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CASE REPORT

Can nasal decongestants trigger a manic episode?

Ali Kandeger[1], Rukiye Tekdemir[1], Baris Sen[1], Yavuz Selvi[1]

[1]Selcuk University, Faculty of Medicine, Department of Psychiatry, Konya – Turkey

ABSTRACT

Among the sympathomimetic drugs, phenylephrine, pseudoephedrine, and ephedrine are the ones that have been used most commonly in oral medication for the relief of nasal congestion. There are reports suggesting that psychiatric cases have been triggered by central nervous system stimulant drugs used as nasal decongestants. In this report, we would like to present a male patient with bipolar disorder undergoing two manic episodes, both triggered by cold medicine. A 25-year-old male patient was seen in the psychiatric outpatient clinic with increasing complaints such as raised level of energy, talkativeness, decreasing sleep, increasing libido, and visual and auditory hallucinations after using an cold medicine containing phenylephrine. Also, 2 years ago, he had a manic attack triggered after the use of cold medication. The patient's manic symptoms were stabilized with lithium 900 mg/day and olanzapine 15 mg/day and his functionality improved. According to his history, the psychometric tests, psychiatric evaluation, and the 6 months follow-up, he was diagnosed with "substance/medication-induced bipolar and related disorder" according to DSM-5 diagnostic criteria. He had not suffered any mood or psychosis episodes before the use of nasal decongestants, no family history of bipolar disorder, a 16-month period of wellbeing without using a mood stabilizer between 2 episodes, and remission after 1-month anti-manic treatment after the cessation of the cold medicine, supporting the view that the adrenergic drugs with a central stimulant effect may have triggered the manic episodes.

Keywords: Ephedrine, manic episode, phenylephrine, pseudoephedrine, substance/medication-induced bipolar and related disorder

INTRODUCTION

Phenylephrine, pseudoephedrine and ephedrine are the most commonly used sympathomimetic drugs included in the orally administered medicines for the relief of nasal congestion (1). These drugs are known to stimulate the central nervous system (CNS) through alpha- and beta-adrenergic agonistic effects (1).

It has been reported in the literature that drugs containing ephedrine and pseudoephedrine trigger manic symptoms and episodes (2-5). To the best of our knowledge, no phenylephrine-induced manic or psychotic attack has been reported. In this article; we want to present a case of bipolar disorder in which two manic episodes, both being triggered by an cold medicine.

CASE

A 25-year-old single male patient working in the industrial labor force consulted his family doctor with complaints of nasal discharge, fatigue, and cough nearly 6 months ago, and an cold medicine containing 10 mg phenylephrine 2 times per day was prescribed. Twenty-four hours after starting the drug (after the 2nd dose), symptoms such as energy increase, talkativeness,

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Correspondence: Rukiye Tekdemir, Selcuk University, Faculty of Medicine, Department of Psychiatry, Konya – Turkey
Phone: +90 332 606 05 05 - 44 047 **E-mail:** dr.rtekdemir@gmail.com
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racing thoughts, lack of sleep, and increase in libido set on. In addition to these symptoms, irritability, auditory verbal hallucinations of voices threatening to catch and kill him, and visual hallucinations of images of policemen coming to arrest him appeared, and the related aggressive behavior began. Subsequently, the patient stopped taking the drug and was taken to our clinic.

Two years ago, three days after starting a prescribed cold medicine (2 doses per day) for an upper respiratory infection, he had developed pressured speech, emotional lability, excessive talking to himself, and visual hallucinations. He was diagnosed with bipolar disorder-manic episode in the psychiatry clinic he consulted. After hospitalization, his symptoms almost completely disappeared within 1 month. One month after discharge, he discontinued his medication and did not visit the outpatient clinic. The patient did not have any psychiatric symptoms for nearly 16 months until his current episode. In the intervening period, he used no psychiatric treatment or cold medicines and his functioning was good.

There were no other mood disorder events in the patient's history except for the two manic episodes described above. The patient had no history of alcohol or substance use in his lifetime. He also had not suffered from any other psychiatric and neurological illnesses or head trauma. In the patient's family history; there was no evidence of any psychiatric disorders, including mood disorders, in first-degree relatives.

The patient was admitted to our clinic for diagnosis and treatment with manic and psychotic symptoms following the use of cold medicine. In mental status examination, the patient's general appearance was overactive, restless, and overly anxious. His speech was fast and copious. His affect was euphoric and sometimes irritable and hostile. He had racing thoughts and delusions of persecution and grandiosity and perceived visual and auditory hallucinations. Psychomotor activity increased in his behavior and there was aggression consistent with the hallucinations. The patient's attention and concentration were decreased. His attention was distractible and his insight was reduced. He scored 44 points on the Young Mania Rating Scale (YMRS) (6).

