USE OF ANTIDEPRESSANT MEDICATION DURING COGNITIVE AND DEPRESSIVE TREATMENT IN BRAZILIAN ELDERLY PATIENTS: A 180 DAY PROGRAM

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Abstract

Objective: There is an association between the severity of depression and functional impairment in the elderly, such that depression may deteriorate individuals' ability to perform daily activities, such as eating, dressing and personal care. The use of antidepressants may indirectly improve cognition, whereas some suggested that cognitive symptoms did not benefit from antidepressant treatment. Investigate the influence of the long-term use of antidepressants for an average period of 10 months on the cognitive and functional performances and psychiatric symptoms of a determined sample of elderly patients with depressive symptoms.

Method: Twenty non-dementia patients with complaints of depressive symptoms, aged between 60 and 90 years, were selected. Half of the sample received antidepressant treatment for 180 days or more. Clinical evaluations were performed using a cognitive scale, two functional scales and two psychiatric scales. A longitudinal analysis was performed comparing the results of the first and second evaluations (after prolonged use of an antidepressant for 180 days or more). These two were used to qualify and quantify the presence of depressive indicators and neuropsychiatric symptoms.

Results: Effect size ranged from –0.21 to 0 in control group and from 0.04 to 0.39 in experimental group. There was a significant effect of depressive symptoms only for the experimental group ($p<0.05$) and medium effect size equal to 0.39. The control group had no significant differences between the first and second evaluations for any of the cognitive, functional and psychiatric instruments. None of the subjects in the experimental group showed a significant effect due to the influence of antidepressants.

Conclusions: Our data suggest that antidepressants contributed to a reduction in depressive complaints in the experimental group, but not to cognitive symptoms. Our data are limited to a general assessment of non-specific cognition, and our patient sample was convenient, although it had specific selection criteria to ensure that all the participants had depressive complaints.

Key words: antidepressant treatment, cognitive symptoms, depression, elderly

Declaration of interest: none

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In the elderly, memory loss, speaking disorders, slow thinking, loss of functioning and psychosocial changes often occur due to different environmental conditions that generate depressive episodes (Argimon and Stein 2005), such as social contact disruption (Wild et al. 2011), social support dissatisfactions (Lieverse et al. 2013), loneliness (Holwerda et al. 2012), institutionalization (Luppa et al. 2010), poor social and economic conditions (Veras 2012), and alcohol dependence (Anstey et al. 2009) or medication abuse (Ekeh et al. 2013).

Submitted November 2012, Accepted April 2013

Depressive episodes

According to the International Statistical Classification of Diseases and Related Health Problems (ICD-10), depressive episodes are classified as 'light' when individuals can perform most of their daily activities, 'moderate' when they begin to have difficulty continuing their daily lives, and 'severe' when they experience remarkable feelings of worthlessness, low self-esteem, and suicidal ideation (Organization 1992, 1993).

Depressive episodes are more frequent among the elderly, and this prevalence is explained by factors associated with aging (Kessler et al. 2010). Subtle differences become more visible with advanced age, such as issues with melancholy and psychomotor disturbances (Blazer and Van Nieuwenhuizen 2012). Moreover, the elderly are more likely to experience reductions in social perspectives (Lapierre et al. 2011). Neuroendocrine and neurochemistry dysfunctions in the brain also occur with aging, and their etiologies are multifactorial (Francis et al. 2010).

The presence of an organic pathology increases the risk of psychiatric depression, which occurs in clinical comorbidities, such as dementia, cardiovascular disease, diabetes, hip fracture, osteoporosis, and weight loss (Francis et al. 2010). Alexopoulus et al. (Alexopoulos et al. 2002) suggest that clinical disease may contribute to the pathogenesis of depression through direct effects on brain function or through psychosocial or psychological effects. Given that chronic depression and chronic diseases exacerbate depressive symptoms, this is a complex relationship that has important implications both for the management of comorbidity and for the treatment of depression (Kok et al. 2011).

