

## CASE REPORT

## Toxicology

## Propafenone and propranolol dual toxicity

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## Abstract

Propranolol is a highly lipid-soluble beta-receptor antagonist and propafenone is a potent class 1c anti-arrhythmic agent with strong Na-channel blockade effect. We describe a novel case of dual overdose of propafenone and propranolol resulting in hypotension, generalized seizures, and reduced level of consciousness that was successfully treated. A 52-year-old female ingested 500 mg of propranolol and 1.5 g of propafenone. The patient was brought to the emergency department (ED) and exhibited signs of systemic toxicity and reduced level of consciousness. The patient was treated as a case of combined  $\beta$ -blocker and propafenone toxicity using high dose insulin,  $\text{NaHCO}_3$ , glucagon, atropine, and dopamine. She started improving and becoming more alert, with subsequent ECGs revealing normal sinus rhythm. The patient was discharged 4 days later. We believe that early administration of  $\text{NaHCO}_3$  should be administered in patients exhibiting signs of Na-channel blockade.

## KEYWORDS

Brugada, Na-channel blockade, overdose, propafenone, propranolol, toxicity

## 1 | CASE PRESENTATION

A 52-year-old woman with a previous medical history of bipolar disorder and supraventricular tachycardia was brought to the emergency department by ambulance in a drowsy state at 0900 hours. Emergency medical services (EMS) reported that on their arrival on scene, the patient was actively seizing, following an overdose with a combination of 1.5 g of propafenone and 25 mg total bisoprolol. Her vitals at presentation were heart rate (HR) = 58 BPM, blood pressure (BP) = 100/50 mm Hg, Glasgow Coma Scale (GCS) = 13/15, and  $\text{O}_2$  saturation = 96% on room air.

At 0910 hours, the repeated vital signs were HR = 50 BPM, BP = 80/50 mm Hg,  $\text{O}_2$  saturation = 97% on room air, and her initial post-ictal GCS was 13/15 (with symmetrically reactive pupils). However,

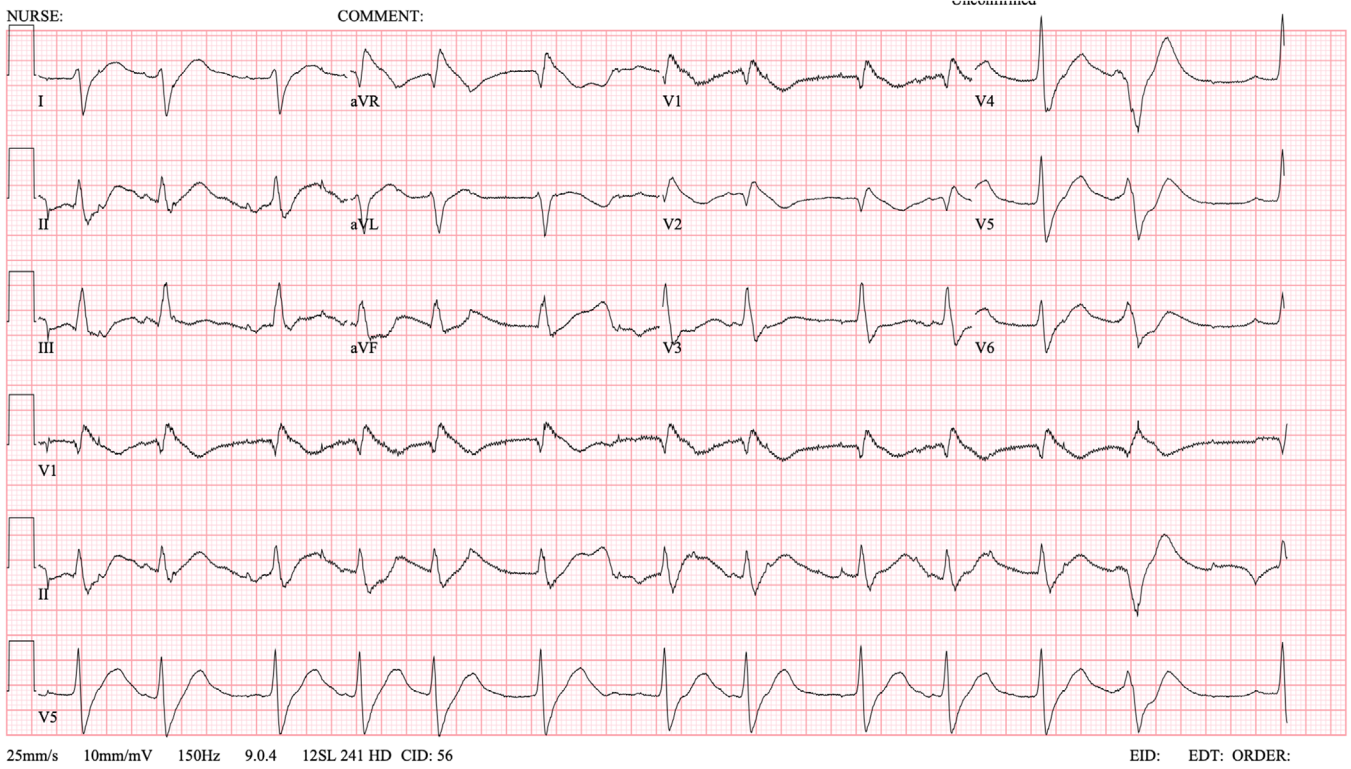
her venous blood gas (VBG) revealed respiratory acidosis with lactate levels of 5.5 mmol/L. The cardiac monitor confirmed a sinus bradycardia, and the patient was administered atropine 0.5 and 10 mg glucagon intravenously. Her BP was rechecked, and it revealed hypotension with 70/50 mm Hg. A large-bore left external jugular intravenous cannula was inserted, and 0.9% normal saline bolus was administered. Her BP was still dropping (80/40 mm Hg), and she then received 0.5 mg atropine twice and an infusion was started at 10 mcg/kg/min. Her QRS was widening, and she was at risk of developing a ventricular arrhythmia (Figure 1). In view of this, she was also administered calcium gluconate 10% 10 mL and  $\text{NaHCO}_3$  42% 50 mL intravenously.

