A study on drug–drug interactions through prescription analysis in a South Indian teaching hospital

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Abstract

Objective: The objective of this study was to assess the drug–drug interactions (DDIs) through prescription analysis among the inpatients of a South Indian teaching hospital.

Methods: The study was a prospective observational prescription analysis conducted for a period of 6 months, from October 2010 to March 2011. The prescriptions having two or more drugs and where a DDI was suspected were selected by the physician in charge of the ward. The drugs in the prescription were then entered into the drug interaction checker software. The DDIs were classified based on the mechanism of interactions, severity of interactions, relation to the number of drugs prescribed, and disease conditions were also determined.

Results: A total of 204 prescriptions were analyzed, of which 186 prescriptions had 856 DDIs. Most of the DDIs were pharmacokinetic drug interactions (42%) followed by unknown mechanisms (34%) and pharmacodynamic mechanisms (24%). The study findings showed that the prescriptions for cardiovascular with respiratory disease conditions had the greatest number of drug interactions on average. A severity assessment showed that majority of the DDIs were moderate (70%) followed by minor (28%). The study results showed that as the number of drugs increases in a prescription, the number of DDIs also increases. The interventions determined showed that dosage adjustment (12%) was to be followed in most of the DDIs.

Conclusion: This study assists in understanding the factors associated with DDIs that can help in safe and effective use of drugs in the future.

Keywords: disease conditions, drug–drug interaction, inpatients, management, mechanism, severity

Introduction

A drug–drug interaction (DDI) is defined as a pharmacokinetic or pharmacodynamic influence of drugs on each other, which may result in desired effects, in reduced efficacy and effectiveness or increased toxicity [Schalekamp, 1997]. DDIs may lead to adverse drug reactions that can be severe enough to necessitate hospitalization. Studies have shown that DDIs may cause up to 3% of all hospital admissions [Huic *et al.* 1994; Jankel and Fitterman, 1993; McDonnell and Jacobs, 2002]. Approximately 37–60% of patients admitted to hospital may have one or more potentially interacting drug combinations at admission [Costa, 1991; Gosney and Tallis, 1984; Manchon *et al.* 1989; Mitchell *et al.* 1979; Schneider *et al.* 1992; Shinn *et al.* 1983]. In inpatients, the risk of having potentially interacting drug combinations can additionally increase because new drugs are often added to the existing drug therapy [Heininger-Rothbucher *et al.* 2001; Herr *et al.* 1992; Wiesner *et al.* 1999]. DDIs are a concern for patients and providers, as polypharmacy is becoming more common in managing complex diseases or comorbidities and the consequences can range from untoward effects to drug-related morbidity and mortality [Juurlink *et al.* 2003; McDonnell and Jacobs, 2002]. Healthcare

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professionals' ability to recognize potential DDIs is important in reducing their potential risks and adverse consequences [Ko *et al.* 2008]. The assessment of prevalence and patients at risk for clinically important DDIs at visit will be useful in minimizing medication-related problems and improving pharmaceutical care [Aparasu *et al.* 2007]. The potential benefits of drug combinations should be weighed against the seriousness of the DDI, taking into account the availability of alternatives. If the benefit of treatment is of such importance that it outweighs the potential risks, and no safer alternatives are apparent, then the risks of a potential DDI may be tolerated and treatment continued [Becker *et al.* 2007].

The objectives of the study included the following: categorization of DDIs in the prescriptions based on the mechanism involved; determination of the severity of DDIs in the prescriptions; determination of the relationship between the number of drugs in the prescription and its potential for DDIs; determination of the potential for DDIs with different diagnoses; determination of the intervention control for various DDIs observed.

Methods

The study was conducted in the South Indian teaching hospital. On average 180 outpatients and 20 inpatients were admitted per day for consultation and treatment, respectively. The hospital had various wards such as an intensive care unit, medical wards, surgical wards, pediatric wards and gynecology department. The prospective observational prescription analysis study was conducted for a period of 6 months from October 2010 to March 2011. The prescriptions from the inpatient medical wards including male and female medical wards, pediatrics ward and intensive care unit were used for the study. The study was approved by the Institutional Ethic Committee, JSS College of Pharmacy, Ooty. Inpatients with two or more drugs in their daily prescriptions were included in the study and patients with a history of drug abuse and surgical patient prescriptions were excluded from the study.

