

## Analysis of safety margin against lamotrigine-induced cardiovascular adverse events in the halothane-anesthetized dogs

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**Introduction:** While lamotrigine is a common antiepileptic drug, it has been reported that overdose of lamotrigine induced the hypotension, cardiac conduction delay, wide complex tachycardia and cardiac arrest. In this study, we tried to bridge the gap between lamotrigine treatment and the onset of these cardiovascular adverse events.

**Methods:** Lamotrigine was intravenously administered in doses of 0.1, 1 and 10 mg/kg/10 min to the halothane-anesthetized dogs under the monitoring of cardiohemodynamic and electrophysiological variables (n=4).

**Results:** The low or middle dose of lamotrigine did not alter any of the variables. The high dose significantly prolonged the PR interval for 45-60 min, QRS width at 10 and 60 min, HV interval at 15 and for 45-60 min, whereas no significant change was detected in the other variables.

**Conclusion:** Lamotrigine may have a wide safety margin against hemodynamic adverse events since the low dose of 0.1 mg/kg in this study would provide clinically-relevant plasma concentrations. Importantly, the atrioventricular nodal and intraventricular conduction delay indicates toxic dose of lamotrigine may inhibit Ca<sup>2+</sup> and Na<sup>+</sup> channels, respectively, which might partly explain clinically-observed cardiovascular adverse events of lamotrigine.