Collateral history from the husband revealed that the patient felt chest pain and discomfort at around 0630 hours, and she ingested 500 mg of propranolol instead of 25 mg total bisoprolol, information

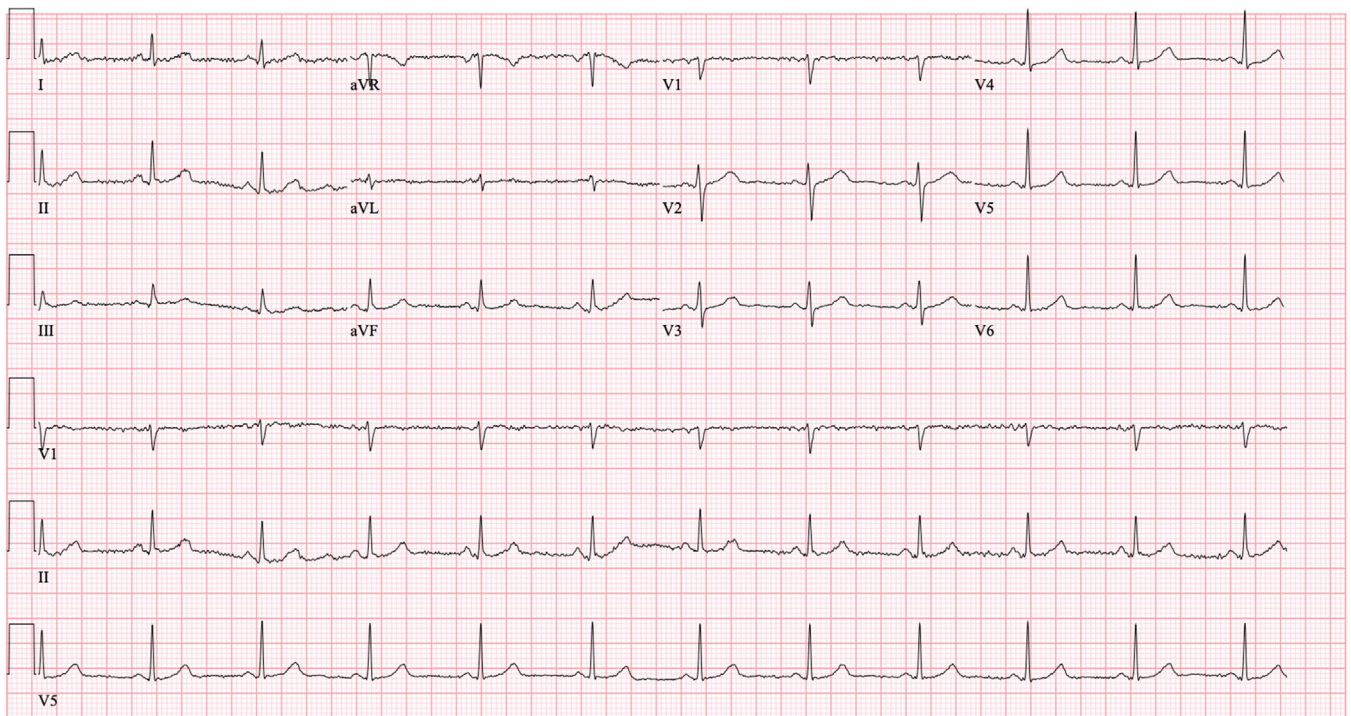
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**FIGURE 1** Initial ECG at ED presentation showing sinus rhythm with few PACs, left axis deviation, broad QRS (164 ms) due to Na-channel blockade. There are coved ST changes in leads V1 and V2, consistent with type 1 Brugada pattern



