

CARDIAC ARREST DUE TO A LETHAL DOSE OF PROPAFENONE AND FIRST CASE TO SURVIVE FOLLOWING TREATMENT WITH INTRAVENOUS FAT EMULSION

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ABSTRACT

Propafenone poisoning is a rare and life-threatening condition with no specific treatment procedure or antidote. The survival rate is low in patients who require cardiovascular resuscitation due to cardiac arrest. This case report described a young female patient who was unresponsive following intake of high-dose oral propafenone in a suicide attempt. The patient developed cardiac arrest

and was administered intravenous fat emulsion (IFE) after failure to respond to standard supportive treatment. Although IFE has been used in two previous cases of high-dose propafenone intake, ours was the first to present with cardiac arrest and to survive and recover without deficit after IFE treatment.

Keywords: Propafenone, intoxication, intravenous fat emulsion. *Nobel Med 2015; 11(3): 89-92*

LETAL DOZ PROPOFENON ALIMINA BAĞLI KARDİYAK ARREST VE İNTRAVENÖZ YAĞ EMÜLSİYON TEDAVİSİYLE YAŞATILAN İLK VAKA

ÖZET

Propafenon zehirlenmesi çok nadir görülen yaşamı tehdit eden bir durumdur. Tedavi için kullanılan spesifik bir prosedür ya da antidot yoktur. Kardiyak arrest nedeniyle kardiyovasküler resüsitasyon gereken hastaların sağ kalım oranı düşüktür. Suisidal amaçlı yüksek

doz oral propafenon alımı sonrası tüm destek tedaviye rağmen yanıt alınamayan ve kardiyak arrest gelişen, intravenous fat emulsion (IFE) tedavisi sonrası taburcu edilen genç bayan hastayı bildiriyoruz. Literatürde IFE tedavisi iki propofenon vakasında daha kullanılmıştır fakat propofenon aşırı alımına bağlı arrest olan ve IFE tedavisi uygulanıp yaşatılabilen ve taburcu edilebilen ilk vaka bizim hastamızdır.

Anahtar kelimeler: Propafenon, intoksikasyon, intravenöz yağ emülsiyon. *Nobel Med 2015; 11(3): 89-92*

INTRODUCTION

Propafenone poisoning is a very rare and life-threatening condition with no specific procedure or antidote available for treatment. The survival rate is low if patients require cardiopulmonary resuscitation (CPR) due to cardiac arrest.¹

Treatment with intravenous fat emulsion (IFE) has been used for cardiac arrests due to local anaesthetic poisoning.² More recently, IFE has been used for lipophilic drug overdoses in animal models as well as for beta-blockers, calcium channel blockers, parasiticides, herbicides, and several varieties of psychotropic agents.³

The present report is the first published case of a patient with propafenone poisoning who fully recovered following IFE treatment after failing to respond to all other supportive treatment, including CPR.

CASE

A female patient 35 years of age without any known disease or drug usage was brought to the emergency room by ambulance after taking 30 tablets of propafenone (150 mg). The patient was non-cooperative and non-oriented with a Glasgow Coma Score (GCS) of 7 (E2M4V1), and her blood pressure was undetectable. QRS duration was 160 ms (electrocardiogram [ECG] 1, Figure 1) with a nodal rhythm rate of 59 beats/minute (min) on her ECG. The patient was administered intravenously 0.5 mg atropine, 1000 cc intravenous (IV) saline solution, and 1 mEq/kg of NaHCO₃ in that order, due to her nodal rhythm bradycardia, altered mental status, and hypotension. Dopamine infusion (20 µg/kg/min) was initiated because the hypotension did not respond to the above treatment. The patient had a tonic-clonic seizure and was administered 5 mg IV diazepam and intubated due to her decreased GCS and development of shock. After dopamine was ineffective to recover blood pressure, noradrenaline was initiated at a dose of 1 µg/kg/min. Measurement of arterial blood gas revealed metabolic acidosis and increased blood lactate. The patient developed pulseless electrical activity and cardiac arrest after 50 min of emergency room care. CPR was administered for 2 min, and pulse was restored. A 1-mEq/kg dose of NaHCO₃ was administered twice. Her control ECG revealed atrial fibrillation (ECG 2) with a wide QRS (160 ms) and a rate of 90 beats/min. (Figure 2) A temporary intravenous pacemaker was attached to the patient due to her continuous wide QRS complex rhythm and hemodynamic instability. The patient was unconscious and intubated, and her vital functions did not improve despite all the above supportive treatment. At 55 min after admission, 100 mL IV bolus of V lipid

(Nutriflex) was administered, followed by continuous infusion at 0.25 mL/kg/min for 1 hour. Blood pressure (114/78 mmHg), pulse (76 beats/min), oxygen saturation (91%) and improved GCS (E1M1VE) were detected minutes after the IFE bolus, and the inotrope doses were reduced. The patient's acidosis and hypoxia improved after the IFE treatment, and the blood lactate was reduced (3 mmol/L). The patient had a total of three tonic-clonic seizures in the emergency room and was administered two doses of intravenous diazepam (5 mg). Complete blood count and biochemical tests were normal. The patient was admitted to the coronary intensive care unit with a blood pressure of 108/88 mmHg, pulse 76 beats/min, oxygen saturation 92%, and GCS E1M1VE. The patient was discharged 6 days after admission to the emergency room with normal function and no long-term consequences.

