Life-threatening overdose with lamotrigine, citalopram, and chlorpheniramine

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ABSTRACT

Lamotrigine is a commonly used agent for seizure control in epilepsy. There are limited data on the adverse effects of lamotrigine in overdose. We report a number of serious side-effects associated with a large overdose of lamotrigine. A 23-year-old female presented to the emergency department after taking an intentional overdose of 9.2 g of lamotrigine, 56 mg of chlorpheniramine, and 220 mg of citalopram. On admission, she had a reduced level of consciousness and electrocardiographic abnormalities; a widened QRS and a prolonged corrected QT (QTc) interval. Prompt treatment with early intubation, along with the use of magnesium for cardioprotection and administration of sodium bicarbonate may have aided in a quick recovery with a short intensive care stay and good outcome.

KEY WORDS: Chlorpheniramine, citalopram, electrocardiography, lamotrigine, magnesium, overdose, sodium bicarbonate

Case Report

A 23-year-old female presented to the emergency department after taking an intentional overdose of 9.2 g lamotrigine, 56 mg chlorpheniramine, and 220 mg citalopram while intoxicated with alcohol. This information was provided by her partner. The attending ambulance crew had found her agitated and vomiting.

Initial examination showed her heart rate was 107 min⁻¹, blood pressure 140/73 mm Hg, and respiratory rate was 36 min⁻¹ with oxygen saturations of 97%. Her temperature was 38.5°C. She was agitated with a reduced conscious level (Glasgow coma scale (GCS): 12/15), a coarse tremor and bilateral horizontal nystagmus. The pupils were equal (5 mm) and demonstrated sluggish reactions. Both plantar responses were flexor. Arterial blood gas analysis indicated a partially compensated metabolic acidosis (pH 7.326; BE: -9.6; pCO₂ 3.90). Her admission electrocardiogram (ECG) showed a sinus tachycardia, a widened QRS (> 120 ms), and prolonged QTc interval (> 470 ms) [Figure 1].

She was initially treated with intravenous fluids and 4 mg lorazepam, for agitation. An hour later, her conscious level reduced further (GCS: 8/15). Therefore, she was intubated and ventilated, and transferred to the Intensive Care Unit (ICU). Specialist advice was sought from Toxbase and the National Poisons Information Service (NPIS). They recommended 8 mmol magnesium and a sodium bicarbonate infusion to maintain arterial pH at ~7.4.

The following morning (Day 2), 15 h post-ICU admission, the ECG changes had resolved [Figure 2]. The sodium bicarbonate infusion was discontinued. The sedation was stopped and the patient was extubated. Subsequently, the plasma lamotrigine levels returned to within the treatment range [Figure 3]. She was discharged to the medical ward 24 h after admission to the ICU.

Discussion

Lamotrigine is a first-line antiepileptic; however, there are limited data regarding its effects in overdose.[4] One large retrospective study showed that the majority experienced no toxic effects.[2] Major effects including respiratory depression, coma, and cardiac conduction disturbances occurred in only
0.6-1.2% of patients. We describe a number of life-threatening consequences associated with a large overdose of lamotrigine.

The QTc (Bazzett’s formula) was prolonged on the initial ECG. Lamotrigine exerts its antiepileptic effect through inhibition of voltage-dependant sodium channels. Furthermore, lamotrigine inhibits cardiac rapid delayed rectifier potassium currents. This is a potential mechanism by which it could, in overdose, cause QRS widening and prolonged QTc. The Naranjo probability scale for lamotrigine being the cause is 5 (probable). A prolonged QTc has been reported with citalopram overdose, though it was associated with higher quantities than described here. Chlorpheniramine toxicity is mainly associated with anticholinergic effects and treatment is rarely required if less than 1 mg/kg is ingested. In our case, it is possible that the QTc prolongation was due to the combination of drugs ingested.

A recent case report documented higher levels of ingestion of lamotrigine without any cardiac conduction abnormalities. A key difference in management between the two cases was the timing of intubation. Earlier intubation in our patient may have resulted in fewer complications through more controlled support. The NPIS recommended 5 mmol magnesium and administration of sodium bicarbonate to raise the arterial pH. Lamotrigine is a weak base with a pKa of 5.7. Alkalinization will decrease the ionized proportion of the drug and therefore reduce toxic effects. It is also possible that sodium bicarbonate contributed by delivering a sodium load and correction of acidosis.

The following day, the plasma lamotrigine level was within the therapeutic range. The measured half-life for the elimination was approximately 15 h. The therapeutic elimination half-life of lamotrigine is between 22 and 36 h, but there have been reports of much shorter half-lives in overdose. The measured plasma levels seem disproportionate to the amount of lamotrigine ingested and may be related to emesis.

In conclusion, our case demonstrates that following lamotrigine overdose, early intubation, the use of magnesium for cardioprotection and administration of sodium bicarbonate may aid a quick recovery with short intensive care stay.

References


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