

Acute intoxication with propafenone and trimethoprim-sulfamethoxazole in a case of suicide attempt

İntihar amaçlı propafenon ve trimetoprim/sulfametoksazol alımı ile akut zehirlenme

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A 17-year-old male ingested about 20 tablets of propafenone (total 6,000 mg) and 24 tablets of trimethoprim (total 1,920 mg) - sulfamethoxazole (total 9,600 mg) with suicidal intent. Within one hour, he was brought to a hospital with vomiting, nausea, and loss of consciousness, where he developed cyanosis and mild acidosis, and eventually cardiorespiratory arrest, despite bicarbonate, saline infusion, and inotropic support. Fortunately, he was fully resuscitated and ventilated, and sinus rhythm was restored. He was then transported to our center. On admission, his heart rate was regular with 55 beats/min and blood pressure was 70/45 mmHg. The 12-lead electrocardiogram (ECG) showed sinus bradycardia, extreme widening of the QRS complex (260 msec) with a right bundle branch block pattern. Intravenous saline, bicarbonate, and dopamine were administered, and respiration was supported mechanically, which resulted in rapid restoration of sinus rhythm and improvement in hemodynamic parameters and acidosis. A subsequent ECG showed shortening of the QRS duration (230 msec). He was discharged with an appropriate hemodynamic balance on the third day with normal ECG findings.

Key words: Anti-Arrhythmia agents/poisoning; electrocardiography; propafenone/poisoning; suicide, attempted; trimethoprim-sulfamethoxazole combination/poisoning.

Propafenone is a class IC antiarrhythmic drug, approved for use in patients with life-threatening ventricular arrhythmias, such as ventricular tachycardia.^[1] It is at least as effective as any other type I agent in converting atrial fibrillation to sinus rhythm. It is also effective in suppressing the recurrence of atrial fibrillation once sinus rhythm has been restored. Class IC antiarrhythmic drugs are the most potent sodium-channel blockers, but do not affect potassium

On yedi yaşındaki bir erkek hasta, intihar amacıyla yaklaşık 20 tablet (toplam 6000 mgr) propafenon ve 24 tablet trimetoprim (toplam 1920 mgr)-sulfametoksazol (toplam 9600 mgr) içtikten sonra bir saat içinde, kusma, bulantı ve bilinç kaybıyla başka bir merkeze getirildi. Burada, uygulanan bikarbonat, salin infüzyonu ve inotropik desteğe rağmen hastada siyanoz, orta derecede asidoz ve sonuçta kardiyorespiratuvar arest gelişti. Hasta başarılı resüsitasyon ve ventilasyon girişimleriyle yaşama döndürüldükten ve sinüs ritmine döndükten sonra merkezimize sevk edildi. İlk muayenede kalp hızı düzenli ve 55 atım/dk, kan basıncı 70/45 mmHg olan hastanın 12 derivasyonlu elektrokardiyografisinde sinüs bradikardi, aşırı derecede genişlemiş QRS kompleksi (260 msn) ve sağ dal bloku paterni izlendi. İntravenöz salin, bikarbonat ve dopamin tedavisi ve mekanik solunum desteğiyle hastanın sinüs ritmi, hemodinamik parametreleri ve asidozu hızla düzeldi. Elektrokardiyogramda QRS süresinin azaldığı (230 msn) görüldü. Üçüncü günde yeterli hemodinamik dengesi sağlanan hasta normal elektrokardiyografik bulgularla taburcu edildi.

Anahtar sözcükler: Antiaritmik ilaç/zehirlenme; elektrokardiyografi; propafenon/zehirlenme; intihar girişimi; trimetoprim-Sulfametoksazol kombinasyonu/zehirlenme.

channels. These agents cause QRS prolongation without QT prolongation. Overdose of sodium-channel blockers causes hypotension, prolonged QRS duration, ventricular arrhythmias, depressed mental status, and seizures. Trimethoprim-sulfamethoxazole (TMP/SMX), on the other hand, is a frequently prescribed antibiotic with a wide spectrum of antimicrobial activity. It may cause QT prolongation, but the risk is very low. Prolonged QT interval may lead to torsade

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de pointes, with potential consequences of syncope or sudden death.^[2,3]

We presented a case in which propafenone and TMP/SMX were found to be the cause of cardiopulmonary arrest in patient with a structurally normal heart.

