

Full Length Research Paper

A prospective study on assessment of clinically potential drug-drug interactions in hospital and community pharmacy prescriptions

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Drug-drug interaction or simply term drug interactions may be defined as the combining of two or more drugs such that the potency or efficiency of one drug is significantly modified by the presence of another. Potential drug-drug interactions (DDIs) are concern for patients and providers, as multiple medication use is becoming more common to manage complex diseases. The consequences of DDIs can range from no untoward effects to drug-related morbidity and mortality. The study was prospective conducted for a period of twelve months in Government Headquarters Hospital Ooty (GHQH) and four community pharmacies that were located in Southern India, Tamilnadu. A total number of 1,066 prescriptions were collected from the patients. A copy of prescription was taken from the patients and data collected included age and sex of the patients, their primary diagnoses presence or absence of comorbidities and the list of medications prescribed concurrently. The potential DDIs were determined through IBM Micromedex Database. However, 147 DDIs were followed up for clinically drug interactions which were found not to be significant. Among the total numbers of prescriptions analyzed 402 (38%) prescriptions showed 462 DDIs and 664 (62.2%) total number of prescriptions collected from inpatient department, GHQH showed 147 DDIs. The DDIs were classified based on the mechanism of interactions, severity of interactions, drug causing DDIs and top combination of drugs and which were determined. This study emphasized on understanding about the most prone age group and the common mechanism that can cause drug interactions which will help in the safety and efficacy of prescribed drugs followed by its management.

Key words: Drug-Drug interactions, prescriptions, prevalence, severity, management.

INTRODUCTION

Drug-drug interactions (DDIs) are defined as the presence of two or more drugs where one drug significantly modifies the action of another drug (Bruno et al, 2007); Jindal et al., (2005) and Janchawee et al., (2005). This is a major concern for patients and health care

professionals as most of the diseases require multiple drug regimen. The consequences of DDIs can range from untoward effects to drug-related morbidity (Vonbach et al., 2007; Lubinga et al., (2011) and David et al., 2003) and mortality. Understanding the prevalence and patients

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At risk for clinically important DDIs at the visit level will be useful in minimizing medication-related problems and improving pharmaceutical care (Kennedy et al., 2015). Previous research has found that drug-drug interactions (potential DDIs) lead to adverse clinical outcomes, hospital admissions and emergency department (ED) visits. Health care professionals' ability to recognize potential DDIs is important in reducing the risk of potential DDIs and their adverse consequences. The consequences of DDIs can range from untoward effects to drug-related morbidity and mortality. Understanding the prevalence and patients at risk for clinically important DDIs at the visit level will be useful in minimizing medication-related problems and improving pharmaceutical care (Jorg et al 2007), (Mitja 2017). Previous research has found that drug-drug interactions (potential DDIs) lead to adverse clinical outcomes, hospital admissions and emergency department (ED) visits.

Health care professionals' ability to recognize potential DDIs is important in reducing the risk of potential DDIs and their adverse consequences (Malone et al., 2005), Elena et al, (2013), Janja et al., (2017). The potential benefits of drug combinations should be weighed against the seriousness of the DDI, taking into account the availability of alternatives. The risk associated with the drug-drug interactions are higher, hence alternative drug should be prescribed as to avoid potential DDI (Kaushikbhai et al., 2016) and Walter et al., (2007).

Understanding the prevalence and clinically DDIs at hospital level will be minimized and improving overall pharmaceutical care (Becker and Kallewaard, 2007). According to a study, the odds ratio of having at least one drug interaction, the rate of the drug interaction was the same for both genders when age was increased by 20 years (Rajender et al., 2007). The objectives of this study were to find out prevalence of potential DDIs among the collected hospital prescriptions and the community pharmacy prescriptions, and to categorize the identified interactions as to assess its severity, mechanisms involved and its management requirements.

MATERIALS AND METHODS

Study design and description of study settings

The study was prospectively cross-sectional design that was conducted for about a period of twelve months. From 12th January, 2018 up to 12th January, 2019 at the Government Headquarters Hospital Ooty (GHQH) and in four community pharmacies which were located at Southern Tamilnadu.

Inclusion criteria

The inclusion criteria were patients with at least more than one prescribed medications for pharmacies and admitted patients in hospital for more than two days consecutively.

Exclusion criteria

Patients prescribed with a single medication and patients prescribed with the topical formulations such as a creams, ointments, and gels.

Ethics

The study was approved by Institution Ethical Committee of JSS Academy of Higher Education and Research (Approval number: JSSAHER/OT/IEC/07/2017-18 Dated (06/01/2018).

