Original Article

A Survey on Psychotropic Prescription Patterns in Elderly Bipolar Patients

Investigação dos Padrões de Prescrição de Psicotrópicos em Pacientes Idosos com Transtorno Afetivo Bipolar

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SUMMARY

There is a lack of knowledge about Bipolar Disorder (BD) in the elderly and also in psychopharmacology among these patients. Current treatment guidelines originate from controlled trials involving only mixed-age or young adult participants. To analyze the psychiatric medication used in a Brazilian sample of elderly bipolar outpatients and compare them to recent guidelines for medication treatment for BD. Bipolar patients aged 60 years and older were selected from two outpatient services in São Paulo, Brazil. Clinical characteristics and the use of psychiatric medications were obtained from medical records and interviews with all patients and relatives. One hundred and thirty five individuals were enrolled in the study. Sixty one percent of the patients were in polytherapy, and the association most commonly used was mood stabilizer with antipsychotic (16.3%). Mood stabilizers were been used by 90.4% of the patients and the most prescribed was lithium. Among the patients using antipsychotics, 80% were using atypical antipsychotics. Thus the patterns prescription of our sample of elderly bipolar patients is in accordance with recent guidelines for medication treatment for BD.

Key words: antidepressant, antipsychotic, benzodiazepines, bipolar disorder, lithium, mood stabilizer, treatment guidelines

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RESUMO

Há uma deficiência no conhecimento do transtorno afetivo bipolar (TAB) e do seu manejo farmacológico em idosos. Guias atuais para o tratamento de idosos com TAB são originários de pesquisas envolvendo, em sua maioria, pacientes adultos. O presente estudo objetivou analisar o padrão de prescrição de medicações psiquiátricas em amostra de idosos com TAB e compará-lo com guias de tratamento para o transtorno. Pacientes com TAB e com mais de 60 anos foram selecionados de dois ambulatórios em São Paulo. Informações sobre características clínicas e uso de medicação psiquiátrica foram obtidas através de pesquisas em prontuários médicos e entrevistas com os pacientes e familiares. Cento e trinta e cinco indivíduos participaram do estudo. Sessenta e um por cento estavam em politerapia, sendo que a associação medicamentosa mais comumente utilizada foi de estabilizador do humor com antipsicótico (16,3%). Estabilizadores do humor estavam sendo utilizados por 90,4% dos pacientes no momento da pesquisa, sendo que o lítio era o mais prescrito. Entre os pacientes usando antipsicóticos, 80% deles utilizavam atípicos. Assim, o padrão de prescrição da amostra de pacientes idosos com TAB, investigada no presente estudo, estava de acordo com os guias propostos para o manejo clínico de pacientes com o transtorno.
Palavras-chave: antidepressivo, antipsicótico, benzodiazepínico, estabilizador do humor, guia de tratamento, lítio, transtorno afetivo bipolar

INTRODUCTION

In 2002, the percentage of persons older than 60 years was 10%, and the estimate is that by 2050 this percentage will have increased to up to 20% [1]. Therefore psychiatric disorders are also representing an increasing burden to society com-paring with other medical conditions. Worldwide, mental disorders will represent 15% of the total disease burden by 2050 [2].

Bipolar disorder (BD) is a chronic condition, and a common diagnosis on psycho-geriatric wards, representing around 25% of all inpatient admissions [3]. In spite of this, there is a lack of knowledge about BD in the elderly and also in psychopharmacology among elderly BD patients. Because of such situation elderly patients with BD pose particular challenges in terms of appropriate pharmaco-therapy[4]. Current treatment guidelines and recom-mendations in general originate from controlled trials involving mixed-age or young adult parti-cipants and do not pay adequate attention to particular situations involving elderly patients [5,6,7]. Only recently, prospective studies on treatment of BD in elderly patients were started but using a small number of participants[8]. However, neither the efficacy nor the minimum and maximum dosages have been clearly established for lithium, valproate, carbamazepine, and other anticonvulsants for elderly patients [4].

Thus the aim of the study was to analyze the psychiatric medication used in a Brazilian sample of elderly BD outpatients and compare them to guidelines for medication treatment for the disorder.

