Acute flecainide overdose and cardiovascular toxicity: the potential utility of Intralipid (lipid emulsion therapy).

0 Mukhtar1,2, JRH Archer2, H Chubb3, P James3, DM Wood2,4, PI Dargan2,4

1 Clinical Pharmacology, King's College Hospital NHS Foundation Trust and King's Health Partners, London, UK, 2 Clinical Toxicology, Guy's and St Thomas’ NHS Foundation Trust and King's Health Partners, London, UK, 3 Paediatrics, Guy's and St Thomas’ NHS Foundation Trust and King's Health Partners, London, UK, 4 King's College London, London, UK

Background:

Flecainide is used in the treatment and prevention of tachyarrhythmias. Blockade of the cardiac sodium channel leads to a rate-dependent prolongation of the action potential; it also has negative ionotropic effects. Unsurprisingly, flecainide overdoses can be associated with significant cardiovascular toxicity.

There is increasing interest in the use of Intralipid (lipid emulsion therapy) for the management of cardiovascular toxicity associated with lipid-soluble drugs. With an octanol:water partition coefficient of 14.0, flecainide is highly lipid soluble. We report the use of Intralipid in a patient with flecainide-related cardiovascular toxicity, with data of its impact on flecainide kinetics.

Case report:

A 13 year old girl attended her local Emergency Department 90 minutes after an intentional overdose with 25mg of bisoprolol, 900mg of flecainide and 225mg of aspirin. Her weight was 45kg. On arrival her GCS was 15/15, heart rate was 65bpm and blood pressure was 70/39mmHg. A 12 lead ECG showed sinus rhythm (rate: 70bpm), first degree AV nodal blockade (PR interval: 215milliseconds), right bundle branch block (QRS duration: 164milliseconds) and a QTc of 452milliseconds. Her serum sodium was 137mmol/L, potassium 3.7mmol/L and magnesium 0.83mmol/L; a four hour salicylate level was <50mg/L. The serum pH was 7.55, pCO2 3.72kPa, bicarbonate 24.1mmol/L and BE 3.0 with a respiratory rate of 12bpm. Two 900ml boluses (20ml/kg) of 0.9% sodium chloride solution were given and advice sought from the clinical toxicology service.

As a result glucagon therapy was advised, along with intravenous 8.4% sodium bicarbonate (to maintain a pH of 7.45-7.50) and an infusion of magnesium sulphate (4mmol). Due to flecainide's lipid solubility and the significant cardiovascular compromise observed, a 200ml bolus of 20% Intralipid was also suggested as a subsequent infusion. Despite these interventions, the patient had a VF arrest an hour after presenting to the ED. Following successful cardiopulmonary resuscitation, she was transferred to a tertiary centre, with ionotrope support.

For the next 8 hours, severe cardiovascular instability was observed with the cardiac rhythm frequently alternating between sinus tachycardia with right bundle branch block, Torsades de Pointes, a Brugada-like syndrome, coarse VT and ventricular standstill. Intravenous bicarbonate, Intralipid and ionotropes were continued throughout this period; although a temporary transvenous pacing wire was inserted, cardiac stability returned soon after [serial 12 lead ECGs showed sinus rhythm, QRS duration of <120milliseconds and QTc of <450milliseconds].
Flecanide toxicokinetics:

The initial flecainide concentration, 120 minutes post-overdose, was 1512 microgram/L, increasing to 2699 microgram/L at 9.5 hours post ingestion. At 12, 24, 60 and 140 hours the flecainide concentrations had fallen to 2075 microgram/L, 1680 microgram/L, 895 microgram/L and <100 microgram/L respectively. With an elimination half-life of 32 hours the use of Intralipid did not appear to have significantly altered the toxicokinetic profile of flecainide; previous reports have established the elimination half-life of flecainide to be 28-30 h.

Conclusion:

We describe a life-threatening flecainide overdose with significant cardiovascular toxicity, where Intralipid was utilised. Although Intralipid did not appear to alter the elimination half-life of flecainide, it may have transiently removed free flecainide from the systemic circulation, thus contributing to a successful outcome.