Case Report

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Intravenous Lipid Emulsion Treatment in The Verapamil Intoxication

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Abstract

The use of intravenous lipid emulsion therapy (ILE) as an antidote in toxicology has become an increasingly popular in recent years. In pediatric age group, the reported number of cases treated with ILE is very low. Successful results have been reported with ILE therapy in tricyclic antidepressant, verapamil, and beta blocker poisonings in cases that are not responsive to the standard treatment methods. In this article, we present a clinical and laboratory finding of a case that did not respond to standard treatment and was successfully treated with ILE therapy.

Key words: child, verapamil, intoxication, intravenous lipid emulsion

Özet

Toksikolojide bir panzehir olarak intravenöz lipid emülsiyon terapisinin (ILE) kullanımı son yıllarda giderek daha popüler hale gelmiştir. Pediatrik yaş grubunda, ILE ile tedavi edilen bildirilen vaka sayısı çok düşüktür. Standart tedavi yöntemlerine yanıt vermeyen trisiklik antidepresan, verapamil ve beta bloker zehirlenmelerinde ILE tedavisi ile başarılı sonuçlar bildirilmiştir. Bu yazıda, standart tedaviye yanıt vermeyen ve ILE tedavisi ile başarılı bir şekilde tedavi edilen bir olgunun klinik ve laboratuvar bulgusunu sunuyoruz.

Anahtar kelimeler: pediatri, verapamil, zehirlenme, intravenöz lipid emülsiyon

Introduction

Verapamil is a potent calcium channel blocker (CCB) used in the treatment of various cardiovascular diseases such as hypertension, cardiac arrhythmias and angina[1]. Its effect is demonstrated by inhibiting L-type calcium channels in the heart and vascular smooth muscle. In verapamil intoxication, clinical conditions such as bradycardia, metabolic acidosis, hypotension, conduction defects and shock may occur. Treatment is based on the reduction of drug absorption, supportive care and stabilization of cardiac functions[2]. There have been many studies showing the efficacy of lipid emulsion therapy in the overdose of verapamil[3,4].

The use of intravenous lipid emulsion therapy (ILE) as an antidote in toxicology has been an increasingly popular issue in recent years. It has been reported in animal trials and case reports that ILE is a successful antidote for cardiac side effects of drugs such as verapamil, beta blocker, and tricyclic antidepressant[5-7]. In this case report, we aimed to share a case of verapamil intoxication with resistant bradycardia and hypotension within the scope of relevant literature

Case Report

A 16-year-old woman ,weighing 64 kg, ingested 2880 mg of sustained release verapamil-active drug in a suicide attempt. The patient was taken to the nearest health center with complaints of nausea, vomiting and malaise in 30 minutes after taking the drug.

In the health center, a nasogastric tube was inserted and gastric lavage and active charcoal were performed. After developing bradycardia and hypotension, the patient was transferred to our intensive care unit for follow-up and treatment. In the initial evaluation of the case, the patient's fever was 37° C, blood pressure (BP) was 90/60 mm Hg, heart rate (HR) was 60 / min, and peripheral oxygen saturation (SpO2) was 96%. During the physical examination (PE), it was seen that the patient's general condition was moderate, she was conscious, heart sounds were rhythmic, lung sounds were normal, had no organomegaly, and Glasgow Coma Score (GCS) was 14. Hemogram and biochemical tests did not show any features. Electrocardiography (ECG) showed sinus bradycardia (Fig. 1). The blood gas was evaluated as normal. The patient received 0.5 g / kg of activated