Data extraction

The collected data was taken from patient's prescription and each prescription was analyzed and checked for potential DDI through Micromedex IBM data base, assessment and categorization of the interaction was found with the indication as per the Classification on Micromedex termed Contraindication. The drugs were contraindicated for concurrent use. Major 1: The interaction may be life threatening and/or require medical intervention to minimize or prevent serious adverse effects. Major 2: The interaction may be life threatening and/or require medical intervention to minimize or prevent serious adverse effects. Moderate: The interaction may result in exacerbation of the patient's condition and/or require an alteration in therapy. Minor: The interaction would have limited clinical effects. Manifestation may include an increase in frequency or severity of the side effects but generally would not require a major alteration in therapy, Unknown (Truven Health Analytics, 2016).

RESULTS

A total of 1,066 prescriptions were analyzed during the study period which was collected from Government Headquarters Hospital Ooty (GHQH) and from the four community pharmacies. Among the total numbers of prescriptions analyzed, 402 (38%) prescriptions showed 462 DDIs and 664 (62.2%) total number of prescriptions collected from inpatient department, Government Headquarters Hospital Ooty (GHQH) showed 147 DDIs (Table 2) where patients were followed up and assessed for clinically DDI and when frequency of administration was taken into consideration was not found clinically significant.

Demographics characteristic

The study showed that among the 402 prescriptions analyzed, 75.1% of drug interactions account for males and only 24.8% drug interactions account for females (Table 1). The grouping of the age categorization showed that as the age increases the chance of more number of drug interactions was observed.

Number of DDIs found in the prescription

The study showed that as the number of drugs prescribed increases the likelihood for a chance of an interaction.

Table 1. Demographic characteristics at four pharmacies.

Characteristics	Number of drug Interactions	Percentage
Gender		
Male (307)	347	75.1
Female (95)	115	24.8
Total (402)	462	100
Age categorization (years)		
Paediatrics (≤ 18)	121	26.1
Adult (19 - 60)	271	58.6
Geriatrics (>60)	70	15.15
Total	462	100

Table 2. Demographic characteristics at hospitalized patients.

Characteristics	Number of drug Interactions	Percentage
Gender		
Male (216)	98	66.67
Female (448)	49	33.33
Total (664)	147	100

Categorization of drug interactions based on mechanism

Categorization of drug interactions based on mechanism are shown in Table 5 and Figure 1, the study showed that prescriptions had more number of pharmacokinetic interactions than compared to pharmacodynamics and interactions due to unknown mechanisms.

Categorization of drug interactions based on severity

Categorization of drug interactions based on severity is as shown in Figure 2. The study showed more number of moderate (32%) interactions as compared to minor (18%) and major (49%) interactions.

Management required for the drug interactions documented

The types of management required for the clinically drug interactions are shown in Table 7. The study showed most of the interactions requires dose adjustment and monitoring for toxicity.

DISCUSSION

Clinically, potential DDI is a major concern for patients and health care professionals as most diseases require multiple drug regimens (Aline et al., 2015) and Raymond

et al. (2008). The consequences of DDIs can range from untoward effects to drug-related morbidity and mortality (Zelalem et al., 2017) and (Rajender et al., 2007). Understanding the prevalence and patients at risk for clinically important DDIs at the visit level will be useful in minimizing medication-related problems and improving pharmaceutical care (Angeles and Sacramento, 2016) and (Catherin et al., 2003). Previous research has found that potential DDIs lead to adverse clinical outcomes, hospital admissions and emergency department (ED) visits (Becker and Kallewaard, 2007). Health care professionals' ability to recognize potential DDIs is important in reducing the risk of potential DDIs and their adverse consequences (Kulkarni et al., 2013; Yu et al., 2007 and Vijay et al., 2013).

A total of 1,066 prescriptions were analyzed during the study period from the government hospital where Number of Drug interactions per Hospitalised Patients found 102(69.4%), 28(19%), 17(11.66%) (Table 4) and selected four community pharmacies of which 402 (38%) prescriptions showed 462 DDIs. Prescriptions with single drug interactions was found to be high 53.73% (n=216) followed by two drug interactions 25.37% (n=102), three drug interactions 11.94% (n=48), four drug interactions 4.47% (n=18), six drug interactions 2.98% (n=12) and five drug interactions 1.6% (n=06). Age categorization revealed that adults (19-60 years) showed a greater number of interactions 58.17% (n=271) compared to pediatrics (≤ 18 years) 26.1% (n=121) and geriatrics (>60 years) 15.15% (n=70). The study prescriptions comprised 73.92% pharmacokinetic, 96% was pharmacodynamic

