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Nota: IPFMC = Instituto Psiquiátrico Forense Maurício Cardoso; UFCSPA = Universidade Federal de Ciências da Saúde de Porto Alegre.
Mais informações, consultar as Instruções aos Autores.

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Mania switch induced by amantadine in bipolar disorder: report of three cases

Virada maníaca induzida pela amantadina no transtorno bipolar: relato de três casos

Dear Editor,

Bipolar disorder (BD) is often a severe and chronic disease. It has been shown that subjects with BD present cognitive impairment during the acute phase of the disease and remission, which seems to worsen with the recurrence of episodes. Available treatments are successful in reducing symptoms in acute mania and depression. However, their effects in the functional recovery of patients are minor. As previously shown in schizophrenia (SZ);[1] BD is associated with cognitive impairment (as seen in psychometric tests), neuroanatomical changes (evidenced in imaging studies), and neurotransmission dysregulation, such as in the case of glutamate.[2] It has also been demonstrated that serum levels of brain-derived neurotrophic factor (BDNF), which is a protein related to neuroplasticity, are decreased during BD mood episodes.[3]

The adjunctive use of amantadine, a memantine derivative, has shown to be conducive to cognitive improvement in subjects with SZ[4] and BD.[5] This is so because amantadine has several properties: a) it increases the monoaminergic tonus via dopamine, norepinephrine, and serotonin in the amygdala and hippocampus b) has an antidepressant activity c) directly modulates glutamate as a partial agonist of N-methyl-D-aspartate (NMDA) receptors, and d) contributes to BDNF increase and stabilizes the neuronal membrane. Amantadine use in patients with BD has not been associated with mood swings.[5]

We evaluated the use of amantadine adjunctive therapy for improving the cognitive impairment of three euthymic DSM-IV BD type I subjects who presented with a standard clinical pattern of cognitive and behavioral impairment or who were unable to live autonomously.[3] Subjects gave informed consent for the experimental use of amantadine administered at increased doses of up to 400mg over a period of 8 weeks. Patients were evaluated by means of a psychiatric interview and their clinical response was assessed using the Young Mania Rating Scale (YMRS) and the 17-item Hamilton Depression Scale (HAMD). The three cases are illustrated in Table 1. All subjects had mania switches and the consequent worsening of cognitive impairment. Subject 3 presented a slightly different evolution, since it tolerated 200mg

Table 1 – Patients with bipolar disorder type I treated with amantadine

Patient	Age (years)	Illness duration (years)	Sex	Dose (mg/day)	Concurrent medications (mg/day)	Mood stabilizers serum levels Baseline	YMRS Baseline	HAMD Baseline	Treatment duration (weeks)	YMRS End of treatment	HAMD End of treatment
1	45	13	Female	400	Lithium(1200), risperidone (1), fluoxetine (20)	0.9 mEq/l for lithium	1	6	2	11	27
2	40	12	Male	200	Lithium (900), carbamazepine (800), risperidone (4)	0.8 mEq/l for lithium and 77 mg/ml for carbamazepine	0	0	2	22	6
3	53	13	Female	200	Carbamazepine (800), olanzapine (10), clonidine (0.100)	71 mg/ml for carbamazepine	3	0	8	9	3

YMRS: Young Mania Rating Scale; HAMD: Hamilton for depression 17-item.

of amantadine for up to 2 weeks and showed some level of cognitive improvement. However, after 8 weeks of treatment, this subject presented with a mania switch associated with cognitive worsening. As a result of that, the administration of amantadine was discontinued.

Although amantadine may improve cognition by acting as a partial agonist at NMDA receptors, it increases the monoaminergic tonus of the amygdala and hippocampus. This may explain the mania switch seen in our subjects. Although subject 3 presented a different evolution, the reason for this remains unclear. This difference in evolution could be attributed to a better disease course or the antipsychotic profile of olanzapine, which this patient made use of while the other two subjects made use of risperidone. In contrast with the findings of Ohlmeier et al.,[5] our results do not support the use of amantadine in BD. Further studies are required to evaluate possible treatments to improve functional outcomes in BD.

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For more information, see Instructions for Authors.

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