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Research Paper

Assessment of potential drug-drug interactions in in-patients of a medicine ward of a tertiary care hospital

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Abstract

Drug-Drug interactions are the common problems during the allopathic drug administration especially with polypharmacy, which may have one of reason for hospital admission and fatal consequences. The current study was carried out to assess the potentiality of drug-drug interactions, the risk associated with drug interactions and to identify the most commonly prescribed drugs which causing drug interactions. The prospective study was carried out between January 2014 to June 2014 for a period of six months in an internal medicine ward. Information on patient's demographic details, medication history and relevant clinical laboratory data were obtained from each patient by interview and medical records. The potential DDIs were identified using Micromedex, Stockleys drug-drug interactions and Medscape. Total 150 patients were reviewed, out of 150 patients, 104(69.33%) patients had 227 PDDIs. Among 104 patients, 56(53.8%) were males (PDDIs (55.9%) were: 18 major, 101 moderate, 8 minor) and 48(46.15%) were females (PDDIs 44.05% were: 13 major, 74 moderate, 13 minor). The average numbers of drugs prescribed were 11, severe PDDIs were 19%, moderate DDIs were 69.6% and mild interactions were 11.4%. Among major therapeutic classes, Antibiotics (25.2%) were having high PDDIs and Anti-Diabetics (5.04%) were low PDDIs. A more number of drug-drug interactions were occurred in male (59) compared to females (45). There were a significant increased in PDDIs with the increased age and increased number of drugs prescribed to a patients. The study showed that regular monitoring of PDDIs will definitely helps in a better patient care.

Keywords: Prospective observational study, Potential Drug-Drug Interactions, in-Patients of a Tertiary care hospital.

Introduction

A drug interaction is defined as a change in the pharmacologic effect of a drug that results when it is given concurrently with another drug or with a food [1]. Potential drug- drug interactions (PDDIs) are the pharmacological or clinical responses to the administration of drug combinations. PDDIs may include, drug contraindications, drug combinations that require monitoring and possible dosage adjustments which may be beneficial when administered together [2]. There are numerous potential drug-drug interactions that can result in toxicity, in an alteration of the desired therapeutic end point or at the very extreme in a life threatening situation. It is important not only to identify PDDIs that are clinically meaningful, but also to understand options to approach the potential loss of efficacy or toxicity that may result when certain combinations of drugs are administered together [3]. Hence this prospective study was carried out from January 2014 to June 2014 for a period of six months in a Tertiary Care Hospital.

Criteria for assessing PDDIs

Criteria	Description
Minor	The effects are usually mild consequences may be bothersome or unnoticeable but should not significantly affect the therapeutic outcome. Additional treatment is usually not required.
Moderate	The effects may cause deterioration in a patient's clinical status. Additional treatment, hospitalization, or extension of hospital stay may be necessary.
Major	The effects are potentially life threatening or capable of causing permanent damage [2].

The factors affecting drug-drug interactions include poly Pharmacy, Age, Gender, and number of patients visited to the hospital [4].

The mechanism of Drug-Drug interaction is pharmacokinetics and pharmacodynamic. Pharmacokinetic parameters such as Absorption, Distribution, Metabolism and Elimination, where as pharmacodynamic characteristics could be affected by unspecific membrane interactions, the drugs synergism or antagonize the effect at the level of target of action. Clinically beneficial and reparative drug interactions are explored to obtain useful drug combinations [5,6].

Drug-Drug interactions (DDI) in patients receiving multi-drug therapy are of wide concern. Such interactions are an important cause of adverse drug reactions and may lead to an increased risk of hospitalization and higher health care costs [7]. Seriousness and severity of Drug-Drug interactions are Hospitalization, Life-threatening and Death [8].

Four steps to manage a drug interaction

- Avoid the combination.
- Adjust the dose.
- Monitor the patient.
- Continue the medication if, the interaction is not clinically significant [9].

Prevention of drug-drug interaction

The number of drugs used to treat patients must be minimized to reduce the incidence of potential drug–drug interactions, and adherence difficulties while at the same time minimizing the costs [10].

Consequences of Drug-Drug Interactions

There are 3 possible outcomes during drug-drug interactions.
1. One (drug) may intensify the effects of other.
2. One may reduce the effects of other.
3. The combination may produce a new response, but not seen when either of the drug is given alone [11].

Materials and Methods

Study design and setting

The prospective study was conducted in the medicine ward in a Tertiary Care 1000 bedded teaching hospital for a period of 6 months. The necessary information was collected under the supervision of clinical pharmacist and other health care professionals for the detection of DDIs.

