Significant lamotrigine overdose associated with acute pancreatitis

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DECLARATIONS

Competing interests
None declared

Funding
None

Ethical approval
Not applicable

Guarantor
KD

Contributorship
All authors contributed equally

Acknowledgements
None

The case

In March 2007, a 24-year-old woman was admitted via the Emergency Department after an act of deliberate self-harm. Five hours prior to admission she had taken 4200 mg of lamotrigine. She denied taking any other medication at the time of this overdose. Her relevant medical history included two previous episodes of mixed overdoses (July 2002 and May 2006), depression and a psychotic episode for which she was treated with mirtazepine 30 mg once daily, lamotrigine 100 mg twice daily and risperidone 2 mg twice daily. At the time of admission she reported a regular intake of two 750 mL bottles of wine per evening, but had no previous history of alcohol-related liver or pancreatic problems. She had drunk two bottles of wine with her overdose.

On admission, she was tachycardic, lethargic, dehydrated, showed slurred speech, with cerebellar signs of nystagmus and ataxia. She had no evidence of abdominal tenderness.

Arterial blood gas measurements revealed a compensated metabolic acidosis. Full blood count, urea, electrolyte and liver function tests were normal. Her blood alcohol level was 100 mg/100 mL. Paracetamol and salicylate were not detected. A lamotrigine level was not taken because it is not routinely available in our institution. An electrocardiogram showed a sinus tachycardia only.

Within 24 hours of admission she complained of upper abdominal pain and vomiting. Serum amylase was 1043 U/L (0–110 U/L). Liver transaminase, full blood count, calcium, glucose, urea and electrolyte levels were within reference ranges. The patient was diagnosed with acute pancreatitis, and at 48 hours achieved a Ranson score of 1 on assessment of severity, predicting a good prognosis, with less than 1% mortality.[1] General supportive treatment was started with intravenous fluid resuscitation, analgesia and antiemetics.

Abdominal ultrasound two days after onset of symptoms showed a thickened gall bladder wall, with some surrounding fluid and no evidence of gallstones.

Her symptoms as well as amylase levels settled within three days and the patient was discharged five days after the initial overdose. An endoscopic ultrasound of the pancreas was performed six weeks after discharge. This showed a normal gallbladder and common bile duct. The pancreas had no features of chronic pancreatitis and had a normal calibre pancreatic duct.

In the 12 months following discharge she was seen twice in the Emergency Department with symptoms and signs consistent with significant alcohol abuse, however on both occasions her amylase was normal.

Discussion

Lamotrigine is a commonly used agent, licensed in the UK for monotherapy and adjunctive treatment of partial seizures, primary, secondary generalized tonic-clonic seizures and seizures associated with Lennox-Gastaud Syndrome.[2] It is also used for the treatment of trigeminal neuralgia and refractory bipolar disorder.[2] It has recently been advocated as first-line therapy for patients diagnosed with partial onset seizures.[3]

Very few cases of lamotrigine overdose have been reported. However, in agreement with previously published data,[4] our experience of this drug is that it is frequently taken during acts of deliberate self-harm but usually in doses not large enough to cause long-term problems. Only one case of pancreatitis linked with lamotrigine has been reported.[5] That case was associated with therapeutic doses of lamotrigine in association with valproate, a drug well-known to be associated with pancreatitis.[2] We have described a case of significant lamotrigine overdose associated with acute pancreatitis.

Our patient exhibited several of the most common clinical features of significant lamotrigine overdose. These include ataxia, nystagmus and vertigo, hypertonia, coma, convulsions, hypokalaemia, encephalopathy and widening of the QRS interval. Other signs include tachycardia and respiratory depression.[4,6] Furthermore, lamotrigine toxicity has been reported to occasionally lead to multi-organ system abnormalities similar to an anticonvulsant hypersensitivity syndrome.[4] Until recently treatment had been mainly supportive, however Sirianni and colleagues used the knowledge that lamotrigine is highly lipophilic to treat a case of refractory cardiovascular collapse due to lamotrigine and buproprion overdose with a lipid infusion.[7] However, there remains the conundrum that while the lipid infusion itself may precipitate a hypertriglyceridaemia and thus potentiate or precipitate acute pancreatitis, the high lipid levels may protect against the cardiovascular consequences of lamotrigine overdose.

In the present case the history of regular alcohol misuse was a significant risk factor for the development of acute pancreatitis. However, the patient had a constant high alcohol intake in the past. The amount of alcohol taken with the drug did not exceed the usual amount. She had not experienced previous episodes of pancreatitis and became symptomatic only one day after a significant overdose of lamotrigine. In addition, neither ultrasound showed features of chronic pancreatitis. Thus, we suggest that it was the lamotrigine that precipitated the pancreatitis.

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