

STUDY OF IDENTIFICATION AND ASSESSMENT OF DRUG-DRUG INTERACTIONSShekar H. S¹, Chandrashekhar H. R², Bhagawan B. C³, Alirezasahebde⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: INTRODUCTION: Drug–drug interactions can be defined as pharmacological or clinical response to the administration of drug combinations that is different from its known effects of two or more than two medicines. It frequently conjures images of a sudden catastrophic and even fatal outcome. While such an event can occur and it is important to prevent in the clinical set up. Drug interactions can occur by pharmacokinetic & pharmacodynamic interactions. The antipsychotics are known to have more drug interactions compared to any other class of drugs hence we aimed for the identification of drug interactions of psychiatric drugs. **METHODOLOGY:** The data was collected from medication chart of inpatients in the psychiatric department and analyzed the interactions using Stockley’s drug interactions, Dipiro etc. **RESULTS AND DISCUSSION:** The study includes 508 samples out of which 368 case were found to have interactions. The cobalamine and pantoprazole interactions were found to be 36.14% and the combination of antipsychotics, anticonvulsants with anxiolytics and anticonvulsants were 10.22 %.

KEYWORDS: Drug-Drug interactions, Disulfiram, NSAIDS.

INTRODUCTION: Drug interaction occurs when the effect of one drug is modified by another drug(s), may arise either from alteration of the absorption, distribution, biotransformation or excretion of one drug by another, or from combination of their actions or effects.^{1,2}

Drug interactions can be a consequence of various situations that reflects the growing number of drugs available in the market, increasing complexity of polytherapy and the very widespread practice of self-medication makes the situation more severe and difficult. Most of the studies evaluated, analysed and estimated that drug interactions may affect up to 63% of all hospitalized patients.^{3,4,5} These may occur due to several reasons. For example, accidental misuse or younger people tend to metabolize drugs faster than older people or those who smoke the cigarettes metabolize clonazepam and olanzapine faster than those who do not. Co-morbid medical conditions that decrease the hepatic functions, such as cirrhosis or congestive heart failure, are likely to decrease the rate of drug metabolism. Cytochrome P450 enzymes are polymorphic; there exist ethnic differences in hepatic enzymes that influence the pharmacokinetics of drugs and also due to lack of knowledge about the active ingredients involved in the relevant substances. Drug interactions are to be avoided, due to the possibility of poor or unexpected outcomes.⁶

Drug-drug interactions are a concern for the prescriber because they have the potential for causing untoward outcomes for everyone involved, morbidity and even mortality for the patients, liability for the prescriber and increased costs for the healthcare system. The risk of unintended and untoward drug interactions is increasing in concert with both the increasing number of pharmaceuticals available and the number of patients on multiple medications. Many studies have found that patients on psychiatric medications, such as antidepressants, are on more medications

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than patients not on psychiatric medications. It is important for prescribers to appreciate that medications interact not on the basis of their therapeutic use but on the basis of their pharmacodynamic and pharmacokinetic characters.²

It is easy to understand that the occurrence of drug interaction and can mimic virtually any clinical presentation imaginable from catastrophic to the everyday problems seen in practice and can present in the multitude of different types of serious adverse events, such as sudden death, seizures, cardiac rhythm disturbances, serotonin syndrome, malignant hypertension, neuroleptic malignant syndrome and delirium.⁷⁻¹⁷ Factors that predispose to drug interaction include poor tolerability (patients sensitive to adverse drug effect),¹⁸⁻²² lack of efficacy (patient resistant to beneficial drug effect),²³ symptoms that mimic or lead to a misdiagnosis of a new disease,²⁴⁻²⁶ the apparent worsening of the disease being treated and withdrawal symptoms or drug-seeking behavior on the part of the patient.^{27,28} All drugs, except anti-infectives, are administered to change human physiology.²⁹

Those changes can present in every way clinically imaginable. For this reason, the prescriber should keep in mind that the patient may not be doing well because of the medications he is receiving rather than despite the medications receiving.³⁰ Understanding and identifying drug interactions with psychiatric medications is perhaps more challenging than in any other area of medicine. The reason is complexity of the organ they affect and its output.³¹

Every identified neurotransmitter has 2-17 receptor subtypes. Thus, the human brain may contain thousands of receptors, which are the primary targets of drug action. There are different enzymes for the synthesis and degradation of these neurotransmitters, different uptake pumps and storage mechanisms. These regulatory proteins can be the target for drug action. Thus, current drugs may interact pharmacodynamically in ways that are neither understood nor predictable at the present time.³² Their detection is dependent on the careful assessment at the time of a medication prescribed by the prescriber.²⁸

METHODOLOGY: The 508 patients who have fulfilled study criteria were included for the study. The study was conducted for a period of 9 months from January-2013 to September 2013. The data was collected from medication chart and Patient attenders. The patients who are admitted to psychiatric department with the clinical conditions and treated with two or more than two drugs and fulfil study criteria in psychiatric department at tertiary care teaching center, Bangalore. The data was interpreted and evaluated using standard references.

