

# Risk of drug interaction: combination of antidepressants and other drugs

## Risco de interação de drogas: combinações de uso de antidepressivos e outras drogas

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### Keywords

Drug interactions. Antidepressive agents. Drug utilization. Risk assessment. Prescriptions, drug.

### Abstract

#### Objective

To assess the frequency of combination of antidepressants with other drugs and risk of drug interactions in the setting public hospital units in Brazil.

#### Methods

Prescriptions of all patients admitted to a public hospital from November 1996 to February 1997 were surveyed from the hospital's data processing center in São Paulo, Brazil. A manual search of case notes of all patients admitted to the psychiatric unit from January 1993 to December 1995 and all patients registered in the affective disorders outpatient clinic in December 1996 was carried out. Patients taking any antidepressant were identified and concomitant use of drugs was checked. By means of a software program (Micromedex®) drug interactions were identified.

#### Results

Out of 6,844 patients admitted to the hospital, 63 (0.9%) used antidepressants and 16 (25.3%) were at risk of drug interaction. Out of 311 patients in the psychiatric unit, 63 (20.2%) used antidepressants and 13 of them (20.6%) were at risk. Out of 87 patients in the affective disorders outpatient clinic, 43 (49.4%) took antidepressants and 7 (16.2%) were at risk. In general, the use of antidepressants was recorded in 169 patients and 36 (21.3%) were at risk of drug interactions. Twenty different forms of combinations at risk of drug interactions were identified: four were classified as mild, 15 moderate and one severe interaction.

#### Conclusion

In the hospital general units the number of drug interactions per patient was higher than in the psychiatric unit; and prescription for depression was lower than expected.

### Resumo

#### Objetivo

Verificar a frequência de combinações de antidepressivos com outros medicamentos e o risco de interações medicamentosas em um hospital público no Brasil.

#### Métodos

Prescrições de todos os pacientes internados em um hospital público, em São Paulo, SP, de novembro de 1996 a fevereiro de 1997 foram analisadas pelo centro de processamento de dados do hospital. Foi realizada busca manual de todos os

### Descritores

*Interações de medicamentos. Antidepressivos. Uso de medicamentos. Medição de risco. Prescrição de medicamentos.*

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Received in 19/2/2002. Reviewed in 5/9/2002. Approved in 12/11/2002.

*prontuários de pacientes internados na enfermaria de psiquiatria do hospital de janeiro de 1993 a dezembro de 1995, assim como de todos os pacientes registrados no ambulatório de doenças afetivas em dezembro de 1996. Foram identificados os pacientes que usaram algum antidepressivo e as drogas utilizadas concomitantemente. Foram identificadas pelo programa Micromedex® as interações medicamentosas.*

#### **Resultados**

*Dentre os 6.844 pacientes internados nas enfermarias gerais (não psiquiátricas) do hospital, 63 usaram antidepressivos (0,9%) e 16 (25,3%) usavam medicações com risco de interação. Dentre os 311 pacientes da enfermaria de psiquiatria, 63 (20,2%) usavam antidepressivos e 13 (20,6%) apresentavam risco de interação. Dos 87 pacientes do ambulatório de doenças afetivas, 43 (49,4%) usavam antidepressivos e 7 (16,2%) apresentavam risco. Em geral, o uso de antidepressivos foi encontrado em 169 pacientes e 36 (21,3%) estavam em risco de interação medicamentosa. Vinte diferentes tipos de interações foram identificados, sendo 4 leves, 15 moderados e um grave.*

#### **Conclusões**

*Nas enfermarias gerais o número de interações medicamentosas foi superior em relação à enfermaria de psiquiatria; e o número de prescrições de antidepressivos foi menor do que o esperado.*

## INTRODUCTION

The association of depression with several clinical conditions has been thoroughly studied.<sup>2,3,4,6-10,12,15</sup> According to a study performed in Brazil, 20% of the patients admitted to a general hospital have depressive symptoms and could benefit from antidepressant treatment.<sup>3</sup>

However, the use of antidepressants by patients with other conditions or in use of other medications require special caution, mainly concerning drug interaction.<sup>1,5,11,13</sup>

Drug interaction is defined as modification of the effect of one drug by previous or concomitant administration of another drug. 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. The clinically significant drug interactions with antidepressants are described in the literature.<sup>1</sup>

The objective of this study is to assess the frequency of combination of antidepressants with other drugs that may result in drug interactions in the setting of public hospital units (general and psychiatric and affective disorders outpatient clinic).

