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Original Research Article

A prospective observational study on drug-drug interactions in department of general medicine at a tertiary care hospital

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ABSTRACT

Background: To assess the prevalence, severity, and significance of potential drug interactions in the Department of General Medicine of a tertiary care hospital.

Subject and Methods: It is a prospective observational study done over a period of six months that includes established cases of Drug Interactions.100 patients were evaluated for their socio-demographic details, clinical characteristics of the disease and medication prescribed. The medications of the patients were analyzed for possible interactions using the standard drug interaction database - Micromedex× 2.0.

Results: A total of 100 cases were reviewed, with the age group between 18 to 75 years. A total of 87 prescriptions were found to have drug interactions. A total of 49 drug interactions were reported to the physician during the study period. Majority (22.8%, n=114) of the i10nteractions were moderate. The Prevalence of drug interactions was 29.3%. The interactions found most frequently in the present study are ceftriaxone and furosemide (21.98%), followed by norfloxacin and ondansetron (13.7%) phenytoin and atorvastatin(11.4%), chlorpheniramine and midazolam (8.04%%), azithromycin and calcium carbonate (2.29%) and enalapril and furosemide (1.14%). The results of our study revealed that the majority of drug interactions were found in the prescriptions of cardiovascular diseases.

Conclusion: Patients with co-morbid conditions and elderly were found to be associated with more number of drug interactions. Potential drug interactions are frequent among patients prescribed with multiple medications and the rate is directly related to the number of drugs prescribed.

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INTRODUCTION

Drug-drug interactions (DDIs) are one of the commonest causes of medication error in developed countries. There is little knowledge in terms of the epidemiology of drug-drug interactions on the clinical level and most evidence and documentation on this come from case reports, voluntary studies and/or through reports from drug-drug interactions admitted in hospital patients. A necessary consequence of this is the danger that interactions between drugs will lead to serious adverse effects or will reduce the therapeutic effect of some compounds (Akram et al., 2012). These medical errors also increase the patient's expenses which ultimately affects the whole society.

A Drug-Drug interaction can be defined as a pharmacological or clinical response to the administration of a drug combination, different from that of anticipated one from the known effects of the two agents when given alone (Rajakananan et al., 2012). The clinical result of a DDI may be manifested as antagonism, synergism or idiosyncratic.

Drug-drug interactions (DDIs) are considered to be an important risk factor in the development of adverse drug reactions. The aging of the population, polymorbidity, and polypharmacy, and the introduction of new drugs are all associated with a high probability of development of DDIs. The clinical outcome of DDIs may be either increased risk of adverse effects/toxicity or loss of efficacy. Since the clinical manifestation of DDIs is not always present they are often referred to as potential DDIs. A study of ADRs from the UK estimated that 16.6% of ADRs leading to hospital admission were associated with DDI. Data suggests that certain population groups like the elderly, patients from intensive care units and oncology patients are at high risk of drug-related morbidity due to DDIs. The recognition and management of potential

DDIs is a matter of good prescribing practice and clinical care for which the use of drug information services is essential. Potential DDIs are usually detected with various computerized screening programs displaying different sensitivity and specificity compared to the gold standard Stockley's Drug Interactions (Arvind et al., 2011).

Among medical errors, potentially serious drug-drug interactions have recently received increased attention. The consequences of mistake and drug errors such as drug interactions affect millions of patients every year and contribute to 5% of patient admissions into hospital. Published studies have reported proportions of potential DDIs ranging from 2.2%-30% in hospitalized patients and from 9.2% to 70.3% in ambulatory patients (Nekanti et al., 2012).

Polypharmacy is an important factor which leads to drug-drug interactions however, the number of items per prescription, the more the likelihood of drug-drug interactions occurrence. Increase in multimorbidity with age often makes it necessary to prescribe several drugs for one patient at a time. As a consequence of this is the danger that interactions between drugs will lead to serious adverse drug effects or will reduce the therapeutic effect of some compounds. Potential drug interactions can arise at any age in life, but the frequency of polypharmacy in older lives increases the risk substantially. Despite a large amount of drug-related information, the analysis and optimization of multi-medications is still complicated and even for experts unmanageable. Substantial improvements in patient safety can be achieved which analyses multi-medications and evaluate with regards to adverse drug reactions and thus Potential drug interactions, drugs, drug side effects, and drug-induced diseases can be avoided.

