Buprenorphine-Induced Psychotic Symptoms: A Case Report

To the Editor: Buprenorphine has been available in the market since the 1980s as an analgesic. It was approved by the US Food and Drug Administration (FDA) for use in opioid addiction in October 2002. Since then, most studies have found buprenorphine to be well tolerated with the added advantage of having a ceiling effect as compared to other opioids such as methadone,[1] showing few if any central nervous system (CNS) side effects. The authors were able to find only a few reports[2,3] of buprenorphine-induced psychotic symptoms in the literature. We therefore present a case of buprenorphine-induced psychotic symptoms.

Case report. Mr A, a 40-year-old man, had a history of multiple substance use since 1989. The patient had been using alcohol and tobacco (chewable form) in a dependent fashion diagnosed according to the criteria of the *International Statistical Classification of Diseases and Related Health Problems*, 10th revision, since the early 1990s. With these substance use disorders, he had marital as well as occupational dysfunctions.

Mr A was diagnosed with human immunodeficiency virus (HIV) in 2007. He switched to injection buprenorphine along with pheniramine (3.6 mg and 227.5 mg/d, respectively) in 2010 out of curiosity, as some of his friends were using the same. The quantity of buprenorphine had been increased to 7.2 mg/d and that of pheniramine to 455 mg/d after 6 months, following which the patient started experiencing delusions of reference and persecution whenever he was in the company of his colleagues. When alone, Mr A reported experiencing tactile hallucinations (insects crawling under the skin) as well as visual hallucinations (small white worms crawling over his skin and burrowing into his skin). These perceptual abnormalities would occur 4 or 5 times a day, lasting for 1 to 2 hours each time. This episode lasted for 15 days, during which time the patient also made a suicide attempt and then was admitted to a drug de-addiction treatment center for further management. The episode ended when he remained abstinent from buprenorphine and pheniramine. The patient had no family history of psychotic disorders.

After a 1-month stay in the de-addiction center, the patient was discharged, following which he restarted consuming buprenorphine (3.6 mg/d) and pheniramine (227.5 mg/d) in the previous amounts. He also became noncompliant with the antiretroviral therapy that was initiated during his hospital stay and remained as such until about 8 months later, when he again increased the dose of buprenorphine to 7.2 mg/d and of pheniramine to 455 mg/d. This led to similar psychotic features as before, following which he was again admitted to the drug de-addiction treatment center. He was detoxified, following which these abnormalities gradually subsided over the course of 2 weeks.

Given Mr A's HIV-positive status, the treating team considered the use of oral opioid substitution therapy. The patient was started on sublingual buprenorphine and naloxone combination treatment (2 mg and 0.5 mg, respectively). Two days later, he started experiencing the same tactile hallucinations as he had experienced in 2010 but without the visual perceptual abnormalities that he had experienced the last time; he had no delusions on this occasion. These perceptual abnormalities gradually decreased in intensity when the buprenorphine-naloxone combination was stopped.

During his stay in the ward, Mr A was also found to be suffering from hepatitis C virus infection, the management of which was started in the inpatient setting after liaison with the hepatology department of the institute. The treating team considered the possibility that these psychotic symptoms were due to organic pathologies such as HIV infection. However, this possibility was ruled out as the patient had contracted HIV in 2007 and these symptoms started in 2010 when the patient increased the dose of buprenorphine. The psychotic symptoms in the later part of the patient's history were also temporally associated with an increase in the dose of buprenorphine. The psychotic symptoms were also unlikely to have occurred with increased dose of pheniramine, as Mr A developed the same when he was given sublingual buprenorphine without pheniramine.

Buprenorphine has been found to be a safe option for opioid substitution therapy in the majority of the literature. A review of buprenorphine on the FDA Web site showed that the most common CNS side effects were anxiety, depression, insomnia, nervousness, and somnolence.[4] Common side effects of buprenorphine on other systems included constipation, nausea, vomiting, headache, dizziness, and flu syndrome. Wiegand[5] opined that serious side effects of buprenorphine such as respiratory depression were more likely to occur in drug-naive pediatric patients or those who were suffering from a concomitant lung disease such as chronic obstructive pulmonary disease. A PubMed search with the keywords *buprenorphine* and *psychosis* revealed no significant information. However, a search using the keywords *buprenorphine* and *hallucination* found a series of 5 cases of reported visual hallucinations; in 1 of the 5, the hallucinations followed epidural administration of buprenorphine.[2] The dose of epidural buprenorphine in that case was 1,159 μg. Another case report described auditory hallucinations in a patient who received buprenorphine to relieve pain after hemorrhoidectomy.[3]

We therefore wish to draw attention to the psychotic side effects of buprenorphine, which, although rare, can be severely distressing.

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