CASE REPORT

Lipid Rescue Therapy and High-Dose Insulin Euglycemic Therapy are Effective for Severe Refractory Calcium Channel Blocker Overdose: Case Report and Review of Literature

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Abstract

Background: High-Dose Insulin Euglycemic Therapy (HIET) and Lipid Rescue Therapy (LRT) are new alternative treatments for acute poisoning with calcium channel blockers. In this report a severely poisoned patient with verapamil and furosemide who was successfully treated with these two treatments is presented.

Case report: A 27-year-old woman was brought to “Mother Theresa” Clinical Center in Skopje with a history of consumption of 24 grams (100 pills) sustained-release verapamil and 4 grams (10 pills) furosemide. She was alert and oriented with 60/35 mmHg blood pressure (BP), her respiratory rate was 25 breaths/min and heart rate was 40 beats/min with first degree atrioventricular (AV) block on electrocardiogram (ECG). In the first 90 minutes, she received activated charcoal, 1 liter of 0.9% saline, 60 mL of calcium chloride (CaCl₂), 40 mg potassium and subsequently dopamine and 100 mg noradrenaline. However, there was no significant improvement in her hemodynamic status (BP = 70/50 mmHg) and she developed second degree AV block. Temporary pace maker was implanted. In the next one hour, the patient had stable vital signs, when she again became hypotensive (BP = 60/35 mmHg) with prolonged QRS complex (20 msec). During this period she was treated with epinephrine (9mg), atropine (2mg), isoprenalin, bicarbonate, CaCl₂ and intravenous fluid. Unsuccessful conventional treatments indicated administration of HIET and LRT. Three hours later, the BP was normalized (110/75mm) and 36 hours later, all ECG disturbances disappeared. She left the Clinic without any sequels, four days later.

Conclusion: LRT in addition to HIET are effective treatments for CCB overdose. LRT can be considered as a standard treatment for CCB overdose. Nevertheless, further investigations are necessary to establish the real value of these treatments.

Keywords: Calcium Channel Blockers; Intravenous Fat Emulsions; Poisoning; Verapamil

INTRODUCTION

Calcium channel blocker (CCB) overdose is emerging as one of the most common causes of prescription drug-related fatalities (1). The use of CCBs as an antihypertensive treatment is increasing worldwide (2,3), leading to a parallel increase in potential CCB overdoses. Calcium channel blockers and beta-blockers (BB) account for approximately 40% of cardiovascular drug exposures reported to the American Association of Poison Centers (1). However, these drugs are responsible for more than 65% of deaths from cardiovascular medications (4). Acute suicidal poisonings with CCBs are common in Macedonia, with more than 7.5% of all suicidal poisonings. In more than 35% of these poisonings, verapamil is the only, or one of the medications (5).

Common clinical manifestations of CCB overdose are nausea and vomiting, hypotension and bradycardia (6). A range of similar adverse effects have been reported in case reports, but death and life threatening complications such as heart block and refractory hypotension are much more common with verapamil than diltiazem (7). Recommended treatments for CCB poisoned patients include gastrointestinal decontamination, bicarbonate, calcium chloride, vasopressors, glucagon and high-dose insulin euglycemic therapy (HIET) (6). Nevertheless, some scientists proposed administration of lipid rescue therapy (LRT) as an alternative treatment for severely CCB poisoned patients (8).

We report a severely poisoned patient with verapamil and furosemide, who was successfully treated with HIET and LRT.

CASE REPORT

A 27-year-old woman (55 kg, 165 cm) was brought to “Mother Theresa” Clinical Center in Skopje with a history of consumption of 24 grams (100 pills) sustained-release verapamil and 4 grams (10 pills) furosemide 4 hours earlier, in a suicidal attempt. She was alert and oriented, while her blood pressure (BP) was 60/35 mmHg, heart rate was 40 beats/min with first degree atrioventricular (AV) block on ECG, and respiratory rate was 25 breaths/min. In the first 90 minutes, she received activated charcoal, 1 liter of 0.9% saline, 60 mL of calcium chloride (CaCl₂), 40 mg potassium and subsequently dopamine and 100 mg noradrenaline. However, there was no significant improvement in her hemodynamic status (BP = 70/50 mmHg), and she...
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Conventional treatments for CCB overdose include supportive care, gastrointestinal decontamination, calcium salts, glucagon, HIET and vasopressors including dopamine, dobutamine and norepinephrine (6,9). Most of these treatments are intended to increase trans-membrane calcium flow (calcium salts) or increase of cyclic adenosine monophosphate (cAMP) concentration by stimulating production of adenylate cyclase (with norepinephrine and glucagon), or by inhibiting production of phosphodiesterase (with amrinone and milrinone) (9). However, the conventional treatments may be unsuccessful in reversing the cardiovascular toxicity of CCBs and they commonly fail to improve the hemodynamic condition of the patient (8,9).

Blockade of the L-type calcium channels that mediate the antihypertensive effect of CCBs also decreases the release of insulin from pancreatic β-islet cells and reduces glucose uptake by tissues (insulin resistance) (10). These, in turn, may be the most important factors in CCB-mediated attenuation of cardiac inotropism and peripheral vascular resistance (10). By targeting this insulin-mediated pathway, HIET appears to have a beneficial role, and its clinical potential is under-recognized in the management of severe CCB toxicity (10).

Another alternative treatment which has been recommended and found to be effective is LRT (8,11-14). The predominant theory for its mechanism of action is that by creating an expanded intravascular lipid phase, equilibria are established that can drive the offending drug from target tissues into the newly formed 'lipid sink' (11). Based on this hypothesis, lipid emulsion has been considered as a candidate for reversal of toxicity caused by overdose of any lipophilic drug (11).

LRT in addition to HIET are effective treatments for CCB overdose. LRT can be considered as a standard treatment for CCB overdose. Nevertheless, further investigations are necessary to establish the real value of these treatments.

All hemodynamic and cardiac conduction disturbances disappeared in next 48 hours. BP was 110/75 mmHg 3 hours later and normal ECG was noted 36 hours after LRT. No further disturbances or any recurrence were noted during the next four days, when she left the hospital without any sequel.

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REFERENCES