Cognitive and functional changes in depression

The following are the most common cognitive impairment dysfunctions in older patients with depression: a lack of initiative, a lack of planning, reduced mental flexibility, reduced verbal and visual memory, disorientation and distraction (Ávila et al. 2007).

There is an association between the severity of depression and functional impairment in the elderly, such that depression may deteriorate individuals' ability to perform daily activities, such as eating, dressing and personal care (Alexopoulos et al. 1988, Blazer and van Nieuwenhuizen 2012, Lenze et al. 2001, Parayba and Simões 2007, Penninx 1999). Over the lifespan depressive symptoms are associated with an increased risk of Alzheimer's disease even in patients who achieve remission in their symptoms of dementia following successful treatment for depression (Alexopoulos et al. 1993, Yaffe et al. 1999).

Antidepressant effects

There has been a growing interest in studies examining the effect of antidepressant treatments on depressive symptoms and cognition in elderly patients both with and without Alzheimer's disease, with a specific focus on identifying the influences of antidepressant drugs on overall performance and on the quality of life of the elderly and their families (Barnes and Yaffe 2011, Robinson et al. 2013). However, these studies are controversial (Byers 2011). The use of antidepressants may indirectly improve cognition (Han et al. 2012), whereas some suggested that cognitive symptoms did not benefit from antidepressant treatment (Fournier et al. 2013, Reifler et al. 1989). In fact, Reifler et al. 1989, noted that cognitive symptoms may be negatively affected by antidepressant drugs, as was evident in a study examining imipramine and amitriptyline in which the worst cognitive symptoms were attributed to the effects of the anticholinergic medication. Knegtering et al. 1994, concluded that the sedative effect of some psychotropic drugs might impair performance on tests that require concentration and attention, whereas anticholinergic medication may directly affect memory.

Thus, the choice of antidepressant is crucial for successful treatment and remission of depressive symptoms in elderly patients given the scope of cognitive decline that may occur, yet this choice depends on the tolerability of associated clinical conditions and on the individual characteristics of the patient (Donohue et al. 2011).

The importance of neuropsychological assessments of cognition during depression

There is controversy regarding the decline of cognition and its etiology in normal elderly patients with depression. Some following important questions can be asked: Does depression causes cognitive decline or vice versa? Does depression in the elderly worsen their prognosis and increase their risk for the occurrence of dementia? (Kessing et al. 2011). Is the presence of cognitive impairment in the depressed elderly the first symptom of dementia? Does depression remission cause cognitive and functional deficits? (Byers 2011, Kessing 2012, Mintzer and O´Neill 2011). Therefore, knowing the main cognitive and functional changes caused by depressive episodes is essential for choosing the right treatment and establishing parameters regarding the prognosis of these patients, given that the first episode is of extreme importance for healthcare professionals when making differential diagnoses.

Neuropsychological assessment plays a key role in the investigation of the relationship between brain and behavior (Lezak et al. 2012, Malloy-Diniz et al. 2010), especially regarding the cognitive dysfunction associated with disorders of the central nervous system. This assessment helps identify variables that determine cognitive impairments, consolidates hypotheses about risk factors for the development of neural diseases, and provides information about the cognitive profiles that illustrate the differential diagnostics between depression and dementia in elderly patients with memory complaints (Lezak et al. 2012). This type of evaluation typically consists of tests that evaluate behavior, cognition and functionality with the aims of detecting diagnostic and prognostic estimations, designing cognitive rehabilitation programs and understanding the impact of psychosocial and pharmacological treatments (Lezak et al. 2012, Malloy-Diniz et al. 2010).

Objectives

Investigate the influence of the long-term use of antidepressants (i.e., selective inhibitors of serotonin, tricyclic, tetracyclic and other reuptakes) for an average period of 10 months on the neuropsychological and functional performances and psychiatric symptoms of a determined sample of elderly patients with depressive symptoms.

Method

Participants

Participants met the following inclusion criteria: a) each was a patient at the Elderly Medicine Center at the University of Brasilia, b) the patient was aged between 60 and 90 years, c) the patient had a Clinical Dementia Rating (CDR) equal to 0 (no dementia diagnostic), d) the patient had subjective complaints of depressive symptoms according to medical records and/or based on the International Statistical Classification of Diseases and Related Health Problems (ICD-10), and e) the patient was not receiving antidepressant treatment for at least 3 weeks prior to the first assessment (study entry) and had experienced more than 180 days of treatment.

