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Can the nasal decongestants trigger a manic episode?

Ali Kandeger, Rukiye Tekdemir, Baris Sen, Yavuz Selvi

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Ali Kandeđer1, Rukiye Tekdemir1, Barıř Ően1, Yavuz Selvi1

1Selçuk University, Faculty of Medicine, Department of Psychiatry, Konya, Turkey

Sorumlu Yazar:

Rukiye Tekdemir, Selçuk University, Faculty of Medicine, Department of Psychiatry, Konya, Turkey

E-mail: dr.rtekdemir@gmail.com

Tel: +90 530 326 49 95

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Nazal dekonjestanlar manik dönemi tetikleyebilir mi?**Özet**

Fenilefrin, psödoefedrin ve efedrin burun tıkanıklığının hafifletilmesi için oral preparatlarda en sık kullanılan semptomimetik ilaçlardır. Literatürde, nazal dekonjestan olarak kullanılan santral sinir sistemi uyarıcı ilaçlar tarafından tetiklenen psikiyatrik vakalar bildirilmiştir. Bu yazıda, iki manik epizod öyküsü olan ve her ikisi de grip ilaçları tarafından tetiklenen bir bipolar bozukluk vakası sunmak istiyoruz. 25 yaşındaki erkek hasta 10 mg fenilefrin içeren grip ilacını kullanmaya başladıktan 2 gün sonra psikiyatri polikliniğine çok konuşma, giderek artan enerji, azalmış uyku ihtiyacı, libido artışı, işitsel ve görsel hallüsinasyonlar gibi şikâyetler ile başvurdu. Bu ikinci manik dönem olan hastanın öyküsünde 2 yıl önce de, grip ilacı kullanmaya başladıktan 3 gün sonra tetiklenen bir manik dönem yaşadığı öğrenildi. Hastanın manik epizodu lityum 900 mg / gün ve olanzapin 15 mg / gün ile kontrol altına alındı. Psikometrik testler, psikiyatrik değerlendirmeler ve 6 aylık izlem tarihine göre DSM 5 tanı ölçütlerine göre "maddenin/ilacın yol açtığı bipolar ve ilişkili bozukluk" tanısı kondu. Olgumuzda; nazal dekonjestan kullanılmadan önce psikotik ya da manik dönem olmaması, ailede psikiyatrik hastalık öyküsü olmaması, 2 manik dönem arasında bir duygudurum dengeleyici kullanmadan 16 ay boyunca iyilik halinin olması, grip ilacı kesilip psikiyatrik tedaviye başladıktan sonra tedaviden fayda görmesi, merkezi sinir sistemi uyarıcı etkisi olan adrenerjik ilaçların manik dönemleri tetiklediği görüşünü desteklemektedir.

Anahtar sözcükler: Fenilefrin, psödoefedrin, efedrin, maddenin/ilacın yol açtığı bipolar ve ilişkili bozukluk, manik epizod

Can the nasal decongestants trigger a manic episode?

Abstract

Phenylephrine, pseudoephedrine and ephedrine are the sympathomimetic drugs that have been used most commonly in the oral preparation medication for the relief of nasal congestion. The psychiatric cases have been reported to be triggered by CNS stimulant drugs which have been used as the nasal decongestants. In this article, we would like to present a male patient with bipolar disorder with two manic episodes and both of them triggered by anti-flu drugs. 25 year old male patient was admitted to psychiatric outpatient clinic with increasing complaints such as increasing energy, talkativeness, decreasing sleep, increasing in libido and visual and auditory hallucinations after using the anti-flu drug containing phenylephrine. Also, 2 years ago, he has had a manic attack triggered after the use of anti-flu drug. The patient's manic symptoms were stabilized with lithium 900 mg / day and olanzapine 15 mg / day and his functionality was improved. According to the history, the psychometric tests, the 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. In our case; no mood or psychosis episode before the use of nasal decongestants, no family history of bipolar disorder, 16 months of well being without using a mood stabilizer between 2 episodes, remission in 1 month anti-manic treatment after the cessation of anti-flu drug strengthens the view that the adrenergic drugs with a central stimulant effect may trigger the manic episodes.

Keywords: Phenylephrine, pseudoephedrine, ephedrine, substance/medication induced bipolar and related disorder, manic episode

INTRODUCTION

Phenylephrine, pseudoephedrine and ephedrine are the sympathomimetic drugs that have been used most commonly in the oral preparation medication for the relief of nasal congestion (1). These drugs are known to stimulate the central nervous system (CNS) by the 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 (2-6). 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 which is triggered by the a anti-flu drug in both of manic episodes.

CASE REPORT

25 years old, single, male patient who works in the industry as a worker applied to the family doctor with complaints of nasal discharge, fatigue and cough nearly 6 months ago and an anti-flu drug containing 10 mg phenylephrine was prescribed. After starting to use of that drug 2 times per day, 24 hours later (after 2 doses), symptoms such as energy increase, talkativeness, racing thoughts, lack of sleep, increasing in libido started. In addition to these symptoms; irritability, auditory verbal hallucinations of voices threatening to catch and kill him and visual hallucinations of images of policemen who came to arrest him, and the relevant aggressive behaviors began. After that he patient had stopped taking the drug and was brought to our clinic.