CASE REPORT

A 17-year-old male ingested about 20 tablets of propafenone (per 300 mg; total 6,000 mg) and 24 tablets of trimethoprim (per 80 mg; total 1,920 mg) - sulfamethoxazole (per 400 mg; total 9,600 mg) with suicidal intent. Within one hour after ingestion, he was brought to a hospital with vomiting, nausea, and loss of consciousness. Moments later he developed cyanosis and mild acidosis. Despite bicarbonate, saline infusion, and inotropic support, cardiorespiratory arrest ensued. The patient was fully resuscitated and ventilated, and sinus rhythm was restored within half a minute. He was then transported to the emergency department of our hospital. On initial evaluation, his heart rate was regular with 55 beats/min and blood pressure was 70/45 mmHg. The initial 12-lead electrocardiogram (ECG) showed sinus bradycardia, extreme widening of the QRS complex (260 msec) with a right bundle branch block pattern (Fig. 1a).

Intravenous saline, bicarbonate, and dopamine were administered, and respiration was supported mechanically, which resulted in rapid restoration of sinus rhythm and improvement in hemodynamic parameters and acidosis. There was no significant abnormality in the levels of sodium, potassium, calcium, and magnesium. He had no prior history of cardiac disease, nor a coronary risk factor other than smoking. A subsequent 12-lead ECG obtained five hours later showed shortening of QRS duration (230 msec) (Fig. 1b). As the patient began to breathe spontaneously and tried to communicate, the endotracheal cannula was removed. Transthoracic echocardiography and thyroid function tests were normal.

The 12-lead ECG at the time of discharge showed normal sinus rhythm with normal axis, P-R interval, and QRS duration (Fig. 1c). Following consultation with psychiatry, he was included in the behavioral treatment program. He was discharged with an appropriate hemodynamic balance on the third day after admission. No medication was prescribed.

DISCUSSION

Propafenone is a class IC antiarrhythmic drug used for the therapy of ventricular arrhythmias