The following exclusion criteria were also applied to all participants in this study: a) the patient met the diagnostic criteria for probable Alzheimer's Disease (DA) according to the National Institute of Neurological, Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (McKhann et al. 1984), b) the patient had to have Alzheimer's Disease, Vascular Dementia, Frontotemporal Dementia or Dementia with Lewy`s Bodies, c) the patient was receiving antidepressant treatment for more than 3 weeks prior to the first assessment (study entry) and had experienced less than 180 days of treatment in the second evaluation, d) the patient was receiving anticholinesterase, anxiolytic, antipsychotic, anticonvulsant treatments, e) the patient was in the Cognitive Stimulation Program, f) the patient had changed antidepressants after the first evaluation, and g) the patient regularly used psychotropic drugs or alcohol.

Based on these inclusion and exclusion criteria, 20 elderly participants were divided into the following two groups: 1) the Experimental Group (N=10): elderly participants with depressive symptoms and CDR=0 who had received antidepressant treatment for 180 days or more and, 2) the Control Group (N=10): elderly participants with depressive symptoms and CDR=0 who were not receiving antidepressant treatment. The two experimental and the control groups did not differ (p<0.05) in age, sex, education or marital status, as is evident in **table 1**.

Procedures

This study was approved by the Ethics in Human Research (CEP-FS/UnB) in the Faculty of Health Sciences at the University of Brasilia, Brazil, in the first regular meeting held on February 1, 2011 with record number 153/10.

All participants were fully informed and advised about the nature and purpose of the study, as well as its voluntary and non-invasive character, by reading the Terms of Consent. After reading and understanding these terms, participants consented to participate in the study according to the universally established ethical rules for human experimentation and Resolution 196/96 of the National Health Council of the Ministry of Health (CNS/MS). This consent procedure occurred on the day that the participants had their medical appointments to receive prescriptions for their antidepressants. After volunteering for the study, patients underwent two sessions of clinical evaluations, with the first occurring on the same day, which marked the beginning of the study. The second evaluation occurred after a minimum period of 180 days and maximum period of 320 days from the beginning of the study, with a study average of 10 months.

Instruments for data collection

Clinical evaluations were performed using a cognitive scale (Mini Mental State Examination, MMSE) (Folstein et al. 1975), two functional scales (Barthel Scale of Basic Activities of Daily Living, BADL) (Mahoney and Barthel, 1965) and Pfeffer Scale of Instrumental Activities of Daily Living (IADL) (Pfeffer et al. 1982), and two psychiatric scales (Cornell Scale for Depression in Dementia, CSDD (Alexopoulos et al. 1988) and Neuropsychiatric Inventory, NPI) (Cummings et al. 1994, Cummings 1997). A longitudinal analysis was performed comparing the results of the first and second evaluations (after prolonged use of an antidepressant for 180 days or more). These two were used to qualify and quantify the presence of depressive indicators and neuropsychiatric symptoms. These instruments are brief, general in nature and aim to track global deficits in cognition and losses in the ability to adequately perform the basic activities of daily living.

Table 1. *Demographic characteristics of participants*

	Experimental group	Control group	*p*
Age	M=74.7, SD=7.3	M=75.2, SD=5.2	0.50
Women	7	4	0.51
Education			
≤ 4 years	9	5	0.48
> 4 years	1	5	
Marital status			
Married	6	5	
Single	1	1	
Widower	3	4	

The BADL (Mahoney and Barthel 1965) consists of 10 categories of activities, as follows: eating, bathing, dressing, personal hygiene, bowel control, urinary control, using the toilet, moving from the bed to the bathroom, walking, and going up and down the stairs. It measures the degree of functionality, or the basic functional ability, of older people when performing these 10 activities in their daily lives. Their score can range from a minimum of zero to a maximum of 100 points, with scores greater than 60 indicating independence with regard to personal care activities, such as moving without assistance, eating, personal hygiene and sphincter control.

