

## Systematic review of adult and pediatric lamotrigine overdose

Bader Alyahya<sup>1,4</sup>, Marjorie Friesen<sup>2</sup>, Bénédicte Nauche<sup>2</sup>, Martin Laliberté<sup>2,3</sup>

<sup>1</sup>*Clinical Pharmacology and Toxicology Program, McGill University, Montreal, Canada,* <sup>2</sup>*McGill University Health Centre, Montreal, Canada,* <sup>3</sup>*Centre anti-poison du Québec, Quebec city, Canada,* <sup>4</sup>*King Saud University, Riyadh, Saudi Arabia*

### Background

Lamotrigine overdose is often described as benign but cases of cardiac arrest and fatalities are reported.

### Research question

What is the range of lamotrigine toxicity in overdose and can serum concentrations predict poisoning severity?

### Methods

This is a systematic review of acute lamotrigine overdose. Eight databases including Medline, EMBASE, and the Cochrane Library were searched through October 2015. Only overdose cases with at least one lamotrigine serum concentration were included. Cases of chronic toxicity and those describing side effects of therapeutic use were excluded. Two independent reviewers blinded to the authors' and journals' names selected the records based on eligibility criteria.

### Results

We retrieved 5315 records; 39 records (43 cases) met our inclusion criteria. Cases involved primarily adults (72%) and potentially life-threatening features included: seizures (51%), GCS  $\leq 8$  (18%), hypotension (14%) and wide-complex tachycardia (WCT) and cardiac arrest (7%). Of 22 cases of lamotrigine-only exposures (12 adult; 10 pediatric) 2 adult fatalities occurred (4 g and 7.5 g ingested) and in 6/10 pediatric cases seizures occurred (all  $\leq 2$  years, 83% with no underlying seizure disorder, minimum 525 mg ingested). The lowest concentration associated with seizures was 3.8 mg/l (pediatric) and 25.6 mg/l (adult), suggesting children may be more susceptible to CNS toxicity.

Cardiovascular toxicities occurred almost exclusively in adult patients (threshold  $> 25$  mg/l). Interventions included: benzodiazepines (58%), propofol or barbiturates (9%), NaHCO<sub>3</sub> (21%) lipid therapy (14%), and extracorporeal elimination (12%). No response to NaHCO<sub>3</sub> was reported in 4/9 cases with conduction delays; subsequent lipid therapy achieved response in 2 cases.

### Discussion

Lamotrigine is associated with sodium channel blockade. An earlier retrospective review of poison center data for lone lamotrigine overdose suggested relatively benign outcomes; the majority experienced no or minor effects (no deaths). Our review found outcomes consistent with the toxicological profile, namely seizures and cardiac arrest. Our findings are limited by the small number of cases and the inherent publication bias of published case reports.

### Conclusion

Lamotrigine concentrations  $> 25$  mg/l may be predictive of severe toxicity in adults; ingestions as low as 525 mg in those  $\leq 2$  years can produce significant CNS toxicity.