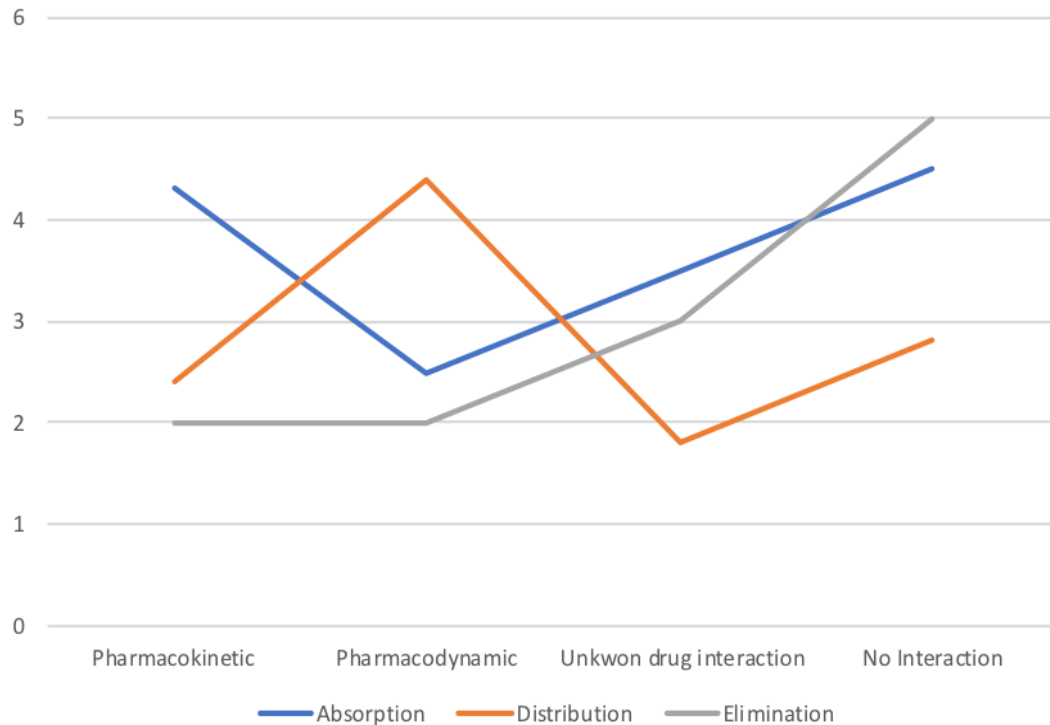


Figure 1. Categorization of the drug-drug interactions based on mechanism.

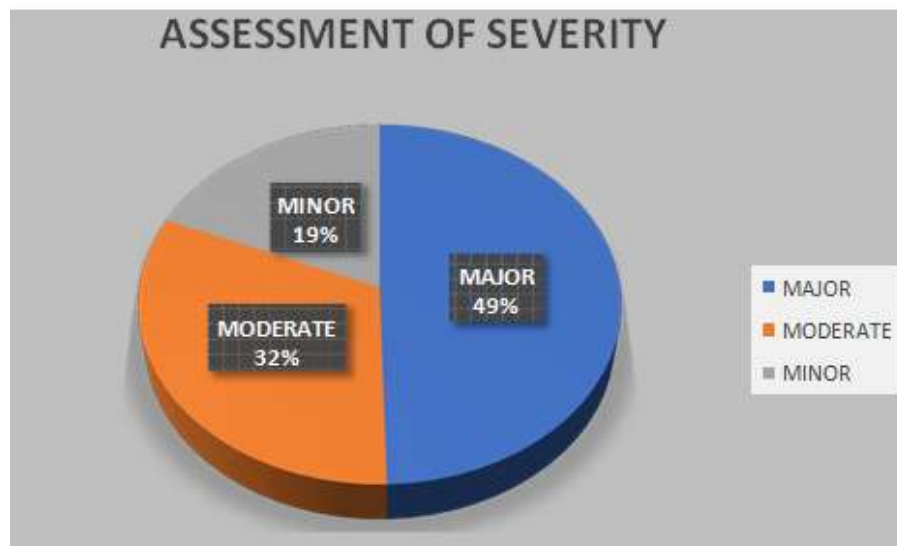


Figure 2. Assessment of severity.

and 6.68% of interactions were due to unknown mechanisms 18% (Table 3). Statistical analysis did not show significant difference within the pharmacokinetic drug interactions, where drug interaction due to altered metabolism occurred most often 67.67%, followed by absorption related drug interaction (4.3%) and interaction related to distribution (1.07%). There were a greater

number of major drug interactions (49%) which among of the potential drug -drug interactions occurred due to mostly frequently Responsible drugs for an Interaction as shown in (Table 6) than moderate (32%) and minor interactions were found among the prescriptions. The present study shows the prevalence of DDIs as 38% which was found similar to the results obtained from the

Table 3. Number of Drug Interactions per patients at four pharmacies.