METHODS

The clinical records of patients with BD type I according to the International Classification of Diseases - 10th edition from the World Health Organization (CID-10) [9], aged 60 years and older, were selected from two outpatient specialized services form university hospitals in São Paulo, Brazil. Demographic and clinical characteristics and the use of psychiatric medications during the treatment of BD were obtained from medical records and interviews with all patients and at least one relative trough the same psychiatrist. Patients with psychiatric comorbidity (axis I) were excluded. The Montgomery-Asberg Depression Scale [10] and the

Young Mania Scale [11] were used to identify whether the patients were euthymics, in depressive (score ≥ 7) or maniac phases (score ≥ 7). We compared the patterns prescription currently used by the elderly BD patients with guidelines for treatment of BD.

This survey was approved by the local ethical committee (CAPPESQ n. 155/02).

RESULTS

A total of 302 medical charts were selected from both medical institutions. One-hundred and sixty-seven subjects were excluded (76 subjects were not found, 52 subjects were incorrectly diagnosed, 17 were deceased, nine subjects refused to participate in the study and 13 subjects were hospitalized at the time of recruitment). One hundred and thirty five individuals were enrolled in the study, with a mean age of 68.7 years (sd = 5.5 years). One third (65.9%) were women and 43% were married. The mean duration of the disease was 28.9 years (sd = 14.9 years), with 0.9 affective episodes per year on average (sd = 0.7 episodes/year)

Six patients (4.4%) were not using psychotropic medication at the time of the study. Eighty three patients (61.5%) were in polytherapy, and the associations most commonly used were mood stabilizer with antipsychotic (16.3%) and mood stabilizer and benzodiazepine (15.5%) (Table 1).

Table 1 - Psychiatric medication currently used for the elderly patients with bipolar disorder (n=135).

	N	%
Mood stabilizers	122	90.4
Benzodiazepines	45	33.3
Antipsychotics	40	29.6
Antidepressants	30	22.2
Mood stabilizers only	44	32.6
Antipsychotics only	2	1.5
Mood stabilizer and antipsychotics	22	16.3
Mood stabilizer and benzodiazepines	21	15.5
Mood stabilizer and antidepressants	14	10.4
Benzodiazepines and antidepressants	4	3.0
Mood stabilizer, antipsychotics and benzodiazepines	10	7.4
Mood stabilizer, antidepressants and benzodiazepines	8	6.0
Mood stabilizer, antipsychotics and antidepressants	3	2.2
Antidepressants, antipsychotics and benzodiazepines	1	0.7
No medication	6	4.4

Eighty two percent of the patients (n = 111) were euthymic, 13.3% (n = 18) were depressive and 4.4% (n = 6) were in maniac episode. Among the patients in maniac episode, all were using mood

stabilizer and half of them were using antipsychotics. None were taking antidepressants.

Antidepressants were being used by ten depressive patients, all of them with polytherapy with mood stabilizers.

Mood Stabilizers

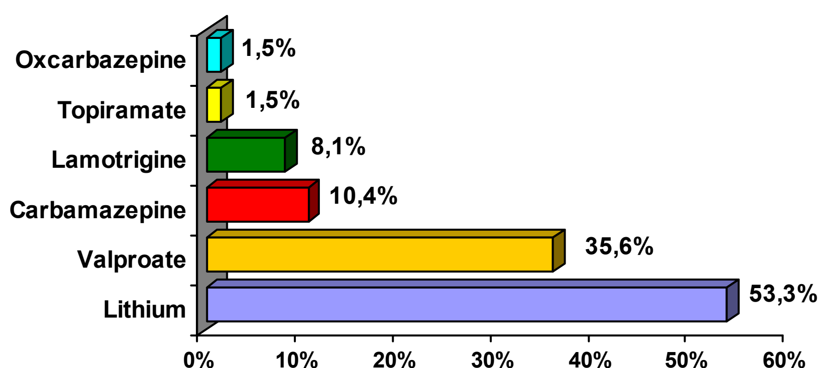
Mood stabilizers were used in all patients during the life course of BD, and 90.4% (n = 122) were still using them. A hundred patients (74.1%) were using only one mood stabilizer and the association most commonly used was lithium and valproate (VAL) (n = 10; 7.4%). Other associations were lithium and lamotrigine (2.2%), carbamazepine (CBZ) and lamotrigine (2.2%), lithium and CBZ (1.5%), oxcarbazepine and lamotrigine (0.7%), VAL and topiramate (0.7%), lithium, CBZ and lamotrigine (0.7%), lithium, VAL and lamotrigine (0.7%), and lithium, oxcarbazepine and lamotrigine (0.7%).

