Erciyes Med J 2015; 37(3): 119-21 • DOI: 10.5152/etd.2015.8381

Clinical Management of Severe Propafenone Intoxication

CASE REPORT

İnci Kara, Jale Bengi Çelik, Seza Apilioğulları, Eyüp Aydoğan

ABSTRACT

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 in 15 $\mu g \cdot kg^{-1}min^{-1}$ and 5 $\mu g \cdot kg^{-1}min^{-1}$, respectively. In addition, intravenous fluids were administered with central venous pressure guidance. Laboratory

Department of Anesthesiology and Reanimation, Selçuk University Faculty of Medicine, Konya, Turkey

Submitted
12.11.2013

Accepted
30.12.2013

Correspondance
Dr. İnci Kara, Selçuk Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Konya, Türkiye
Phone: +90 505 483 18 19
e.mail: drincikara@yahoo.com

This study was presented at the 46th TARD National Congress, 7-11 November 2012, Cyprus

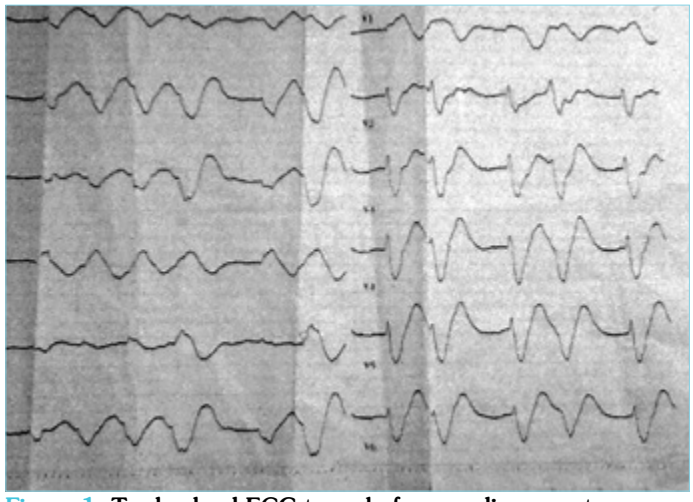

Figure 1. Twelve-lead ECG trace before cardiac arrest

tests including serum electrolyte, cardiac enzyme levels, and coagulation were carried out. Mechanical ventilation was adjusted, and the patient received 20 mL of 8.4% sodium bicarbonate infusion to titrate to an arterial pH of less than 7.5. Meanwhile, she had a seizure in response to 15 mg/kg^{-1} of phenytoin.

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-l min^{-1} oxygen support was given via an oxygen mask. Forty-eight hours after extubation, she was consulted with a cardiologist without any recommendation, discharged from the intensive care unit with a full neurological and hemodynamical recovery, and transferred to a phychiatry clinic for neurobehavioral examination. She was discharged in an appropriate condition with the recommendation to continue neurobehavioral therapy on the sixth day after intoxication.

DISCUSSION

Propafenone is a class 1C antiarrhytmic 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 upto 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 ß-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.

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authors' Contributions: Conceived and designed the experiments or case: İK, JBÇ, SA, EA. Performed the experiments or case: İK, JBÇ, SA, EA. Analyzed the data: İK, JBÇ, SA, EA. Wrote the paper: İK, JBÇ, SA, EA. All authors read and approved the final manuscript.