The IADL (Pfeffer et al. 1982) consists of nine cognitive categories that assess short-term memory, spatial-temporal orientation, calculation and recall. It evaluates the functional capacity of the elderly and their degree of commitment, i.e., it assesses whether the patient can live alone. In the IADL, functional disability and cognitive impairment are calculated as follows: a) a score greater than five indicates the presence of declined functional ability and cognitive impairment, whereas b) a score higher than five (minimum five and maximum 27) indicates a less functional decline and cognitive impairment of the patient and greater functionality with regard to performing the instrumental activities of daily living.

The MMSE (Folstein et al. 1975) consists of several questions grouped into the following seven categories: temporal orientation (5 points), spatial orientation (5 points), registration of three words (3 points), attention and calculation (5 points), recall of three words (3 points), language (8 points) and visuo-constructive ability (1 point). The MMSE ranges from 0 to 30 points and constitutes a scale of cognitive screening, which correlates with the evolution of the dementia process in the Brazilian population when the degree of individual education is considered. The cutoff points are as follows: a) illiterate: cutoff score of 13, b) individuals with low levels of education (1-4 years) or a middle school level of education (4-8 years of age): cutoff score of 18, c) individuals with high levels of education (over 8 years): cutoff score of 26 (Bertolucci et al.1994).

The CSDD (Alexopoulos et al., 1988) consists of 19 questions grouped into five categories with regard to depressive symptoms in dementia, as follows: signs related to mood (e.g., anxiety, sadness, lack of reaction to pleasant events, and irritability), behavioral disturbances (e.g., agitation, retardation, multiple physical complaints, and loss of interest), physical symptoms (e.g., loss of appetite, weight loss, and lack of energy), cyclical functions (e.g., diurnal variation of mood symptoms, difficulty falling asleep, waking up often during the night, and waking up too early), and disturbance of ideation (e.g., suicide, low self-esteem, pessimism, and humor-related delusions). This measure includes clinical characteristics of patients with dementia through both clinical examinations of the patients and examinations of completed by the patients. This measure is used to quantify the symptoms and is not used to make a diagnosis, which requires other instruments. Scores range from eight to 38 points, with higher scores indicating more depressive symptoms.

The NPI (Cummings et al. 1994, Cummings 1997) is an instrument that assesses 12 categories of common neuropsychiatric symptoms in dementia, such as delusions, hallucinations, agitation, depression/dysphoria, anxiety, euphoria, apathy, disinhibition, irritability/lability, abnormal motor behavior without a purpose, sleep disorders and nocturnal behavior, eating disorders and eating habits. Each item is assessed in relation to its frequency (1=absent to 4=very often) and severity (1=mild to 3=severe). The total score is obtained by multiplying the frequency score by the severity score, with a range from 0 to 144 points. Patients' stress levels or their sense of being overwhelmed is also observed, although not counted in the total score for this test. Higher scores on the NPI indicate more depressive symptoms in the evaluated subjects. The NPI is a widely used tool for characterizing the psychopathology of dementia, as it enables the investigation of neuropsychiatric symptoms to distinguish between the different dementia syndromes.

The CDR (Hughes et al. 1982) scale is widely used in longitudinal studies as it classifies the severity of Alzheimer's disease. This scale is derived from a semi-structured form completed by the patient and an informant, and it quantifies the change in the following six cognitive categories: memory, orientation, judgment, problem-solving skills, community tasks and personal care. Each category is scored on a scale of 5 points, with memory as the main category and the others as secondary categories. A CDR score of 0 indicates no dementia, CDR=0.5 indicates questionable dementia and CDR=1, 2 or 3 indicates mild, moderate or severe dementia, respectively. This scale is analyzed based on clinical data, which are independent of psychometric tests.

Description of participants' pharmacological use

To describe the pharmacological profiles of the drugs that were used in this experiment, the medical records for the 20 participants were studied. Their medications were classified according to the Relation of Essential National Medication (RENAME), see **table 2**.