The most common mood stabilizer prescribed during the treatment of BD was lithium, in 119 patients (88.1%). At the time of the study, 72 elderly patients (53.3%) were using it, in a daily dose ranging from 300mg to 1500mg (mean dose = 755.2 mg per day, sd = 260.5mg) during 6.5 years on average (sd = 5.8years).

Valproate was being used by 35.6% of the patients at the time, in a mean dose of 1022 mg per day (sd = 383mg) during 3.4 years on average (sd = 1.9 years). Patients with mixed episodes had a tendency to use VAL more frequently than the patients without a history of these episodes (p = 0.05).

Fourteen patients (10.4%) were using carbamazepine and its daily dose ranged from 400mg to 800mg (mean = 585.7 mg/day; sd = 146.0mg). Other mood stabilizers used were lamotrigine (n=11; 8.1%), topiramate (n=2; 1.5%) and oxcarbazepine (n=2; 1.5%) (Graphic 1).

Graphic 1 – Use of mood stabilizers in elderly bipolar patients (n=135)



Antidepressants

Antidepressants were being used by 22.2% of the patients (n=30), and 105 patients (77.8%) had already used some antidepressant in their lives. Fifteen patients (11.1%) were using selective serotonin reuptake inhibitors (SSRI) (ten patients with sertraline, two with paroxetine, two with fluoxetine and one patient using citalopram). Tricyclic antidepressants were being used in nine patients (6.7%) (six patients in use of nortriptyline, two with imipramine and one with amitriptyline), and three patients (2.2%) were using monoamine oxidase inhibitor (MAOIs) tranilcipromine. Others antidepressants used were bupropion (n=3; 2.2%),

venlafaxine (n=1; 0.7%) and mirtazapine (n=1; 0.7%).

Two patients were using association of antidepressants (fluoxetine and nortriptyline, nortriptyline and tranilcipromine), both still presenting depressive episode.

Antipsychotics

Eighty two percent of the patients (n = 111) had used some antipsychotics during the treatment of BD and forty patients (29.6%) were still taking antipsychotics at the time of the study. Among these patients, the majority were using atypical antipsychotics (n=32; 80%) and olanzapine was the most used (n=20; 50%).

Eleven patients (8.1%) were using risperidone, five (3.7%) were using haloperidol, two (1.5%) levomepromazine and chlorpromazine and quetiapine were being used by one patient each.

Benzodiazepines

One third of the patients (n = 44) were using benzodiazepines and 23.7% (n = 32) were taking clonazepan. Other BDZ used were diazepam (n = 4; 3%), flunitrazepan (n = 2; 4.5%), lorazepan (n = 1; 0.7%), alprazolan (n = 1; 0.7%), midazolan (n = 1; 0.7%), bromazepan (n = 1; 0.7%) and flurazepan (n = 1; 0.7%).

DISCUSSION

There are only a few reports in the medical literature concerning the psychotropic medication in elderly BD patients. The present description aims to present a broad view of this situation, helping clinicians, hospital managers and health policy makers.

In our survey, the most commonly used medication by patients with BD was lithium carbonate. During life-time treatment, 88% of the patients had used this medication, a similar percentage found by Snowdon (1991) [12]. In such study, the author described that 90% of elderly BD patients used lithium [12].