Acknowledgement: Would like to thank to Department of Cardiology for their support.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Söyüncü S, Bektaşi F, Yiğit O. Propafenone overdose: two case reports. Turk J Emerg Med 2007; 7(3): 127-31.
2. Clarot F, Goullé JP, Horst M, Vaz E, Lacroix C, Proust B. Fatal Propafenone Overdoses: Case Reports and A Review of the Literature. J Analytical Toxicology 2003; 27(8): 595-9. [CrossRef]
3. Ardıç I, Günebakmaz Ö, Yarlioglues M, Kaya MG. Acute intoxication with propafenone and trimethoprim-sulfamethoxazole in a case of suicide attempt. Turk Kardiyol Dern Ars 2009; 37(6): 410-3.
4. Amerini S, Bernabei R, Carbonin P, Cerbai N, Mugelli A, Pahor M. Electrophysiological mechanism for the antiarrhythmic action of propafenone: a comparison with mexiletine. Br J Pharmacol 1988; 95(4): 1039-46. [CrossRef]
5. Köppel C, Oberdisse U, Heinemeyer G. Clinical course and outcome in class Ic antiarrhythmic overdose. J Toxicol Clin Toxicol 1990; 28(4): 433-44. [CrossRef]
6. Siddoway LA, Thompson KA, Mc Allister CB, Wang T, Wilkinson GR, Roden DM. Polymorphism of propafenone metabolism and disposition in man: clinical and pharmacokinetic consequence. Circulation 1987; 75(4): 785-91. [CrossRef]
7. Ledda F, Mantelli L, Manzini S, Amerini S, Mugelli A. Electrophysiological and antiarrhythmic properties of propafenone in isolated cardiac preparations. J Cardiovasc Pharmacol 1981; 3(6): 1162-73. [CrossRef]
8. Ustundag M, Orak M, Guloğlu C, et al. Lethal toxicity of propafenone in a case of suicidal attempt. Turk J Emerg Med 2007;7(3):132-5.
9. Fonck K, Haenebalcke C, Hemeryck A, Belpaire F, Jordaens L, Calle P, et al. ECG changes and plasma concentrations of propafenone and its metabolites in a case of severe poisoning. Clin Toxicol 1998; 36(3): 247-51. [CrossRef]
10. Budde T, Beyer M, Breihardt G, Passlick J, Grabensee B. Therapy of severe propafenone poisoning: an attempt at elimination by hemoperfusion Z. Kardiol 1986; 75(12): 764-9.
11. Kerns W, English B, Ford M. Propafenone overdose. Ann Emerg Med 1994; 24(1): 98-103. [CrossRef]
12. Mc Hugh TP, Perina DG. Propafenone ingestion. Ann Emerg Med 1987; 16(4): 437-40. [CrossRef]
13. Ielasi G, Panagia M, Grasso L, Caminiti G. Acute voluntary poisoning with propafenone. A clinical case. Minerva Anestesiol 1993; 59(1-2): 69-73.
14. Picciotto G, Siragusa V, Cellura M, Ventimiglia C, Rotolo L. Acute propafenone poisoning. Description of a case. Minerva Cardioangiol 1990; 38(12): 555-8.
15. Lanquetot H, Furet Y, Kerourédan V, Poitrineau O, Hubiche M, Autret E. Fatal poisoning caused by the combination propafenone-amitriptyline; apropos of a case. Agressologie 1988; 29(1): 39-42.
16. Friocourt P, Martin C, Lozac'h L. Intoxication volontaire à la propafénone: a propos d'un cas. Ann Cardiol Angeiol 1988; 37(3): 133-6.
17. Eray O, Fowler J. Severe propafenone poisoning responded to temporary internal pacemaker. Vet Hum Toxicol 2000; 42(5): 289.
18. Camous JP, Ichai C, Meyer P, Gibelin P, Baudouy M, Varenne A, et al. Traitement des intoxications aux nouveaux antiarythmiques (cibenzoline, flécaïnide, propafénone). Presse Méd 1987; 16(41): 2076.
19. Rambourg-Schepen MO, Grossenbacher, Buffet M, Lamiable D. Recurrent convusions and cardiac conduction disturbances after propafenone overdose. Vet Hum Toxicol 1999; 41(3): 153-4.
20. Olm M, Jimenez MJ, Munne P. Efficacité de la methoxamine par voie veineuse lors des intoxications à la propafénone. Presse Méd 1989; 18(22): 1124.
21. Maxeiner H, Klug E. Lethal suicidal intoxication with propafenone, after a history of self-inflicted injuries. Forensic Sci Int 1997; 89(1-2): 27-32. [CrossRef]
22. Lanari A, Brun M, Dormi A, Giunti M, Mariani A, Mariotti V, et al. Propafenone and verapamil poisoning. Report of two clinical cases. Clin Ther 1994; 145(12): 457-61.
23. Naccarelli GV, Sager PT, Singh BN: Antiarrhythmic agents. In: Podrid PJ, Kowey PR eds. Cardiac arrhythmias. Mechanisms, diagnosis and management. 2nd ed. Philadelphia: Lippincott-Williams & Wilkins; 2001.p.265–301.
24. Benowitz N, Goldschiager N: Cardiac disturbances. In: Haddad L, Shannon M eds. Clinical management of poisoning and drug overdoses. 3th Ed., New York: Saunders Company; 1998.p.1181.
25. Müller-Peltzer H, Greger G, Neugebauer G, Hollmann M. Beta-blocking and electrophysiological effects of propafenenone in volunteers. Eur J Clin Pharmacol 1983; 25(6): 831-3. [CrossRef]
26. Odeh M, Seligmann H, Oliven A. Propafenone-induced ataxia: report of three cases. Am J Med Sci 2000; 320(2): 151-3. [CrossRef]