

Fatal Venlafaxine poisoning: Case Report

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Teaching Points

1. Overdosage with venlafaxine can have serious consequences.

2. Careful monitoring and early involvement of critical care teams should be considered if significant toxicity is suspected.

Introduction

Venlafaxine is a selective serotonin and noradrenaline re-uptake inhibitor (SNRI), used in the treatment of depressive illness and anxiety disorder. Overdose may result in cardiac and neurotoxicity, but there are very few case reports of fatal isolated Venlafaxine overdose.¹ The following case highlights the potentially serious consequences of overdose of this drug.

Case History

A 26 year old male presented in the Emergency Department (ED), two hours after ingesting 112 Venlafaxine modified release 150mg tablets (total 16.8g) along with 4 cans of beer. This gentleman had a past medical history of depression and borderline personality and was known to abuse alcohol but had no previous documented overdoses or other forms of deliberate self harm. His only regular prescribed medication was venlafaxine 150mg bd.

Investigation	Day 1	Day 2	Day 3	Day 4
Hb (g/dl)	16.5	13.2	9.6	8.7
WCC (x10 ⁹ /l)	13.9	21.6	19.4	26.2
Platelets (x10 ⁹ /l)	309	185	20	55
Na (mmol/l)	140	142	156	142
K (mmol/l)	4.0	3.9	4.5	5.2
Urea (mmol/l)	3.9	5.5	8.3	8.6
Creatinine (umol/l)	88	197	364	452
CK (U/l)		1543		
ALT (U/l)	59	68	9721	>20000
INR	1.0	1.4	3.6	6.3
APTT (secs)	25	34	65	87
Glucose (mmol/l)	5.5	6.9	2.4	2.2
Total Protein G/l	83	51	42	42

Table 1. Results of Laboratory Investigations During the Patient's Admission.

He was initially apyrexial and alert with GCS 15/15, pulse 130/ min, and blood pressure 212/118. ECG revealed sinus tachycardia. Laboratory investigations were unremarkable (see table 1). Paracetamol and salicylate were not detectable in his blood. He was treated with intravenous fluid, and oral administration of 50g activated charcoal. He was connected to a cardiac monitor and underwent neurological observation every 30 minutes.

Over the next 6 hours the patient became increasingly diaphoretic, tremulous and agitated. He suffered 8 grand mal seizures, of which 7 required termination with intravenous diazepam. Arterial blood gas analysis, taken 4 hours after arrival in the hospital revealed a marked metabolic acidosis (pH of 7.18 KPa, pCO² 4.77 KPa, HCO³ 12.9 mmol/L, base deficit 13.8 mmol/L).

His condition continued to deteriorate with the development of broad complex tachycardia, hypotension, pyrexia (38c) and hypoxaemia (saturation 77-83 % on 100% O₂). The patient was transferred to ITU where he was intubated and mechanically ventilated. Sinus rhythm was restored by synchronised DC cardioversion, following which he received loading doses of intravenous fosphenytoin and amiodarone.

Persistent hypotension and acidosis required administration of adrenaline, noradrenaline and bicarbonate infusions. He also became oliguric, which was refractory to colloid and furosemide challenges resulting in haemofiltration.

On the third day bleeding was noted from the patient's eyes, nose and mouth and crepitations were heard throughout the lung fields. Chest x-ray showed features consistent with acute respiratory distress syndrome. Blood testing showed worsening coagulopathy and thrombocytopenia, suggesting the development of disseminated intravascular coagulation. Renal and liver function had also deteriorated, implying the development of multiple organ failure. Elevation of the creatinine kinase level on day 2 was suggestive of rhabdomyolysis, which may have contributed to his renal impairment.

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Despite continued intensive inotropic support, platelet, bicarbonate and fluid infusions his condition deteriorated further. At 11.15 on the fourth day after his admission he suffered an asystolic cardiac arrest and was subsequently declared dead.

Discussion

There were 3.2 million Venlafaxine prescriptions in the UK in 2003.² Although generally considered to be less dangerous in overdose than older tricyclic antidepressant drugs, this case highlights the potential dangers of massive overdose with SNRIs, including venlafaxine. Fatalities have been described previously^{3,4} although more commonly where taken in combination with other drugs.¹ The fatal dosage is variable with deaths reported following ingestion of as little as 8.4g.⁵ Cardiac and neurological toxicity may be dependent on genetic factors relating to cytochrome p450 phenotype,⁶ which may explain this variation.

The National Poisons Information Service⁷ lists a variety of serious consequences of venlafaxine overdose, including many of those exhibited by our patient in the hours following his presentation to the ED. Tachycardia, hypertension, convulsions and ventricular arrhythmias are recognised complications of overdose. Agitation, fever, sweating and neuromuscular instability are seen as part of the 'serotonin syndrome' (SS) which may accompany overdose with both SNRIs and selective serotonin uptake inhibitors (SSRIs). In severe cases of SS, rhabdomyolysis, coagulopathies and renal dysfunction have also been described.

Treatment options following overdose with venlafaxine are limited. There is no specific antidote, and therapy is therefore supportive. Complications such as convulsions are usually treated with benzodiazepines followed by infusions of phenytoin or fosphenytoin if refractory. Arrhythmias may settle following administration of bicarbonate or may require DC cardioversion. Gastric lavage and activated charcoal administration is usually recommended only if the patient presents within 1 hour of ingestion; unfortunately our patient presented after 2 hours, and although he agreed to take 50g charcoal orally, any benefit would have been limited.

Electrocardiographic abnormalities, including prolongation of the QRS and corrected QT interval (QTc), are well recognised following overdose with venlafaxine. Such abnormalities may lead to the development of ventricular arrhythmias, including Torsades de pointes. Retrospective review of serial ECGs taken during the first 24 hours following our patient's admission showed progressive prolongation of the QRS duration (85ms at admission compared to 101ms after 4 hours). Current texts⁸ favour the administration of sodium bicarbonate when there is evidence of a QRS interval of greater than 100 ms, although there is no definitive evidence base to support this. Our patient did not receive sodium bicarbonate until the following day.

This case illustrates that physicians should be aware that overdoses with modern antidepressants can have very serious consequences. There are some concerns that Venlafaxine is more dangerous in overdose than drugs in the SSRI class.¹ Careful monitoring and early involvement of the critical care team is essential if significant toxicity is suspected.

References:

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