

Full recovery after prolonged resuscitation from cardiac arrest due to propafenone intoxication

A case report

Bingyu Ling, MM^a, Ping Geng, MD^a, Dingyu Tan, MD^{a,*}, Joseph Walline, MD^b

Abstract

Rationale: The prognosis of cardiac arrest (CA) induced by propafenone intoxication was thought to be very poor. The maximal duration of cardiopulmonary resuscitation (CPR) for propafenone induced CA is unknown.

Patient concerns: We describe a case that was successfully resuscitated after prolonged CPR (totaling 340 minutes during one hospital visit) for propafenone intoxication without subsequent neurological sequela.

Diagnoses: A previously healthy 36-year-old female who developed multiple and prolonged CAs after consuming 98 tablets of 50mg propafenone. The CPR duration of this case, to the best of our knowledge, is the longest of all existing propafenone-induced CPR events to still have full recovery. We also analyse the contributing factors to this successful CPR.

Interventions: Sodium bicarbonate, inotropic drugs and pacemaker application did not prevent the occurrence of CA. A full recovery was eventually achieved after prolonged CPR with a mechanical CPR device, blood purification and other aggressive supportive treatments.

Outcomes: Full recovery without neurological sequela.

Lessons: Prolonged CPR including the application of mechanical CPR devices should be considered in propafenone-related CA, especially in young patients without significant comorbidities and delayed resuscitation.

Abbreviations: BP = blood pressure, CA = cardiac arrest, CPR = cardiopulmonary resuscitation, CVWH = continuous veno-venous hemofiltration, ECG = electrocardiogram, HR = heart rate, ROSC = restoration of spontaneous circulation.

Keywords: cardiopulmonary resuscitation, hemodialysis, hemoperfusion, propafenone

1. Introduction

Propafenone is a class 1C anti-dysrhythmic agent that blocks sodium channel, calcium channel, and beta-adrenergic receptors. Propafenone intoxication can lead to severe myocardial depression, ventricular arrhythmias, and refractory seizures is a rare yet life-threatening situation.^[1] Cardiac arrest (CA) induced by propafenone overdose has been occasionally, reported in recent years. Like CA of other causes, the maximal duration of cardiopulmonary resuscitation (CPR) for propafenone induced CA is unknown. However, drug overdose may be one of the

etiologies of CA that deserves prolonged resuscitation.^[2] In this paper, we present a case that was successfully resuscitated after prolonged CPR for CA induced by propafenone intoxication without subsequent neurological sequela.

2. Case presentation

A previously healthy 36 year-old woman presented with impaired consciousness and sporadic, bilateral limb tremors to our emergency department. Her family stated that the patient had consumed 98 tablets of 50mg propafenone 1 hour prior to arrival, and they had tried to induce vomiting without success. On arrival to our hospital, she had a Glasgow Coma Scale of 7/15, and her blood pressure (BP) was 53/31mmHg with an irregular heart rate (HR) of 50 bpm. Her electrocardiogram (ECG) showed a ventricular escape rhythm, and an intraventricular conduction delay. She was intubated and ventilated. The patient's HR continued to slow despite intravenous sodium bicarbonate, atropine, dopamine, and adrenaline. A temporary pacemaker was then inserted and gastric lavage was performed. However, the patient showed no significant response to these treatments. CA developed 22 minutes after her admission, and CPR was started. Restoration of spontaneous circulation (ROSC) was achieved after 11 minutes of CPR with a HR of 48 bpm (ventricular escape rhythm on monitor) and a BP of 91/32 mmHg. Activated charcoal was administered via nasogastric tube, and hemoperfusion combined with continuous veno-venous hemofiltration (CVWH) were also initiated. However, the patient remained extremely unstable over the next 4 hours,

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^a Department of Emergency Medicine, Northern Jiangsu People's Hospital, Yangzhou China, ^b Division of Emergency Medicine, Department of Surgery, Saint Louis University Hospital, Saint Louis, Missouri, USA.

