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A STUDY ON POTENTIAL DRUG-DRUG INTERACTIONS AMONG PATIENTS ADMITTED UNDER DEPARTMENT OF MEDICINE IN A TERTIARY CARE HOSPITAL IN INDIA

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Abstract

Objective: This study was conducted to evaluate the potential drug-drug interactions (pDDIs) among patients admitted in a tertiary care hospital in India.

Methods: This was anobservational and cross sectional study for 3 months. All the patients admitted in the general ward under Department of Medicine. Pre-structured proforma and patient's charts were be used for data collection on the 2nd day of admission. For drug interactions, online 'Medscape Drug Interaction Checker' was used.

Results: A total of 61 charts were screened. A total of 304 drugs with 57 different types were admitted to these patients (including all dosage forms and routes). The total number of pDDIs were 217, of them 69 were minor, 130 were significant and 18 were serious (including repetitions in different patients). There were 13 unique serious pDDIs.

Conclusion: The incidence of pDDIs in our study was high. Controlled study to evaluate whether good clinical management of DDIs can reduce drug-related morbidity or mortality is needed.

Keywords: Potential drug-drug interactions (pDDIs), adverse drug reactions (ADRs), poly-medication, hospitalization, pharmacokinetic and pharmacodynamics interactions.

Introduction

Adverse drug reactions (ADRs) are a major cause of hospital admissions leading to significant medical and economic problems. Drug-drug interactions (DDIs) contribute to a major part of ADRs, especially in elderly patients and in patients under poly-medication, in whom the risk of drug interactions increases exponentially with number of drugs (1).In Harvard Medical Practice Study of adverse events, 20% of events in an acute hospital in-patient setting were drug related and of these 8% were considered to be DDIs (2).It can occur either pharmacokinetically or pharmacodynamically. Pharmacokinetic interaction occurs when both of the concurrently administered drugs have potential to alter other's pattern of absorption, distribution, metabolism and excretion, and similarly, pharmacodynamic interaction occurs if concurrently administered drugs have similar or opposite effects.

Various studies in India have also shown significant DDIs resulting in increased morbidity among patients admitted in Medicine, Cardiology and Nephrology wards in various tertiary care hospitals (3-5).Thus, it is essential to screen for potential DDIs (pDDIs) among the admitted patients receiving multiple medications for various disorders. With this background, the present was done to evaluate pDDIs among patients admitted in a tertiary care hospital in India.

Materials and Methods

Ethics:

This study was conducted according to the guidelines of the Declaration of Helsinki and Tokyo for human studies. The study design was approved by the institutional ethics committee. Informed consent was obtained from all the patients prior to enrollment.

Study type:

This was an observational and cross sectional.

Study duration:

This study was conducted for duration of3 months.

Study population:

All the patients admitted in the general ward (non-emergency) under Department of Medicine. The admission days were twice a week.

Study tools:

Pre-designed and pre-structured proforma and patient's chartswere be used for data collection. For DIs, online 'Medscape Drug Interaction Checker' (6)wasused.It grades DIs into 3 categories:

a) Serious (use alternative),
b) Significant (monitor closely),
c) Minor.

Study method:

Patient's charts were looked for all the prescribed drugs on the second day of admission and evaluated for pDDIs.

Statistical analysis:

Descriptive statistics was used.

Results

A total of 538 charts were screened. A total of 546 drugs with 87 different types were administered to these patients (including all dosage forms and routes). The most commonly used drugs are enumerated in Table 1. The total number of pDDIs were 417, of them 69 were minor, 330 were significant and 18 were serious (including repetitions in different patients). There were 13 unique serious pDDIs. The list of the different serious pDDIs is enumerated in Table 2.

Table 1: Most commonly used drugs (n = 546 prescribed drugs).