DISCUSSION

Propafenone overdose may lead to hypotension; prolongation of PR, QRS, and QT intervals; ventricular tachyarrhythmia; bradycardia; seizure; and sudden death.¹ IFE treatment has been used to treat a variety of poisonings for nearly 10 years.²⁻⁸ In 1998, Weinberg presented the "lipid sink" theory, which is the most widely accepted mechanism of action for IFE treatment.⁴ IFE forms a lipid phase, and the toxic drug passes from the tissue to the aqueous plasma phase to the lipid phase. Drug diffusion into the lipid compartment creates a concentration gradient that removes drug from the tissues into the plasma. Theoretically, this reduction in drug concentration in the tissue reduces the toxicity of the drug.⁵ Supporting this hypothesis, IFE also reverses neurologic signs and symptoms, such as seizures and altered mental status, related to lipophilic drug intoxications, indicating the efficacy is not limited to cardiovascular system.⁶

The potential mechanism involves augmenting cardiac energy supplies. Fatty acids are the primary substrate for myocardial ATP production in the nonstressed, resting heart. Although study results vary on the importance of fatty acid substrate during times of cardiac stress, some investigations indicate that augmented fatty acid supply improves cardiac performance in the ischemic, hypodynamic heart.^{9,10} IFE may restore myocyte function by increasing intracellular calcium. In isolated cardiac tissue, free fatty acids directly activate the voltage-gated calcium channel similar to known calcium channel openers.⁵

Recommended protocol is 1.5 mL/kg, or 100 mL 20% lipid bolus, with subsequent 0.25 to 0.5 mL kg⁻¹ min⁻¹ infusion.¹¹ There is not a consensus about the infusion dose and time. The American College



Figure 1. Electrocardiogram 1

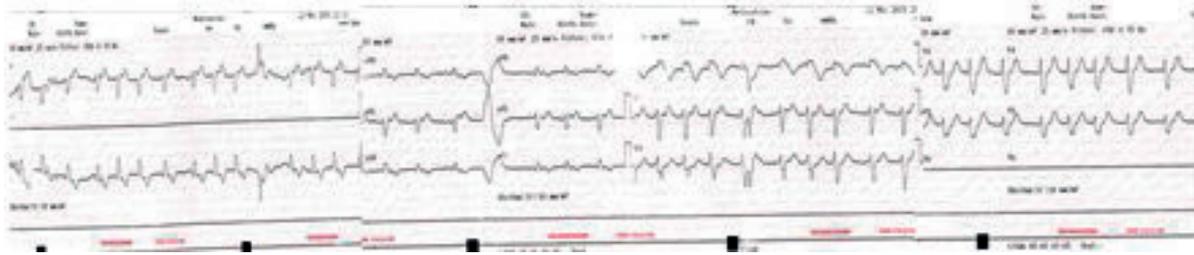


Figure 2. Electrocardiogram 2

of Medical Toxicology Position Statement on use of intravenous fat emulsion (ILE) rests the decision to initiate lipid resuscitation therapy solely on the discretion of the treating physician; however, they consider it a reasonable treatment option in cases where serious hemodynamic or other instability from a xenobiotic with a high degree of lipid solubility exists, even if the patient is not in cardiac arrest.¹²

We only found two cases of propafenone overdose for which the IFE treatment has been used.^{7,8} The first case 7 was a 21-year-old female patient with sinus bradycardia, first-degree atrioventricular (AV) block, and a wide QRS (320 ms) interval after consuming 4500 mg propafenone. The patient was brought to the emergency room after unsuccessful administration of CPR and other supportive therapy (intravenous fluids, sodium bicarbonate, dopamine, noradrenaline, calcium chloride, and glucagon) for 30 min. IFE treatment was initiated, which decreased inotrope requirement by 40% and reduced QRS duration to 200 ms. However, the patient died 3 days later.

The second case 8 was a 59 year-old male patient who had taken multiple drugs (150 mg dabigatran, 6 tablets of sildenafil [100 mg total], and an unknown dose of enalapril). It was not clear whether the patient had a history of propafenone use, had taken propafenone in a suicide attempt, and if so, the dose the patient took. The patient was admitted with hypotension, coma, and QRS duration of 450 ms. The patient was administered IFE after he did not respond to the initial supportive treatment. After treatment, QRS duration decreased to 110 ms and inotrope support was discontinued. The patient recovered but was sent to rehabilitation with tracheostomy.

Our case was the first to survive IFE treatment following high-dose propafenone intake and to be discharged with normal function. The treatment was administered

Table 1. EKG results		
Laboratory Parameters	IFE Before Treatment	IFE After Treatment
EKG		
QRS duration	0.16 ms	0.16 ms
PR duration	Nodal Rhythm	Atrial Fibrillation
	Undetectable P wave	Undetectable P wave
QT duration	0.48 ms	0.44 ms

IFE: Intravenous fat emulsion, EKG: Electrocardiogram

Table 2. Laboratory results		
Laboratory Parameters	IFE Before Treatment	IFE After Treatment
Blood Gases		
pH	7.32	7.44
pO ₂ (mmHg)	42.6	83.8
pCO ₂ (mmHg)	32	34.9
HCO ₃ (mmol/L)	16.8	25.1
Laktate (mmol/L)	6.9	1.3

IFE: Intravenous fat emulsion

55 minutes after admission to the emergency room and played a life-saving role. Both our patient and other patients with propafenone intoxication showed increases in blood pressure, elimination of inotrope requirement, shortening in QRS duration, and control of seizures following IFE treatment.

CONCLUSION

Currently, intravenous lipid treatment is not recommended as the first treatment option for propafenone intoxication. However, it may increase rate of survival rate when administered to patients at an early stage of cardiac arrest.

* The authors declare that there are no conflicts of interest.

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