## METHODS

The present study was carried out in three areas of

the hospital studied: general and psychiatric units, and affective disorders outpatient clinic. Prescriptions for 6,844 patients admitted to all hospital units from November 1996 to February 1997 were surveyed at the hospital's Data Processing Center. A manual survey of case notes of all patients admitted to the psychiatric unit from January 1993 to December 1995 was performed, as well as a manual survey of all case notes of patients registered in the affective disorders outpatient clinic in December 1996. Any patient who took any antidepressant was identified, and then the drugs concurrently used were checked. By means of a software program (Micromedex®) all possible combinations were surveyed.

All antidepressants available were included. Lithium, valproic acid and carbamazepine were not included for being considered mood stabilizers and not exactly antidepressants.

Micromedex® is a software program that has an interactive system to check drug interactions. Approximately 8,000 medications may be tested as to possible drug interaction. It also tests drug-food, drug-diseases, drug-alcohol, and drug-laboratory tests interactions, classifies interactions as minor, moderate and major,\* and presents interactions mechanisms and references.

## RESULTS

Of the total of patients studied (6,844) in the mentioned period, 63 (0.9%) used antidepressants. The antidepressants used were amitriptyline (n=51\*\*),

\*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.

imipramine (n=7), clomipramine (n=4), and nortriptyline (n=1). Twenty-five combinations with risk of developing drug interaction were identified in 16 patients (25.3%).

There were 350 admissions to the psychiatric unit and a total of 311 patients, from January 1993 to December 1995. Twenty-three patients were admitted twice, five patients were admitted three times, and two patients were hospitalized four times in this period. Out of the total number of patients, 63 patients received antidepressants (20.2%). The public hospital has only a psychiatric unit for female patients. The antidepressants used were: imipramine (n=37), amitriptyline (n=15), clomipramine (n=9), tranylcypromine (n=7), moclobemide (n=4), nortriptyline (n=3), fluoxetine (n=3) and maprotiline (n=2). Fourteen drug interactions were observed in 13 patients.

There were 87 patients registered in the affective disorders outpatient clinic in December 1996. Forty-three of these patients used antidepressants (49.4%). The antidepressants prescribed, in order of frequency, were clomipramine (n=12), imipramine (n=7), sertraline (n=7), fluoxetine (n=6), nortriptyline (n=5), maprotiline (n=3), moclobemide (n=2), tranylcypromine (n=2), paroxetine (n=1), amineptine (n=1), and mianserin (n=1). Seven drug interactions were observed in seven patients.

A total of 169 patients received antidepressants and drug interactions were observed in 36 subjects (Table). There were 20 different forms of drug interaction. As to severity, four were minor, 15 moderate and one major.

**DISCUSSION**

In the study it was observed that approximately 20% of the patients admitted to a general hospital with depressive symptoms would benefit from taking antidepressants. At the public hospital, the proportion of patients using antidepressants in the general (non psychiatric) units is quite small (0.9%). 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 affective disorders outpatient clinic. Also it was noted that few of the new antidepressant drugs are used but this probably reflects the medications available in public health facilities in Brazil.

Todi et al <sup>14</sup> give 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.

In conclusion, 25% of the patients in the general hospital units, 20% in the psychiatric unit, and 16% in affective disorders outpatient clinic of the public hospital 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 unit; and prescription for depression was lower than expected.

**ACKNOWLEDGMENTS**

To Dr Bernardo Garcia de Oliveira Soares and Dr Sebastião Marcos R. Carvalho of the Cochrane Centre of Brazil for their careful advice.

**Table** - Drug interactions observed through a software at hospital studied (general and psychiatric units, and affective disorder outpatient clinic).

	General units	Psychiatric unit	Affective disorder outpatient clinic	Total
Total number of patients	6,844	311	87	7.242
Patients using antidepressants	63 (0.9%)	63 (20.2%)	43 (49.4%)	169 (2.3%)
Patients with drug interactions *ns	16 (25.3%)	13 (20.6%)	7 (16.2%)	36 (21.3%)
Total number of interactions	25	14	7	46

\*ns chi=1.29 p=0.52

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