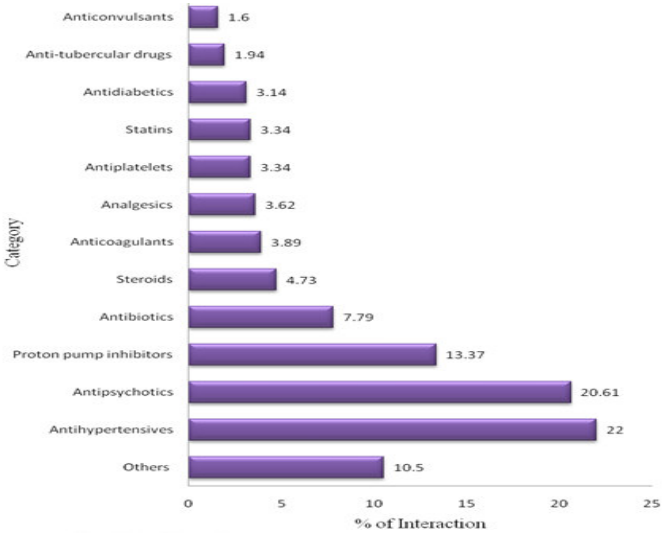

Figure 5
Category of drugs causing PDDIs

The detailed descriptions of all identified DDIs are given in table 2.Among the antihypertensive drugs, beta blockers (6.4%), calcium channel blockers (4.4%), angiotensin converting enzyme inhibitors (3.6%), angiotensin receptor antagonists (3.3%), diuretics (2.9%) and other antihypertensive drugs (1.4%) were found to cause PDDIs.

Table 2
Prevalence of potential drug-drug interactions (n = 207)

Interacting Drugs	Potential Adverse Outcome	Prescription (n)
Anticoagulant+Aspirin+ Clopidogrel	Increased risk of bleeding	16
Beta Blockers+ CCB	Increased risk of hypotension, bradycardia, AV conduction disturbance	14
Benzodiazepines+ SSRIs	Increased risk of drowsiness, dizziness, and confusion	11
Clopidogrel+ PPIs	Increased risk of thrombosis	9
Risperidone+Escitalopram	Increased risk of irregular heart rhythm	8
CCB+Atorvastatin	Increased exposure to statins and increased risk of myopathy or rabdomyolysis	8
Insulin+Ciprofloxacin	Increased risk of hypoglycemia or hyperglycemia	6
Ondansetron+Antibiotics	Increased risk of irregular heart rhythm	6
BetaBlockers+ Antidiabetics	Increased risk of hypoglycemia or hyperglycemia	5
Haloperidol+ SSRIs	Increased risk of drowsiness, dizziness and confusion	5
Atorvastatin+Ranolazine	Increased exposure to statinsand increased risk ofmyopathy or rhabdomyolysis	5
ACEI + Thiazide Diuretics	May result in postural hypotension	4
ACEI+Spironolactone	Hyperkalemia	4
Warfarin+ PPIs	Increased risk of bleeding	4
Rifampicin+Isoniazid	Hepatotoxicity	4
ACEI+NSAIDs	Decreased antihypertensive effects	3
Beta Blockers+NSAIDs	Decreased antihypertensive effects	3
Diuretics +NSAIDs	Decreased antihypertensive effects	3
Tramadol+Amitriptylline	Increased risk if seizures	1
Others		88

