



Case Report

Management of lamotrigine overdose using hemodialysis

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ABSTRACT

Lamotrigine [LTG] is primarily an anti-epileptic drug used to treat seizure disorders, depression, and bipolar disease. It is generally well tolerated with limited side effects reported during routine use. Adverse events after overdose include neurotoxicity in the form of sedation and seizure activity, as well as cardiopulmonary toxicity in the form of sodium-channel blockade and cardiovascular collapse. There is no consensus regarding the role of hemodialysis (HD) in management of lamotrigine toxicity. Based on pharmacological properties, LTG is a candidate for extracorporeal removal, however, the successful use of HD for the treatment of this poisoning is not well described. We report the case of a 44 year-old female after a LTG overdose that experienced prolonged sedation that was ultimately treated with HD with an excellent response.

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1. Introduction

Lamotrigine [LTG] is primarily an anti-epileptic drug used to treat seizure disorders, depression, and bipolar disease. It is generally well tolerated with limited side effects reported during routine use. Adverse events after overdose include neurotoxicity in the form of sedation and seizure activity, as well as cardiopulmonary toxicity in the form of sodium-channel blockade and cardiovascular collapse. There is no consensus regarding the role of hemodialysis (HD) in management of lamotrigine toxicity.

2. Case report

A 44 year-old female with a history of depression and bipolar disorder was brought to the emergency department (ED) after being found unresponsive at home next to empty bottles of LTG. Upon ED presentation, the patient was obtunded with no response to verbal commands. There was no seizure activity or myoclonus. Vital signs were HR of 119 bpm, BP of 151/84 mm Hg, RR of 24 bpm, O₂ saturation of 98% on 2 L supplemental oxygen. The patient underwent endotracheal intubation for airway protection and was admitted to the intensive care unit. CT head was negative for acute intracranial pathology. Her CBC showed a slightly elevated WBC count with a slight left shift. A complete metabolic panel showed elevated serum creatinine of 1.32 mg/dl. The rest of her electrolyte panel was normal. Her serum creatinine kinase (CK) was

elevated at 881 U/L. Her serum LTG level was 41.7 mg/L (ref: 2.5–15 mg/L). Her serum and urine toxicology screen was positive for phencyclidine. Electrocardiogram showed sinus tachycardia with a QRS duration of 90 ms, and QTc of 440 ms. On post-intubation day 2, no purposeful neurological activity was noted and thus an electroencephalogram was performed which demonstrated moderate diffuse slowing without any epileptiform activity. A repeat head CT did not show any intracranial pathology to explain the lack of neurological recovery. This lack of neurological recovery was attributed to the CNS-depressing effects of LTG. A multi-disciplinary meeting was held with Toxicology and Nephrology and the decision was made to initiate HD in an attempt to promote neurologic recovery. The patient underwent one 4-hour session of HD. Shortly after hemodialysis the patient began following simple commands. The patient underwent another 4-hour session of HD the next day after which marked neurological improvement was observed. The patient was subsequently extubated. The patient was noted to be following complex commands and answering questions appropriately. The hemodialysis catheter was removed and the patient was transferred to a regular medical floor. The remainder of her clinical course was unremarkable.

3. Discussion

Lamotrigine, an anti-epileptic agent, is a phenyltriazine derivative which works by inhibiting the high-voltage activated calcium channels and voltage-sensitive sodium channels as well as by reducing neuronal glutamate release [1,2]. It also has an effect on the serotonergic pathway with reuptake inhibition, which accounts for the majority of its use as an anti-depressant [3]. Indications for LTG use include partial, primary generalized tonic-clonic seizures, as well as generalized seizures of Lennox-

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Gestalt syndrome [4]. It is also used in the treatment of bipolar depression as well as the prophylaxis of rapid-cycling bipolar disorder [5].

While most anti-epileptic medications have side-effects, lamotrigine is considered one of the safest in its class. With therapeutic dosing, central nervous system toxicity is rare, but includes anxiety, confusion, headache, insomnia, irritability, confusion and diminished cognitive function [6]. The most common adverse events from LTG use are dermatologic hypersensitivity reactions which can range from a mild rash to Stevens-Johnson syndrome [6].

In the overdose setting, patients have demonstrated ataxia, CNS depression, seizures, and QRS prolongation [7,8]. False-positive urine drug screens for PCP are commonly described.