Increasing multimorbidity with age often makes it necessary to prescribe several drugs for one patient at a time. As a consequence, the average 65-year-old patient is on five drugs simultaneously. Prescription peaks in the 75- to 84-year-old group; a European study showed among patients with a mean age of 81 years that 34% to 68% were taking six drugs or more (Delafuante, 2003). A necessary consequence of this is the danger that interactions between drugs will lead to serious adverse effects or will reduce the therapeutic effect of some compounds. Potential interactions can arise at any age in life, but the frequency of polypharmacy in older life increases the risk substantially. Meta-analyses of the reasons for inpatient admission to medical wards showed that in 7% of cases serious drug interactions were the cause for admission or for prolonged hospital stays (Carruther et al., 2000).

The treatment of disease usually requires the use of more than one drug. When Patients have multiple symptoms, it becomes necessary to prescribe a number of drugs. DDIs mostly occur among drugs with the low therapeutic index having a small difference between their therapeutic and toxic or lethal dose (Bertoli et al., 2010). This means with the slightest change in the dosage of a drug it can produce dangerous and harmful effects. The severity of illness in the patient being treated is also another predisposing factor to DDIs such that treating cardiovascular, infectious diseases and psychiatric disorders which have the greatest potential for dangerous drug interactions.

SUBJECTS AND METHODS

Subject

A 6 months prospective and observational study on "drug-drug interactions" was carried out in the Department of General Medicine, Osmania General Hospital, Hyderabad, Telangana, India. The present study was approved by the Institutional Ethics Committee (MCP/IEC/PD/PR/24). A total of 100 cases were included in this study. The study included all patients admitted to the hospital with the age group of 18 and above of either gender who were admitted and received inpatients services of more than 24 hours with two or more medications. The patients under 18 years age group, pregnant and lactating women and out-patients were excluded from the study.

Methodology

Patients were enrolled as per the inclusion criteria of the study. Their demographic and medical details were properly documented in the self-designed patient profile form. The medications taken by the patients during their hospital stay were analyzed for possible drug interaction via the electronic database Micromedex × 2.0. The potential drug interactions of major, moderate and minor severity were documented. These interactions were also classified in terms of their documentation status and mechanism. Some risk factors were studied to predict the presence of DDIs. These included the number of medicines, length of hospital stay and concurrent illnesses. Available data on prescriptions included are Physicians identification, name, strength, and quantity of medications dispensed. The results were analyzed based on severity and corresponding documentation for each drug interaction. Due to the greater clinical importance of drug interactions, all the three types of interactions-major, moderate and minor were considered in the present study.

Sources of data

The required details were obtained from the Case sheet of the Patients from which all the medications being given to the Patient were recorded. The laboratory data and ECG were also ascertained from the case sheets. The Past Medication History of the patient was also obtained from the patients and their attainders to find out if there were any past events of adverse drug reactions or drug interactions.

Parameters assessed

The parameters which were assessed are Evidence relating to the interaction, clinical relevance of the potential adverse reactions resulting from the interactions and risk factors identifying patient, medication or disease characteristics for which the interaction is of particular importance.

Drug interaction checker

The undesirable drug interactions were identified by the online Medscape drug interaction checker. This software has the appropriate sensitivity and specificity to detect possible drug interactions. DDIs were also checked with the help some standard textbooks of pharmacology.

Medscape categorizes the drug interactions into serious, significant, minor. Serious meant use alternative, significant meant monitor closely and minor (non-significant) meant to continue in therapy. Potential for drug-drug interactions were analyzed for variables like age, comorbid conditions, number of drugs prescribed, and days of hospital stay.

On the basis of severity, Micromedex classifies DDI as major, moderate and minor.

Major: Potentially life-threatening; requires medical intervention to minimize or prevent the serious adverse effects

Moderate: Results in potential deterioration of patients clinical condition and may require an alteration in therapy.

Minor: The effects are usually mild and may not require

change in therapy.

It also classifies potential DDI as excellent, good, fair, poor or unlikely on the basis of documentation status as mentioned follows:

1. Excellent: The existence of drug interaction has been clearly established by the controlled studies.

2. Good: The existence of drug interaction is suggested by documentation, but well-controlled studies are lacking.

3. Fair: Available documentation is poor.

4. Poor: Documentation is scant; however, the possibility of a clinical conflict exists.

5. Unlikely: Documentation as well as a sound pharmacological

For each interaction, the DDI checker listed the expected or possible effects of the drug combination, and the proposed mechanism of the interaction.

RESULTS

A total of 100 cases were reviewed, with the age group between 18 to 75 years. A total of 87 prescriptions were found to have Drug Interactions. A total of 49 Drug interactions were reported to physician during the study period. Majority (22.8%, n=114) of the interactions were moderate.

