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CASE REPORT

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# Intravenous lipid emulsion therapy for flecainide toxicity

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**ABSTRACT**

Intravenous lipid emulsion (ILE) is an accepted antidote for systemic local anesthetic toxicity and may be useful for other lipophilic drugs with cardiac toxicity. Flecainide is a class IC antiarrhythmic drug related to lidocaine. Flecainide is highly lipophilic with an octanol/water partition coefficient of 3.8 (similar to that of bupivacaine). In overdose, flecainide produces wide complex dysrhythmias and cardiogenic shock. We describe two patients with life-threatening flecainide overdoses which were refractory to standard treatment and which responded rapidly to ILE. Patient 1 was a 49-year-old man who had bradycardia (31 bpm) and hypotension (50 mmHg systolic) after taking 2400 mg of flecainide. His ECG showed a wide complex bradycardia (QRS 178 ms). Bradycardia and hypotension persisted despite atropine, glucagon, CPR, endotracheal intubation, epinephrine, dopamine, magnesium sulfate, and sodium bicarbonate. Patient 2 was a 69-year-old man who ingested 1 g of flecainide, 12 mg of clonazepam, and 1 mg of ropinirole. His ECG showed a rate of 76 bpm with QRS of 268 ms. His blood pressure fell to 66/29 mmHg. Both patients rapidly improved with ILE bolus and infusion. ILE appears useful in severe flecainide toxicity with cardiogenic shock that fails to respond to conventional therapy.

**KEYWORDS**

Flecainide; toxicity; overdose; cardiotoxicity; lipid emulsion; antidote; treatment

## Background

Flecainide is a class IC anti-arrhythmic agent indicated in patients with structural heart disease for the prevention of atrial and ventricular dysrhythmias. The primary mechanism is blockade at the cardiac $N_{av}1.5$ sodium channels and prolongation of phase 0 of the myocardial action potential. After overdose, this can result in a significant widening of the ECG QRS interval. Flecainide has a large volume of distribution (Vd) of 5.5–10 L/kg and an octanol/water partition coefficient (log P) of 3.8. Intravenous lipid emulsion (ILE) has been used successfully to treat toxicity from bupivacaine [1] and other cardiotoxic drugs [2]. We report two cases of lipid emulsion therapy successfully used to treat severe flecainide overdoses.

## Case 1

A 49-year-old man with history of alcohol abuse, hypertension, and atrial fibrillation presented to the emergency department (ED) unresponsive and bradycardic with a heart rate of 31 bpm. Initially, EMS reported potential metoprolol ingestion based on an inconclusive history at the scene. In the ED, he received atropine 0.5 mg IV and glucagon 1 mg IV but deteriorated to asystole. After CPR, intubation, and epinephrine 1 mg IV, he had a return of spontaneous circulation with a HR 45 bpm. Severe hypotension persisted (systolic BP as low as 50 mmHg), and he received dopamine infusion at 10 mcg/kg/min (increased to 25 mcg/kg/min) and magnesium 2 g IV. ECG demonstrated a HR 64, QRS 178 ms, and QTc 367 ms. His wife arrived at the ED with an empty bottle of flecainide with forty-eight 50 mg tablets missing (2.4 g). She denied the use of metropolol. He received an IV bolus of $NaHCO_3$ (150 mEq) followed by $NaHCO_3$ infusion at 37.5 mEq/h. Despite these treatments, he remained hypotensive with a wide QRS interval. At this point, he received 20% lipid emulsion 1.5 mL/kg bolus followed by an infusion at 0.25 mL/kg/h. After treatment began, SBP stabilized at 85–100 mmHg and repeat ECG demonstrated a narrowing of the QRS to 147 ms. After a two hour infusion of ILE was complete, the SBP increased to 124–144 mmHg and HR to 105–120 bpm. Dopamine was weaned, $NaHCO_3$ was discontinued after 12 h while his QRS interval remained $<$100 ms.

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**Prior presentation:** Case 1 was presented as an abstract at the North American Congress of Clinical Toxicology, September 2014. Case 2 was presented as an abstract at the European Association of Poisons Centres and Clinical Toxicologists Annual Congress in May 2016.

## Case 2

A 69-year-old man with history of depression, atrial fibrillation, and restless leg syndrome informed his spouse that he had ingested 1 g of flecainide, 12 mg of clonazepam, and 1 mg of ropinirole. She drove him to the hospital. On arrival, he complained of dyspnea and dry cough, but had no other complaints. Initial vital signs one hour after ingestion were pulse 75/min, respiratory rate 16/min, blood pressure (BP) 119/62 mmHg, and oxygen saturation 98% on room air. Initial electrocardiogram 70 min after ingestion demonstrated a wide complex irregular tracing with heart rate of 76/min, QRS duration 268 ms, and QTc interval 644 ms (Figure 1). At 79 min after ingestion, his BP fell to 66/29 mmHg. He received a bolus of 150 mEq of sodium bicarbonate followed by a continuous infusion, with no improvement in hypotension or shortening of QRS duration. Coughing, rales, and hypoxia developed two hours after ingestion. Chest radiography confirmed pulmonary edema. He underwent rapid sequence intubation and placement of central venous and arterial lines. He received a 135 mL bolus of a 20% lipid emulsion followed by a continuous infusion of 1350 mL over two hours. BP rose to 100/66 mmHg at 2.5 h after ingestion, then to 152/94 mmHg. There were no further hypotensive episodes. The patient was admitted to the cardiac intensive care unit. His hospital course was complicated by atrial fibrillation requiring medication adjustment and pulmonary edema requiring diuresis. He made an uneventful recovery with transfer to the psychiatric service two weeks after admission.