The recommended treatment of LTG toxicity is typically supportive. Early management involves GI decontamination, if appropriate. Cardiotoxicity due to sodium channel blockade should be treated with sodium bicarbonate in a rationale similar to that of tricyclic antidepressant toxicity [9,10]. Seizures can be treated with benzodiazepines or propofol. Finally, given the lipophilic characteristics of LTG, intravenous lipid emulsion has been suggested as a possible treatment strategy in cases of severe toxicity [9].

There is no consensus regarding the role for extracorporeal removal of LTG. In a study by Fillastre et al., the elimination half life of LTG was reduced from 59 ± 28.1 h to 12.2 ± 6.4 h through the use of dialysis [11]. The LTG extraction factor associated with hemodialysis is reported to be around 17–20% [11,12]. Lu et al. reported a decrease in the serum concentration of lamotrigine from 61.2 mg/L to 7.2 mg/L over a 62 hour period using HD and hemoperfusion [13]. Our patient was found to have serum LTG levels of 41.7 mg/L and much of her clinical course is consistent with previously described LTG overdoses [7,8,14]. After a prolonged ICU course of neurologic inactivity our patient underwent 2 cycles of HD with a rapid positive clinical response that manifested as an improved respiratory rate and wakefulness.

In summary, we present a case of a 44 year-old female with profound CNS depression due to a LTG whose recovery was successfully expedited with HD. While first-line therapy in patients presenting with LTG overdoses is aimed at supportive care, HD may play an important role in reducing intubation time, as well as ICU and overall length-of-stay.

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None.

Declaration of Competing Interest

The authors report no conflict of interest.

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References

- [1] Stefani A, Spadoni F, Siniscalchi A, Bernardi G. Lamotrigine inhibits Ca^{2+} currents in cortical neurons: functional implications. *Eur J Pharmacol* 1996;307:113–6.
- [2] Biton V. Pharmacokinetics, toxicology and safety of lamotrigine in epilepsy. *Expert Opin Drug Metab Toxicol* 2006;2:1009–18.
- [3] Sagud M, Pivac N, Mustapic M, Nedic G, Peles AM, Kramaric M, et al. The effect of lamotrigine on platelet serotonin concentration in patients with bipolar depression. *Psychopharmacology (Berl)* 2008;197:683–5.
- [4] Goldenberg MM. Overview of drugs used for epilepsy and seizures: etiology, diagnosis, and treatment. *P T* 2010;35:392–415.
- [5] Alabi A, Todd A, Husband A, Reilly J. Safety profile of lamotrigine in overdose. *Ther Adv Psychopharmacol* 2016;6:369–81.
- [6] Egunsola O, Choonara I, Sammons HM. Safety of lamotrigine in paediatrics: a systematic review. *BMJ Open* 2015;5:e007711.
- [7] Lofton AL, Klein-Schwartz W. Evaluation of lamotrigine toxicity reported to poison centers. *Ann Pharmacother* 2004;38:1811–5.
- [8] Nogar JN, Minns AB, Savaser DJ, Ly BT. Severe sodium channel blockade and cardiovascular collapse due to a massive lamotrigine overdose. *Clin Toxicol (Phila)* 2011;49:854–7.
- [9] Castanares-Zapatero D, Wittebole X, Huberlant V, Morunglav M, Hantson P. Lipid emulsion as rescue therapy in lamotrigine overdose. *J Emerg Med* 2012;42:48–51.
- [10] Miller J. Managing antidepressant overdoses. *Emerg Med Serv* 2004;33:113–9.
- [11] Fillastre JP, Taburet AM, Fialaire A, Etienne I, Bidault R, Singlas E. Pharmacokinetics of lamotrigine in patients with renal impairment: influence of haemodialysis. *Drugs Exp Clin Res* 1993;19:25–32.
- [12] Lacerda G, Krummel T, Sabourdy C, Ryvlin P, Hirsch E. Optimizing therapy of seizures in patients with renal or hepatic dysfunction. *Neurology* 2006;67:S28–33.
- [13] Lu J, Xiong C, Wang X, Hu J, Chen X. Successful treatment of severe lamotrigine and clonazepam poisoning by blood purification. *Blood Purif* 2012;34:18.
- [14] Moore PW, Donovan JW, Burkhart Haggerty D. A case series of patients with lamotrigine toxicity at one center from 2003–2012. *Clin Toxicol (Phila)* 2013;51(7):545–9. <https://doi.org/10.3109/15563650.2013.818685> Aug.