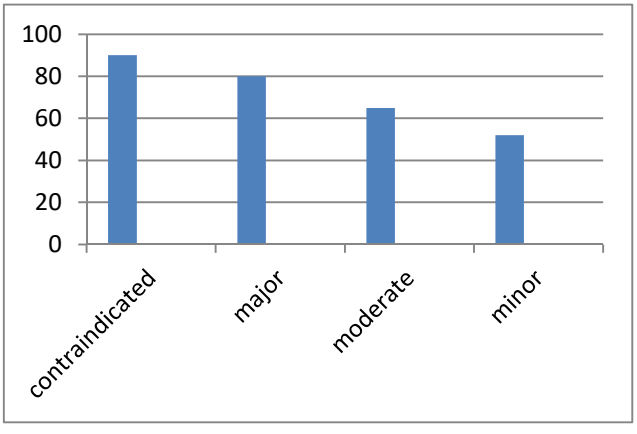

Figure 1. Interventions done in drug interactions.

Figure 1 shows that 90% of interventions were done in contraindicated interactions and least interventions were done in minor interactions. Moderate reactions are classified as significant interactions if they require intervention and Non-significant if change of therapy is not required.

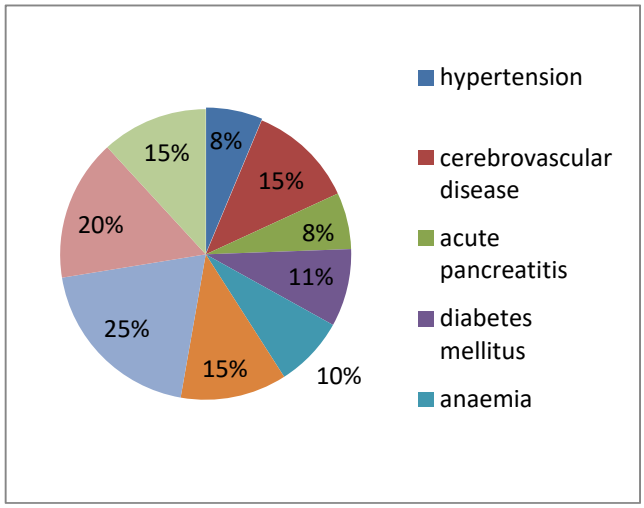

Figure 2. Disease and drug interactions.

Figure 2 shows the number of drug interactions found in each disease.

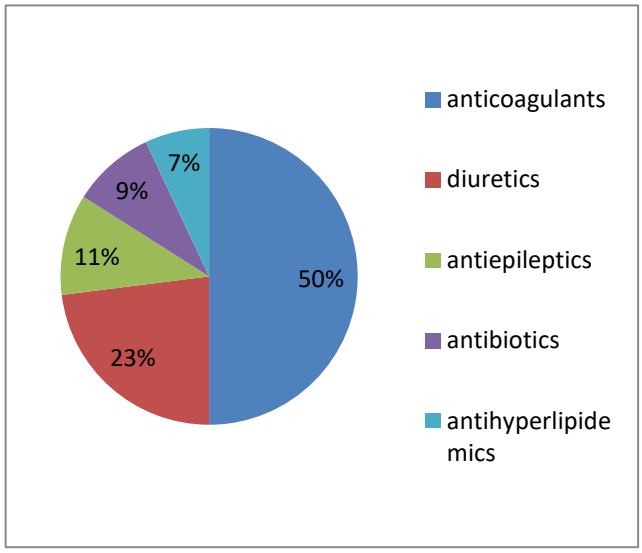

Figure 3. Drug categories found to show more drug interactions.

Figure 3 shows that the drug category of anticoagulants (50%) has most drug interactions and anti hyperlipidemics (7%) have least drug interactions.

DISCUSSION

With every day passing by a new drug is coming in the market and the availability of multiple options can drag prescriber towards polypharmacy which increases the chances of DDIs. There is a need to raise the awareness of possible DDIs in all hospital departments and all DDI should be identified, managed and recorded. The age, gender, polypharmacy, and co-morbidities are known as the risk factors for developing DDIs. Furthermore, it has been observed that the use of polypharmacy was related to widely increased risk of unsafe drug-drug combinations (Bertoli et al., 2010).

Table 1. Major drug interactions.