In recent years, however, it has been observed an increased use of anticonvulsants as mood stabilizers [13]. This change can be observed in the reports about mood stabilizers use in the last 10 years. In 90's, Tohen *et al*. (1990) [14], Dhingra & Rabins (1991) [15] and Lish *et al*., (1994) [16], had shown that the percentages of patients who were taking lithium was 67%, 83.3% and 77% respectively. In Kupfer *et al*. (2002) [17] and Raymont *et al*. (2003) [18] described that only 37.1% and 33% of patients respectively, were using this medication. The use of lithium in BD patients has become restricted, especially in the elderly. Some possible reasons for that are: a) the possible greater incidence of collateral effects, which involve higher repercussions when associated with clinical comorbidities; b) introduction of new effective drugs for BD treatment which are supported by commercial interests; c) lithium requires a more carefully follow-up from the psychiatrists, whom must have more attention and medical skills [19]. Shulman *el al*. (2003) [20] have shown that the number of new valproate users surpassed the number of new lithium users in 1997, so while the curve from the lithium was going down, the curve for the VAL was going up, and crossed in 1997. VAL has gained more attention and is being more widely prescribed, although there is no evidence that this medication is superior to lithium in this population. In the last decade there was a changing prescription patterns involving mood stabilizers without research evidences [20].

However in special situations, there are some evidences confirming good response for VAL use. The association found between mixed episodes and VAL is in accordance with the literature and guidelines, which shows that the presence of mixed states as one predictive factor for good response to VAL [5].

No depressive patient was in monotherapy with antidepressants, and all of them were in therapy combined with mood stabilizer, following orientations from treatment guidelines. The guidelines recommend the SSRIs for BD depression (these antidepressant agents were the most frequent used

by our sample). The guidelines also do not recommend the use of antidepressant drugs for BD manic patients [21,22].

Due the increased risk to induce movement disorders like distonia and discinesia, and serious parkinsonism symptoms with classical antipsychotics, atypical antipsychotics have become an option for this population, with good tolerance and effectiveness [23]. A demonstration of this was the number of 32 patients (23.7%) of our sample, who were currently in use of atypical antipsychotics. Such medication has also been preferred by the consensus of APA [5,24]. In a study with BD patients from Frangou *et al*. (2002) [25], only 7.9% of the patients were using atypical antipsychotics. This increase in the percentage of patients using atypical antipsychotics can be justified by the number of recent publications on the use of these medications in BD showing the efficacy in mania and also by the fact that these medications may produce a lower switch rate into depression than haloperidol [26,27]. However, In 2005, the US Food and Drug Administration (FDA) issued warnings on the use of second-generation antipsychotics for the treatment of behavioral disorders in elderly patients with dementia because of increased risk of death. Whether similar concerns apply to elderly BD patients without dementia is unclear [23]. Drug concentrations in plasma are affected by age, sex, genetic differences, co-morbid diseases, physiological variations, and drug-drug interactions. For older patients, polypharmacy and multiple comorbidities are two of the most prominent considerations in choosing the right drug and dosage by the clinician. Sajatovic *et al*. (2005) [23] has showed that individuals with BD may develop dementia at a greater rate than others at the same age without BD, and that adverse drug reactions increase dramatically with advancing age.

Almost 75% of the patients using benzodiazepines in our sampler were in use of clonazepan at the time of the evaluation. There are a few studies analyzing the use of benzodiazepines in BD in the elderly, and the majority of them is about clonazepan [23]. The percentage of patients using benzodiazepines in our sample (33.3%) was higher than in other studies with BD patients, which ranged from 9.5% to 28% [16,17,25]. It's important to beware of the risks of these medications, especially in the elderly population, due to collateral effects such as sedation, cerebelar ataxia, mental confusion, somnolence and cognitive impairment.

The patterns prescription of our sample of elderly BD patients is in accordance with recent guidelines for medication treatment for BD. With few studies approaching treatment BD in old age, the professionals have used the knowledge gotten in studies with adult patients. Future studies research is needed to understand if this adherence is adjusted for the aged population.

In conclusion, in spite of the growing use of anticonvulsants as mood stabilizers, lithium was the mood stabilizer most used by the elderly BD patients of our sample. Psychiatrists are managing BD in the elderly according to treatment guidelines for adult BD patients. However in order of the pharmacokinetic and pharmacodynamic changes associated with aging the dosage guidelines derived from clinical trials in younger adults should not be automatically extrapolated to older adults.

We are aware some limitations of the present work. The sample size was modest. The study was not an epidemiological investigation. Our sample was specific from two academic hospitals of São Paulo and may not represent the elderly BD population in the community. The retrospective nature of this investigation may have produced less reliable and clear information on the clinical feature of BD and about the psychotropic drugs used by the patients.

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