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## Evaluation of the use of Tricyclic Antidepressants Vs. Selective Serotonin Reuptake Inhibitors and Benzodiazepines in Geriatric Patients

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### ABSTRACT

To evaluate the use of tricyclic antidepressants, selective serotonin reuptake inhibitors and benzodiazepines in elderly patients aged over 60 years. Prospective, cross sectional, descriptive type of study was carried out in the general medicine department of a 640 bedded multispecialty tertiary care teaching hospital, South India. Benzodiazepines were prescribed in 79.6% patients, selective serotonin reuptake inhibitors in 12.3% and tricyclic antidepressants in 8.27%. The study identified 81.7% inappropriateness in prescriptions. Initiation of treatment with high dose after admission contributed to 32.6% while prescribing without proper indication accounted for 31.7%. Significant reduction of inappropriateness (48%) was observed during the post implementation phase, especially in the number of prescriptions of tricyclic antidepressants. The initial dose of alprazolam was reduced to 0.25 mg in all elderly patients. Prescribing benzodiazepines without proper indication reduced from 31.7% to 22%. Long acting benzodiazepines were not prescribed during this phase. The study demonstrated an overall improvement in the prescribing pattern of tricyclic antidepressants, selective serotonin reuptake inhibitors and benzodiazepines in elderly patients.

**Key Words:** Antianxiety agents, tricyclic antidepressants, selective serotonin reuptake inhibitors, benzodiazepines, elderly, prescriptions.

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## INTRODUCTION

Depression and anxiety are common among elderly patients. Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines (BZDs) are commonly used to treat this condition. SSRIs represent a major advance over tricyclic antidepressants because of their lower toxicity<sup>1</sup>. Elderly patients are particularly susceptible to adverse reactions of long and short acting benzodiazepines. Their use is associated with an increase in the incidence of falls and hip fractures, cognitive impairment, CNS depression, day time drowsiness and day time withdrawal effects<sup>2</sup>. In spite of the risks, there is evidence that benzodiazepines may be overprescribed to elderly patients<sup>3</sup>. However, the research available on appropriate use of TCAs, SSRIs and BZDs in elderly patients in India is surprisingly deficient for the magnitude of this issue. Therefore, the aim of the present study was to determine the prevalence of prescribing TCAs, SSRIs and BZDs for elderly inpatients, to identify inappropriate prescriptions of these groups of drugs, and to provide pharmacist intervention in order to improve appropriateness in prescribing pattern of these antianxiety agents and antidepressants in elderly patients.

## MATERIALS AND METHODS

A prospective, cross sectional descriptive study was carried out in the general medicine department of a 550 bedded multispecialty tertiary care teaching hospital, South India for a period of six months. Study protocol was approved by hospital authorities and permission to carry out the study was obtained from the hospital ethical committee. Patients aged over 60 years and above who were prescribed with TCAs, SSRIs or BZDs were included in the study. Written informed consent was obtained from each patient after explaining the purpose of the study. Their clinical, demographic and prescribing data were collected using data entry forms specially prepared for this purpose. Prescribing of antianxiety agents and antidepressants was considered inappropriate if the drug was started after admission for no acceptable indication or if the patient was admitted on a TCA, SSRI or BZD with a history of falls or impaired conscious level and no dose reduction was attempted. High initial doses, drug interactions, contraindications and long acting benzodiazepines were also considered inappropriate in elderly. Appropriate use of antianxiety agents and antidepressants was assessed for each patient. Therapeutic guidelines were prepared for the treatment of anxiety and major depressive disorder in elderly patients and circulated among the physicians. Pharmacist intervention was provided during the initial phase in order to reduce inappropriate prescriptions. A postimplementation study was conducted for assessing the effectiveness of pharmacist intervention in improving prescribing pattern of TCAs,

SSRIs and BZDs in elderly patients.

### Statistical Analysis:

Statistical analysis was performed using SPSS 11.0. Descriptive statistics were described as means with range and frequencies. A p value less than 0.05 was considered statistically significant.

## RESULTS AND DISCUSSION

Data were collected from 104 medical inpatients aged over 60 years and above. TCAs were prescribed in 8.27% of patients (mean  $0.105 \pm 0.30$ , 95% CI 0.04-0.16), SSRIs for 12.03% (mean  $0.153 \pm 0.362$ , 95% CI 0.08-0.22) and BZDs in 79.6% patients (mean  $1.125 \pm 0.386$ , 95% CI 1.05-1.2). The mean age of patients prescribed with TCAs, SSRIs and BZDs was  $67 \pm 4.47$  years and their mean length of stay was  $4.96 \pm 0.81$  days. Table 1 shows the list of TCAs, SSRIs and BZDs prescribed to elderly patients. Major diagnoses and concurrent medications prescribed for the patients were identified. Most of them were admitted with either diabetes (33.6%) or hypertension (29.8%). The average number of medical diagnosis per patient was  $5 \pm 7.6$ . Table 2 shows the combination of TCAs, SSRIs, and BZDs or with other antipsychotics prescribed for the elderly.

