Varenicline Precipitating Psychosis in a Patient with no Previous Psychiatric History: A Case Report of a Spanish Patient Who was Later Diagnosed with Paranoid Personality Disorder

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Abstract

Varenicline is gaining popularity for the treatment of nicotine dependence. General treatment guidelines recommend monitoring for behavioral changes in patients with a mental illness. There are very few cases reported on patients developing psychiatric symptoms with no previous history. We are reporting the case of a Spanish patient who had developed a first-psychotic episode after he was started on varenicline. He was ultimately diagnosed with a paranoid personality disorder. Therefore, prior to starting a patient on varenicline, the clinician must identify possible paranoid and other cluster A personality traits. It is essential to monitor for new onset of psychotic symptoms during the treatment with this drug.

Key Words: Nicotine, Paranoia, Side Effects, Psychopharmacology, Psychosis

Introduction

Varenicline is a medication widely used for the treatment of nicotine dependence. It is believed to work by partially blocking alpha 4 and beta 2 nicotinic receptors, making this drug ideal for patients with moderate to severe tobacco dependence (1).

When used in a population with previous psychiatric history, varenicline has been associated with worsening of depression, mania or psychosis (2-4). Also, it is believed to possibly induce psychosis in patients with a diagnosis of borderline personality disorder, drug dependence or other nonspecified psychotic disorders (5-8). As a result, it is generally recommended to watch for behavioral changes in all patients taking varenicline (9).

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Despite these side effects, varenicline is not thought to cause psychiatric side effects in patients with no previous history. One study carried out in a general population showed no development of major psychiatric symptoms with treatment on this drug when compared with a group that received nicotine replacement therapy (10). Only two cases have been published involving patients with no previous psychiatric history. In one of them, a patient was admitted voluntarily to an inpatient unit after she developed anxiety, depression, paranoia and suicidal ideation when she was started on this drug (11). In the other case, a patient with family history of psychiatric illness developed withdrawal symptoms, including visual hallucinations, after abrupt cessation of varenicline (12). Neither of these studies included personality assessments.

We are reporting a patient who suffered a first-psychotic episode after he was started on varenicline for the treatment of nicotine dependence. He had no known history of mental illness and no psychiatric symptoms during his first visit to

Table 1 MCMI-II Scores

MCMI-II	(p) Paranoid	(1) Schizoid	(s) Schizotypal	(pp) Psychotic Delusions	(7) Compulsive	(3) Dependent
3rd week	83	106	85	85	120	97
6th week	69	93	42	83	120	75

Note: Scores of 75–84 indicate personality traits or the presence of clinical syndrome; scores of 85 or above indicate the persistence of a personality trait or a clinical syndrome.

the office. He was ultimately diagnosed with a paranoid personality disorder according to the psychometric and clinical evaluation.

Case

Mr. A is a 48-year-old single, unemployed male with a 30-year history of smoking 18 to 20 cigarettes daily. He had no previous psychiatric or medical history, including alcohol or illicit drug abuse. He went to the chemical dependency unit at the University Hospital of Virgen de la Arrixaca in Murcia, Spain, in order to receive treatment for nicotine dependence. He was started on 0.5 mg of varenicline daily after the first visit. His smoking habit decreased progressively during the first week. His dose was increased up to 0.5 mg twice daily during that week.

At the beginning of the second week of treatment, the patient started to develop symptoms concurrently with the increase of varenicline to 1 mg twice daily. At that time he came back to the office accompanied by his supervisor at work. He had stopped smoking, but presented clinically with intense fear and anxiety. He thought his coworkers were planning a conspiracy against him. He strongly believed they wanted to hurt him and get him fired. He had thought that they were going to break into his house to rob him. He was scared of people and spoke softly because he did not want to be heard by others. He also complained of insomnia. He denied auditory or visual hallucinations. On the basis of his fears, he admitted to aggressive and violent thoughts. During this time, he was not taking any other medication. A physical examination done by an internist, basic metabolic panel, complete blood with differential and thyroid hormones did not show abnormalities. A urine toxicology screen was negative for opiates, cannabis, amphetamines and cocaine. Blood alcohol level was also negative. Previous toxicology screens were not available. A CT scan of the head showed no acute intracranial pathology. Varenicline was stopped and the patient was discharged to a family member's home on lorazepam 1 mg q 8 hours PRN for anxiety and zolpidem 10 mg qhs PRN for insomnia. These doses were gradually tapered between the first and the fourth week. He refused to try antipsychotic medications, and the clinical presentation was not severe enough to warrant hospitalization. In addition, he had a supportive family system that could monitor his behavior at home.