## Case discussion

Flecainide is a potent anti-arrhythmic agent with high mortality in overdose [3,4]. In the two cases reported here, one with cardiac arrest and the other with severe cardiogenic shock, toxicity resolved after treatment with ILE therapy. Sodium bicarbonate has demonstrated efficacy in reversing QRS prolongation and cardiotoxicity following overdoses of tricyclic antidepressant [5] and other sodium channel blockers, but it was ineffective in these two cases.

Based upon its log(P) of 3.8, flecainide should concentrate in the lipid phase at roughly 6300 times the concentration in the aqueous phase. This "lipid sink" effect is a likely explanation for the effect of ILE in these cases, although ILE may also improve cardiac function by supporting metabolic demands of cardiac myocytes.

Two prior case reports described successful reversal of cardiogenic shock after flecainide ingestion after ILE infusion [6,7]. Two additional cases presented as abstracts similarly describe successful use of ILE in two pediatric cases of flecainide poisoning [8,9]. Three other

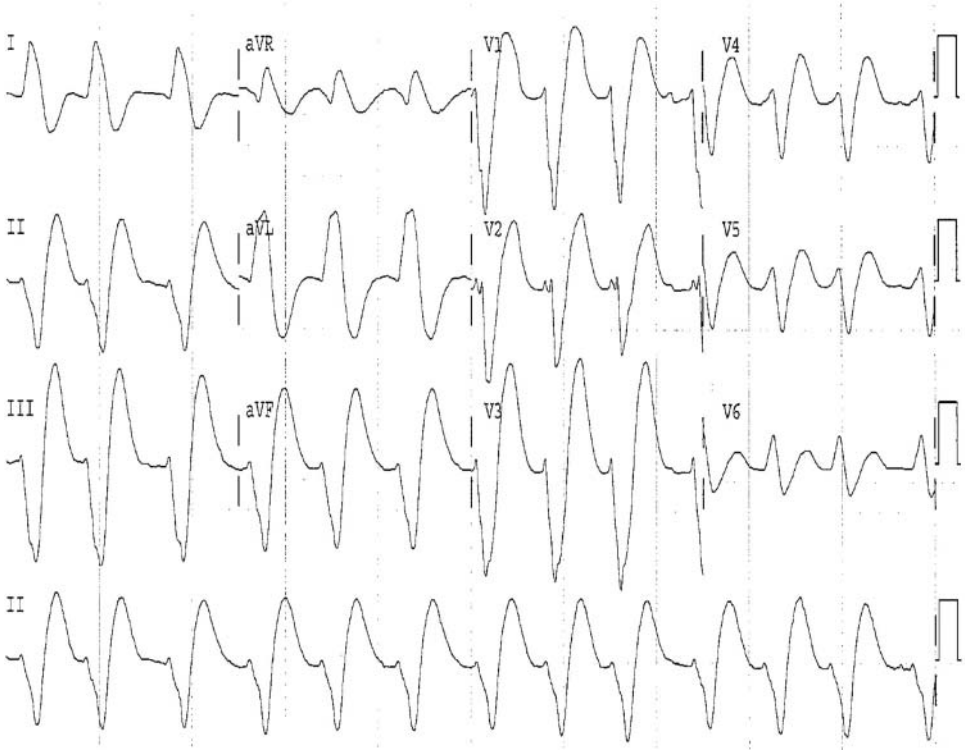


**Figure 1.** Electrocardiogram for patient 2 at approximately 70 minutes after ingestion of approximately 1 g of flecainide. QRS = 268 msec; uncorrected QT = 572 ms; QTcB = 644 ms.

case reports describe survival after a severe flecainide overdoses with shock and cardiac arrest treated with a combination of ILE and extra-corporeal membrane oxygenation [10–12]. Concurrent use of ILE may cause mechanical difficulties with flow through an ECMO apparatus, although none of these three cases indicated this problem. Data from Steinmetz et al illustrate that hemoperfusion is ineffective in removing flecainide from blood [13].

## Conclusion

ILE improved severe flecainide toxicity in two cases that were unresponsive to conventional therapy including sodium bicarbonate, magnesium sulfate, and vasopressors. One of the two cases had asystolic cardiac arrest before receiving ILE. Based on these experiences, we recommend early use of ILE in the treatment of severe toxicity after a flecainide overdose.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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