

## Varenicline Induced Psychosis

**Bilge Burçak Annagür, Özkan Guler,  
Emine Tekinarslan**

To the Editor,

Varenicline is a novel treatment for smoking cessation. This agent is a partial agonist that binds at the nicotinic  $\alpha 4\beta 2$  receptor, and it seems to be the most effective smoking cessation product currently available (1). As a partial agonist, varenicline produces low to moderate levels of dopamine release, which reduces craving and withdrawal symptoms. Additionally, varenicline stimulates the central nervous mesolimbic dopamine system. This system is believed to be involved in the reinforcement and reward neuronal mechanism associated with smoking.

As it acts on the central nervous system and its effects include the stimulation of dopamine release, it is possible that it may have an impact on mood and suicide risk (2). Increased neuropsychiatric symptoms such as depressed mood, agitation, and suicidal ideation and behavior have been reported with the use of varenicline. A published case report of varenicline exacerbating symptoms of schizophrenia exists (3). Due to these adverse effects, FDA added a black box warning in 2009 to alert physicians and patients about these risks (4). Individuals with psychiatric history might be particularly vulnerable to these side effects, but empirical evidence is limited (5).

Although not all reported cases about the side effects of varenicline had a psychiatric history, some reports in the current literature have shown exacerbation of symptoms or recurrence of pre-existing psychiatric disorder in those patients who had a psychiatric history (3,6).

This is a case report of varenicline induced psychosis: Mr. X is a 50-year-old man. His psychiatric history started 18 years ago. He began to live with a friend when he went to work in a city away from his family. He had some paranoid ideas such as his friend added poison to his meals and was planning to do harm to and besides his wife deceived him. Haloperidol 5 mg/day was prescribed at that time, his paranoid ideas decreased but continued. Two years after the beginning of the illness, he left work and turned back to his home and began to work in marketing sector. For last ten years he has been on olanzapine treatment (5mg/day) and had no psychotic symptoms. Oral varenicline tablet (2 mg/

day) was prescribed to him 14 days ago in a smoking cessation clinic. His paranoid ideas began shortly after the start of varenicline such as he was defrauded and given bogus cheque by others in the marketing sector. He also began to check his wife's mobile phone because he thought that she deceived him. The patient reported that there were not any stressors and he was taking olanzapine regularly. Routine laboratory examination was normal. The recurrence of preexisting psychotic symptoms was suggested to be resulted from varenicline. Varenicline was immediately stopped and olanzapine dosage was increased to 10 mg/day. All psychiatric symptoms significantly improved within three weeks after varenicline cessation. The patient is still on olanzapine treatment.

The exacerbation of psychosis in this patient after initiation of varenicline treatment for smoking cessation certainly suggests that varenicline has the capacity to induce psychosis at least in patients with a history of psychosis. This has been also reported in another patient with a documented history of mental illness (7). Possible mechanisms include dopaminergic stimulation secondary to agonism of the  $\alpha 4\beta 2$  nicotinic receptor.

Some of the behavioral changes and mood changes seen in patients who use varenicline may be associated with nicotine withdrawal. However, some occurred in people who continued smoking while they were on varenicline medication (8). In our case, rapid improvement in psychotic symptoms and remission of the disease forced us to evaluate these symptoms with a mechanism other than nicotine withdrawal.

This case report provides valuable support of previously published cases that demonstrate the risk of exacerbation of psychotic symptoms with varenicline use in patients with major mental illness. With proper assessment and management of varenicline induced neuropsychiatric effects, health care professionals can help to prevent and manage potential worsening of psychiatric symptoms.

Bilge Burçak Annagür  
Selcuk University, Selcuklu Medical Faculty,  
Department of Psychiatry, Konya -Turkey  
e-mail address: bilgeannagur@yahoo.com

*This letter was accepted for publication in December 12, 2011.*

## References:

1. Cahill K, Stead L, Lancaster T. A preliminary benefit-risk assessment of varenicline in smoking cessation. *Drug Saf* 2009;32(2):119-35.
2. Hays JT, Ebert JO. Varenicline for tobacco dependence. *N Engl J Med* 2008;359(19):2018-24.
3. Freedman R. Exacerbation of schizophrenia by varenicline. *Am J Psychiatry* 2007;64(8):1269.
4. Food and Drug Administration. FDA Med Watch Alert, Varenicline (marketed as Chantix): Information, February 1, 2008, and November 20, 2007. Available at [www.fda.gov/cder/drug/infopage/varenicline/default.htm](http://www.fda.gov/cder/drug/infopage/varenicline/default.htm).
5. Kuehn BM. Varenicline gets stronger warnings about psychiatric problems, vehicle crashes. *JAMA* 2009;302(8):834.
6. DiPaula BA, Thomas MD. Worsening psychosis induced by varenicline in a hospitalized psychiatric patient. *Pharmacotherapy* 2009;29(7):852-7.
7. Pumariega AJ, Nelson R, Rotenberg L. Varenicline-induced mixed mood and psychotic episode in a patient with a past history of depression. *CNS Spectr* 2008;13(6):511-4.
8. Xi ZX. Preclinical Pharmacology, Efficacy and Safety of Varenicline in Smoking Cessation and Clinical Utility in High Risk Patients. *Drug Health Patient Saf* 2010;(2):39-48.