Statistical analysis

To perform a longitudinal analysis of the effect of antidepressants on cognition, function and symptoms, as identified in the tests and scales used, we conducted the nonparametric related-samples Wilcoxon signed rank test and effect size (Cohen's *d*) on the experimental group (with antidepressant treatment) and the control group (without antidepressant treatment). We compared participants' performances from the first and second assessments. **Table 3** presents the means and standard deviations of their performances during the first and second evaluations for both groups on the following scales: a) the BADL, b) the IADL, c) the MMSE, d) the CSDD, and e) the NPI. Significant differences were found in the distribution and characteristics of the groups.

Results

To examine the longitudinal effects of antidepressants on cognition, function and symptoms, we compared the results of the first and second clinical assessments for the experimental and control groups.

Effect size ranged from –0.21 to 0 in control group and from 0.04 to 0.39 in experimental group. There was a significant effect of depressive symptoms (CSDD scale) only for the experimental group (-1.94, $p<0.05$) and effect size equal to 0.39 (see **table 3**). The control group had no significant differences between the first and second evaluations for any of the cognitive, functional and psychiatric instruments. None of the

Table 2. *Categories of medications taken by these study participants following the classification of national essential medicines*

Medications in use	Experimental group	Control group
Antidepressant selective inhibitor of serotonin reuptake	70%	
Antidepressant tetracyclic	20%	
Antidepressant tricyclic	10%	
Drugs acting on Cardiovascular and Renal Systems	90%	100%
Drugs acting on Reproductive and Endocrine Systems	40%	20%
Mineral Substancie	20%	30%
Vitamines	10%	
Drugs used in the treatment / prevention of osteoporosis	30%	10%
Drugs acting on Digestive Systems	10%	10%
Drugs acting on Respiratory Systems		10%
Anti-inflammatory drugs and drugs used to treat gout	20%	10%
Analgesic drugs for fever and migraine relief	30%	20%

Table 3. *Nonparametric statistics and effect size of the first and second clinical evaluations to control and experimental groups*

	Control Group (n=10)								Experimental Group (n=10)							
	1st Evaluation		2nd Evaluation						1st Evaluation		2nd Evaluation					
Evaluation	Mean	SD	Mean	SD	Std Wilcox	*p*	Cohen's *d*	Effect Size	Mean	SD	Mean	SD	Std Wilcox	*p*	Cohen's *d*	Effect Size
BADL	98.5	3.4	100	0	1.34	0.18	-0.42	-0.2	98.0	3.5	96.5	7.8	-0.82	0.41	0.16	0.08
IADL	0.5	1.6	1.4	2.5	0.94	0.34	-0.43	-0.21	8.0	5.9	6.8	7.2	-0.28	0.78	0.18	0.09
MMSE	27.7	1.9	27.9	2.0	1.41	0.16	0	0	22.0	6.6	20.4	7.8	-1.44	0.15	0.28	0.14
NPI	5.6	8.7	5.9	8.3	0.07	0.94	-0.04	-0.02	22.7	18.9	21.4	29.1	-0.66	0.51	0.08	0.04
CSDD	2.4	2.9	2.8	3.4	0.54	0.59	-0.13	-0.06	10.2	6.4	5.3	5.3	-1.94	<0.05*	0.84	0.39

** $p<0.05$ using Wilcox statistics to nonparametric related samples. SD = standard deviation; BADL = Barthel Scale of Basic Activities of Daily Living; IADL = Pfeffer Scale of Instrumental Activities of Daily Living; MMSE = Mini Mental State Exam; NPI = Neuropsychiatry Inventory; CSDD = Cornell Scale for Depression in Dementia.*

subjects in the experimental group showed a significant effect due to the influence of antidepressants, which means there were no increases or reductions in the BADL, IADL, MMSE or NPI scores. However, scores on the CSDD scale showed improvement in patient performance, such that there was a significant reduction in these scores (M=10.2, SD=6.4 and M=5.3, SD=5.3) during the second evaluation, which was after 25.7 to 45.7 weeks of treatment with antidepressants.