Drug Interactions	Effects
Ceftriaxone+ Heparin	Ceftriaxone increases the levels of heparin and may decrease prothrombin activity
Ceftriaxone+ Calcium Salts	Risk of potentially fatal particulate precipitation in lungs and kidneys
Ceftriaxone+ Enoxaparin	Ceftriaxone increases the levels of enoxaparin and may decrease prothrombin activity
Ceftriaxone+ Furosemide	Acute nephrotoxicity
Levofloxacin+ Ondansetron	Both increase QT interval
Ciprofloxacin+ Ondansetron	Both increase QT interval
Aspirin+ Heparin	Both increase anticoagulation
Levofloxacin+ Insulin	Acute hypoglycaemia

Table: 2. Drug interactions effecting serum potassium

Drug interactions	Effect on serum Potassium	Incidents reported
Aspirin+Diclofenac	Increase in serum potassium	2
Carvedilol+Aspirin	Increase in serum potassium	1
Losartan+Aspirin	Increase in serum potassium	-
Metoprolol+Aspirin	Increase in serum potassium	1
Adrenaline+ Salmetarol	Decrease in serum potassium	-
Epinephrine+ Furosemide	Decrease in serum potassium	1
Furosemide+ Hydrocortisone	Decrease in serum potassium	1

Table 2 shows the Drug combinations which produces interactions that affect the serum potassium.

Table 3. Drug interactions effecting ECG.

Drug interaction	Affect on ECG	Incidents reported
Ciprofloxacin +Ondansetron	Prolong QT interval	1
Levofloxacin+ Ondansetron	Prolong QT interval	-

Table 3 shows the drugs interactions that were found to be associated with prolongation of QT interval.

Table 4. Drug interactions most commonly found.

	Drugs	Interaction	No. of occurrences
1.	Ceftriaxone+ Furosemide	Risk of nephrotoxicity	19
2.	Ceftriaxone+ Heparin	Risk of anticoagulation	19
3.	Ceftriaxone+ Calcium Gluconate/Carbonate	Risk of particulate precipitation in lungs	16
4.	Norfloxacin+ Ondansetron	Risk of prolongation of qtc interval	12
5.	Phenytoin+ Atorvastatin	Decrease in levels of atorvastatin	10
6.	Chlorpheniramine+ Midazolam	Increase in sedation	7
7.	Azithromycin+ Calcium Carbonate	Risk of acute hypotension and renal insufficiency	2
8.	Enalapril+ Furosemide	Risk of hypotension	1
9.	Ciprofloxacin+ Metformin	Risk of hypoglycaemia	1

Table 4 is a list of most commonly occurring drug interactions along with their occurrences.

A total of 100 prescriptions were included from the General medicine department of a tertiary care hospital with the aim to analyze the potential for drug-drug interactions within the prescriptions. The overall incidence rate of DDIs in the present study was found to be 29.3% which was lower than the incidence rate of DDIs study conducted by Virendra et al. (2010) which was found to be 30.67% and more than the study conducted by Eslami et at. (2008) which was 14.66%.

In general, elderly patients are at higher risk for DDIs because they are likely to have multiple diseases and polypharmacy that usually occur with an increased duration of disease condition and altered physiology. In many of the reported studies, age more than 60 was reported as an independent risk factor for DDI (James et al., 2004). The results are in line with other studies which also showed that DDIs are more frequent in older patients who are on polypharmacy (Bjorkman et al., 2002).

Most frequent comorbid conditions were cardiac diseases (25%), infectious diseases (20%), cerebrovascular diseases and epilepsy (15%), diabetes mellitus (11%), anemia (10%), hypertension and acute pancreatitis (8%) and chronic kidney disease (5%).

Ceftriaxone was the most frequently prescribed drug in a total of 100 prescriptions. The most common DDI identified was ceftriaxone with furosemide (19%), heparin (19%) and calcium-containing salts(16%). Out of all interactions, 11 (2.2%) were serious, 114 (22.8%) moderate, and 48 (9.6%) were minor interaction. Age of the patients and the number of drugs prescribed are significantly correlated with drug interactions.

87 prescriptions out of 100 had DDIs. The total number of DDIs was 173 with a mean number of 5.90 ± 6.01. Most common drug category implicated in DDIs was anticoagulants 50.9%. Most common DDI was seen with ceftriaxone and least common with calcium-containing salts. Other frequently prescribed drug pairs responsible for DDIs were ceftriaxone + furosemide, ceftriaxone + heparin, ceftriaxone + calcium carbonate, norfloxacin +ondansetron, phenytoin + atorvastatin, chlorpheniramine + midazolam, enalapril + furosemide and ciprofloxacin + metformin.

Drug interactions were found to be more associated with the class of Anticoagulants drugs. This was similar to the study of Smithburger et al. (2010) reported the involvement of blood coagulation modifier in a maximum number of DDIs.

Out of the total DDI identified, 27.9% were pharmacodynamic interactions and (60.3%) were pharmacokinetic interactions and (8.04%) interactions had an unknown mechanism of drug interaction The findings obtained here are similar to those reported by Vonbach et al. (2008) who reported 76% of pharmacokinetic and 22% of pharmacodynamic interactions respectively.