**FIGURE 2** Repeat ECG 4 days later at discharge showing normal sinus rhythm.



that was initially misreported by the EMS, along with 1.5 g of propafenone. He presented the empty medication leaflets of propranolol and propafenone, which confirmed this.

After treatment with NaHCO<sub>3</sub>, she was administered high dose insulin at 1 U/kg (60 units total as bolus) and started on an insulin infusion. Concomitantly, dextrose 50% bolus was administered, and a dextrose 10% infusion was started at 80 mL/h. Blood glucose assessments were carried out every 30 minutes.

The patient was maintaining the patency of her airway and intubation was withheld. Her vitals were HR = 90 BPM, BP = 110/60 mm Hg, O<sub>2</sub> saturation = 97% on room air, and GCS = 13/15. When the patient became more alert, she confirmed that she had consumed 500 mg propranolol and 1.5 g propafenone, and she denied taking any bisoprolol. Before her transfer to the ICU, her repeat ECG revealed normal sinus rhythm, and she was hemodynamically stable. Lab values before transfer were: Trop = 0.02 ng/mL, INR = 0.83, APTT = 22.5, Na = 143 mmol/L, K = 4 mmol/L, WBC = 12.04, Hb = 12.2 g/dL, urea = 4.8 mmol/L, and creatinine = 126 umol/L (urine drug panel was not sent). The patient had an uncomplicated stay in the ICU for 2 days and was then transferred to the ward in a stable state and discharged home after another 2 days. Her ECG upon discharge showed normal sinus rhythm (Figure 2).

## 2 | DISCUSSION

In the United States, there were 9041 single  $\beta$ -blocker exposures reported to poison centers in 2006.<sup>1</sup> In contrast, according to one literature review, propafenone poisoning is rarer, with only a handful of cases being reported in the literature.<sup>2</sup> To our knowledge, there was no published material on concurrent poisoning from both agents in a single patient, and this is the first instance of combined overdose we have observed.

Propafenone is a class 1c anti-arrhythmic agent that works as a potent Na-channel blocker and can cause QRS prolongation without QT prolongation.<sup>3,4</sup> Like propranolol, it can cause hypotension, ventricular dysrhythmias and seizures especially when combined with a non-selective  $\beta_1$ -blocker.  $\beta$ -blocker toxicity algorithms also work for class 1c anti-arrhythmic agents. This is because they both target rapid-acting Na channels in the myocyte.<sup>5</sup> Reversal of the blockade of these channels is the mainstay target of treatment.