With regard to functionality, the experimental group showed less independence in the second clinical assessment for the BADL (M=96.5, SD=7.8) compared to the control group M=100, SD=0) and this was also evident for the IADL (M=8.0, SD=5.9) when compared to the control group M=0.50, SD=2.54).

Discussion

The interest in studying pharmacological influences on cognition has been increasing, especially the interest in topics regarding antidepressant use in elderly patients with depression and their risk of developing Alzheimer's disease (Byers 2011, Kessing 2012, Mintzer and O´Neill 2011).

The literature suggests an association between depression and dementia, and growing evidence implies that timing of depression may be important to defining the nature of the association. Recently studies suggest that some forms of depression is associated with increased risk of subsequent development of dementia, and have supported the relationship between depression and Alzheimer's disease to understand whether depression is a risk factor for cognitive impairment and eventually dementia, or whether depression is an independent event that aggravates cognitive impairment owing to its impact on an emotionally related cognitive function, such as attention and motivation. The existence of a clinical association between changes in mood (depression) and cognitive impairment is clearly established (Mintzer

and O´Neill 2011). In particular, earlier-life depression or depressive symptoms consistently have been shown to be associated with a 2-fold or greater increase in risk of dementia. However, the discuss whether depression is a prodromal state of dementia or an independent risk factor for dementia, as well as to discuss how the type of depression (Byers 2011), the type of dementia, and antidepressant treatment influence the association, have been discussed (Kessing 2012). If a patient presents with depression or depressive symptoms, particularly in late life, then screening for cognitive deficits should become part of the patient's management or clinical care (Byers 2011). In addition, studies on earlier-life depression suggest that older adults with a history of previous depression should be closely monitored for both recurrent depression and cognitive decline.

Our results show there is a significant decrease in depressive symptoms, as measured by the CSDD, following antidepressant treatment over an average period of 25.7 weeks to 45.7 weeks for patients in the experimental group, yet there was no significant effect on cognition.

Constantine Lyketsos and his collaborators (Lyketsos et al. 2000) suggested that patients suffering from Alzheimer's disease and depression appear to respond to antidepressant treatments that improve activity of these very same neurotransmitters that seem to be decreased in Alzheimer's disease. A study conducted with a larger sample of patients found that in those individuals who met all criteria for depression of Alzheimer's disease, this very same treatment (sertraline) was not more effective than placebo. No differences in cognitive function were noted between participants receiving drug or placebo. Furthermore, biological studies have suggested a decrease of neurotransmitters known to be involved in the regulation of mood, such as serotonin, in patients with Alzheimer's disease and other types of dementia. It was then expected that the antidepressant treatment of patients with dementia with these compounds will result in an improvement in mood (Mintzer and O´Neill 2011). Some studies have shown that treatment of depression in elderly patients (i.e., pharmacological, behavioral or other modalities) improves cognition, leading to improved memory and other cognitive performance (Byers 2011) and may reduce pathophysiological alterations related to dementia, but other studies have shown that cognitive deficit either persists or still ensues after successful treatment for depression.

The BADL data support previous studies showing that pharmacological treatment for depression is better for patients with functional impairments than for those complaining of depression without functional impairments. Additionally, this type of treatment is not recommended for older adults with depressive symptoms (as they are more likely to have Alzheimer's disease) who do not have functional impairments (Fitz and Teri 1994). Thus, the functional inability to perform daily living activities is a prescription factor for pharmacological depression treatment (Blazer and van Nieuwenhuizen 2012). Concerning the necessity of treating depression, Xavier et al. (2001) suggest that there is a greater likelihood that depression impacts the physical health of the weak, particularly the elderly, and has a significant impact on functionality, including a lower level of independence for more susceptible individuals. These negative effects are not evident for aspects of cognition. Additionally, previous literature suggests that depression in the elderly increases the risk of being unable to participate in daily life activities by 67% and increases the chance for a loss of mobility by 73% in 6 years (Penninx 1999). These increases may be due to the negative effects of depression that undermine individuals' social functions, which reduces the quality of social support available. This lead to the restriction of social or leisure activities, isolation, and decreased quality of life, which may explain why depressed people are more functionally disabled (Lenze et al. 2001).