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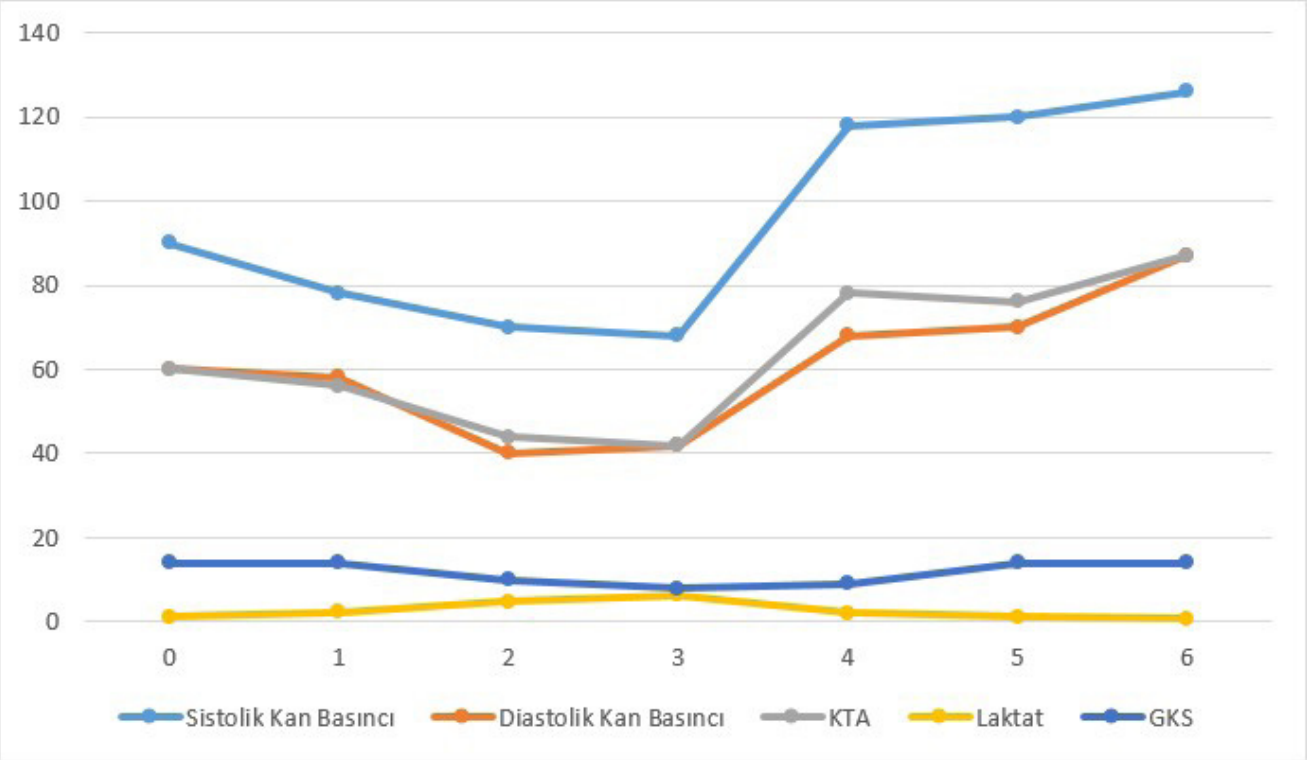
Grafik 1: Hastanın yoğun bakım takipleri



charcoal and fluid support, ECG monitoring and close haemodynamic follow-up were conducted.

During the second hour of follow-up, intravenous calcium, fluid and dopamine treatment were given to the patient with blood pressure (BP): 70/40 mm Hg and HR: 44 / min. Neuroadrenaline and adrenaline therapy were initiated in patient with hypotension and bradycardia. At the third hour of the follow-up, the patient's blood gas pH was 7, 24, PaO2 was 92 mmHg, PaCO2 was 56 mmHg, HCO3 was 14.3 mmol / L, BE was -13.5, and lactate was 6.3 mEq. As confusion occurred and GCS was 8, the patient was intubated (Figure 1).

At the same time, hyperinsulin / euglycemia (HIE), glucagon and ILE therapy were started, respectively. A 1.5 ml / kg 20% lipid emulsion, iv bolus for 1 minute followed by a 0.25 ml / kg / min 30 minute infusion was started to the patient who did not respond to initial treatment. In approximately 10 minutes, the pulse rate and blood pressure values attained normal levels and the ECG returned to normal sinus rhythm. The inotropic support of the patient was reduced and cut at the 24th hour because the patient reached normal blood pressure and pulse rate. The patient was extubated. The patient whose cardiac evaluation was normal without complication on follow-up was discharged on the 4th day.