Propranolol is the most potent sodium channel blocker among  $\beta$ -blockers,<sup>6,7</sup> because sodium channels play an important part in the development of action potential in the cardiac muscle, and bradycardia caused by  $\beta$ -blocker overdose in normal hearts is due more to sodium channel block rather than a  $\beta$ -block.<sup>7,8</sup> Therapeutic intervention used in the management of both propranolol and propafenone ingestion includes atropine, dopamine, NaHCO<sub>3</sub>, glucagon, and high dose insulin.<sup>9,10</sup>

In our patient, the ECG changes observed initially were reverted with NaHCO<sub>3</sub> administration. It is difficult to say, however, whether the changes were because of propafenone alone, propranolol alone, or due to dual toxicity, because we were unable to obtain quantitative

drugs levels during the hospitalization. However, we corroborated collateral history from the spouse with that of the patient, and it is highly likely that the toxicity was from propafenone and propranolol ingestion, rather than just a single agent. The presence of type-1 Brugada pattern, seen in both propranolol toxicity and propafenone toxicity<sup>9,11</sup> and the presence of generalized tonic-clonic seizures (also a clinical sign of toxicity caused by both agents) support this.<sup>12</sup>

In summary, patients suffering from an overdose of combined  $\beta$ -blockers and propafenone present with variable signs and symptoms such as bradycardia, hypotension, unresponsiveness, generalized seizures, or even cardiac arrest.<sup>12</sup> It is important that these patients receive aggressive airway management with the possibility of mechanical ventilation. All patients require close monitoring of their initial treatment, and treatment should consist of fluid boluses, vasopressors, and glucagon. No single therapy is considered as definitive treatment in the literature. There have been cases where temporary intravenous pacing, and/or particularly intravenous lipid emulsion therapy have been used.<sup>13</sup> Lipid emulsion therapy has been successfully used in treating lipophilic drug poisoning (eg, from propranolol) by acting as a "lipid-sink" that attracts substances away from the brain and heart and toward the lipid-sink preventing toxic accumulation of the substances in those tissues.<sup>14</sup> In addition to the aforementioned treatments, we believe that early administration of NaHCO<sub>3</sub> should take place in patients exhibiting signs of Na-channel blockade, due to its ability to prevent cardiac dysrhythmias by reversing Na-channel blockade.<sup>11</sup>

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## REFERENCES

1. Bronstein AC, Spyker DA, Cantilena LR, Jr, Green J, Rumack BH, Heard SE. 2006 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS). *Clin Toxicol*. 2007;45(8):815-917.
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 Anal Toxicol*. 2003;27(8):595-599.
3. Funck-Brentano C, Kroemer HK, Lee JT, Roden DM. Propafenone. *N Engl J Med*. 1990;322(8):518-525.
4. McHugh TP, Perina DG. Propafenone ingestion. *Ann Emerg Med*. 1987;16(4):437-440.
5. Kerns W, II, English B, Ford M. Propafenone overdose. *Ann Emerg Med*. 1994;24(1):98-103.
6. Lauterbach M. Clinical toxicology of beta-blocker overdose in adults. *Basic Clin Pharmacol Toxicol*. 2019;125(2):178-186.
7. Bailey B. Glucagon in  $\beta$ -blocker and calcium channel blocker overdoses: a systematic review. *J Toxicol Clin Toxicol*. 2003;41(5):595-602.
8. Rennyson SL, Littmann L. Brugada-pattern electrocardiogram in propranolol intoxication. *Am J Emerg Med*. 2010;28(2):256.e7-8.
9. Köppel C, Oberdisse U, Heinemeyer G. Clinical course and outcome in class IC antiarrhythmic overdose. *J Toxicol Clin Toxicol*. 1990;28(4):433-444.
10. Bayram B, Dedeoglu E, Hocaoglu N, Gazi E. Propafenone-induced cardiac arrest: full recovery with insulin, is it possible? *Am J Emerg Med*. 2013;31(2):457.e5-7.

11. Gil J, Marmelo B, Abreu L, Antunes H, Santos LF, Cabral JC. Propafenone overdose: from cardiogenic shock to Brugada pattern. *Arq Bras Cardiol.* 2018;110(3):292-294.
12. Rambourg-Schepens MO, Grossenbacher F, Buffet M, Lamiable D. Recurrent convulsions and cardiac conduction disturbances after propafenone overdose. *Vet Hum Toxicol.* 1999;41(3):153-154.
13. Brubacher J. Bicarbonate therapy for unstable propafenone-induced wide complex tachycardia. *CJEM.* 2004;6(5):349-356.
14. Lashari BH, Minalyan A, Khan W, Naglak M, Ward W. The use of high-dose insulin infusion and lipid emulsion therapy in concur-

rent beta-blocker and calcium channel blocker overdose. *Cureus.* 2018;10(11):e3534.

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