Patients

All patients admitted to the medicine wards were screened for eligibility to enter the study. Patients with more than a 48 h stay were included in the study.

Source of data

The data were collected from the patient case records, patient history, laboratory data, medication history and patient progress report.

Data evaluation and analysis

All the data were tabulated according to the combinations of drugs in treatment chart, intravenous fluids and nutritional supplements were excluded from the study. Verification of potential drug interactions was carried out using the software Truven Micromedex database, Medscape, Epocrates, Stockleys Drug-Drug Interactions. The occurrence and severity of potential drug interactions were evaluated by cross-checking each patient's prescription profile. The collected data were analyzed for the followings.

- Age distribution
- Gender distribution
- Classification of Drug Interactions
- Drug-Drug Interactions in Different Age Groups
- Gender wise categorization of subjects enrolled with and without potential Drug-Drug interactions
- Correlation between No. of Drugs and Drug-Drug Interactions
- No. of Potential Drug-Drug Interactions in Gender Wise
- Mechanism of Potential Drug-Drug Interactions
- Severity of Drug-Drug Interactions
- Major Therapeutic Classes involved in Drug- Drug Interactions

Inclusion criteria

- Patients on polypharmacy.
- Patients with more than a 48 hrs stay in hospital.
- Inpatients admitted to medicine wards.
- All the patients above the age of 18years.
- Patients of both the sexes.

Exclusion criteria

- Patients on herbal medicines.
- Pregnant and lactating women.
- Patients on non-prescription or self medications.
- Patients treated on outpatient basis.

Results and Discussion

In the present study, 150 subjects were reviewed and 104 had an experienced of drug interactions. The drug-drug interactions were classified as mild, moderate and severe according to their severity and undesirable effects. Drug-drug interactions limit the clinical effects. Mild interaction may not need any change in the treatment plan, where as moderate drug-drug interactions may result in exacerbation of the disease of the patient and/or a change in the therapy. The severe drug-drug interactions are life threatening and/or they may require medical treatment or an intervention to minimize or to prevent the severe adverse effects [12].

During the six month study period, 150 patients cases were collected and studied as follows

- Out of 150 subjects, 104 (69.33%) subjects had 227 PDDIs, 85(56.66%) were males and 65 (43.33%) were females (Table 1). It was observed that the maximum number of patients were in the age group of 39-48 years (23.07%) (Table 2). These findings are similar to the study conducted by Nag et al., Elderly individuals were exposed to more multiple drug regimens than younger individuals, which increase the risk of PDDIs.
- A total of 227 drug-drug interactions were seen in 104 patients, among 227, 28 (12.33%) were mild, 156 (68.72%) were moderate and 43(18.94%) were severe (Table 3). A maximum number (51) of drug interaction were seen in the age of above 69 years, followed by between 59-68 years

(40) and a minimum number of interaction were in between the age group of 49-58 (28), one of factor may have involved in interaction is poly pharmacy (Table 4). Among 104 PDDIs, 59 were observed with males and 45 were in females, 46 patients did not show any PDDIs (Table 5).

Table 1: Gender distribution of patients

Gender	No. of Cases	Percentage
Males	85	56.66%
Females	65	43.33%
Total	**150**	**100%**

Table 2: Distribution of Age Groups (N =104)

Age in years	No. of Cases	Percentage
18-28	11	10.5%
29-38	16	15.38%
39-48	24	23.07%
49-58	12	11.53%
59-68	18	17.30%
>69	23	22.11%
TOTAL	**104**	**100%**

Table 3: Classification of Drug Interactions (N = 227)

Type of interaction	No.	Percentage
Major	43	18.94%
Moderate	156	68.72%
Minor	28	12.33%
Total	**227**	**100%**

Table 4: Distribution of Drug-Drug Interactions in different Age Groups

Age	Drug-Drug Interactions			total	percentage
	Major	Moderate	Minor		
18-28 years	12	15	06	33	14.53%
29-38 years	07	25	06	38	16.74%
39-48 years	05	30	02	37	16.29%
49-58years	01	25	02	28	12.33%
59-68 years	05	29	06	40	17.62%
>69 years	13	32	06	51	22.46%
Total	**43**	**156**	**28**	**227**	**100%**

Table 5: Gender Wise Categorization of Subjects Enrolled With and Without Potential Drug-Drug Interactions, Where (N=150)

Gender	Drug-Drug Interaction		Total
	With	Without	
Male	59	26	85
Female	45	20	65
Total	**104**	**46**	**150**

- The number of DDIs increases with the increase in number of drugs per prescription, where maximum (35) DDIs were seen with 15 number of drugs, and minimum (03) DDIs were occurred with 4 number of drugs per prescription (Table 6), the results are comparable to previous studies as Kohler GI et al. Study, the numbers of drugs taken per patient as well as the number of interactions per patient are higher during hospitalization. According to Cruciol-Souza the rate of potential DDI was also associated with prescription size.