Discussion

Verapamil, a lipophilic calcium channel blocker, reduces the level of cytosolic calcium by inhibiting voltage-dependent L-type calcium channels found in the smooth muscle of the myocardium and veins and reducing calcium entry into these cells. Verapamil has the most potent negative inotropic effect among CCB. Cardiotoxic effect of verapamil overdose may cause more deaths than all other CCBs. In a study conducted in the United States in 2004, 10513 high-dose calcium channel blocker cases were identified. 5202 of those were high-dose verapamil, and 356 had major toxic effects[8].

Intoxication usually starts at 1-5 hour after ingestion of the drug, while it might be up to 48-72 hours in slow-release formulations[9]. In verapamil intoxication, cardiovascular, gastrointestinal, central nervous system related and metabolic effects can be seen. Treatment is based on reduction of drug absorption, supportive care and stabilization of cardiac functions[10]. When its effect on the cardiovascular system is examined, bradycardia and hypotension are the most common findings[9]. Findings of central nervous system include vertigo, confusion, hallucinations, epileptic seizures, and coma. In the onset of neurological symptoms, direct toxic effects have also been observed although cerebral hypoperfusion has been mainly considered[10].

Metabolic acidosis and hyperglycemia are the most common metabolic effects. Hypoperfusion occurs elevation of lactate level in resulting metabolic acidosis. In this case, blood gas analysis revealed that metabolic acidosis developed with lactate elevation. No response to advanced cardiac life support theraphy that was received, hypotension

and bradycardia continued, and there was a consciousness change and a decrease in GCS, which was thought to be due to decreased cerebral perfusion.

There are two hypotheses related to the ILE mechanism. In 1998, Weinberg et al. argued that the ILE formed a separate compartment for drugs after being intravenously injected. This mechanism is referred to as the Lipid Sink Theory and is still considered the most valid opinion[5]. Ion Channel Theory is an alternative theory that was put forward in the following years. In these studies, it was claimed that ILE increased myocardial energy substrates and high-energy phosphate content in the heart, or triglyceride levels increased the calcium level through calcium ion channels in cardiomyocytes[11]. Sirianni (2008) was the one clinically using lipid emulsions on a 17-year-old girl in whom cardiac arrest developed after taking bupropion and lamotrigine and no response to advanced cardiac life support therapy was received. She was treated successfully with ILE therapy [7]. Reported ILE treatment in pediatric age group is relatively small. Hendron et al. successfully used the ILE therapy on a 20-month-old girl who took high-dose tricyclic antidepressant, was unresponsive to standard treatment, and had resistant convulsions and ventricular tachycardia. She had no complication and was discharged on the 3rd day without sequelae[12]. Levine et al. applied ILE therapy in addition to standard treatment to a 13-year-old female patient who took high-dose amitriptyline, developed seizure, and then ventricular tachycardia and arrest. She was discharged on the 28th day without sequelae[13]. Our patient who developed severe hypotension and bradycardia after taking high dose verapamil and was non-responsive to standard treatment was successfully treated with ILE therapy, and cardiac functions improved. She was discharged on the 4th day of follow-up without sequelae.

Despite the widespread use of ILE, no standard dose proposal is available. There are different opinions about the subject: some publications suggest infusion after the dose to be given as bolus; while others suggest only low-dose and relatively long-standing infusions[14, 15]. In pediatric age group intoxication, the same indications as the adult and the same treatment doses are recommended as a treatment. In this case, 1.5 mL / kg of 20% lipid emulsion was applied as iv bolus for 1 minute followed by 0.25 mL / kg / min for 30 minutes infusion.

The most important and frequent problem caused by the use of ILE as an antidote is that excessive amounts of triglyceride prevents serum laboratory analysis and causes allergic reaction, acute lung injury, pancreatitis, and venous thromboembolism. Levine et al.[13] reported a case of pancreatitis after ILE. Nonetheless, there was no complication after ILE application in our case.

In conclusion, the use of intravenous lipid emulsion therapy for lipophilic drug intoxication has become an increasingly popular in recent years. In pediatric age group intoxication, the same indications as the adult and the same treatment doses are recommended as a treatment. Clinicians should be aware of these treatment indications, treatment doses, possible complications and side effects, and should consider ILE treatment as an alternative treatment method in cases that do not respond to standard treatments.

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