A case of near-fatal flecainide overdose in a neonate successfully treated with sodium bicarbonate

David H. Jang, Robert S. Hoffman, Lewis S. Nelson

Abstract

Background—Flecainide is a class IC antidysrhythmic primarily indicated for ventricular dysrhythmias and supraventricular tachycardia (SVT). Class IC antidysrhythmic overdoses has a reported mortality of 22% and death results from dysrhythmias and cardiovascular collapse. We report a near-fat al flecainide overdose in an 18-day old treated successfully with sodium bicarbonate.

Case Report—An 18-day old, 2 week premature, 4-kg boy developed persistently high heart rates (220-240 beats/min) and ECG changes consistent with supraventricular tachycardia. There was minimal response to vagal maneuvers, adenosine, and esmolol, and a transthoracic echocardiogram showed no underlying structural abnormality. He was then started on flecainide 4 mg PO Q8h. Following the fourth dose he developed lethargy, cold clammy skin and a heart rate of 40 beats/min with no palpable pulse. Patient was given 0.1 mg of atropine intravenously with an increase to 160 beats/min of the patient's heart rate. The child's cardiac monitor revealed a wide-complex tachycardia with left bundle branch morphology with associated pallor and poor cap refill. Sodium bicarbonate was administered intravenously due to suspected flecainide toxicity. Approximately five minutes after 10 mEq of 8.4% sodium bicarbonate intravenously twice his rhythm converted to a narrow-complex tachycardia. A serum flecainide concentration was 1360 mcg/L (therapeutic, 200-1000 mcg/L) drawn one hour prior to the cardiac arrest. It was later discovered that a 2-fold dosing error occurred: the patient received 8 mg Q8h instead of 4 mg Q8h for four doses.

Conclusion—Flecainide toxicity in children is rare, especially in neonates. It is important for clinicians to be able to identify and treat this uncommon poisoning.
Keywords
Flecainide; sodium bicarbonate; dysrhythmias

Introduction
Flecainide is a class IC antidysrhythmic that is primarily indicated for ventricular dysrhythmias and supraventricular tachycardia. Overdose with class IC antidysrhythmics is reported to have a mortality of up to 22% and death results from sudden cardiovascular collapse due to the prodysrhythmic effects of this class of drugs. [1] There is a paucity of reports of class IC antidysrhythmic overdoses in children, and flecainide toxicity in neonates is even rarer. We report a case of life-threatening flecainide toxicity in an 18-day old neonate being treated for supraventricular tachycardia (SVT) successfully resuscitated with sodium bicarbonate.

Case Report
An 18-day old, 2 week premature, 4-kg boy with a past medical history of supraventricular tachycardia presented to a local emergency department with decreased feeding. Initial vital signs: Blood pressure, 70/50 mmHg; pulse rate, 220 beats/min; respiratory rate, 40 breaths/min; oral temperature, 36.6°C (98°F); room air pulse oximetry, 98%. The general physical examination was normal with warm skin and a 2-second capillary refill. Laboratory studies included a normal complete blood count and a basic metabolic panel. An electrocardiogram (ECG) demonstrated narrow-complex tachycardia at approximately 220 beats/min. Each episode of SVT lasted for 1-2 minutes with frequent recurrence. The patient was admitted for further management of his SVT. During his admission at the outside hospital, the patient received adenosine and esmolol with no success and after two days of unsuccessful treatment, the patient was transferred the pediatric intensive care unit (PICU) at a tertiary care center for further evaluation by the pediatric cardiology service.

At the receiving hospital, the patient underwent a transthoracic echocardiogram that showed no underlying structural abnormality. An order was written for flecainide acetate 4 mg PO every eight hours with rate control following the second dose. However, following the fourth dose of flecainide, the child was found to be lethargic with cold clammy skin and a heart rate of 40 beats/min with no palpable pulse. Patient underwent endotracheal intubation followed by chest compressions. Patient was given 0.1 mg of atropine intravenously with an increase to 160 beats/min of the patient's heart rate. The child's cardiac monitor revealed a wide-complex tachycardia with left bundle branch morphology with associated pallor and poor cap refill. During this time the poison center was contacted and recommended sodium bicarbonate due to suspected sodium channel blockade from flecainide. Patient was given 10 mEq of 8.4% sodium bicarbonate intravenously twice. Within one minute his cardiac rhythm converted to a narrow-complex tachycardia at 170 beats/min with a measurable blood pressure of 90/61 mmHg. An echocardiogram showed normal anatomy with normal function.

