VAN TIP DERGİSİ Medical Journal

OLGU SUNUMU / CASE REPORT

Van Tıp Derg 25(4): 535-537, 2018
DOI: 10.5505/vtd.2018.88709

Venlafaksin İntoksikasyonu ve Serotonin Sendromu

Venlafaxine Intoxication and Serotonin Syndrome

Mehmet Fatih Yörük[1], Onur Avcı[2*], Göze Çayırlı Demir[1]

[1]Yüksek İhtisas Hastanesi Anesteziyoloji ve Reanimasyon Bölümü Kırıkkale/Türkiye
[2]Numune Hastanesi Anesteziyoloji ve Reanimasyon Bölümü Sivas/Türkiye

ABSTRACT

A second-generation antidepressant called venlafaxine serotonin and norepinephrine reuptake inhibitors (SNRI). Venlafaxine is used in the treatment of depression, anxiety and attention deficit hyperactivity disorder in children and adolescents. Compared with tricyclic antidepressants, tolerance and safety profiles of SNRI's are positive, and their use in terms of patient compliance and overdosage is increasing day by day. Symptoms that should be paid attention to in severe toxicity are CNS (central nervous system) depression, serotonin syndrome and cardiac conduction abnormalities. We aimed to present a 10.5 gr long venlafaxine intoxication with rhabdomyolysis, muscle rigidity and epileptic seizures.

Key Words: Serotonin syndrome, rhabdomyolysis, venlafaxine

ÖZET

Venlafaksin; serotonin ve norepinefrin geri alım inhibitörleri (SNRI) olarak isimlendirilen ikinci nesil bir antidepresandır. Venlafaksin çocuk ve ergenlerde depresyon, anksiyete ve dikkat eksikliği hiperaktivite bozukluğu tedavisinde kullanılmaktadır. Trisiklik antidepresanlar ile karşılaştırıldıklarında SNRI'ların tolerabilite ve güvenlik profilleri olumlu olup, hasta uyumu ve doz aşımı açısından da kullanımı gün geçtikçe artmaktadır. Ciddi toksisitede en çok dikkat edilmesi gereken semptomlar SSS (santral sinir sistemi) depresyonu, serotonin sendromu ve kardiyak iletim anormallikleridir. Biz rabdomyoliz, kas rijiditesi ve epileptik nöbetleri olan toplam 10,5 gr uzun salınımlı venlafaksin zehirlenmesini sunmayı amaçladık.

Anahtar Kelimeler: Serotonin sendromu, rabdomyoliz, venlafaksin

Introduction

Venlafaxine is a second generation antidepressant, which inhibits serotonin and noradrenaline reuptake. Overdose can cause tachycardia, high blood pressure, fatigue, headache, nausea, xerostomia, changes in mental state, mydriasis, even seizures and attacks (1). Overdose of many newer generation antidepressants are safer than old tricyclic antidepressants (TCA) (2). We aimed to present a case report regarding intoxication from venlafaxine from the SNRI group (serotonin noradrenaline reuptake inhibitory).

Case Report

A 35 year old female patient with depression history is using venlafaxine (sulinex XR) tablet 150 mg/day. The patient is brought to the emergency service after taking some amount of venlafaxine in an attempt to suicide. Her husband stated that she took 56 x 75 mg and 42 x 150 mg tablets so a total of 10.5 grams of extended release venlafaxine. These were not taken with alcohol or any other drugs. The patient was immediately transferred to intensive care unit after being treated with activated charcoal and gastric lavage. Upon arrival, the patient was agitated and had muscular rigidity. Pupils were dilated and light reflex was +/+. Arterial blood pressure was: 100/60 mmHg, heart rate: 150/min, SpO2: 85, GCS (Glasgow Coma Score): 9 (E:3-M:4-V:2), axillary body temperature: 37.3 °C. In addition, the patient had grand mal seizures. 2-6 L/min oxygen with mask and midazolam 3 mg IV (0.05 mg/kg IV) was applied to suppress the seizures. Upon neurologic consultation, 5 mg/kg/day IV phenytoin sodium infusion was started after 15 mg/kg IV loading dose. Routine blood tests were analyzed for the patient who did not have respiratory problems. Arterial blood gas showed pH: 7.29, pCO2: 42.7 mmHg, pO2: 83.3 mmHg, H2CO3: 19.6 mmol/L, anion gap: 5.9 mmol/L and lactate: 1.4 mmol/L. IV saline infusion and esmolol hydrochloride infusion at 0.1 mg/kg/min were started to prevent sinus tachycardia.

*Sorumlu Yazar: Onur Avcı, Kardeşler Mah. Birlik Cad. Eğriköprü 2 Konakları No:85 A Blok D:20 Merkez/Sivas
E-mail: dronuravci@gmail.com, Tel: 0(530) 112 64 08
Geliş Tarihi: 09.12.2017, **Kabul Tarihi:** 21.01.2018

The patient was consulted with cardiology after checking her ECG. Echocardiography results were normal and close ECG follow-up was suggested by cardiology. Blood gases returned to normal after 3 hours. Leucocyte count was 17.5x10^9, which returned to normal values after 3 days. CK (Creatin kinase) was 424 U/l and CK-MB was 171 U/L. After 5 days of hospitalization, CK values were 22846 U/L. At day 9 of hospitalization, blood CK levels were normal, too. BUN and creatinine levels were in normal range. On day 9, upon clinical recovery and blood values being normal, the patient was discharged with suggestions after consulting with psychiatry.