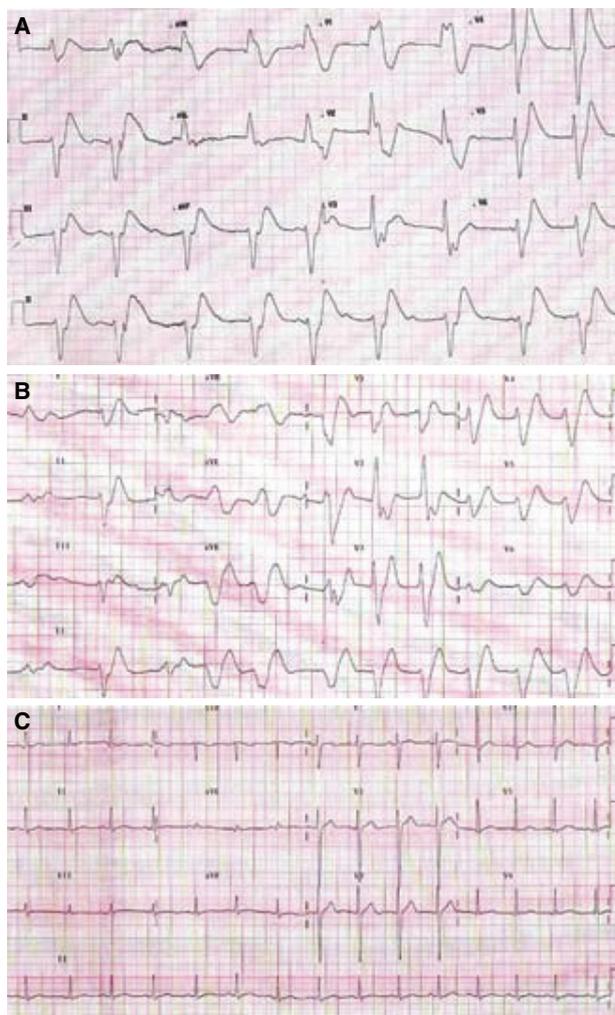


Figure 1. Twelve-lead electrocardiograms (ECG) demonstrating the three stages of the patient's prognosis. **(A)** 3.5 hours after admission: sinus bradycardia, extreme QRS complex widening (260 msec), right bundle branch block pattern, and QT prolongation (QTc interval 569 msec). **(B)** 5 hours later: shortening of QRS duration (230 msec) and QTc interval (545 msec). **(C)** At discharge: normal sinus rhythm with normal axis, normal P-R interval, with QRS duration of 88 msec and QTc interval of 407 msec.

and supraventricular tachycardia. It is available in tablets of 150 and 300 mg, the recommended daily therapeutical dose for an adult being 450-600 mg. Propafenone is 95% protein bound, and the metabolism is 99% hepatic with an elimination half-life of 2 to 12 hours.^[4] It is metabolized into two major metabolites, 5-hydroxypropafenone and N-depropylpropafenone. Both propafenone and its metabolites have a negative inotropic activity at high concentrations. Propafenone acts by slowing the influx of sodium ions into the cardiac muscle cells, causing a decrease in excitability of the

cells.^[5] Propafenone and its metabolites differ in their affinity and duration of binding to the sodium channel, in their effects on potassium and calcium channels, and in other effects such as antimicrobial properties. Because of its class IC antiarrhythmic properties, propafenone may show a significant proarrhythmogenic effect even at therapeutic doses. Relatively infrequent complications are hematologic reactions and those of neurological (convulsions, amnesia, peripheral neuropathy), gastrointestinal, and hepatic.^[6-9] Toxic effects of high doses including a fatal outcome have been sporadically reported.^[10,11] Vomiting, nausea, and loss of consciousness are the earliest symptoms of intoxication, and are observed within a half hour after ingestion.^[10] Severe complications resulting from high overdoses occur within a few hours.^[10,12] Fatal course is usually associated with cardiac conduction abnormalities with progression to electromechanical dissociation or asystole as in our patient. Propafenone intoxication-induced ECG changes have been reported as QRS prolongation usually with a right bundle branch block pattern. Complications of acute propafenone overdose also include hypotension, cardiovascular collapse and, in most cases, seizures.^[13]

Trimethoprim-sulfamethoxazole is known to cause hepatitis and may be associated with prolonged QT interval, though the risk is low. Syncope (fainting) due to ventricular arrhythmias may result in prolonged QT interval, possibly of torsade de pointes type, which can progress to ventricular fibrillation and ultimately sudden death.

Although intoxications with class IC antiarrhythmic drugs have been reported, there has been no report on intoxications caused by propafenone and TMP/SMX in concert. In our case, the right bundle branch block pattern was accompanied by QRS prolongation (260 msec) and QT prolongation (569 msec). Since propafenone has no effect on potassium channels nor on ventricular repolarization, QRS prolongation is usually seen without QT prolongation in propafenone intoxications. Thus, prolongation of QTc must have occurred as a consequence of TMP/SMX intoxication in our patient. On the other hand, the JT interval, which is measured from the end of the QRS complex to the end of the T wave, has been proposed as an alternative way to measure the duration of ventricular repolarization and is useful especially in patients with a QRS interval of ≥ 120 msec. In our case, the JTc interval was in normal range with 311 msec (normal < 350 msec).

Intoxications with TMP/SMX usually result in torsade de pointes and eventually ventricular fibrillation. In our case, cardiac arrest occurred because of bradycardia, and no ventricular fibrillation was seen, suggesting that the main cause of cardiac arrest was propafenone intoxication, with the concomitant effect of TMP/SMX intoxication manifested as QT prolongation.

In our case, the main clinical findings were hypotension, coma, acidosis, bradycardia, and ventricular arrhythmias. Treatment with gastric lavage, mechanic ventilation, and administration of alkalinizing solutions were the most important therapeutic applications resulting in a successful outcome. The use of sodium bicarbonate has also been reported to treat adverse cardiac effects associated with propafenone treatment.^[14]

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