- According to Gender wise, In male patients major PDDIs were18, moderate were 101 and 08 were minor interactions, where as in female patients major and minor were 13 and moderate were 74 (Table 7).
- As concern with the mechanism of PDDIs, Pharmacokinetic interactions were 84, Pharmacodynamic were 110 and 33 were non-specified interactions (Table 8).

Table 6: A relation between number of drugs prescribed and number of Drug-Drug Interactions encountered

No. of Cases	No .of Drugs	No. of Drug –Drug Interactions
03	04	03
03	05	04
12	06	07
05	07	12
12	08	20
09	09	14
15	10	23
09	11	21
12	12	30
05	13	20
06	14	28
09	15	35
04	>15	10

Table 7: Number of Potential Drug-Drug Interactions in Gender Wise

Gender	Major	Moderate	Minor	Total
Males	18	101	08	127
Females	13	74	13	100
Total	**31**	**175**	**21**	**227**

Table 8: Mechanism of Potential Drug-Drug Interactions

Pharmacokinetic	Pharmacodynamic	Non specified	Total
84	110	33	227

Table 9: Major Therapeutic Classes involved in Drug- Drug Interactions

Classes	No. of Drugs	Percentage
Anti tubercular drugs	39	12.30%
Diuretics	48	15.14%
Antibiotics	80	25.2%
Anti-Diabetics	16	5.06%
Anti coagulants	37	11.67%
Anti hypertensive's	34	10.72%
Proton pump inhibitors	23	8.25%
Total	**277**	**100 %**

Among all the prescribed major therapeutic classes, PDDIs were observed as follows, Antibiotics were 80 (25.2%) and Anti-Diabetics were 16 (5.04%), Anti-TB drugs were 39 (12.30%), Anti-Diuretics were 48(15.14%), steroids were 40 (12.61%), Anti Coagulants were 37 (11.67), Anti-Hypertensive's were 34 (10.72%), and PPIs were 23 (8.252%). Antibiotics were found highly intractable substances, whereas anti Diabetics were less intractable **(**Table 9).

Some of important PDDIs occurred between the drugs are summarized in Table 10. In the present study the most commonly observed interactions were in between aspirin with clopidogrel and ofloxacin with ondansetron (Table 10) [13]. However, it should be remembered that the clinical outcome

of most drug interactions depends on several factors like, frequency, route of administration, age, number of drugs per prescription, dose of each drug and even the influence of other drugs.

Table 10: The often drugs involved in PDDIs and type of interaction

Combination of drugs	Type of interaction
Major interactions	
Ofloxacin + Ondansetron	Combination may Increase in QTc Prolongation
Rifampicin + Dexamethasone	Rifampin will decrease the effect of Dexamethasone by affecting Cyp3A4 metabolism.
Moderate interactions	
Aspirin + Clopidogrel	Combination may Increase risk of Bleeding.
Hydrocortisone + Theophylline	Hydrocortisone will decrease the level or effect of Theophylline by affecting Hepatic or Intestinal enzyme cyp3A4 metabolism.
Minor interactions	
Cefuroxime + Furosemide	Cefuroxime increases the toxicity of Furosemide by Pharmacodynamic synergism.
Pantoprazole + Vitamin B 12	Pantoprazole decreases the effect of vit B12 by inhibiting the GI absorption.

Conclusion

The regular monitoring of PDDIs will definitely help in better patient care with co-morbidities and polypharmacy. There is a significant increase in PDDIs with the increase in age of the patient and the number of drugs prescribed to a patient, most of the DDIs was preventable. The more number of PDDIs were due to aspirin with clopidogrel, and ofloxacin with ondansetron. This study has put forth the common interactions which we come across in a tertiary care hospital. A thorough knowledge of these can decrease the incidence of DDIs, particularly during the prescription of multiple medications.

The risk of drug interactions increases exponentially with the number of drugs given to a patient, our study indicates that prescribing fewer drugs can reduce the risk of suffering from symptoms/condition secondary to drug interactions [14]. Taking this risk into an account may help to improve the quality of drug treatment and to decrease the economic burden to the patient. Pharmacists must take the responsibility for monitoring of the drug interactions and notifying the physician and patient about potential problems. The presence of clinical pharmacist in medicine department obviously reduces the drug related problems.

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