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Study of Drug-Drug Interactions in General Medicine Department of a Tertiary Care Hospital

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ABSTRACT

Objectives Drug therapy (DT) is growing more complex, thus appropriate drug prescription becomes increasingly challenging. Drug interactions (DI) are one of the important factors that modify the response to a drug. The main objective of this study was to monitor the potentially serious and significant Drug-Drug Interactions (DDIs).
Material and methods The number of drugs prescribed for each patient, drugs taken by the patient and the drug interactions were recorded. The interactions between the drugs were assessed using Micromedex software and Stockley's Drug Interaction. The type and severity of prescription with DDIs was also assessed.
Results The number of potential DDIs for the study population was 390 and each prescription had at least one interaction. Of the total potential DDIs (n=390) identified, majority were of moderate severity (n = 257, 65.90%). Most frequent DDI was seen between Metformin + Ranitidine (moderate interaction) in 70 prescriptions (50%) and between Ranitidine + Acetaminophen (minor interaction) in 48 prescriptions (34.29%). The common major interactions were seen between Rabeprazole + Clopidogrel in 4 prescriptions (2.86%), Enalapril + Spironolactone and Ciprofloxacin + Tramadol in 3 prescriptions (2.14%).
Conclusion The drug related problems, primarily the drug interactions is a permanent patient related risk in hospitals and the utilization of computer software has become the best way to identify and prevent them.

INTRODUCTION

Drug therapy (DT) is growing more complex, thus appropriate drug prescription becomes increasingly challenging. Drug interactions (DI) are one of the important factors that modify the response to a drug. Drug-Drug Interactions (DDI) can result in anything from minor morbidities up to fatal consequences. The main causes of hospital admission and mortalities are related to DI and their corresponding adverse effects (AE). It has been estimated that 10-20% of hospital admissions are caused by drug related events, and about 1% are caused by Drug Interactions (Jankel and Fitterman, 1993). Drug Interactions may produce beneficial or desirable, or undesirable or harmful effects (Doubova *et al*., 2007). The beneficial effects are those whose purpose is to treat concomitant disease, enhancing the effectiveness, reducing AE and allowing to reduce the dose, while the undesirable effects may reduce the drug effectiveness and may produce unwanted, noxious and even life threatening effects in the body, along with the increased treatment cost. The undesirable interactions may result in impact on the patient. DDIs can lead to alteration of therapeutic response or increase untoward effects of many drugs (Baxter and Stockley, 2010). Adding each drug combination increases chances of further DDI. Special attention and thorough monitoring is definitely required for the patients who are at the most risk of developing pDDIs (Rana *et al*., 2014). Now-a-days, many patients are on polypharmacy for treating their disease conditions and there are many interactions between the drugs prescribed in each prescription.

There are very less number of Drug-Drug Interaction studies that focus on type, severity of potential for adverse drug-drug interactions. The main aim and objective of this study was to monitor the potentially serious and significant Drug-Drug Interactions (DDIs), to evaluate the nature and mechanism of these interactions and to identify the common and causal drug groups for these DDIs. Hence this study was carried out to evaluate the types and severity of possible DDIs in General Medicine department.

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MATERIALS AND METHODS

This cross-sectional study was carried out in the department of General Medicine after getting approval from the Institutional Ethics Committee, School of Pharmaceutical Sciences, Vels University. All the patients coming to the inpatient general medicine department, who were greater than 18 years and who were prescribed with 4 or more drugs were included in the study.

Pregnant ladies and psychiatric patients were excluded from the study. Prior approval from all the patients was obtained in the patient consent form. The patients were followed from the time of admission till discharge. The patient demographics, details of prescribed medication and discharge medications were all recorded in a specially designed proforma. The interactions between the drugs were assessed using Micromedex software and Stockley's Drug Interaction (Baxter and Stockley, 2010). The type and severity of prescription with DDIs was also assessed.

RESULTS

In this study, 140 patients were on polypharmacy. The most common medications include anti-hypertensives and oral hypoglycaemic drugs. Majority of patients were in the age group of 51-60 years (n=34, 24.28%), followed by 41-50 years (n=33, 23.57%). Among 140 patients, majority were male. Majority of the patients do not have any social habits of smoking or drinking.

The diagnosis and co-morbidities in General Medicine department were given in table 1.

Table 1: Diagnosis and co-morbidities in general medicine department.

Co-morbidities	No. of patients (n=140)
Ischemic Heart Disease (IHD)	10
Diabetes Mellitus (DM)	42
Hypertension (HTN)	34
Gastrointestinal (GI) Problems	32
Pyrexia	22
Renal Disorders	15
Blood Disorders	5
Poisoning	2
Respiratory Problems	27
Headache/Cerebrovascular Accident (CVA)	12
Thyroid Disorders	8
Ortho Problems	7
Dermatological Problems	3
Neurological Problems	5

Among 140 prescriptions, 390 interactions were found. Among them, 51.8% were of pharmacodynamic interactions and 48.2% were of pharmacokinetic interactions.

