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Low-Dose Combination of Aripiprazole for Treatment of Severe Depression with Cognitive Impairment: Case Report

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Abstract

Even with adequate treatment and relevant symptomatic recovery from major unipolar depressive disorder, some symptoms may persist causing significant functional impairment. The use of atypical antipsychotics in combination with antidepressants in the treatment of major depressive disorder has increased in last year's and demonstrated good efficacy regardless of the presence of psychotic symptoms. The following case exemplifies a patient recovering from severe depressive episode, with cognitive and functional improvement after a low dose combination of aripiprazole. Aspects related to the refractory symptoms of depression as well as the treatment of this condition will be discussed.

Keywords: Aripiprazole; Cognitive impaiment; Depressive disorder

Introduction

Major depressive disorder has been a relevant cause of concern for the public health of several countries, causing personal, family and economic losses of great proportions. The rehabilitative treatment of patients suffering from this disorder has been pursued by clinicians to occur as quickly as possible. However, even when significant improvement is achieved, symptoms may persist and contribute to the maintenance of disability. Cognitive dysfunctions, for example, may persist even after recovery from the classic symptoms of psychiatric disorders [1,2], have been reported in pre-morbid stages and in healthy first-degree relatives of patients who developed schizophrenia and bipolar disorder [3], are strongly associated with functional impairment even when other symptoms are controlled [1,4], as well are related to worsening quality of life and the well-being of patients and caregivers [5,6].

In recent years, an emerging number of researches have demonstrated the existence of deficits in cognitive functions in various psychiatric disorders. In general, cognitive dysfunctions are not considered as classic symptoms of mental disorders, they are neglected in clinical practice and do not yet have effective pharmacological treatment [5]. Finding ways to treat remaining cognitive deficits in psychiatric disorders may be an interesting pathway for reducing morbidity and functional rehabilitation of these patients. The following case exemplifies a patient recovering from severe depressive episode, with cognitive and functional improvement after a low dose combination of aripiprazole.

Case Report

A Brazilian male patient, 58 years old, married, trained in mathematics, Catholic, presented the first depressive episode at age 19 and the second at 38 years. At age 50, he had the third depressive episode, at that time with psychotic symptoms (delirious ideation). Although the relatives describe him as very sociable, playful and little hyperthymic, they denied any phase of hypomania or mania. He began follow-up with the current assistant psychiatrist in October 2011 for presenting three months of the initial consultation the fourth depressive episode. At that time, the severe clinical picture was marked by intense anergy, a lot of insomnia and a lot of cognitive impairment (intense thinking slowing, memory impairment, intense hypoprosexia and being unable to make decisions). In addition, he had prominent psychotic symptoms with delusional ideas,

some guilty congruent with humor (for example, he was sure that the war in Iraq was on his account), and others of greatness not congruent with humor (eg, Said to be the king of the cangaço [1]). Some drug regimens were tried without much success, and the patient only achieved resolution of the condition with the combination of 60mg of fluoxetine and 15mg of olanzapine in May 2012, including returning to work.

Despite this improvement in mood symptoms and good functional recovery, there were persistent memory lapses (he got lost on the street once) and hypoprosexia (which harmed him in college studies). Cerebral neuroimaging (magnetic resonance imaging) and laboratory tests were performed (blood count, serum biochemistry, ionogram, anti-HIV, VRDL and FTA-Abs, vit-B12, serology for hepatitis B and C, lipid profile, fasting glycemia, hepatic function, renal function and thyroid exams), all without alterations. Neuropsychological evaluation evidenced major impairment in executive functions, concentration, episodic memory and prospective memory. A diagnosis of mild amnestic cognitive impairment of multiple domains was done and the case was followed up.

In February of 2014 he assumed managerial positions in the job and displayed new depressive episode. This time without psychotic symptoms, however with intense cognitive impairment and psychomotor retardation, in addition to severe initial insomnia. The drug regimen was changed to tranylcypromine, reaching over the months until the dosage of 60mg daily, associated with flunitrazepam 2mg at night. The patient had only partial response. Nine months later the depressive symptoms of humor and cognition presented only partial response. It was decided to try electroconvulsive therapy (ECT). As in the Brazilian state where this case occurred, there is only one public service that provides this treatment, and the family did not have the financial means to pay for the treatment of a particular outpatient ECT, the patient had to stay in a university hospital under the Care of another assistant team. However, because the patient had atrial flutter (using amiodarone, digoxin, and acetylsalicylic acid), the hospital staff decided not to do ECT and to modify the drug regimen by withdrawing tranylcypromine and slowly introducing venlafaxine up to 300mg / day associated with mirtazapine 30mg / day.

Seventy days after the onset of hospitalization, the patient did not present improvement and the family decided to remove him from the hospital and continue ambulatory follow-up with the assistant psychiatrist. At that time, aripiprazole 2.5 mg / day was associated with the hospital discharge regimen (venlafaxine 300mg / day and mirtazapine 30mg / day). About 45 days after the combination of aripiprazole, the patient had no depressive symptoms (both moody and cognitive) and went back to work. During 1 year and 9 months of clinical follow-up, the patient was able to perform well, returned to the engineering course that was put aside,had no cognitive complaints (neither the family complained about it) and the Montreal Cognitive Assessment (MoCA) test score always was around 26 (out of 30).

Discussion

Among the cognitive deficits found in psychiatric disorders, the most important are the impairments involving the so-called executive functions [4-6], particularly decision-making [7,8]. Thus, in addition to difficulties in concentration, problems in decision making were recently specified within the diagnostic criteria of depression [9].Our case exemplifies the existence of cognitive deficits in depression regardless of cardinal humor symptoms. Recently, medications such as vortioxetine have been designed to treat both spheres of depression: cognition and mood [10-12]. However, the commercialization of this drug only began to be performed in Brazil in early 2016, that is after the treatment reported in this article. The efficacy of an augmentation of antidepressant drugs with second generation antipsychotic drugscould be demonstrated in a large number of randomized clinical trials and meta-analyses [13-15] andcan be considered as first-line medication in treatment-resistant unipolar depression [16].

Studies have shown there has been a considerable increase in prescription in recent years for the treatment of major unipolar depressiondespite the presence of psychotic symptoms [16,17]. Aripiprazole has the approval of adjunctive treatment for these cases, after non-response to prior antidepressant monotherapy, by the US Food and Drug Administration (FDA) but the recommended doses are lower than the doses used in schizophrenia, starting at a dose of 2-5mg/d with a maximum dose of 15mg/d [18]. Aripiprazole has been considered as an effective adjuvant treatment strategy in randomized clinical trials and review articles [13-16]. The association of aripiprazole with atidepressants is currently considered to have more robust evidence than association with lithium [16,18] and has been shown to be related with increased plasma BDNF levels after 4 weeks of combination [19].

The case described demonstrates that total remission of symptoms, including cognitive recovery, should be the focus of treatment for depression. This approach facilitates recovery of functionality and improvement of the patient's quality of life with recurrent depressive symptoms. In this way, drug combinations may be necessary and low doses of aripiprazole appear as a good option.

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