Except for mild hyperlipidemia, no abnormalities were found in the results of hemogram, biochemistry, thyroid function tests, and other hormone tests. No organic pathology was detected in electroencephalographic examination and brain magnetic resonance imaging.

When the patient was admitted to our clinic, he had no insight and he was very aggressive and agitated. Physical restraints had to be used on the first day and haloperidol 10mg/day intramuscularly was given on the first 3 days of hospitalization. The patient was followed up in our psychiatry service with lithium 900 mg/day and olanzapine 15mg/day for nearly 1 month. During follow-up, lithium blood level was in the range of 0.95-0.88 mmoL/L. Severity of hallucinations decreased within 1 week. Subsequently, emotional lability symptoms such as anger, euphoria, and irritability quickly disappeared. Within nearly 1 month, all of the patient's symptoms completely disappeared and the YMRS score declined to 4 points. The patient was followed in the outpatient clinic for nearly 6 months after discharge. During these 6 months, the patient was in remission with lithium 900 mg/day and olanzapine 2.5 mg/day and his function improved, with a YMRS score of 0. According to history, psychometric tests, psychiatric evaluation, and 6 months follow-up, the patient was diagnosed with "substance/medication induced bipolar and related disorder" according to DSM-5 diagnostic criteria.

DISCUSSION

Ephedrine is an agonist of both alpha- and beta-adrenergic receptors, enhancing the release of norepinephrine from sympathetic neurons; in addition, it is an amphetamine-like substance with mixed-action sympathomimetic properties and a potent CNS stimulant. Pseudoephedrine is a sympathomimetic stereoisomer of ephedrine. Phenylephrine is an alpha-1-selective agonist that activates beta-adrenergic receptors only at much higher concentrations. Pseudoephedrine and phenylephrine have the potential to cause psychiatric disturbances, although they seem to have less effect on the CNS than ephedrine (1,7). Phenylephrine, ephedrine, and pseudoephedrine are thought to produce psychotic and manic symptoms by acting like amphetamine, leading to a release of catecholamine, noradrenaline, and dopamine from the anterior synaptic nerve terminals (8). The second manic episode of our case occurred with the use of an cold medicine containing phenylephrine. Our patient and his family told us that the patient had also used an cold medicine before his first manic episode nearly two years ago, but they did not remember the name of the drug. Anti-flu drugs in Turkey contain ephedrine, pseudoephedrine, or phenylephrine as nasal decongestants. This suggests that our patient may have

experienced a manic episode triggered by one of these agents in the first episode.

Manic episodes with/without psychotic properties, psychotic attacks, and chronic psychosis triggered by ephedrine and pseudoephedrine have been reported in the literature. In one of the published cases, a 40-year-old female patient with no previous psychiatric diagnosis developed manic symptoms using a weight-loss medication containing ephedrine. Although there was improvement within 20 days of treatment, she had mixed and depressive episodes independent of ephedrine during follow-up (2). In the last case, a 13-year-old girl developed manic symptoms after receiving an amount 6 times greater than the recommended 60 mg dose of pseudoephedrine prescribed for nasal congestion and started treatment for drug-induced affective disorder. However, the patient's family history of bipolar disorder and the presence of pseudoephedrine-independent affective episodes in the follow-up changed the diagnosis to bipolar disorder (5). The common feature of these cases, in which manic symptoms were triggered by nasal decongestants with stimulant properties, was that remission was achieved with treatment in a short time. In our case, remission was achieved within 1 month after each of the two manic episodes. In addition, in contrast with our case, in the cases discussed affective episodes independent of stimulant-acting drug use had been reported.

In conclusion, when the presented case and the reference cases are examined, the importance of differential diagnosis of substance/drug-induced bipolar disorder and bipolar I/II disorder is significant. In our case, the absence of mood or psychosis episodes before the use of nasal decongestants, a family history without psychiatric anomalies, a 16-month-period of wellbeing without using a mood stabilizer between 2 episodes, and remission in 1 month with anti-manic treatment after stopping the cold drug strengthen the diagnosis of the presented case as substance/medication-induced bipolar and related disorder according to DSM-5.

In Turkey, isolated forms (in 2003) and combined forms (in 2013) of nasal decongestants have been added to the list of "prescription drugs" by the Republic of Turkey's Ministry of Health, Turkish Medicines and Medical Devices Agency (9). The authors believe that the over-the-counter sale of anti-flu drugs is risky due to their stimulating effects.

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Category 1	Concept/Design	A.K., R.T., Y.S.
	Literature review	A.K., R.T., B.S.
	Data analysis/Interpretation	A.K., R.T.
	Case follow-up (if applicable)	A.K., R.T., B.S., Y.S.
Category 2	Drafting manuscript	R.T., B.S.
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Category 3	Final approval and accountability	A.K., R.T., B.S., Y.S.
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