Number of drugs	Number of patients	Number of drug interactions (%)
2 - 5	254	297 (64)
6 - 10	144	151 (32.54)
> 10	4	14 (3.44)

Table 4. Number of Drug Interactions per hospitalized patients at GHQH

Number of drugs	Number of patients	Number of drug interactions (%)
2 - 5	209	102 (69.4)
6 - 10	310	28 (19)
> 10	145	17 (11.66)

Table 5. Categorization of drug interactions based on the mechanism.

Categorization	No. of drug interaction	Percentage	
Pharmacokinetic Drug Interactions	Absorption	20	4.3
	Distribution	5	1.07
	Metabolism	314	67.67
	Excretion	04	0.86
	Total	343	73.92
Pharmacodynamic Drug Interactions	88	18.96	
Unknown Mechanism	31	6.68	
Total	462		

Table 6. Mostly frequently responsible drugs for an interaction.

Class/Name of the drugs	No. of interactions found (295)
Antiplatelet	24 (8.13%)
Clopidogrel	19
Prasugrel	05
NSAIDS	33 (11.1%)
Aspirin	14
Aceclofenac	08
Diclofenac	08
Ibuprofen	03
Oral Hypoglycaemic	27 (9.1%)
Metformin/Glimepiride	24
Sitagliptin	03
Calcium channel blockers	16 (5.4%)
Amlodipine	11
Verapamil	05
Antiarrhythmic	12 (4.06%)
Amiodarone	09
Quinidine	03

Table 6. Cont'd

PPIs	14 (4.7%)
Rabeprazole	03
Omeprazole	07
Propanazole	04
Loop Diuretics	21 (7.1%)
Furosemide	18
Torsemide	03
Antifungal	09 (3.0%)
Fluconazole	09
Anticonvulsant	18 (6.1%)
Phenobarbital	08
Clonazepam	06
Carbamazepam	04
Antidepressant	13 (4.4%)
Amitriptyline	07
Citalopram	04
Duloxetine	02
Corticosteroids	21 (7.1%)
Prednisolone	12
Dexamethasone	09
Vit. Supplementants	09 (3.05%)
Niacin	03
Vit.B12	02
Vit.B	04
Fluoroquinolones	34 (11.52%)
Levofloxacin	16
Norfloxacin	08
Ofloxacin	06
Ciprofloxacin	04
K⁺Sparing lactone	09 (3.05%)
Spirolactone	09
Macrolide antibiotics	18 (6.1%)
Azithromycin	11
Erythromycin	07
D2 Receptor blocker	17 (5.7%)
Domperidone	17
Total	295 (100%)

studies conducted by Patel Jaskumar et al. (2016) and Kafeel et al. (2014) (Fantaye et al 2016). The underlying mechanism in the 462 interactions was found to be 73.92% of pharmacokinetic mechanism, 18.96% of pharmacodynamics mechanism and 6.68% involving

unknown mechanisms. While assessing the severity of the drug interactions, 49% were major, 32% were moderate, and 19% of the interactions were minor. The study showed that majority of the interactions require dose adjustments and monitoring for signs and symptoms

Table 7. Management requirements for the drug interactions documented.

Management	Number of drug interactions (%)
Monitor for drug levels	46(9.9)
Dosage adjustment	62 (13.4)
Monitor for electrolyte levels	28 (6.0)
Avoid the combination	37 (8.0)
Monitor for signs and symptoms	55(11.9)
Monitor for biochemical parameters	39 (8.44)
Monitor for drug level and biochemical parameters	7 (1.5)
Monitor for signs and symptoms and biochemical parameters	28(6.0)
Monitor for signs and symptoms and drug level	12 (2.6)
Monitor for patient response	17(3.62)
Monitor for patient response and dose adjustment	21 (4.54)
Dose titration	15(3.3)
Monitor for electrolyte and drug level	05(1.08)
Change dosing interval	39 (8.44)
No management required	51 (11.0)

for toxicity as compared to other methods of management which is similar results were obtained from the study (Murphy and Armstrong, 2009).

Conclusion

The present research study assessed the clinically potential DDIs in a hospital and community pharmacy prescriptions. The study analyzed that most of the interactions would be managed by dose adjustment, monitoring patients for signs and symptoms for toxicity and a long term need to follow up patients for clinically DDI. This study elaborates that the nature of clinically drug interaction is a complex process due to involvement of multiple mechanism and thus impossible to document all clinically significant DDIs.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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