Discussion

Venlafaxine is a noradrenaline and serotonin reuptake inhibiting antidepressant, which was approved in 1994 by FDA. IT is being used for treating major depression, generalized anxiety disorder, social phobia and panic attacks. It is metabolized in the liver by sit p450. Half-life of the extended release type is around 5 hours and is eliminated through the kidneys. Among side effects of venlafaxine use are: nausea, vomiting, headache, stomach ache, sleepiness, discomfort, dizziness, nervousness, xerostomia, increased muscular tonus, tremor, confusion, hypertension, tachycardia, anorexia, constipation, sweating and skeletal muscle breakdown (1).

On venlafaxine overdose, severe complications like cardiac toxicity (prolonged QT, arrhythmia, hypertension, hypotension), serotonin related toxic effects (mental changes, neuromuscular anomalies, autonomous dysfunction) and CNS (central nervous system) depression can be seen (1). Our patient had sinus tachycardia, and responded to esmolol hydrochloride infusion quickly. Serotonin syndrome on the other hand is a drug related toxic condition caused by serotonergic agents as a result of increased serotonin activity in the brain (3). It is characterized with a triad of neuromuscular hyperactivity (hyperreflexia, myoclonus, coordination disorder, tremor), autonomous disorders (hyperhidrosis, hyperthermia, diarrhea, hyper/hypotension, nausea-vomiting) and changes in consciousness (confusion, hypomania, agitation) (3). The patient in this report showed tachycardia, mydriasis, xerostomia, muscular rigidity, coordination disorder and agitation.

According to Sternbach criteria; our patient was concordant with serotonin syndrome (4). In addition, patient's CK levels were high (22846 U/L). Plasma CK elevation was probably caused by skeletal muscles. In a study of Wilson et al; relation between venlafaxine usage and muscle damage was observed (5). It was also stated, that CK levels may not rise in the first 12 hours of drug intake (5). In our report, CK levels elevated after 11 hours of drug intake. For this reason, CK levels right after drug intake may not be realistic. Severe risk of death, including seizures and serotonin syndrome, was reported in a case with 8 g or more intake of venlafaxine (6). Another case reported that intakes of 30 g or more had caused death (7). In our case of 10.5 g oral intake, grand mal seizures and serotonin syndrome were observed; with treatment, seizures stopped after 1 day and serotonin syndrome was treated in 36 hours. High doses of venlafaxine (>900 mg) are reported to trigger epileptic seizures (8). Occurrence of seizures is related to the dosage of the taken antidepressant; seizure risk is increased by 4-30% in patients who take high doses of drugs (8). Due to the wide volume of distribution of venlafaxine, it has no specific antidote, and force diuresis, dialysis and hemoperfusion are not very useful in cases of intoxication. Activated charcoal is helpful to prevent absorption of the drug when administered in time.

In conclusion, as a result of venlafaxine overdose, our patient showed changes in mental state, grand mal seizures, muscular rigidity, rhabdomyolysis and elevated plasma CK. Early diagnose and supportive care treated the patient's clinical picture. With this in mind, physicians should be prepared for complications caused by intoxications.

References

1. Johnson EM, Whyte E, Mulsant BH, Pollock BG, Weber E, Begley AE, et al. Cardiovascular changes associated with venlafaxine in the treatment of late-life depression. Am J Geriatr Psychiatry 2006; 14(9): 796-802.
2. Doğan BE. "Serotonin Syndrome, Rhabdomyolysis and Cardiovascular Toxicity in Venlafaxine Poisoning: A Case Report." Kocatepe Medical Journal 2012; 13: 173-175.
3. Koçak O, Yarar C, Çarman KB, Işık İ. Ciddi Bir İlaç Reaksiyonu: Serotonin Sendromu İKSST Derg 2015; 7(3): 144-146.
4. Sternbach H. The serotonin syndrome. Am J Psychiatry 1991; 148(6): 705-713.
5. Wilson AD, Howell C, Waring WS. Venlafaxine ingestions is associated with rhabdomyolosis in adults. The J of ToxicolSci 2007; 32 (1): 97-101.
6. Hojer J, Hulting J, Salmonson H. Fatal cardiotoxicity induced by venlafaxine overdosage.

ClinToxicol (Phila) 2008; 46(4): 336-337.
7. Mazur JE, Doty JD Kyrygiel AS. Pharmocotherapy 2003; 23(12): 1668-1672.
8. Ateş MA. Venlafaksinin Uzun Salınımlı Formunun Kullanımı Sonucu Tetiklenen Epileptik Nöbet: Bir Olgu Sunumu Nöropsikiyatri Arşivi 2008; 45: 62-64.