During the third week since his first visit in the office our patient was evaluated again. The psychotic symptoms were decreased, and the patient was less anxious. The Naranjo Scale was performed. This is a questionnaire that determines the likelihood that an adverse drug reaction is, in fact, due to the drug rather than other factors. He had a score of 5, consistent with a probable adverse drug reaction due to the drug (13). Also during this visit, a Millon Clinical Multiaxial Inventory II (MCMI-II) was completed (see Table 1) (14).

In the sixth week, the patient was seen again. He was calm and denied paranoid ideation. He was functional at his job, but still seemed to be slightly suspicious of others. His sister was called to obtain collateral information. She described him as a lonely person who had no known romantic involvement and was fearful, reserved and distrustful. She reported that her brother had had previous problems with the neighbors. There was no known psychiatric family history. During this visit, the MCMI-II (see Table 1) and the Symptom Checklist-90-Revised (SCL-90-R) tests were performed (see Table 2) (14, 15). Moderate personality traits still persisted at a relatively high level. MCMI-II results showed a baseline pathological personality in our patient as schizoid, compulsive, and dependent values were still elevated after four weeks (see Table 1). SCL-90-R was significant for persistent paranoid and psychotic features (see Table 2). As a result of the clinical evaluation, interviews with the family and the psychometric evaluation, the team concluded that the patient suffered from a paranoid personality disorder (*DSM-IV* Criteria 301.0). The patient was not started on antipsychotic medications since these medications are generally not indicated in paranoid personality disorders and, as mentioned before, the patient was not interested in taking antispychotics.

Discussion

To our knowledge, this is the first description of an acute psychotic reaction to varenicline in a patient with no previous psychiatric history diagnosed with a paranoid personality disorder.

The mechanism of how varenicline may induce psy-

Table 2 SCL-90-R Scores

SCL-90-R	Paranoid Ideation	Psychoticism	Phobic Anxiety
6th week	90	85	80

Note: Scores represent percentiles and indicate the probability of a symptom compared to the sample (in this case, the general male population without clinical symptoms).

chotic episodes is still not well understood. Studies have shown that the risk of developing psychotic symptoms is greater for people with previous mental illness. In regards to the central nervous system, nicotinic receptors are widely distributed throughout (16). Varenicline is a partial agonist of alpha 4 and beta 2 and a full agonist of alpha 7 nicotinic receptors (17). It has a long half-life of 24 hours. The partial agonist activity at alpha 4 and beta 2 nicotinic receptors in the ventral tegmental area would increase the release of dopamine in the nucleus accumbens, thereby decreasing the need to smoke. It would also promote dopamine transmission through the cortex causing psychotic symptoms (18). It also acts on alpha 7 nicotinic receptors, which have been linked to major psychiatric disorders (19).

This report has some limitations. The symptoms that the patient presented with could be a result of the patient's abrupt smoking cessation; however, this hypothesis is unlikely since varenicline is believed to improve mood and cognition during the withdrawal syndrome (20). Despite the remittence of symptoms after varenicline was stopped and that Naranjo Scale results showed a probable association between the drug and the onset of symptoms, we cannot rule out with absolute certainty that the patient was not suffering from a primary psychotic episode. Definite association between varenicline and the adverse drug reaction could not be established by rechallenging with the offending agent (13). While varenicline has proven to be effective for treating a smoking habit, it seems, quite infrequently, to carry possible serious side effects in patients with previous mental illness. Secondary psychotic episodes seem to be a possible side effect of treatment with this drug.

We think this case illustrates the importance of monitoring for the development of psychotic symptoms when starting a patient on varenicline. In patients with no previous psychiatric history, early identification of paranoid or other cluster A personality traits would be of significant relevance.

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