Majority of the interactions were of moderate severity (n=257, 65.9%), followed by minor interactions (n=120, 30.77%).

The commonly found potential drug drug interactions along with the severity and number of patients were shown in table 2.

Among 390 interactions, 13 were of major interactions. The major interactions were listed in table 3. The frequency of drug-drug interactions among 140 interactions was depicted in table 4.

Table 2: Commonly found potential Drug-Drug Interactions.

Severity level	Interacting drugs	No. of patients
Major	Ciprofloxcin / Prednisolone	2
	Enalapril / Spironolactone	3
	Ciprofloxacin / Tramadol	3
	Rabeprazole / Clopidogrel	4
	Ciprofloxacin / Theophylline	1
Moderate	Metformin / Ranitidine	70
	Enalpril / Asprin	35
	Aspirin / Insulin	51
	Enalapril / Metformin	64
	Enalapril / Insulin	37
Minor	Ranitidine / Acetaminophen	48
	Enalapril / Amlodipine	30
	Aspirin / Rabeprazole	16
	Ranitidine / Diclofenac	26

Table 3: List of Major Drug-Drug Interactions.

Drugs	No. of patients (%)	Potential effect
Ciprofloxcin / Prednisolone	2 (15.38%)	Ciprofloxacin given together with prednisolone can increase the risk of tendinitis and tendon rupture.
Enalapril / Spironolactone	3 (23.08%)	Concomitant use of angiotensin converting enzyme (ACE) inhibitors and potassium-sparing diuretics may increase the risk of hyperkalemia.
Ciprofloxacin / Tramadol	3 (23.08%)	The risk of seizures may be increased during co administration of tramadol with any substance that can reduce the seizure threshold, such as selective serotonin reuptake inhibitors.
Rabeprazole / Clopidogrel	4 (30.76%)	Co administration with proton pump inhibitors (PPIs) may reduce the cardio protective effects of clopidogrel.
Ciprofloxacin / Theophylline	1 (7.7%)	Co administration with ciprofloxacin may increase the serum concentration of theophylline and the associated risk of toxicity.

Table 4: Frequency of drug-drug interactions.

Frequency of DDIs	Number of patients (n=140)	Percentage
1	64	45.72%
2	14	10%
3	8	5.71%
4	14	10%
5	28	20%
>5	12	8.57%

DISCUSSION

Drug-drug interactions (DDIs) are a concern for all stake holders, especially patients and this risk increases as greater number of medications was commonly used to manage complex conditions. The study utilized a computer system to verify the possibilities of drug interactions in medical prescriptions.

During 6 months of study, 140 prescriptions were analysed out of which 76 (54.2%) were male and 64 (45.8%) were female. Among them, 13 prescriptions were with major interactions, 257 prescriptions with moderate and 120 prescriptions with minor interactions. Major DDIs were identified

in about 3.33% of the study subjects and majority of the patients do not have any social habits.

Majority of the patients were in the age group of 51 – 60 years (n=34, 24.28%), which was similar to the study conducted by Doubova *et al*., 2007.

The number of pDDIs for the study population was 390 and each prescription had at least one interaction. Of the total pDDIs (n=390) identified, majority were of moderate severity (n = 257, 65.90%). It was similar to the study conducted by Patel *et al*., 2011, Riechelmann *et al*., 2007, Riechelmann *et al*., 2008, Dinesh *et al*., 2007.

Of the pDDIs (n=390) observed, majority were of pharmacodynamic (n=202, 51.80%) in nature followed by pharmacokinetic (n=188, 48.20%). These findings were contrast to the study reported by Vonbach *et al*., 2008 and Aparasu *et al*., 2007.

Most frequent DDI was seen between Metformin + Ranitidine (moderate interaction) in 70 prescriptions (50%) and between Ranitidine + Acetaminophen (minor interaction) in 48 prescriptions (34.29%). The common major interactions were seen between Rabeprazole + Clopidogrel in 4 prescriptions (2.86%), Enalapril + Spironolactone and Ciprofloxacin + Tramadol in 3 prescriptions (2.14%). The major interaction seen between Rabeprazole + Clopidogrel was similar to the study conducted by Juurlink *et al*., 2001 in which the major interaction was found between Clopidogrel and Proton Pump Inhibitors other than Pantoprazole.

CONCLUSION

The drug related problems primarily the drug interactions is a permanent patient related risk in hospitals and the utilization of computer software has become the best way to identify and prevent them. Pharmacist involvement may not only highly increase the reporting rate but also the quality of reporting. Hence the pharmacist participation in the multidisciplinary healthcare team can improve the treatment to hospitalized patients and promote drug safety.

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