**Table-1: TCAs<sup>\*</sup>, SSRIs<sup>†</sup> and BZDs<sup>‡</sup> prescribed for elderly patients (N=104)**

Treatment variable	No. of patients
Benzodiazepines only	79 (75.9)
Alprazolam 0.25 mg/day	66 (63.4)
Alprazolam 0.5 mg/day	25 (24.0)
Alprazolam 0.5-10 mg/day	02 (01.9)
Lorazepam 1-2 mg/day	06 (05.7)
Clonazepam 0.25 mg/day	03 (02.8)
Clonazepam 0.5 mg/day	01 (0.96)
Nitrazepam 0.25 -5 mg/day	02 (01.9)
Diazepam 2mg/day	01 (0.96)
Amitriptyline 10-25 mg/day	02 (01.9)
Amitriptyline 75 mg/day	07 (67.3)
Clomipramine 25 mg/day	02 ( 01.9)
Escitalopram 5 mg/day	04 (03.8)
Sertraline 25 mg/	08 (07.6)
Sertraline 50 mg/day	04 (3.8)

\* tricyclic antidepressants

† Selective serotonin reuptake inhibitors

‡ Benzodiazepines

Figures in parentheses represent percentage

**Table-2:Fixed dose combinations of TCAs, SSRIs, BZDs, or antipsychotics prescribed (N=53).**

<b>Drug combination</b>	<b>No. of patients</b>
BZDs +Zolpidem	19 (18.26 )
BZDs + BZDs	11 ( 10.57)
SSRIs + BZDs	10 (9.61 )
SSRIs + Zolpidem	04 (3.84 )
TCAs +BZDs	02 (1.92 )
TCAs +Zolpidem	02 ( 1.92)
BZDs + Haloperidol	02 (1.92 )
TCAs +SSRIs	01 (1.92 )
SSRIs + Hydroxyzine	01 (1.92 )
BZDs + Hydroxyzine	01 (1.92 )

Figures in parentheses represent percentage.

Drugs were prescribed inappropriately for 85/104 (81.7%) prescriptions. Initiation of treatment with high dose after admission to hospital accounted for 34/104 (32.6%) inappropriate prescriptions and initiation of treatment without proper indication accounted for another 33/104 (31.7%) inappropriateness. Among the 51 drug interactions identified, 22 were of major severity. A feedback on study report and therapeutic guidelines on the use of TCAs, SSRIs or BZDs in elderly were prepared and circulated among the physicians. During the post implementation period, data from 50 patients were obtained. The study identified several prescriptions with amitriptyline though literatures suggest avoiding this drug in old age. Elderly patients are more susceptible to adverse effects, in particular to confusional states and orthostatic hypotension, and have a tendency to decreased biotransformation of the drug. There is an appreciable risk of toxic anticholinergic syndrome with amitriptyline in older patients<sup>4</sup>. SSRIs were less frequently prescribed than TCAs. Sertraline was the most commonly prescribed SSRI. In case of sertraline, no dose modification appears to be required<sup>4</sup>. Their relative safety and better acceptability has made them first line drugs in depression and allowed their extensive use in anxiety and depression<sup>5</sup>. Current study shows that 87.7 % of patients received alprazolam which is a short acting BZD. A study by Gurvich *et al* (2000)<sup>6</sup> also reported that short acting BZDs are commonly prescribed (93.3 %) among the elderly. Initial dose of alprazolam should be reduced in the elderly<sup>6</sup>. In elderly patients, BZDs may be dosed as follows: alprazolam 0.25-0.5 mg 3 times daily, lorazepam 2-3 mg daily divided in 2 or 3 doses and clonazepam 1-2 mg/daily<sup>7</sup>. Long acting BZDs (clonazepam, diazepam) should be avoided because they are likely to accumulate and have adverse effects (eg: drowsiness, impaired memory, impaired balance leading to falls and fractures). Short or intermediate acting BZDs with half life <24 hours (eg: alprazolam,

lorazepam) may be preferred over long acting BZDs<sup>8</sup>. In the present study 4.8 % of patients received long acting BZDs which is not recommended in elderly. Drug interactions were classified according to their severity as major, moderate and minor. Major and moderate drug interactions were observed in 43.1% and 56.8% of prescriptions respectively. A significant reduction in the inappropriateness (48%,  $p < 0.05$ ) was observed in the post implementation phase. During this phase, none of the prescription contained TCAs. The initial dose of alprazolam was reduced to 0.25 mg in all prescriptions. Number of prescriptions containing BZDs without proper indication reduced from 31.7% to 22% ( $p < 0.05$ ). In this phase there was no long acting BZDs and no prescriptions containing interacting drug combination such as alprazolam+codeine, alprazolam+ sertraline, alprazolam+ theophylline and theophylline+ lorazepam but some new interacting drug combinations (18%) were recorded. However, there was an overall improvement in the prescribing pattern of TCAs, SSRIs and BZDs in elderly patients.

## CONCLUSION

Current study recorded a large number of prescriptions with higher initial dose of TCAs, SSRIs and BZDs in elderly patients. Treatment with these drugs was initiated without proper indication in many instances. The study has also recorded certain clinically significant interacting drug combinations and long acting BZDs which are normally contraindicated in elderly. Though post implementation study revealed a significant reduction in overall incidence of inappropriateness in the prescribing of TCAs, SSRIs and BZDs in elderly patients, future research should document more evidence regarding the adverse impact of inappropriate prescribing on total health care cost and patient health outcomes.

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