Name of drug	Percentage
Paracetamol	6.2%
Pantoprazole	5.9%
Omeprazole	4.9%
Insulin	4.2%
Calcium carbonate-vitamin D_3	4.1%
Furosemide	3.9%
Tramadol	3.0%
Folic acid	3.0%
Amikacin	2.9%
Famotidine	2.8%
Ceftriaxone	2.6%
Atorvastatin	2.5%
Ferrous sulfate	2.2%
Aspirin	2.2%
Ondansetron	2.2%
Prednisolone	2.2%
Salbutamol	1.9%
Vitamin B complex	1.7%
Potassium chloride	1.6%
Metoclopramide	1.4%
Cough syrup	1.3%
Lactulose	1.2%
Metformin	1.0%
Ipratropium	1.0%
Other drugs individually	< 1.0%

Table 2: Different types of serious pDDIs observed in this study.

Offending drug combination	Results of serious pDDIs	Comments
Azithromycin + ondansetron	Both increase QTc interval, ECG monitoring recommended	Granisetron can be used as an alternative
Rifampin + dexamethasone	Rifampin decreases the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism	Prednisolone/methyl prednisolone should be also avoided
Metoprolol+propranolol	Both increase anti-hypertensive channel blocking	-
Isoniazid + omeprazole	Isoniazid increases the level or effect of omeprazole by affecting hepatic enzyme CYP2C19 metabolism	Pantoprazole can be used as an alternative
Artesunate + ondansetron	Both increase QTc interval	Granisetron can be used as an alternative
Amisulpride + fluconazole	Both increase QTc interval	Nystatin can be used as an alternative
Fluconazole + ondansetron	Both increase QTc interval, combination may increase ondansetron levels	Granisetron can be used as an alternative
Ondansetron + risperidone	Both increase QTc interval	Granisetron can be used as an alternative
Spironolactone + potassium chloride	Both increase serum potassium	-
Digoxin + metoprolol	Digoxin increases toxicity of metoprolol by unspecified interaction mechanism, increase risk of bradycardia	-
Omeprazole + Clopidogrel	Omeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism; inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite formed by CYP2C19	Ranitidine can be used as an alternative
Omeprazole + digoxin	Omeprazole increases the level or effect of digoxin by increasing gastric pH	Ranitidine can be used as an alternative
Piperacillin + warfarin/heparin	Piperacillin increases the effects of warfarin/heparin by anticoagulation, piperacillin can inhibit platelet aggregation	Meropenem can be used as an alternative

Discussion

In our study, both pharmacokinetic and pharmacodynamics interactions have played role. The incidence of pDDIs is similar with other Indian studies. The patterns of incidence of DDIs are positively associated with patients' age, gender, number of drugs prescribed and length of hospital stay (7).

Two Indian studies revealed that the overall incidence of clinically important DDIs in cardiology department to be 14.66%[7]and 30% (3).In another Indian study involving renal failure patients from nephrology ward, among the 205 prescriptions included, a total of 474 interactions were reported, making 2.7 interactions per prescription with incidence rates of 76.09%.

A study in Britain reported that drug interactions accounted for around 16% of ADRs resulting in hospital admissions (8).In another review, it has been reported that globally approximately 0.05% of the emergency department visits, 0.6% of the hospital admissions and 0.1% of the re-hospitalizations are caused by ADRs due to DDIs (9).A prospective study reported that 30.3% of patients admitted to an emergency department in USA were at the risk of pDDIs and that increased to up to 48% after being treated at the emergency department (10).Another study conducted in Germany reported that pDDIs dramatically

increased during the hospital admission period compared to the pre-hospitalization period and fell after discharge (1).

It is to be borne in mind that some of the pDDIs describedmight have potential benefits and were prescribed intentionally. Using 'Medscape Drug Interaction Checker' (6)alone, without considering the clinical scenario as a case to case basis won't give us much insight. Also, these were all potential ADRs resulting from DDIs and actually all were not manifested in our patients. Our study had a short duration and looked for a small number of patients in a selected unit and selected ward and so couldn't reflect the actual scenario in the whole hospital. The number of pDDIs might increase in other wards and intensive care units.

Conclusions

Thus, to conclude, the incidence of pDDIs in our study was high. Controlled study to evaluate whether good clinical management of DDIs can reduce drug-related morbidity or mortality is needed.

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Conflict of interest

The authors declare that there is no conflict of interest.

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