Kocatepe Tıp Dergisi
Kocatepe Medical Journal
13: 173-175/ Eylül 2012

OLGU SUNUMU

Serotonin Syndrome, Rhabdomyolysis and Cardiovascular Toxicity in Venlafaxine Poisoning: A Case Report

Venlafaxin Zehirlenmesinde Serotonin Sendromu, Rabdomyoliz ve Kardiyak Toksisite: Olgu Sunumu

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ABSTRACT
More selective antidepressant agents are increasingly being used on first-line treatment. We present a case of 6gr venlafaxine intoxication with rhabdomyolysis,cardiac toxicity including patologic Q and serotonin syndrome. The patient was haemodynamically stable but musculer rigitidy, hyperreflexia, dilated pupils and raised creatinin cinase (CK) were prominent on presantation to our Intencive Care Unit (ICU). It was seen that venlafaxine causing cardiac toxicity and death after large overdoses in the literature. Physicians should be aware of rhabdomyolysis and cardiac toxicity with venlafaxine poisoning.
Keywords: rhabdomyolysis, serotonin syndrome, venlafaxine

ÖZET
Selektif antidepresan ajanların birinci sıra tedavi kullanımları giderek artmaktadır. Biz rabdomyoliz, patolojik Q'lar içeren kardiyak toksisite ve seratonin sendromlu 6gr venlafaxine zehirlenmesini sunuyoruz. Hasta yoğun bakım ünitemize geldiğinde hemodinamik olarak stabildi fakat kas rijiditesi, hiperrefleksisi, pupil genişlemesi ve yükselmiş kreatinin kinaz (CK) seviyesi mevcuttu. Literatürde yüksek doz aşımlarında venlafaksinin kardiyak toksisite ve ölüme neden olduğu görülmektedir. Doktorlar venlafaxine zehirlenmelerinde rabdomyoliz ve kardiyak toksisite açısından dikkatli olmalıdırlar.
Anahtar Kelimeler: rabdomyoliz, serotonin sendromu, venlafaxin

INTRODUCTION

Venlafaxine is a phenylethylamine derivative whose pharmacological mechanisms of action are related to inhibition of serotonin and norepinephrine neuronal reuptake (1). It is associated with a number of predictable adverse effects that are generally mild, including tachycardia, increased blood pressure, fatigue, headache, dizziness and dry mouth (2). Many of the newer antidepresants have been shown to be safer in overdose compared with the older tricyclic antidepressants. Venlafaxine appears to be more toxic than the newer antidepressants with a higher rate of fatalities (3), increased risk of seizures (4) and cardiac toxicity reported with massive ingestions (5). We present a case of an intoxication to the serotonin noradrenergic reuptake inhibitors venlafaxine .

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CASE REPORT

A 24-year old young man with a history of depression was admitted to the emergency department four hours after intoxication with the antidepressant venlafaxine. He reported to have ingested a total of 6gr of the extended-release formulation.He had not taken any other medications or alcohol. He was transferred to our ICU (Intensive Care Unit). On presentation he was agitated, disorientated, had musculer rigitidy, hyperreflexia and his pupils were dilated and responsive to light. He was haemodynamically stable with a blood pressure of 137/86 mmHg and a sinus tachycardia of 120 to 140 beats/min. There were no signs of respiratory distress. His axillary temperature was 37.2C. His treatment was started with gastric lavage and activated charcoal. Routine blood analysis was performed. Leucocytosis (18.3 $x10^9$/l) was found and returned to normal within five days. Creatine

kinase was increased to 17948U/l with creatinin kinase-MB at 166 U/l. Treatment was started with hydration and bicarbonate infusion. As it is known,

sodium bicarbonate increases cardiac contractility and prevents ventricular ectopies. Renal function was not affected. Miyoglobine values were increased 3548ng/ml and returned normal within three days. Also LDH was increased to 166 U/l and returned normal within three days too. All other electrolytes, blood urine nitrogen, total protein, creatinin, glucose, hepatic transaminases and coagulation study were within normal range. Nausea, sweating and muscle rigidity and agitation were prominent. Midazolam 1-2mg was administered for his agitations. Three days later he became fully orientated and muscle rigidity was improved. When we detected pathological Q in his initial electrocardiogram (ECG) (six hours after ingestion) we wanted consultaion from Cardiology Department. They also saw pathological Q and incomplet left branch block with prolonged QRS in his ECG. They found no abnormalities in his ecocardiography. Treatment was started with Karvedilol by their suggestion. Twelve hours after ingestion pathological Q were prominent in his ECG. Pathological Q was disappeared forty four hours later after ingestion. Thereafter, we saw his ECG normal at the fourth day of ICU.