Regarding the cognitive stability observed in the first and second clinical evaluation, we found that neither the normal elderly patients with depressive complaints in the control group nor the patients with depressive symptoms receiving antidepressant treatment in the experimental group showed a decline in cognition. Rubin et al. (Rubin 1998) found that older people without dementia show stable cognitive performance levels when measured longitudinally with careful clinical assessments and repeated cognitive testing. This stability tends to be maintained unless the patients develop a dementing illness. Moreover, epidemiological studies by Barker and colaborators (Barker et al. 1995) suggest that between 4-54% of normal elderly with memory complaints associated with normal aging also have depression. Taken together with our findings showing a lack of influence of antidepressants on improving cognition, these prevalence data converge with Portella et al. 2003 findings that, even after 12 weeks of antidepressant treatment (mean dose of 20 mg/day), cognitive impairment in patients was still present. Thus, there was no significant difference caused by the use of antidepressants with regard to reducing cognitive symptoms (Lyketsos et al. 1997, Lyketsos et al. 2000, Lyketsos 2000).

Regarding the neuropsychiatric symptoms, our data revealed that treatment with antidepressants for a minimum of 25.7 weeks resulted in significant improvements in depressive symptoms when compared to the first neuropsychological assessment. This finding confirms Lyketsos et al. 1997, Lyketsos et al. 2000 and Petracca et al. 1996, results showing that depressed patients treated with antidepressants for an average of 12 weeks showed improvement in both neuropsychiatric and depressive symptoms when compared to a placebo group.

However, our data contradict the results of Salamero et al. 2003, who investigated cognition in elderly patients with a mean age of 71 years who had major depression. These authors found that the group treated with antidepressants showed MMSE improvement in scores at the end of 12 months compared with a placebo group. Alexopoulus et al. 2002, also suggest that older adults with cognitive impairments can improve their performances after antidepressant treatment, particularly with regard to memory and executive functions, yet they will not reach normal levels in specific areas. Contrary to this, our sample showed normal levels.

Regarding pharmacological effects on depressive and neuropsychiatric symptoms, our data suggest that antidepressants contributed to a reduction in depressive symptoms in the experimental group, which supports the results of a study by Lyketsos 2000, verifying the effectiveness of serotonin reuptake inhibitors on neuropsychiatric depressive symptoms in patients with and without AD. These authors found that an experimental group that was treated with sertraline (mean dose 150 mg/day) for 12 weeks showed improvement in both depressive and neuropsychiatric symptoms compared to a placebo group. This improvement was evident for both the NPI and CSDD scales.

Concluding, the literature is quite controversial regarding the influence of antidepressant treatment

on cognition in patients with depression. Our study highlights the need for more research in this area, given that the present results do not converge with previous literature. For instance, we found that antidepressants do not influence the improvement of cognition when the effect of antidepressants was associated with cognitive improvement.

Our data are limited to a general assessment of non-specific cognition, and our patient sample was convenient, although it had specific selection criteria to ensure that all the participants had depressive complaints. Only the experimental group (elderly participants with depressive symptoms and CDR=0) who had was prescribed an antidepressant for the first time at study entry and for a long period for 180 days or more. None of the participants showed cognitive decline, meaning that everyone had a CDR= 0, i.e., most likely did not have Alzheimer's dementia status. Although a considerable number of studies have compared antidepressant treatment, psychotherapy, whether combined treatment are more effective in depressed older adults, and some preliminary results are useful for deciding which treatment is best for which patient (Cuijpers et al. 2012).

The main limitations of this study, despite the conclusions, were not using other scales for clinical assessment of cognition in elderly patients, in addition to the Mini-Mental State Examination, since they did so for the ongoing of care of the patients in this Medicine Center for the Elderly, were not injured, since the demand is high. However, further studies are necessary to the mental health of elderly patients with and without Alzheimer's disease, to a better understanding of disease and promotion of health and quality of life.

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