

## Exacerbation of Recurrent Depression as a Result of Treatment With Varenicline

TO THE EDITOR: Varenicline, a partial  $\alpha_4\beta_2$ -nicotinic receptor agonist, was approved by the Food and Drug Administration in 2006 for smoking cessation. Recently, Robert Freedman, M.D., (1) reported the exacerbation of schizophrenia in a patient after 1 week of varenicline use (2 mg daily), and Kohen and Kremen (2) described the induction of a manic episode in a bipolar patient who was challenged with 1 week of treatment with varenicline at 2 mg daily. The case reported below is of a patient who demonstrated exacerbation of recurrent major depressive disorder following 6 weeks of treatment with varenicline.

A 75-year-old Caucasian married man, with a 20-year history of recurrent major depressive disorder, presented with an acute exacerbation of depressive symptoms. The patient, who had been stable for several years while being treated with fluoxetine (20 mg), reported 3 weeks of mounting despondency. He correlated the onset of these symptoms with a fall in which he bruised several ribs and his shoulder, although he did not seek medical attention. After 2 days of hypersomnia, he experienced reversal of his sleep cycle, "unusual" dreams, and decreased appetite. He was anergic, irritable, sad, and preoccupied with guilt and the past. He also had thoughts of giving up.

The patient suffered from long-standing, chronic obstructive pulmonary disease and had smoked more than one pack of cigarettes per day for more than 45 years. Six weeks prior to presentation in the psychiatry clinic, he started varenicline for smoking cessation (under the care of an internist). Treatment began with 0.5 mg, once per day, for 3 days and then increased to 0.5 mg twice daily. After 1 week, varenicline was increased to 1 mg b.i.d. However, the patient continued to smoke three to four cigarettes daily. Additional medications included aspirin, niacin, and metoprolol. Reconsultation with the internist was advised, together with the discontinuation of varenicline and a brief course of clonazepam (0.5 mg nightly) to facilitate sleep. The patient chose to discontinue the use of varenicline immediately. On the third day, treatment with clonazepam was instituted (which has continued). The patient subsequently reported resolution of the depressive constellation within 2 weeks of discontinuing varenicline. He was no longer preoccupied with guilt and the past. His sadness, suicidal ruminations, and irritability were no longer present, and his mood returned to the previous baseline. His sleep substantially improved, and he no longer experienced unusual dreams. Treatment with fluoxetine was continued throughout the sequence. The patient's smoking increased from three to four cigarettes daily to six to seven cigarettes daily; however, no challenge with varenicline was attempted.

When varenicline was discontinued and low-dose clonazepam was instituted, the patient's acute depressive symptoms remitted and his clinical presentation returned to baseline. Dosages of fluoxetine and metoprolol were not changed, and the patient continued to smoke cigarettes on a daily basis throughout the sequence. His fall and physical injuries may have confounded any association of his depressive symptoms with the use of varenicline. It appears that the use of varenicline was instrumental, if not causal, in the exacerbation of his mood disorder.

Unlike earlier reports (1, 2), the interval to the induction of the psychiatric presentation following the challenge with varenicline in the patient was nearly 6 weeks. Additionally, treatment with varenicline proceeded in a stepwise fashion, starting at 0.5 mg daily. Clinicians should exercise caution when prescribing varenicline to their patients with established psychiatric disorders.

### References

1. Freedman R: Exacerbation of schizophrenia by varenicline. *Am J Psychiatry* 2007; 164:1269
2. Kohen I, Kremen N: Varenicline-induced manic episode in a patient with bipolar disorder. *Am J Psychiatry* 2007; 164:1269–1270

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## Bizarre Behavior in a Patient Treated With Prazosin for PTSD

TO THE EDITOR: Prazosin is an  $\alpha_1$  antagonist that is often used to treat hypertension and benign prostatic hypertrophy. However, prazosin has also been shown to alleviate posttraumatic stress disorder (PTSD) symptoms, particularly nightmares (1). Although prazosin can cause dizziness and drowsiness, there are no reports of psychiatric side effects. We present the case of a patient who experienced dissociative symptoms and bizarre behavior after starting prazosin for PTSD nightmares.

"Mr. A" was a 42-year-old Caucasian man who served in the first Gulf War. Since the war, he experienced flashbacks, nightmares, hypervigilance, and avoidance. In addition to PTSD, he was being treated for type 2 diabetes mellitus and unclassified erosive arthritis. His diabetes and arthritis were both stable. As a result of his worsening nightmares, the patient was started on prazosin (1 mg by mouth every night). He was also being treated with citalopram, hydroxychloroquine, insulin, lisinopril, and oxy-codone, none of which reportedly interact with prazosin or each other. Over the ensuing week, Mr. A experienced what he described as blurred awareness of the line between dreaming and reality. He was terrified of what he might do in his dreamlike state, and this fear peaked on the night prior to admission. On that evening, he recalled having a conversation with his fiancée in which he stated that he was suicidal and that he "wanted to take someone with him," particularly his mother who was ill in a nursing home. He was uncertain whether the conversation with his fiancée took place while he was dreaming or awake, but his fiancée confirmed that he was awake. By the time he was admitted to our unit, he said that he was horrified that he had felt the way that he did about his mother and that he would never kill himself or anyone else. As a result, he was scared of being unsupervised for any length of time.

Mr. A's fiancée described other behaviors that she noticed since he started treatment with prazosin. In a recent incident, he had been driving with his family in the car, who noted that he began to swerve on the gravel shoulder erratically, and they had to yell at him repeatedly in