DISCUSSION

Venlafaxine is an antidepressant that causes selective inhibition of neuronal reuptake of serotonin and norepinephrine with little effect on other neurotransmitter systems in the liver by cytochrome P450 enzyme system. Because of genetic polymorphisms, the metabolism of venlafaxine varies between patients. The primary route of excretion of venlafaxine and its metabolites is renal elimination, but is not possible to eliminate venlafaxine by haemodialysis. Several cases of seizures indicating neurological toxicity, tachycardia and QRS prolongation indicating cardiac toxicity as well as serotonin syndrome have been reported following a venlafaxine overdose (6, 7).The serotonin syndrome is a potentially life-threatening disorder of excessive serotonergic activity. It presents as a triad of altered mental status, neuromuscular abnormalities and autonomic dysfunction (8). The patient reported in this case had clinical signs and symptoms of an altered mental status, autonomic disorders (tachycardia, pupillary dilatation, dry mouth, tremor and sweating), muscular rigidity. Guided by the Sternbach criteria the diagnosis of the serotonin syndrome was seen in our patient (9). The raised

plasma CK reported in our patient is most likely to have originated from skeletal muscle. Wilson et all determined a relationship between venlafaxine ingestion and acute muscle injury in their study (10). And they also suggested that CK levels might not become elevated until more than 12hr post-ingestion. In our case CK levels increased after 10hr post-ingestion. Therefore, measurement of CK levels immediately after aningestion might underestimate the true prevalence of acute myopathy after venlafaxine overdose.

Venlafaxine poisoning is also associated with high prevalance of cardiovasculer adverse effects. A previous study by Howell et al. on the cardiovasculer toxicity of venlafaxine in overdose concluded that venlafaxine overdose is associated with a prolonged QT in ECG and this may pose an arrhytmogenic risc, despite no cases of malignant arrtythmias occuring in their study (11). In our case pathological Q and incomplet left branch block with prolonged QRS were seen. It was seen that venlafaxine causing cardiac toxicity and death after large overdoses in the literature. There was one report of an ingestion of 30g-venlafaxine overdosage resulted in death (12). There is one report of QRS widening after a dosage of 3g; howewer the patient also ingested thioridazine (13). Other reports all include doses>8g (5), where patients also manifest other features of venlafaxine toxicity, including seizures and serotonin toxicity, and there is a significant risc of death. No seizures were seen in our patient ingested 6g of venlafaxine but pathological Q and incomplet left branch block with prolonged QRS were prominent and his ECG was normal within three days.

Due to the large distribution volume of venlafaxine, forced diuresis, dialysis, haemoperfusion and exchange transfusion are of no benefit. Activated charcoal should be administered to prevent absorbtion and might be useful when administered timely.

Venlafaxine remains a commonly prescribed antidepressant and will continue be taken in overdose.Venlafaxine poisoning is associated with cardiovascular adverse effects. Routine cardiac monitoring and ECG is necessary in venlafaxine overdose of mas-

sive ingestions. And venlafaxine can cause a delayed rise in plasma CKs. Physicians should be aware of this phenomenon.

REFERENCES

1. Holliday SM, Benfield P. Venlafaxine. A review of its pharmacology and therapeutic potential in depression. Drugs 1995;4:280–82.

2. Johnson EM, Whyte E, Mulsant BH, Pollock BG, Weber E, Begley AE, Reynolds CF. Cardiovascular changes associated with venlafaxine in the treatment of late-life depression. Am J Geriatr Psychiatry 2006;14:796–802.

3. Buckley NA, McManus PR. Fatal toxicity of serotoninergic and other antidepressant drugs: analysis of United Kingdom mortality data. BMJ 2002;325:1332–3.

4. Whyte IM, Dawson AH, Buckley NA. Relative toxicity of venlafaxine and selective serotonin reuptake inhibitors in overdose compared to tricyclic antidepressants. QJM 2003;96:369–74.

5. Hojer J, Hulting J, Salmonson H. Fatal cardiotoxicity induced by venlafaxine overdosage. Clin Toxicol (Phila) 2008;46:336–7.

6. Kelly CA, Dhaun N, Laing WJ, et al. Comparative toxicity of citalopram and the newer antidepressants after overdose. J Toxicol Clin Toxico. 2004;42(1):67-71.

7. White CM, Gailey RA, Levin GM, et al. Seizure resulting from a venlafaxine overdose. Ann Pharmacother 1997;31(2):178-80.

8. Boyer EW, Shannon MPH: The Serotonin Syndrome. N Engl J Med 2005;352:1112-20.

9. Sternbach H. The serotonin syndrome. Am J Psychiatry 1991;148:705-13.

10.Wilson AD, Howell C, Waring WS. Venlafaxine ingestions is associated with rhabdomyolosis in-adults.The J of Toxicol Sci 2007;32(1):97-101.

11. Howell C , Wilson AD, Waring WS. Cardiovasculer toxicity due to venlafaxine poisoning in adults: a review of 235 cobsecutive cases. Br J Clin Pharmocol 2007;64:192-7.

12. Mazur JE, doty JD Kyrygiel AS. Pharmocotherapy 2003;23(12):1668-72.

13. Combes A, Peytavin G, Theron D. Conduction disturbances associated with venlafaxine. Ann Intern Med. 2001;134:166–7.