Research Article

Kousalya Kaliamurthy et al. /BioMedRx 2013,1(1),11-14

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A study on drug-drug interactions in inpatients of general medicine department in a tertiary care teaching hospital

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Received on:16-10-2012; Revised on: 22-11-2012; Accepted on:27-12-2012

ABSTRACT

Objective: Many studies have been done on drug interactions in their local hospitals. Drug interactions may lead to an increase or decrease in the beneficial or the adverse effects of the given drugs. We want to know the incidence rate of drug interactions in a tertiary care hospital in Chennai, our hospital setting, so that this data will be useful in creating awareness among the health care professionals. To study the incidence, frequency and severity of drug-drug interactions in patients admitted in General Medicine Department of Sri Ramachandra Hospital, and to create awareness among the health care professionals. **Methods:** A prospective observational study was carried out in Inpatient department of General Medicine in a tertiary care teaching hospital. All inpatients of both sex and who were taking at least four or more drugs (polypharmacy) were included in the study. Over dosage cases were excluded from the study. The medications of the patients were analyzed for possible drug interactions by using computerized data base systems. Statistical analysis was done by Pearson correlation and nonparametric correlation to see the relationship between the number of drugs prescribed and the occurrence of pDDIs. **Results and Discussion:** 425 cases were analyzed. 342 prescriptions were with interactions. pDDIs were identified in about 80.5% of the study subjects. Of 1872 pDDIs, the major interactions were seen in 4.5%, moderate in 75.6% and minor in 19.9% of the patients. Among the DDIs, the majority were of pharmacodynamic (69.5%), followed by pharmacokinetic (23.4%) and unknown (7.1%). Statistical analysis by Pearson correlation and also by Nonparametric correlation (Kendall's tau) showed that there was an extremely significant linear relationship ($r = 0.623$, $r=0.496$) ($p<0.0001$) between the number of drugs prescribed for a patient and the occurrence of pDDIs. **Conclusion:** This article will be useful in rationalizing the prescribing pattern by creating awareness among the physicians about the drug interactions. Detection and reporting of DDIs should be done by all health professionals to ensure patient's safety. The pharmacist participation in the multidisciplinary team can improve the treatment to hospitalized patients and promote drug safety.

KEYWORDS: Potential Drug-Drug Interactions (pDDIs), Severity, Pharmacokinetic, Pharmacodynamic

INTRODUCTION

Drug therapy is a complex process and hence rational drug prescribing is increasingly challenging. The isolated utilization of such drugs may bring various benefits, but the drug interactions may affect the expected therapeutic benefits. Drug-drug interactions can result in anything from minor morbidities up to fatal consequences.

The main reason for patients admitted to hospital and the mortalities are related to drug-drug interactions and their harmful effects. Drug-related events cause about 10-20% of hospital admissions and drug interactions cause 1% of hospital admissions. [1]

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A potential drug interaction is a situation in which one drug affects the activity of another drug, when both are administered together. It may result in increased or decreased effects of the drugs or a new effect can be produced that neither produces on its own. [2] The drug-drug interaction increases as the number of medications increase. Drug-drug interactions may produce beneficial effects or unwanted effects. [3]

When two or more drugs are administered, the activity of one or both the drugs may be altered, resulting in the formation of a new compound, before the administration of drug in the body is pharmaceutical interaction. When the pharmacological effect of the drug is altered during its absorption, distribution, metabolism or elimination process, it is known as pharmacokinetic interaction. The synergism and antagonism effects among drugs occurring at the site of action are called pharmacodynamic interactions. [4,5]

The pharmacist, along with the prescriber must ensure that the patients are aware of the side effects caused by the drugs. The role of a pharmacist is to promote drug utilization evaluation to minimize the drug interactions. The nature and severity of all drug-drug interactions should be identified to educate the staff (physician, nurses, etc.). [6,7]

Hence the main objective of the study was to report the incidence, frequency and severity of drug-drug interactions in patients admitted in General Medicine Department of Sri Ramachandra Hospital.