* Correspondence: Dingyu Tan, Department of Emergency Medicine, Northern Jiangsu People's Hospital, No.98, Nantong West Road, Guangling District, Yangzhou City, Jiangsu Province, China (e-mail: webtan1981@gmail.com).

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even though supported with high-dose vasoactive drugs, and CPR was repeatedly performed due to repeated asystole. 4.5 hours after her admission, the patient demonstrated persistent asystole, and mechanical CPR was performed with a Thumper device (Michigan Instruments, Grand Rapids, Michigan, USA; Device 1007 CVV), accompanied by CVVH, intravenous hydration, and inotropic agents.

After an additional 155 minutes of persistent mechanical CPR, an autonomous ventricular rhythm was recovered with a HR of 51 bpm, and a BP of 91/75 mmHg. The patient was no longer in CA, although her hemodynamics were still unstable. The total duration of CPR was 340 recorded minutes. The patient was transferred to the emergency department's Intensive Care Unit (ICU) for ongoing care. She experienced several episodes of generalized seizures after ROSC. Laboratory tests revealed hypoglycemia (2.2 mmol/L), metabolic acidosis (PH 7.32, HCO_3^- 15.9 mmol/L, BE -10 mmol/L), lactic acidosis (3.78 mmol/L), and liver function impairment (lactate dehydrogenase [LDH] 1711 U/L, aspartate aminotransferase [AST] 225 U/L, alanine aminotransferase [ALT] 153 U/L). Otherwise, the patient's urea, creatinine and electrolytes were in the normal range. ECG showed a wide-complex bradycardia with a QT interval of 640 ms, ST-segment elevation, and T wave inversions in V1-V3. Support therapies included the induction of a mild hypothermia were implemented. The plasma propafenone concentration of the patient at 10 hours post-poisoning (and 2 hours post-ROSC) was 2.13 mg/L (normal therapeutic range is 0.1–1.0 mg/L).

A weak corneal reflex, and pupillary light reflex (PLR) were detectable 1 hour after ROSC. Another 3 sessions of hemoperfusion were performed, and the patient's circulation gradually stabilized although her creatine kinase, and creatine kinase-MB levels began to elevate. Spontaneous respiration, and normal sinus rhythm recovered 7 hours post-ROSC. The patient regained full consciousness 15 hours post-ROSC, and CVVH and hypothermia were discontinued. Over the next 48 hours, inotropic support was gradually weaned, and she was extubated on day 4. A total of 37 mg, and 19.5 mg epinephrine were used before, and after sinus rhythm was recovered, respectively, while the amount of isoprenaline (isoproterenol) used was 2 mg, and 11 mg, respectively. Propafenone was undetectable approximately 32 hours post-poisoning in our patient. She was discharged on day 8, with a normal ECG, normal liver function tests, and full neurological recovery.

3. Discussion

The patient gave her permission to publish this case, and written informed consent has been obtained. Hypotension, bradycardia, widened QRS, and even CA can be observed after severe propafenone overdoses. It has been reported recently, that sodium bicarbonate, glucagon, insulin+dextrose, calcium, intravenous lipid emulsion, and/or temporary cardiac pacing are helpful to reverse the cardiac effects induced by propafenone overdose.^[3–8] However, all these potential remedies were from case reports, and there was not enough evidence to clearly demonstrate the efficacy of these treatments in propafenone intoxication. Sodium bicarbonate and a pacemaker were tried in our case without significant effect. We think the successful rescue of this patient was mainly, due to timely and aggressive supportive therapies. Cardiac toxicity is the main cause of death caused by propafenone.^[9] Significant negative inotropic and negative dromotropic activity is common in propafenone

overdose, while large doses of positive inotropic drugs, and catecholamines such as epinephrine, and isoproterenol are obligatory, and inevitable, as in our case.

