

**ASSESSMENT OF DRUG INTERACTION OF ANTIDEPRESSANTS WITH OTHER PRESCRIBED DRUGS**SAMEER DHINGRA<sup>1,2</sup>, MILIND PARLE<sup>1</sup>

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**ABSTRACT**

**Objective:** The purpose of this study was to assess the frequency of combination of antidepressants with other drugs and risk of drug interactions in the setting of two private hospitals' units in India.

**Methods:** Prescriptions of patients admitted to two private hospitals from April 2010 to June 2010 were surveyed from the hospitals' data processing center. A manual search of case notes of all patients admitted to the psychiatric units from April 2007 to March 2010 and all patients registered in the psychiatric outpatient clinics in May 2010 was carried out. Patients taking any antidepressant were identified and concomitant use of drugs was checked by means of a software program (Micromedex DrugReax®) drug interactions were identified.

**Results:** Out of 5,632 patients admitted to the hospitals, 73 (1.3%) used antidepressants and 21 (28.7%) were at risk of drug interaction. Out of 476 patients in the psychiatric units, 112 (23.5%) used antidepressants and 27 of them (24.1%) were at risk. Out of 92 patients in the psychiatric outpatient clinics, 47 (51%) took antidepressants and 11 (23.4%) were at risk. In general, the use of antidepressants was recorded in 232 patients and 59 (25.4%) were at risk of drug interactions. Twenty-two different forms of combinations at risk of drug interactions were identified: six were classified as mild, 14 moderate and two severe interactions with acute clinical toxicities.

**Conclusion:** In the hospitals general units' prescriptions, the number of drug interactions per patient was higher than in the psychiatric units; and prescription for depression was lower than expected.

**Keywords:** Drug interactions, Antidepressants, Drug utilization, Severity, Prescriptions.

**INTRODUCTION**

Depression represents a major and growing public health burden: it is estimated to be the leading cause of mental disability worldwide and is predicted to be the 2<sup>nd</sup> leading cause of all health disability by 2030<sup>1</sup>. Though estimates from developing countries are not available, depression costs the US economy more than US\$ 43 billion annually in medical treatment and lost productivity<sup>2</sup>.

The association of depression with several clinical conditions has been thoroughly studied in various studies<sup>3-12</sup>. Multiple medication use is common in clinical practice especially in patients with comorbid conditions<sup>13</sup>. Antidepressant drugs are effective in the treatment of depression and various other medical conditions along with other prescribed drugs<sup>14</sup>.

Over the past decade, there has been an increase in the number and types of antidepressants available and very little is known about their interactions with other prescribed drugs. These drug interactions may be due to pharmacodynamics or pharmacokinetic causes. Pharmacokinetics comprehends the processes of drug absorption, distribution, metabolism and excretion. Pharmacodynamics is related to drug biochemical and physiological processes<sup>15</sup>. However, the use of antidepressants by patients with other conditions or in use of other medications requires special caution because of potentially harmful drug interactions<sup>15-18</sup>. The clinically significant drug interactions with antidepressants are described in the literature<sup>19</sup>.

Literature review indicates that most of the studies pertaining to drug interactions of antidepressants with other prescribed drugs have been carried out in other countries and perhaps this is the first-time a study has been carried out in India. The objective of this study was to assess the frequency of combination of antidepressants with other drugs that may result in drug interactions in the setting of two private hospitals' units (general, psychiatric and psychiatric outpatient clinic).

**MATERIALS AND METHODS**

The present study was carried out in three areas of the hospitals studied: general, psychiatric units, and psychiatric outpatient clinics. Prescriptions for 5,632 patients admitted to all hospitals' units from April 2010 to June 2010 were surveyed at the hospitals' Data Processing Center. A manual survey of case notes available of all patients admitted to the psychiatric units from April 2007 to March 2010 was performed, as well as a manual survey of all case notes of patients registered in the psychiatric outpatient clinics in both the hospitals in May 2010.

Any patient who took any antidepressant was identified, and then the drugs concurrently used were checked by means of a software program (Micromedex DrugReax®), all possible combinations were reviewed.

All antidepressants available were included. Lithium, valproic acid and carbamazepine were not included for being considered mood stabilizers and not exactly antidepressants. Micromedex DrugReax® is an interactive drug interactions program that allows clinicians to check for interacting drug ingredients, their effects, and clinical significance.

It classifies interactions as minor, moderate and major\*. It provides drug-drug (including additive adverse effects), drug-food, drug-disease, drug-ethanol, drug-tobacco, drug-alternative medicine, and drug laboratory interactions, along with previous allergic reactions. More than 8,000 medications may be tested as to possible drug interaction with any number of drugs may be entered.