Patient case sheets, patient medical records and a DDI documentation form were used. A drug interaction check was performed using the www.drugs.com database; this 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 are categorized as minor, moderate or major which indicates the possible risks of occurrence of DDIs which can occur in patients, but not the actual severity of DDI.

The initial part of the study was designed to provide awareness about DDIs and their impact on healthcare 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.

The case sheets that had two or more drugs in the prescription were selected by the clinical pharmacist. Among these selected case sheets, the physician chose 204 prescriptions where he or she expected a DDI. After the prescription selection by the physician in charge, the relevant data from the prescription were entered into the DDI documentation form. The drugs in the prescription were further entered into the drug interaction checker on www.drugs.com and any DDIs in the prescription of the patients were assessed. The data obtained was used to categorize interactions based on the mechanism as pharmacokinetic or pharmacodynamic. The pharmacokinetic drug interactions were further categorized into interactions based on absorption, distribution, metabolism and elimination. 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). The relationship between the number of drugs in the prescription and the potential for drug interactions was also assessed. The drugs prescribed for disease conditions which were most prone to DDIs, and the age groups of the patients where DDIs were common were also assessed.

Statistical analysis

Statistical analysis was performed using Epi Info 2002 statistical software. Differences were considered statistically significant for p values <0.05.

Results

A total of 204 prescriptions were analyzed during the study period, of which 186 (91%) prescriptions

Table 1. Categorization of drug–drug interactions based on mechanism.

Mechanism	Number of interactions (n = 856)	Percentage	p value
Pharmacokinetic drug-drug interactions	**361**	**42**	–
Absorption	135	16	
Distribution	3	1	
Metabolism	166	19	<0.05
Excretion	57	7	
Pharmacodynamic drug-drug interactions	206	24	–
Unknown mechanism	289	34	–

Table 2. Categorization of drug–drug interactions based on severity.

Severity	Number of drug interactions (n = 856)
Major	13 (2%)
Moderate	602 (70%)*
Minor	241 (28%)

*p value <0.05 compared with moderate or minor drug interactions.

showed 856 DDIs. The study prescriptions comprised 42% pharmacokinetic DDIs, 34% were by an unknown mechanism and 24% were pharmacodynamic DDIs (Table 1). Statistical analysis showed a significant difference within the different pharmacokinetic DDIs, where drug interaction due to altered metabolism occurred most often (19%) followed by absorption-related drug interaction (16%) then interaction-related elimination changes (7%).

There was a greater number of moderate DDIs than minor or major interactions (602 *versus* 241 or 13, respectively, $p < 0.05$; Table 2).

Prescriptions for patients with cardiovascular and respiratory disease conditions led to the greatest average number of DDIs (7.33/patient), followed by cardiovascular disease prescriptions (6.34/patient) then hepatic disease prescriptions (6.00/patient); see Table 3.

The results showed that when the number of drugs increased in a prescription, the number of DDIs also increased (Table 4).

The drug interaction software showed that dosage adjustment was the most popular intervention following a DDI (102 of 856 cases; Table 5).

Discussion

Our study found that among the 856 interactions, 42% were pharmacokinetic DDIs, 24% were pharmacodynamic DDIs and 34% involved unknown mechanisms. These findings were different from another study reported in the literature where the discharge medications of the inpatients were of concern and pharmacodynamic DDIs were dominant [Egger *et al.* 2003].

The severity assessment of DDIs in our study showed that most of the interactions were moderate (70%) followed by minor (28%) and major (2%) interactions. This trend is similar to that found in another report [Dambro and Kallgren, 1988].

Our study found that the average number of DDIs per patient increased as the number of drugs in the prescription increased. This finding was similar to another published report where the potential for a drug interaction increased from 13% to 82% as the number of medications increased from 2 to 7 or more [Goldberg *et al.* 1996].