Both reducing absorption, and promoting excretion are important treatment principles of drug overdoses. In this case, we administered early gastric lavage, and activated charcoal, which were also recommended to reduce propafenone absorption in other reports.^[5] Hemoperfusion or hemodialysis are some of the key ways to promote toxicant excretion extracorporeally, especially, in lethal poisonings without an antidote.^[10] Literature discussing hemoperfusion or hemodialysis in propafenone poisoning are rare, but they were performed in a couple of early case reports.^[11,12] Hemodialysis is typically, suitable for small molecular weight toxicants which are water-soluble,^[13] but propafenone is hard for hemodialysis to remove because it is a lipophilic drug with a high serum protein binding rate of more than 90% (as seen in a recent case report).^[3] Hemoperfusion decreases the concentration of toxicants in the blood through absorption, and it is especially, preferred for lipophilic compounds with a limited volume of distribution (generally less than 1L/kg).^[14] We performed hemoperfusion early in our patient's course (within 3 hours of presentation), though propafenone's volume of distribution is relatively, high at 1.9 to 3L/kg, because much of the poison is probably, intravascular rather than extravascular at this early stage.^[15]

The role of hemoperfusion in the treatment of the poisoned patient is thought to be limited in industrialized countries, as newer, and more efficient dialysis modalities are more preferred.^[13] However, for hemodynamically unstable patients, as in our case, hemodialysis is relatively, contraindicated, while CVVH can be safely, performed to continuously, remove toxins that are unbound to proteins, and extravascular tissues. Based on the above theory, the combined use of hemoperfusion and CVVH seemed logical in our case. Additionally, CVVH was performed with the aim of correcting the patient's refractory acidosis, and facilitate targeted temperature management, and fluid balance.

The most shocking aspect of this case report is undoubtedly the total CPR duration of approximately, 340 minutes. To the best of our knowledge, the CPR duration of our case is the longest amongst all existing propafenone toxicity case reports, while still successfully, resulting in a full recovery for the patient. The maximal duration of CPR for CA of all etiologies including poisoning is unknown, and traditionally, efforts are usually, terminated after 15 to 30 minutes. For patients with CA due to propafenone overdoses, the prognosis was thought to be very poor in most early case reports, and the survival rate was reported as very low.^[12] However, multiple cases of successful resuscitation with neurologically, intact survival have been reported more recently, and the CPR duration of several cases was more than 20 minutes.^[3,6,7,9,16]

Prolonged CA is usually associated with high mortality rates, and the survival usually, has neurologic sequelae. However, for patients who are young without significant comorbidities, whose CA etiologies are reversible, and in whom CPR is started immediately, prolonged CPR may be associated with a favorable outcome.^[2] Drug overdose is one of the CA etiologies which is treatable and reversible. Our experience described here as well as others suggest that prolonged CPR should be considered in the treatment of propafenone-related CA.

Persistent high-quality CPR played a vital role in our patient's survival, and helped protect her brain from irreversible ischemic damage. However, maintaining effective manual chest compressions during an unusually, prolonged period of

CPR is full of challenges. Mechanical chest compression devices may be a valid alternative to manual chest compressions during prolonged CA, though their efficacy has been subject to debate under normal circumstances.^[17] In prolonged CA related to propafenone, mechanical CPR can serve as a last-resort “bridge” to allow time for the cardiac effects of the toxin to decrease until ROSC.

In conclusion, our case report suggests that in a patient with propafenone related CA, comprehensive, and aggressive supportive therapies are the cornerstone of treatment. CPR duration should be established on a case-by-case basis, and prolonged CPR should be considered in patients under specific conditions. Blood purification techniques such as hemoperfusion may deserve to be performed in these “nothing to lose” cases.

Author contributions

Conceptualization: Bingyu Ling, Dingyu TAN.

Investigation: Bingyu Ling, Ping Geng, Dingyu TAN.

Methodology: Joseph Walline.

Writing – original draft: Bingyu Ling, Ping Geng, Dingyu TAN.

Writing – review & editing: Dingyu TAN, Joseph Walline.

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