MATERIALS AND METHODS

A prospective observational study was carried out for a period of nine months (July 2011- March 2012) in a tertiary care teaching hospital. Ethical approval was obtained from the Research and Ethics Committee, prior to study initiation. Patients admitted in general medicine department of male and female medical wards were included in the study. Prescriptions with four or more drugs prescribed were selected for the study. Over dosage cases were excluded from the study.

All the necessary and relevant data were collected from inpatient case notes, treatment charts, and laboratory data reports and were entered in the patient proforma. The patient and their case notes were followed till discharge. Drug interactions were identified using computerized drug-drug interaction data base systems such as drugs.com, medscape, uptodate and micromedex. Then by using these computerized data bases, the drug-drug interactions were identified and classified according to databases. According to severity, PDDIs were classified as

1) MAJOR- Life threatening effects or permanent damage may be caused.
2) MODERATE- Patient's clinical status may be diminished and hospital stay may be extended or additional treatment needed.
3) MINOR-Mild effects.

Depending upon the mechanism of interaction, drug interactions are subdivided into three groups: pharmaceutical, pharmacokinetic and pharmacodynamic interactions. Statistical analysis was done by Pearson correlation and nonparametric correlation to see the relationship between the number of drugs prescribed and the occurrence of pDDIs.

RESULTS

During the study period, 425 prescriptions were analyzed out of which 198(46.6%) were male and 227(53.4%) were female, who were randomly selected. Among them 342 prescriptions were with interactions and 83 prescriptions were without interactions. The no. of drugs dispensed and the severity of drug-drug interactions were shown in table 1.

The commonly found pDDIs were shown in table 2.

The classification of the pDDIs was made based on their mechanism like pharmacodynamic, pharmacokinetic and unknown. Of the pDDIs (n=1872) observed, majority were of pharmacodynamic 1302(69.5%) in nature followed by pharmacokinetic 438(23.4%) and unknown 132 (7.1%) interactions which were shown in table 3.

The number of drug interactions present in the prescription based on age was shown in table 4.

In our study, the average number of patients =48 years of age were 36.43 and >48 years of age were 61.8 and t-test showed that there was a statistically significant difference found between the 2 age groups ($p<0.0001$). The average number of drugs prescribed was 7.725 and 8.24 respectively. There was no significant difference between the two groups in relation to the drugs prescribed. The average number of interactions was 4.08 and 6.26 respectively and the interactions between the 2 groups were extremely significant (Table 5).

Table.1. No. of Drugs Dispensed and Severity of Drug-Drug Interactions

Characteristics No. of drugs dispensed	Number No. of patients (n=425)	Percentage (%)
≤5	93	21.9
6-10	281	66.1
11-15	45	10.6
16-20	6	1.4
>20	0	0
Severity of DDI	**No. of Interactions (n=1872)**	
Minor	373	19.9
Moderate	1415	75.6
Major	84	4.5

Table.2. Commonly Found Potential Drug-Drug Interactions

Severity Level	Interacting Drugs	No. of Patients
Major	Hydrocortisone/Levofloxacin	13
	Enalapril/Spironolactone	10
	Enalapril/Potassium chloride	8
	Ciprofloxacin/ Tramadol	7
	Potassiumchloride/ Spironolactone	6
Moderate	Metformin/ Ranitidine	38
	Enalapril/ Aspirin	32
	Aspirin/Insulin	30
	Enalapril/ Metformin	28
	Insulin/Metformin	25
	Enalapril/Insulin	24
	Atorvastatin/Clopidogrel	22
	Atorvastatin/Pantoprazole	19
Minor	Ranitidine/ Acetaminophen	84
	Enalapril/ Amlodipine	26
	Aspirin/ Metoprolol	22
	Aspirin/ Rabeprazole	14
	Rantac/Diclofenac	14

Table.3. Classification of PDDIs

Potential DDIs	Number (n=1872)	Percentage (%)
Pharmacodynamic	1302	69.5
Pharmacokinetic	438	23.4
Unknown	132	7.1