**Data analysis and Ethical consideration**

The data was subjected to descriptive analysis using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 15.0 for Windows). The study was approved by the institutional ethics committee. Additionally, there were no known conflicts of interest with this study

**Table 1: Drug interactions observed in general, psychiatric units and psychiatric outpatient clinics of two private hospitals**

	General units	Psychiatric unit	Psychiatric outpatient clinic	Total
Total number of patients	5632	476	92	6200
Patients using antidepressants	73 (1.3%)	112 (23.5%)	47 (51%)	232 (3.7%)
Patients with drug interactions *ns	21(28.7%)	27 (24.1%)	11 (23.4%)	59 (25.4%)
Total number of interactions	32	30	07	69

\*ns chi= 0.63 p=0.7298

## RESULTS

Of the total of patients studied (5,632) in the mentioned period, 73 (1.3%) used antidepressants. The antidepressants used were amitriptyline (n=42\*\*), imipramine (n=12), fluoxetine (n=10), nortriptyline (n=6), and sertraline (n=3). Thirty-two combinations with risk of developing drug interaction were identified in 21 patients (28.7%).

There were 512 admissions to the psychiatric units and a total of 476 patients, from April 2007 to March 2010. Thirty-two patients were admitted twice, four patients were admitted three times, and two patients were hospitalized four times in this period. Out of the total number of patients, 112 patients received antidepressants (23.5%). The antidepressants used were: imipramine (n=34), amitriptyline (24), sertraline (n=22), paroxetine (n=16), fluoxetine (n=14), venlafaxine (n=13), duloxetine (n=9), bupropion (n=7), nefazodone (n=4), and citalopram (n=3). Thirty drug interactions were observed in 27 patients (24.1%).

There were 92 patients registered in the psychiatric outpatient clinic in May 2010. Forty-seven of these patients used antidepressants (51%). The antidepressants prescribed, in order of frequency, were amitriptyline (n=21), imipramine (n=18), sertraline (n=13), fluoxetine (n=10), paroxetine (n=07), venlafaxine (n=06), bupropion (n=04), nefazodone (n=03), citalopram (n=03), duloxetine (n=03), mianserin (n=2), and amineptine (n=2). Seven drug interactions were observed in seven patients. A total of 232 patients received antidepressants and drug interactions were observed in 59 subjects (Table 1). There were 22 different forms of drug interaction. As to severity, six were minor, 14 moderate and two major.

\*Minor: The interaction would have limited clinical effects. Manifestations may include an increase in the frequency or severity of side effects but generally would not require a major change in drug therapy. Moderate: The interaction may result in an exacerbation of the patient's condition and/or require changes in drug therapy. Major: The interaction may be life threatening and/or require medical intervention to minimize or prevent serious adverse effects.

\*\*n= number of times the medication was used.

## DISCUSSION

In the study it was observed that approximately 23% of the patients admitted to private general hospitals with depressive symptoms would benefit from taking antidepressants. At the private hospitals, the proportion of patients using antidepressants in the general (non psychiatric) units is quite small (1.3%). Identifying patients with depressive symptoms and giving them appropriate treatment not only improves their quality of life, but also results in better prognosis and shorter hospital stay. However, prescription of antidepressants to patients who are already taking several medications and suffer from other conditions (hepatic, renal, cardiac conditions, etc.) requires special care regarding possible drug interactions. The use of a software program makes practice easier at bedside and in private offices.

A limitation of this study is its small sample size, particularly in the psychiatric outpatient clinics. Also it was noted that few of the new antidepressant drugs are used but this probably reflects the medications available in private health facilities in India.

Todi et al<sup>20</sup> gave the following recommendations to minimize the risk of drug interaction:

1. Check medications every day.
2. Learn about the therapeutic and toxic effects of each drug.
3. Bear in mind the pharmacokinetic profile of each drug.
4. Remember that systemic conditions (renal and hepatic diseases) might require changes in dosage. An increase in the distribution volume might require higher doses; and reduced clearance might require decreased maintenance doses.
5. Check for possible drug interactions.
6. Minimize the number of drugs prescribed.
7. Whenever possible, replace medication with similarly effective but cheaper drugs. Prescribe generic drugs if efficacy is similar.
8. Plan monitoring of therapeutic and toxic effects. Check serum levels properly.

## CONCLUSION

28% of the patients in the general hospitals' units, 24% in the psychiatric units, and 23% in psychiatry outpatient clinics of the private hospitals who used antidepressants were exposed to the risk of drug interactions during the study period. In the general units, the number of drug interactions per patient was higher than in the psychiatric units; and prescription for depression was lower than expected. Drug interactions with antidepressants are an important cause for concern and we recommend caution while prescribing with other drugs.

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