Blood was drawn 1 hour after the cardiac arrest and sent to an outside laboratory for a flecainide concentration. The plasma concentration of flecainide later returned at 1360 mcg/L with a therapeutic reference range of 200-1000 mcg/L. It was later discovered that a 2-fold dosing error occurred: the patient received 8 mg every 8 hours instead of 4 mg at the same interval. The flecainide acetate was compounded at the hospital pharmacy with a concentration of 10 mg/mL. Analysis of the flecainide showed the correct concentration. The error was thought to be due to improper labeling of the patient's medication.
The patient was further managed with mechanical ventilation in the PICU. The patient's skin was warm and showed good perfusion and he was responsive to noxious stimuli. He maintained a heart rate of 140-150 beats/min. The patient showed neurologic improvement and was started on oral timolol with no evidence of SVT. Patient was eventually discharged in good health.

Discussion

While there are case reports that describe flecainide toxicity in children, pure flecainide overdoses are rarely reported in neonates. A case report described a 2 year-old boy on nadolol and flecainide for persistent junctional tachycardia received a 5-fold dosing error of flecainide due to a medication error. The patient became bradycardic followed by a wide-complex tachycardia that responded to intravenous sodium bicarbonate. [2]

Another report describes a premature neonate who received the appropriate dose of flecainide for supraventricular tachycardia at 24-hours of life and then a day later, developed a wide-complex tachycardia followed by ventricular fibrillation. The baby went into shock requiring prolonged resuscitation. Return of spontaneous circulation occurred after 2 hours of resuscitation. Unfortunately the patient was neurologically devastated and life-support was withdrawn. However, the reported flecainide concentration was within the therapeutic range which demonstrates the narrow therapeutic index of flecainide [3]

Flecainide overdoses are associated with a high mortality. This is not surprising given the combination of negative inotropy, prodysrhythmic affect, and potent ability to slow cardiac conduction. [4] Other features that make flecainide toxicity difficult to treat are the lack of effective antidotes and its high volume of distribution which renders hemodialysis relatively ineffective.

Pharmacologic interventions such as amiodarone and lidocaine have been used with success. [5] Sodium bicarbonate has been advocated as the treatment of choice for flecainide toxicity. The use of sodium bicarbonate therapy in the setting of class IA toxicity and drugs with similar mechanisms of toxicity such as tricyclic antidepressants have a sound pharmacologic basis along with animal evidence and controlled studies showing its efficacy. [6] Theoretically, the treatment for class IA toxicity with sodium bicarbonate could also be applied to toxicity from class IC agents such as flecainide. The combination of sodium loading and alkalinization is thought to reverse the sodium channel blockade and narrow the QRS interval. Review of experimental evidence as well as case reports on bicarbonate therapy in the setting of flecainide toxicity shows mixed results.

Salerno et al. used a canine model of ventricular dysrhythmia induced by flecainide. Flecainide was infused at 1.0 mg/kg/min load (0.5 mg/kg/min maintenance) stepwise until the QRS was widened 50%, 75%, and 100% with the endpoint of ventricular arrhythmia. Dogs that developed spontaneous arrhythmia received either three doses of either sodium bicarbonate (3 mEq/kg/dose, with 1 minute between doses) or normal saline. All 7 dogs treated with sodium bicarbonate had increased survival, compared with only 1 of 7 dogs treated with saline. [7] A case reported by Devin et al. demonstrates the efficacy of sodium bicarbonate in a massive flecainide overdose. The patient reportedly ingested 4500 mg of flecainide and soon after had a cardiac arrest with bradycardia. The patient was intubated and ACLS was initiated. The patient received a total of 450 mEq of sodium bicarbonate over three hours during her resuscitation which resulted in an increase in her heart rate, narrowing of her widened QRS complex, and improvement in her hemodynamics. A serum flecainide concentration of 3600 mcg/L (therapeutic range 200–1000 mcg/L) was reported from blood taken approximately 2.5 h post ingestion. [8]
There are several reported cases that use invasive treatment modalities for flecainide toxicity. [9-11] The few reported cases that use extracorporeal membrane oxygenation (ECMO) have had success, but is considered invasive with complications and is not readily available. [12] A limitation to these cases is while ECMO was successful in these case reports, sodium bicarbonate use was relatively small (<100 mEq) when compared to reports of successful use with sodium bicarbonate. These case reports typically used sodium bicarbonate in much greater amounts (usually >300 mEq) without resorting to invasive treatment modalities.

**Conclusion**

Although overdoses with class IC such as flecainide are relatively rare, not surprisingly mortality is high. Flecainide toxicity in children, in particular in neonates, is exceedingly uncommon. Management of flecainide toxicity in this setting is unexplored. Based on limited case reports as well as experimental evidence, the use of sodium bicarbonate should be the cornerstone of treatment along with maximal supportive care. Aggressive supportive care should be continued to support the cardiovascular and neurologic system until the drug effect dissipates.

**Acknowledgments**

Supported in part by grant 1UL1RR029893 from the National Center for Research Resources, National Institutes of Health.

**References**