DISCUSSION

Currently, data regarding types and frequency of PDDIs in Indian settings is limited. Also, the prescribing pattern for most diseases differs in India with the western and other countries. Hence, the present study was conducted to evaluate the PDDIs in hospital pharmacy with reference to their nature, mechanisms, clinical significance and common drug group's involved.[9]In the current study, out of 500 prescriptions, 291(58.2%) were males and 209(41.8%) were females which was similar to a study carried out by Kafeel, et al., (2014) to evaluate the prevalence of DDIs among dispensed medications in Karachi.[10] In the present study, the mean age of the sample was 49.25 years, which was similar to that reported in other studies conducted by Patel, et al., (2014) in Gujarat on PDDIs among prescribed drugs in medicine outpatient department of a tertiary care teaching hospital. [3]In a total of 500 prescriptions, 293 (58.60%) prescriptions were without DDIs and remaining 207 (41.4%) had atleast one interacting combination with 14.20% major, 72.70% moderate and 13.09% minor interactions which was in accordance with studies performed by Dirin, et al., (2014) on PDDIs in prescriptions dispensed in community and hospital pharmacies in East of Iran[11] and by Kapadia, et al., (2013) on PDDIs in indoor patients of medicine department at a tertiary care hospital in India.[9]A total of 359 PDDIs were recorded with a mean of 2.0 ± 1.47. The frequency of PDDIs were found to be 71.8%. Among 207(41.4%) prescriptions with atleast one identifiable PDDIs, 44.60% were found among males and 36.84% among females which is contrary to a study carried by Kapadia, et al., (2013) in India[9]and many similar studies[12-13]which concluded that there is no statistically significant differences regarding the presence/absence of PDDIs between men and women. Out of 500 patients enrolled, majority of the patients (53%) belongs to the age group of 50 and above years, which is in line with pharmacoepidemiological study conducted by Cruciol-Souza, et al., (2006) on DDIs in Brazil[14] and in the current study, it was observed that it showed 71.8% of total PDDIs which was similar to other studies carried out by Kashyap, et al., (2013) to understand DDIs and their predictors in Indian elderly population[15] and Bertoli, et al., (2010) for assessing PDDIs at hospital discharge in Switzerland.[16]Out of the total PDDIs identified, 60% were PD interactions, 38% were PK interactions and 2% had interactions of unknown mechanism. The study carried out by Patel, et al., (2014)[6] and Kapadia, et al., (2013)[9]on PDDIs suggested higher number of PD mechanism of PDDIs similar to our study. PDDIs were significantly associated with prescriptions of three or more drugs. The largest number of active drugs prescribed with major DDIs were related to the cardiovascular system (diuretics, ACE inhibitors, digoxin, beta-blockers and calcium channel blockers), which is similar to the findings described in studies conducted in different settings. A Brazilian study carried out by Teixeira,et al., (2012) to investigate PDDIs in patients treated in primary care of Southern Brazil[1]reported that aspirin, metoprolol, amlodipine and enalapril were the most prescribed drugs which is in concordance to the current study. In the present study, the most commonly prescribed drugs were cardiovascular agents (32.63%) followed by drugs acting on CNS (22.28%) and on alimentary tract and metabolism (13.37%), which is similar to the study conducted by Doubova, et al., (2007)[13].The top most identified interacting drugs of high severity were found to be aspirin or combination of aspirin and clopidogrel along with anticoagulants. This result was found to be in line with study conducted by Kashyap, et al., (2013) to evaluate DDIs and their predictors in Indian elderly population.[15-1715]The results of the present study showed a high frequency rate of the PDDIs in prescriptions received at hospital pharmacies. The occurrence rate is directly proportional to increasing age of patient and the number of drugs in the prescription. Along with the observed PDDIs, drug utilization pattern[18] and standard treatment guideline should be provided to practicing physicians to improve the quality of patients health. The study showed the potential for PDDIs in the prescriptions but, whether they have actually occurred in the patients could not be determined because the study was a single point observational and outpatient based. Also, study was carried out for less period of time and alert card was not provided to patients.

CONCLUSION

Our study gives a preliminary data regarding an extent of PDDIs in outpatient; it provides a backbone on which further studies on PDDI can be planned focusing on particular drug groups frequently identified as culprits for adverse drug interactions.Facing the results of the current study, we can assume that the prevalence of PDDIs among elderly was high. Collaboration of health care professionals with the pharmacist can contribute in early detection and prevention of DDIs and its related hazard.A computerised DDI program (detection) together with clinical pharmacological experience (interpretation/evaluation), continuingeducation and vigilance on the part of prescribers toward drug selection can be useful for decreasing the number of potentially harmful drug combinations. This approach may lead to an improvement in the quality of prescription, reducing possible risks and thus contributing to patient safety.