Two years ago, three days after prescribed anti-flu drug (2 doses per day) for an upper respiratory infection, he had 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. He was hospitalized and his symptoms were completely disappeared nearly in 1 month. One month after the discharge, he discontinued his medication and did not go to the outpatient clinic. The patient did not have any psychiatric symptoms for nearly 16 months until his current episode. In

the interim period, there was no use of psychiatric treatment or anti-flu drug use in patients with the good functioning.

There was no mood episode on the patient's history except from these two manic episodes. The patient did not use alcohol or substance in his life. Also he haven't got any other psychiatric and neurological illness and head trauma. In the patient's family history; there was no evidence of any psychiatric disorder in first-degree relatives, including mood disorders.

The patient was accepted to our clinic for diagnosis and treatment with the manic and psychotic symptoms following anti-flu drug use. In mental status examination, the general appearance of the patient was overactive, restless and over-cared. 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. The visual and auditory hallucinations were perceived. The psychomotor activity increased in behavior and there was an aggression consistent with the hallucinations. The patient's attention and concentration was decreased. There was distractibility in attention and his insight was reduced. He scored 44 points on the Young Mania Rating Scale (YMRS) (7).

No abnormality was found except from the mild hyperlipidemia as a result of hemogram, biochemistry, thyroid function tests and other hormone tests. No organic pathology was detected in the electroencephalogram examination and brain magnetic resonance imaging of the patient.

When the patient was admitted to our clinic, he had no insight, he was very aggressive and agitated, physical restraints had to be used on the first day and haloperidol 10 mg/day intramuscularly were given on the first 3 days of hospitalization. The patient was followed up in our psychiatry service with lithium 900 mg/day, olanzapine 15 mg/day for nearly 1 month. During follow-up, lithium blood level was in the range of 0.95-0.88 mmol / L. Severity of the visual and auditory hallucinations decreased within 1 week. Subsequently, the emotional lability symptoms such as anger, euphoria and irritability quickly disappeared. Within nearly 1 month, all of the patient's symptoms completely disappeared and YMRS declined to 4 points. The patient was followed in the outpatient clinic for nearly 6 months after the discharge. During this 6 months, the patient was in remission with lithium 900 mg / day and

olanzapine 2.5 mg / day and his function improved, YMRS score was zero. According to the history, the psychometric tests, the psychiatric evaluation, and the 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 both in alpha and beta adrenergic receptors, and enhances their release of norepinephrine from sympathetic neurons; in addition, it is an amphetamine like substance with mixed-action sympathomimetic properties and potent CNS stimulant. Pseudoephedrine is a sympathomimetic stereoisomer of ephedrine. Phenylephrine is an alpha-1 selective agonist and 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 CNS than ephedrine (1, 8). Phenylephrine, ephedrine, and pseudoephedrine are thought to produce psychotic and manic symptoms by acting like amphetamine, leading to release of catecholamine, noradrenaline and dopamine from the anterior synaptic nerve terminals (9). The second manic episode of our case has been with the use of anti-flu drug which includes phenylephrine. Our patient and his family told us that the patient had also used an anti-flu drug before their 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 and phenylephrine as nasal decongestants. This suggests that our patient had experienced a manic episode triggered by one of these agents at the first episode.

Manic episode with/without psychotic properties, psychotic attack and chronic psychosis triggered by ephedrine and pseudoephedrine have been reported in the literature. In one of the reported 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 benefit within 20 days of treatment, she had mixed and depressive episodes independent of ephedrine during follow-up (2). In another case presentation; A 72-year-old female patient with bipolar disorder who had been in remission for a long time was reported to have a manic episode after using 60 mg pseudoephedrine for nasal congestion.

Remission was achieved shortly after discontinuation of pseudoephedrine (5). In the last case, a 13-year-old girl developed manic symptoms after receiving (6 times) more than the recommended dose of pseudoephedrine 60 mg prescribed for nasal congestion and started treatment with 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 (6). 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 both manic episodes. In addition, in the cases discussed, as distinct from our case, there were affective episodes independent of stimulant-acting drugs.

In conclusion, when the presented case and the referenced cases are examined, the importance of the differential diagnosis of substance / drug-induced bipolar disorder and bipolar I / II disorder is remarkable. In our case; no mood or psychosis episode before the use of nasal decongestants, no family story in psychiatric terms, 16 months of well being without using a mood stabilizer between 2 episodes, remission in 1 month with anti-manic treatment after anti-flu drug has stopped strengthens that diagnosis of presented case is substance/medication induced bipolar and related disorder according to DSM 5.

In Turkey, isolated forms (at 2003) and combined forms (at 2013) of nasal decongestants have been added to the list of "prescription drugs" by the Republic of Turkey Ministry of Health, Turkish Medicines and Medical Devices Agency (10). The authors believe that the over-the-counter sale of anti-flu drugs is risky due to their stimulating effects.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report.

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