

## Memantine-Related Psychotic Symptoms in a Patient With Bipolar Disorder

**To the Editor:** Memantine is an *N*-methyl-D-aspartate (NMDA) receptor agonist. It was recently approved in Europe and the United States for treating dementia and has been shown to reduce clinical deterioration in moderate-to-severe Alzheimer's disease and in vascular dementia.<sup>1</sup>

Although memantine has been reported to be useful for psychotic symptoms (delusions and hallucinations) in patients with Alzheimer's disease,<sup>2,3</sup> a few anecdotal reports have noted that it may conversely cause hallucinations and delusions.<sup>4,5</sup>

Herein, we report the case of a patient with bipolar disorder and Alzheimer's disease who developed delusions and auditory hallucinations as a result of memantine therapy. Significant resolution of these symptoms occurred once treatment was discontinued. To our knowledge, this report is the first to describe psychotic symptoms in a patient with bipolar disorder and comorbid Alzheimer's disease as a result of memantine treatment.

**Case report.** Ms A was a 63-year-old retired teacher who was being followed for DSM-IV–defined bipolar I disorder. She experienced her first manic episode when she was 24 years old. She had been in remission for 3 years with lithium carbonate (900 mg/d), quetiapine (400 mg/d), and lamotrigine (150 mg/d). She was admitted to our clinic in April 2009 with complaints of memory deficits and behavioral disturbances (apathy, lack of inhibitions, untidiness) that had started 7 months before. On clinical mental state examination, she displayed reduced working memory capacity, impaired attention, and anomia. Results of a physical and neurologic examination, routine blood tests, and electrocardiogram were normal. Results of magnetic resonance imaging of the brain were unremarkable. Neuropsychological assessment revealed moderate dementia (Standardized Mini Mental State Examination<sup>6</sup> score: 18/30). Ms A was diagnosed with probable early Alzheimer's disease (DSM-IV-TR criteria) and was started on treatment with memantine 5 mg twice daily. Her treatment dose was then increased to 10 mg twice daily.

On the fourth day after she began taking memantine, Ms A reported persecutory delusions (she thought that cars were trying to do bad things to her) and auditory hallucinations (of people calling her name). She was readmitted to our clinic shortly after these symptoms were visible to her family members. We discontinued memantine treatment and started treatment with donepezil 5 mg/d. Significant resolution in her psychotic symptoms was noticed at the fifth day of the new treatment regimen. Ms A has been followed for 4 months with no evidence of recurrence of psychotic symptoms.

Memantine is structurally similar to amantadine, an influenza drug used for the treatment of Parkinson's disease, which has been reported to cause visual hallucinations in patients with Parkinson's disease.<sup>7</sup> Both drugs bind with low affinity to the ion channel phencyclidine site at the NMDA receptor.<sup>8</sup> Phencyclidine, an NMDA receptor antagonist with high affinity, induces psychotomimetic effects, including hallucinations, agitation, and delusions.<sup>8</sup> The worsening of psychotic symptoms, including visual hallucinations, as a result of memantine treatment in patients with Alzheimer's disease has been described.<sup>4,5</sup>

In a few case reports, memantine was found to be useful in treatment-resistant bipolar disorder.<sup>9,10</sup> However, our patient developed delusions and auditory hallucinations shortly after beginning memantine therapy. The strict temporal relationship between the use of the drug and the onset of the psychotic symptoms, as well as the resolution once treatment was discontinued, suggests a causal link between the two phenomena. Because the patient was

also receiving other drugs for bipolar disorder, another possible explanation is that a drug interaction between memantine and the other drugs might have occurred. However, despite inhibition of cytochrome P450 (CYP) 2B6 activity, inhibition of other CYPs during memantine therapy has been reported to be unlikely.<sup>11</sup>

Further studies or case reports are required regarding the incidence of these side effects and the underlying mechanisms of action before definitive conclusions can be reached. Clinicians should be vigilant when prescribing memantine for the treatment of coexisting Alzheimer's disease and bipolar disorder or of treatment-resistant bipolar disorder.

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