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CONFLICT OF INTEREST

Conflict of interest declared none.

REFERENCES

1. Teixeira JJV, Crozatti MTL, Santos CA, Lieber NSR. Potential drug-drug interactions in prescriptions to patients over 45years of age in primary care, Southern Brazil. PLOS ONE. 2012;7(10): e47062.
2. Baxter K, Lee A, Stockley I. Drug-drug interactions in drug benefits and risks revised 2 edition Editors: Boxtel C, Santoso B, Edwards IR. Publishers: IOS Press Amsterdam, 2008; 247-262.
3. Patel PS, Rana DA, Suthar JV, Malhotra SD, Patel VJ. A study of potential adverse drug-drug interactions among prescribed drugs in medicine outpatient department of a tertiary care teaching hospital.J Basic ClinPharma. 2014;5(2):44-48.
4. Yeh YT, Hsu MH, Chen CY, Lo YS, Liu CT. Detection of potential drug-drug interactions for outpatients across hospitals. Int. J. Environ. Res. Public Health, 2014;11:1369-1383.
5. Rama et al. Assessment of drug-drug interactions among renal failure patients of nephrology ward in a south indian tertiary care hospital. Indian J. Pharm. Sci, 2012;74(1):63-68.
6. Cremades J, Gonzalo M, Arrebola I. Relationship between drug interactions and drug-related negative clinical outcomes in two community pharmacy. Pharmacy Practice. 2009;7(1):34-39.
7. Nabovati E, HasanVakili-Arki, ZhilaTaherzadeh, Hasibian MR, Ameen Abu-Hanna, SaeidEslami. Drug-drug interactions in inpatient and outpatient settings in Iran: a systematic review of the literature. DARU Journal of Pharmaceutical Sciences. 2014;22:52-65.
8. Nag KA, Umesh M, Churi S. Assessment of drug-drug interactions in hospitalised patients in India. Asian. J. Pharm. Clin. Res. 2011;4(1):62-65.
9. Kapadia J, Thakor D, Desai C, Dikshit RK. A study of potential drug-drug interactions in indoor patients of medicine department at a tertiary care hospital. J App Pharm Sci, 2013;3(10):089-096.
10. Kafeel H, Rukh R, Qamar H, Bawany J, Jamshed M, Sheikh R et al. Possiblity of drug-drug interaction in prescription dispensed by community and hospital pharmacy. Pharmacology and Pharmacy. 2014;5:401-407.
11. Dirin MM, Mousavi S, Afshari AR et al. Potential drug-drug interactions in prescriptions dispensed in community and hospital pharmacies in East of Iran. Journal of Research in Pharmacy Practice. 2014 ;3 (3):104-107.
12. Nagavi BG, Adepu R, Singhal R. Drug interactions in prescriptions from selected Indian community pharmacies. J Pharm Practice and Research. 2005;35(4):332.
13. Doubova SV, Reyes-Morales H, Torres-Arreola LP, Suárez-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;7:147-155.
14. Cruciol-Souza JM, Thomson JC. A pharmacoepidemiologic study of drug interactions in a brazilian teaching hospital. Clinics. 2006;61(6):515-520.
15. Kashyap M, D'Cruz S, Sachdev A, Tiwari P. Drug-drug interactions and their predictors: Results from Indian elderly inpatients. Pharmacy Practice. 2013;11(4):191-195.
16. Bertoli R, Bissig M, Caronzolo D, Odorico M, Pons M, Bernasconi R. Assessment of potential drug-drug interactions at hospital discharge. Swiss Med Wkly. 2010;140(3):1-6.
17. Manchon ND, Bercoff E, Lemarchand P, Chassagne P, Senant J, Bourreille J. Incidence and severity of drug interactions in the elderly: a prospective study of 639 patients. Rev Med Interne. 1989;10(6):521-525.
18. Sandozi T, Nausheen F. Drug utilization study in ischemic heart diseases associated with diabetes and hypertension. IJPBS. 2010; 1(3):1-419. Drug interaction facts. St. Louis, Mo.: Facts and Comparisons ; 2001.