In our study we also reported high drug interactions and most frequent drug interaction were between ceftriaxone and furosemide 19 (21.98%), followed by norfloxacin and ondansetron 12 (13.7%) phenytoin and atorvastatin 10 (11.4%), chlorpheniramine and midazolam 7 (8.04 %%), azithromycin and calcium carbonate 2(2.29%) and enalapril and furosemide 1 (1.14%).

The findings of this study revealed that the prevalence of DDIs was higher in prescriptions related to cardiac diseases (28.7%). Conversely, the least number of DDIs was observed in CNS related diseases (3.44%). While the prevalence of DDIs in prescriptions with respiratory

disease, GI problems, endocrine diseases, and infectious diseases were 25.2%, 16.9%, 3.4%, and 5.74% respectively.

The results of our study revealed that the most common drugs associated with major interactions of significant clinical importance were those prescribed in cardiovascular diseases. With regard to the interactions detected, our studies found more DDIs in the fields of cardiovascular diseases, hematology, neurology, Gastrointestinal.

Management of DDIs, medication withdrawal and change with another alternative or dose reduction should be the first step to be employed for the rectification of this problem and improve patient safety in hospital setups. The results of this study brought into light an important aspect for future research which is focused on the geriatric population. This study has revealed that this sect of the group is more prone to drug interactions, thus it is the need of time to explore this area in order to promote safe, and effective therapies without any drug-related problems like drug-drug interactions.

CONCLUSION

The study was conducted to assess the prevalence, severity, and significance of potential drug interactions the DDIs in the hospitalized patients of general medicine wards of tertiary care hospital. This study demonstrated a high prevalence of potential DIs due to the complexity of pharmacotherapy. The interactions were associated with a number of drugs, the length of stay and the characteristics of the administered medication.

The result of the study showed a frequency of DDIs to be 29.3%. The study concluded that DDIs are more prevalent in patients suffering from co-morbidities due to increasing the number of drugs in their prescription. The frequency of drug interactions could have been less with more judicial use of the drugs.

Patients with co-morbid conditions and elderly were found to be associated with more number of drug interactions. Potential drug interactions are frequent among Patients prescribed multiple medications and the rate is directly related to the number of drugs prescribed.

CONFLICT OF INTEREST

None declared.

REFERENCES

Akram A, Parimalakrishnan S, Mohanta GP, Manna PK, Manavalan R. Incidence of adverse drug reactions with commonly prescribed drugs in tertiary care teaching hospital in India. International Journal of Pharmaceutical Sciences. 2012;3(1):1-5.

Arvind K, Shobha Churi. Assessment of drug-drug interactions in hospitalized patients in India. Asian Journal of Pharmacy Clinical Research. 2011;1(4):62–65.

Bertoli R, Bissig M, Caronzolo D. Assessment of potential drug-drug interactions at hospital discharge. Swiss Medical Weekly. 2010;140:w13043.

Bjorkman IK, Fastbom J, Schmidt IK, Bernsten CB. Drug-drug interactions in the elderly. Annals of Pharmacotherapy. 2002, 36, 1675–1681.

Carruthers S, Hoffman B, Melmon K, Nierenber D, Hoffman BB, et al. Melmon and Morrelli's Clinical Pharmacology. 4ed. McGraw-Hill; 2000, 1259-67.

Delafuente JC. Understanding and preventing drug interactions in elderly patients. Critical Review Oncology Hematology. 2003;48(2):133-43.

Eslami S, de Keizer NF, Abu-Hanna A. The impact of computerized physician medication order entry in hospitalized patients–a systematic review. International Journal of Medical Informatics. 2008;77(6):365-76.

James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM:Adverse drug reactions as cause of admission to hospital: prospective analysis of 18820 patients. BioMedical Journal. 2004, 329,

Nekkanti H, Mateti UV, Vilakkathala R, Rajakannan T, Mallayasamy S, Padmakumar R. Predictors of warfarin-induced bleeding in a South Indian cardiology unit. Journal of Clinical Pharmacology. 2012;3(1):22-25.

Rajakannan T, Mallayasamy S, Guddattu V, Kamath A, Vilakkthala R, Rao PG, et al. Cost of adverse drug reactions in a South Indian tertiary care teaching hospital. Journal of Clinical Pharmacology. 2012;52(4):559-65.

Vonbach P, Dubied A, Krahenbuhl S, Beer JH. Evaluation of frequently used drug interaction screening programs. Pharmacy World & Science. 2008; 30:367–374.