MATERIAL AND METHODS: A prospective study was conducted on inpatients of psychiatric department at tertiary care teaching Hospital, Bangalore, who have fulfilled inclusion criteria and on therapy. The patient consent form was taken from the patient care taker. The Medical record, case sheets of patients was reviewed and the drug data was collected. Any identified Drug interactions assessment was done for their severity of reactions and the mechanism and time of onset of Drug interactions using recourses like Stockley's drug interaction, patient drug facts etc.

RESULTS: The work illustrates the drug interactions at psychiatric department in tertiary care teaching Hospital, Bangalore. Around 508 patients were included for the study, among this 368 patients were found to have drug interactions in 11 different forms has been observed as shown in the below table.

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SL. NO.	NAME OF DRUGS	INTRACTION WITH	INTERACTION EFFECTS	NO. OF CASES	% OUTCOME
1	CHLORDIAZPOXIIDE	DISULFIRAM	INCREASES SERUM LEVEL OF CHLORDIAZPOXIDE AND CAUSE DROWSNESS	26	7.06%
2	INJ NEUROBION	PANTAPRAZOL	DECREASES EFFECT OF VIT B12	133	36.14%
3	OLENZAPINE	LORAZPAM	ADDITIVE TOXICITY OF LORAZPAM/CNS DEPPRESION/SEIZURE//STROKE	31	8.42%
4	VALPORIC ACID	LORAZPAM	INCREASES LORAZPAM CLEARANCE AND DECREASES THE VALPORIC ACID CLEARANCE /STROKE	10	2.71%
5	VALPORIC ACID	OLENAZPINE	ADDITIVE TOXICITY /TACHYCARDIA/ AGITATION/COMADYSTHERMIA	7	1.90%
6	VALPORIC ACID	CLONAZPAM	INCREASES CLONAZPAM CLEARANCE AND DECREASES THE VALPORIC ACID CLEARANCE	11	2.98%
7	VALPORIC ACID	RISPERIDON	OEDEMA	4	1.08%
8	RISPERIDON	HALOPERIDOL	NEUROLEPTIC MALIGNANT SYNDROME	19	5.16%
9	RISPERIDON	FLOUXETIN	AKATASIAPAINFUL BILATERAL BREAST ENLARGMENT/OBSSEIVE AND COMPULSIVE DISORDER/SEDATIVE AND CONSTIPATION	7	1.90%
10	BUPRION	HALOPERIDOL	BUPRION INCREASE PLASMA LEVEL OF HALOPERIDOL	1	0.27%
11	FLOUXETIN	OLENAZPINE	SEROTONIN SYNDROME	3	0.81%

DISCUSSION: The study illustrates total sample size of 508 among this 368 samples were found to have drug interactions each other. 26 patients who were treated by chlordiazapoxide with disulfiram account for 7.06% of drug-drug interactions which increase the concentration of chlordiazapoxide and causes drowsiness.

Buprion with haloperidol was prescribed for one patient accounting for 0.27% of drug interactions and buprion is reported to increase plasma concentration of haloperidol.

Out of 368 patients 133 patients were found to have drug interactions. The combination between cobalamine and pantaprazole which accounts for 36.14% of the total sample size. Pantoprazole was found to decrease the effects of vitamin B 12.

The 3patients were prescribed olanzapine with flouxetin which causes postural hypotension, drowsiness/increased heart rate/CNS depression and accounts 0.59% of drug interactions. The combination of antipsychotics, anticonvulsants with anxiolytics, anticonvulsants were prescribed for 52 patients, which accounts for 10.22 % of drug interactions. Among 52 patients 31 patients were with olanzapine and lorazepam which causes additive toxicity of lorazepam accounting for 8.42% of drug interactions and causes CNS depression, seizures and stroke. Ten patients were prescribed valproic acid and lorazepam which causes increased lorazepam clearance and decreases the valproic acid clearance, which account for 2.71% of drug drug interaction. The 11 patients were treated with valproic acid and clonazepam which causes increased clonazepam clearance and decreases valproic acid clearance accounting for 2.98% of drug interactions.

The co-administration of anticonvulsants with antipsychotics prescribed for 30 patients out of 508 patients accounts for 5.85% of total drug interactions. The7 patients were treated with valproic acid and olanzapam which accounts for 1.90% of drug interactions, causes additive toxicity, tachycardia, agitation, coma, dysthermia and 4 patients were treated with valproic acid and

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risperidon which causes edema, accounts for 1.08 % of drug interactions and 19 patients were treated with risperidone and haloperidol which causes neuroleptic malignant syndrome accounting for 5.16 % of drug drug interactions.

The co-administration of antipsychotics and anticonvulsants with antidepressants were 10 patients out of 508 cases accounts for 1.96% of drug interactions. The 7 patients were treated with risperidone and fluoxetine which causes akathisia, painful bilateral breast enlargement, obsessive and compulsive disorder. Three patients were prescribed with sedatives and constipation accounts 1.90% of (fluoxetine+olanzapine) drug drug interactions causes serotonin syndrome.

CONCLUSION: Drug drug interactions are more serious around the world, to be avoided unintended and untoward Drug interactions. The prescriber must understand the fundamental principles of pharmacology and good clinical practice and must follow the knowledge of the pharmacokinetic and pharmacodynamic characteristics of the drugs prescribed to patients. This educational review has addressed these principles summarizing the major pharmacodynamic and pharmacokinetic interactions affecting and/or caused by commonly used neuropsychiatric medications.

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