Table.4. No. of Drug Interactions Present in the Prescription Based on Age

Age	No. of Patients (n=342)		Drugs (n=2757)		Interactions (n=1872)	
	Number	Mean	Number	Mean	Number	Mean
18-27	20	22.2	136	6.8	58	2.9
28-37	34	32.5	277	8.14	135	3.9
38-47	58	42.01	448	7.7	245	4.2
48-57	94	52.6	814	8.6	563	5.98
58-67	74	62.18	593	8.01	481	6.5
68-77	51	71.58	400	7.8	317	6.2
>77	11	82	89	8.09	73	6.6

Table.5. Drug Interactions Based on Age (≤48 & >48)

Characteristics	Age		P value
	≤48	**>48**	
No. of patients	120	222	**<0.0001**
Mean	36.43	61.8	Considered extremely significant
Interactions	481	1391	**<0.0001**
Mean	4.08	6.26	Considered extremely significant
Drugs	927	1830	**0.0666**
Mean	7.72	8.24	Considered not quite significant

In our study, statistical analysis by Pearson correlation and also by Nonparametric correlation (Kendall's tau) showed that there was an extremely significant linear relationship ($r = 0.623$, $r=0.496$) ($p<0.0001$) between the number of drugs prescribed for a patient and the occurrence of pDDIs. 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 patient.

DISCUSSION

Drug-drug interactions (DDIs) are a concern for all stake holders, especially patients and this risk increases as greater numbers of medications are commonly used to manage complex conditions. Computer system was utilized to verify the possibilities of drug interactions in medical prescriptions. [8]

pDDIs were identified in about 80.5% of the study subjects. The average number of pDDIs per patient for the study population was 5.46±4.56.

The mean age of the patients was 51±15.577 (range 18-90, 95% CI 48.485-52.556) years. Majority of the patients fall in the age group of 48-57 (n=105, 24.7%). The total number of medicines prescribed to the 425 patients was 3,214 with an average of 7.562±2.525 drugs per patient (range 4-17). The study conducted by Doubova et al (2007) on 'Potential drug-drug and drug-disease interactions in prescriptions for ambulatory patients over 50 years of age in family medicine clinics in Mexico city' reports that the total number of medicines prescribed to the 624 patients was 3,739 with an average of 5.9±2.5 drugs per patients. [9]

Out of 342 patients with interactions, 48 had atleast one interaction. Of the total pDDIs (n=1872) identified majority were of moderate severity 1415(75.6%). It is similar to the study conducted by Patel VK et al (2011), Zimmermann C et al (2008), Riechelmann RP et al (2007), Dinesh KU et al (2007). [8, 10-12]

Most frequent drug-drug interactions were seen between metformin and ranitidine (moderate interaction) in 38 prescriptions (2.7%) and also between ranitidine and acetaminophen (minor interaction) in 84 prescriptions (22.5%). The major interactions were seen between Hydrocortisone+ Levofloxacin in 13 prescriptions (15.5%) and Enalapril+ Spironolactone in 10 prescriptions (1%). The major interaction seen between Clopidogrel+ Rabeprazole in 2 prescriptions (2.4%) is similar to the study conducted by Juurlink DN et al (2001) in which the major interaction was found between clopidogrel and proton pump inhibitors other than pantoprazole. [13]

Of the pDDIs (n=1872) observed, majority were of pharmacodynamic in nature followed by pharmacokinetic interactions. These findings were in contrast to the study reported by Vonbach and Aparasu, who reported 76% of pharmacokinetic and 22% of pharmacodynamic interactions. [14,15]

These potential drug-drug interactions were reported to the consulting physician and the patients prescribed with these drugs were monitored. Hence any serious or harmful effects of the drugs due to interactions were prevented.

- The best way to identify and treat drug interactions is the use of computer programs.
- Detection and reporting of DDIs should be done by all health professionals to ensure patient's safety.
- Pharmacists' involvement may not only greatly increase the reporting rate but also quality of reporting.
- The pharmacist participation in the multidisciplinary team can improve the treatment to hospitalized patients and promote drug safety.

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Source of support: Nil, Conflict of interest: None Declared