We found that prescriptions for patients with cardiovascular disease with comorbid conditions led to the greatest average number of drug interactions, followed by cardiovascular disease (without comorbid conditions). This result is similar to the finding obtained from another study where cardiovascular disease prescriptions had a relatively high risk of drug interactions [Goldberg *et al.* 1996].

Table 3. Drug–drug interactions based on organ system disorders.

Organ system disorder	Number of drug interactions (n = 856)	Number of patients (n = 186)	Average number of drug–drug interactions
Cardiovascular and respiratory system	66 (8%)	9	7.33
Cardiovascular system	279 (33%)	44	6.34
Hepatic system	12 (1%)	2	6.00
Renal system	10 (1%)	2	5.00
Respiratory system	164 (19%)	33	4.97
Respiratory and endocrine system	4 (1%)	1	4.00
Neurology	95 (11%)	24	3.96
Gastrointestinal system	56 (7 %)	15	3.73
Hematology	11 (1%)	3	3.67
Endocrine system	28 (3%)	8	3.50
Others	70 (7%)	21	3.33
Cardiovascular and hematology	3 (1%)	1	3.00
Infectious disease	56 (6%)	22	2.55
Gastrointestinal and alcoholic liver disease	2 (1%)	1	2.00

Table 4. Number of drug interactions per patient.

Number of drugs	Number of patients (n = 186)	Number of drug interactions (n = 856)	Average number of drug–drug interactions with number of drugs in the prescription
2–5	35	78 (9%)	2.23
6–10	146	731 (85%)	5.01
>10	5	47 (6%)	9.40

The most common management plan found in our study for most of the DDIs was dose adjustments; this is similar to the results reported by Bergk and colleagues [Bergk *et al.* 2004].

The significance of using electronic software has been reported in the literature [Taegtmeyer *et al.* 2012]. The authors found that checks by a pharmacologist agreed with only 11% of DDI alerts from electronic software, and the remaining 89% were not thought clinically relevant. Our study showed the same finding. Waring and McGettigan stated that the occurrence of adverse effects is more difficult to detect for newer drugs, where there is less clinical experience and fewer data, emphasizing the role for clinical interpretation [Waring and McGettigan, 2011]. The result obtained in our study was based on the classification as minor, moderate or major according the interaction checker that was used. Sepehri and colleagues used a similar software detection approach, and found the occurrence of DDIs in 20% of patients [Sepehri *et al.* 2012].

Conclusion

Our study helped in understanding about the most prone age groups, disease conditions, and the common mechanisms that can cause DDIs in inpatient prescriptions. This may help in improving the safe and effective use of drugs in our hospital. The use of the drug interaction checker software has greatly aided our study by assessing the findings mentioned above more easily; this would have been harder to achieve if done manually. Our study also helped to define the significant role of the pharmacist in assessing and controlling DDIs. Further research may include

Table 5. Management requirements for the drug–drug interactions documented.

Management	Number of drug–drug interactions (n = 856)
Dosage adjustment	102 (12%)
No management required	94 (11%)
Monitor for signs and symptoms	93 (11%)
Monitor for drug levels	79 (9%)
Monitor for biochemical parameters	74 (9 %)
Change dosing interval	64 (8%)
Avoid the combination	62 (7%)
Monitor for electrolyte levels	60 (7%)
Monitor for patient response	54 (6%)
Monitor for signs and symptoms and biochemical parameters	42 (5%)
Monitor for serum creatinine levels	41 (4%)
Dose titration	28 (3%)
Monitor for signs and symptoms and drug level	23 (3 %)
Monitor for patient response and dose adjustment	17 (2%)
Monitor for drug level and biochemical parameters	13 (2%)
Monitor for electrolyte and drug level	10 (1%)

an evaluation of the economic, clinical, and humanistic outcomes of clinically important DDIs, especially among those at risk.

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Conflict of interest statement

The authors declare no conflict of interest.

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