Clinical Management of Severe Propafenone Intoxication

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We present a case of cardiopulmonary arrest after propafenone intoxication in a patient with normal cardiovascular function. She was admitted to the critical care unit within 40 min after 9000 mg propafenone consumption. Main findings were cardiac arrest, instable hemodynamics, and atrioventricular junction block. For its management, transient pacing was performed with catecholamine infusion. We achieved a good outcome in this case because of rapid resuscitation and aggressive treatment with monitoring and supportive care, including mechanical ventilation.

Keywords: Propafenone, suicide, cardiac arrest, transient pacing

INTRODUCTION

Intoxication with drugs ingested while attempting suicides is frequently treated in critical care units. Propafenone was first synthesized in the year 1970, and 5-OH-propafenone is its active metabolite. Propafenone is a class IC antiarrhythmic drug according to the Vaughan Williams classification and is used in the treatment of supraventricular and ventricular tachyarrhythmias (1). Propafenone has been widely used in Europe since 1977 for the management of supraventricular and ventricular arrhythmias. After the approval by the Food and Drug Administration, the use of propafenone was started in the United States in 1989. Propafenone usage has been restricted since 1990 because of life-threatening ventricular arrhythmias that increased mortality (2). Class IC antiarrhythmic drugs cause QRS prolongation without QT prolongation. Overdose of sodium-channel blockers causes hypotension, prolonged QRS duration, ventricular arrhythmias, depressed mental status, and seizures (3). In microelectrode studies of isolated cardiac tissue, propafenone decreases the maximum rate of depolarization of phase 0 of the action potential, without changing the resting membrane potential, in both atrial and ventricular muscle fibers. These studies also showed that propafenone reduces the amplitude of delayed depolarizations induced by ouabain in Purkinje fibers and ventricular muscle. As a result, propafenone shortens the effective refractory period, exerts a ß-adrenoceptor blocking action, and has a calcium antagonistic activity (4). Propafenone overdose is not a common situation, and a few cases of lethal self-poisoning have been reported in the literature (2). We present a case of cardiopulmonary arrest after propafenone intoxication in a patient with normal cardiovascular function.

CASE REPORT

An 18-year-old female, a student at a high school, ingested about 30 tablets of propafenone (Rytmonorm-300; total: 9000 mg) and two tablets of captopril (Kapril 25 mg; total: 50 mg) with an intent of committing suicide. She referred to a rural medical center on her own and told that she ingested some medicines. Before she was admitted to a ward for mechanical and pharmacological detoxification, a written informed consent was obtained from her parents. On examination, she was conscious, oriented, and stable with regard to hemodynamic parameters. She vomited with gastric decompression and became unconscious after a few minutes. She was intubated and referred to our intensive care unit for advanced therapy within 40 min.

On arrival in the critical care unit, her heart rate was 80 bpm and blood pressure was 50/30 mmHg. An electrocardiogram (ECG) was taken and the prolongation of QRS and QT internal (QTc) was determined (Figure 1). Since the case was accepted as a complete atrioventricular block, she was immediately prepared for temporary pacing (70 bpm), but a sudden circulatory arrest occurred before pacing. Within minutes, a successful resuscitation was performed with pacing via right femoral venous cannulation. The electrical function of the heart was restored; however, she was still unstable in terms of hemodynamic parameters. For the medical treatment of hypotension, norepinephrine and dobutamine were administered at infusion rates of 15 µg·kg⁻¹·min⁻¹ and 5 µg·kg⁻¹·min⁻¹, respectively. In addition, intravenous fluids were administered with central venous pressure guidance. Laboratory
On the second day after intoxication, inotropic support and sedation were gradually decreased, and the patient was evaluated with respect to neurological and hemodynamic features. When p waves and normal sinus rhythm reappeared in ECG, the pacing support was weaned. Over the next 6 h, she was also weaned from mechanical ventilation and 2.1 min⁻¹ oxygen support was given via an oxygen mask. Forty-eight hours after extubation, she had a seizure in response to 15 mg/kg⁻¹ of phenytoin.

We achieved a good outcome in this case because of rapid resuscitation and aggressive treatment with monitoring and supportive care, including mechanical ventilation.

**DISCUSSION**

Propafenone is a class 1C antiarrhythmic agent, and 150 or 300 mg tablets are available in markets. The recommended therapeutic dose for an adult is 450–600 mg per day (2). Trials regarding the pharmacokinetic properties of the drug demonstrated that after an oral dose, propafenone is absorbed rapidly and approximately up to 100%. After 2–3 h of ingestion, peak serum concentration occurs. In a previously reported study, Köppel at al. (5) showed the onset of cardiovascular symptoms after 30–120 min and a first-pass effect by a saturable enzyme, with bioavailability varying from 4.8% to 23.5% depending on the preparation (6). Because propafenone has a polymorphic metabolism, it is thought to be toxic. In some clinical studies, poor metabolizers demonstrate significantly higher β-blockade during therapeutic use, but this difference becomes less significant at higher doses (2). ECG anomalies, particularly prolongation of the PR interval may be caused by propafenone. Other ECG changes are bundle branch block, wide QRS and QT intervals, ventricular tachycardia, and bradycardia (6, 7). Propafenone overdose can cause seizure, and this sign is very important for clinical diagnosis. This is unclear and may be related to a toxic effect or secondary to cerebral hypoperfusion caused by arrhythmia and conduction disturbance (2). Review of the literature revealed 55 cases of propafenone intoxication with ingested doses from 1800 to 9000 mg (1, 2, 5, 8-22). The main clinical warning signs are cardiac insufficiency, conduction disturbance, and seizures. In the review of the literature, the number of deaths reported was 11, which appears to be very low considering the extensive use of propafenone. Poor metabolizers are much more susceptible to therapeutic and toxic effects of the drug. The half-time of the parent compound ranges from 2 to 12 h, with a mean of 6 h and from 10 to 12 h in case of poor metabolizers (24). An overdose of propafenone causes the following: hypotonia, sleepiness, convulsions, PQ interval prolongation, conduction disorder, life-threatening dysrhythmia, ventricular tachycardia, ventricular flutter, fibrillation, and cardiac arrest. Cardiovascular disorders in acute overdosing of propafenone are one of the major causes for morbidity and fatality (25). The progression of the condition was remarkable, and the patient survived with rapid resuscitation, mechanical ventilation, transient pacing, treatment of acidosis, and intravenous catecholamine administration. There is no efficient method for eliminating propafenone in the case of its overdosed apart from quickly performing lavage of the stomach (26). Temporary pacing may prove inefficient in the case of severe electrical and mechanical heart depression. Relatively infrequent complications are hematological reactions and those of neurological (convulsions, amnesia, peripheral neuropathy), gastrointestinal, and hepatic disorders (27).

Major clinical findings in our case were hypotension, coma, acidosis, bradycardia, and ventricular arrhythmias. Treatment with early resuscitation, transient cardiac pacing, gastric lavage, mechanical ventilation, and administration of alkalinizing solutions were the reason for a good outcome. The use of sodium bicarbonate has also been reported in the management of adverse cardiac effects associated with propafenone treatment.

**CONCLUSION**

We achieved a good outcome in this case because of rapid resuscitation and aggressive treatment with monitoring and supportive care, including mechanical ventilation.
REFERENCES


