Case Report

The use of extracorporeal life support in adolescent amlodipine overdose

Elizabeth A. Persad, Lakshmi Raman, Marita T. Thompson, Paul W. Sheeran

Abstract

Calcium channel blocker (CCB) toxicity is associated with refractory hypotension and can be fatal. A 13 year old young woman presented to the emergency department(ED) six hours after an intentional overdose of amlodipine, barbiturates, and alcohol. She remained extremely hypotensive despite the administration of normal saline and calcium chloride and despite infusions of norepinephrine, epinephrine, insulin, and dextrose. Due to increasing evidence of end organ dysfunction, Extracorporeal Life Support (ECLS) was initiated 9 hours after presentation to the ED. The patient's blood pressure and end organ function immediately improved after cannulation. She was successfully decannulated after 57 hours of ECLS and was neurologically intact. Patients with calcium channel blocker overdose who are resistant to medical interventions may respond favorably to early ECLS.

Keywords: Amlodipine overdose, calcium channel blocker, extra corporeal life support.

Access this article online
Website: www.ijccm.org
DOI: 10.4103/0972-5229.106502
Quick Response Code:

Introduction

Calcium channel blocker (CCB) toxicity is associated with refractory hypotension and myocardial depression which can be fatal. Amlodipine is a dihydropyridine CCB that inhibits calcium entry into slow L-type calcium channels in vascular smooth muscle, the myocardium, and pancreatic beta cells. The hemodynamic consequences of CCB toxicity are peripheral vasodilation, decreased contractility, and bradycardia.[1] Suppression of insulin release from the pancreas leads to hyperglycemia and to decreased free fatty acid utilization by the myocardium.

CCB's undergo extensive first pass metabolism and 90% of the parent drug is metabolized in the liver. Amlodipine is 95% protein bound and so cannot be dialyzed. In therapeutic concentrations, amlodipine has a half-life of 30 – 50hrs. After CCB overdose, however, hepatic enzymes become saturated and so the half-life of amlodipine can be even longer.

From:
University of Texas Southwestern, Dallas, Texas, USA

Correspondence:
Dr. Elizabeth A Persad, Department of Pediatrics, Division of Critical Care, Mail Code 9063, University of Texas Southwestern, 5323 Harry Hines Blvd, Dallas, TX 75390 USA. Email: elizabeth.persad@utsouthwestern.edu

Case Report

A thirteen year old, 61kg young woman intentionally ingested thirty 10 mg tablets of amlodipine, six bottles of beer, and an unknown quantity of barbiturates. She presented to the Emergency Department (ED) six hours after the ingestion complaining of tiredness and increased heart rate. She had a blood pressure of 73/34 (mean 47) mmHg, heart rate of 103/min, and respiratory rate of 16/minute. Her blood pressure did not improve despite the administration of multiple boluses of normal saline, two grams of calcium chloride, and infusion of norepinephrine (0.1 mcg/kg/min). The urine toxicology screen was positive for butalbital and caffeine. The serum alcohol concentration was 0.2 g/dL. The patient was transferred to the pediatric intensive care unit (PICU). On admission to the PICU she was hypotensive and drowsy, but would awaken and respond to questions. She had nausea and vomiting. During the first 3 hrs following admission to PICU, the patient had worsening metabolic and lactic acidosis [Table 1], increased creatinine concentration, oliguria, and decreased mental status. The local Poison Control was consulted. Another gram of calcium chloride was administered. The norepinephrine infusion was increased (0.4 mcg/kg/min) and epinephrine infusion (0.1 mcg/kg/min) was added. Insulin (0.1 unit/kg/hour) and dextrose (D12.5 at 100 cc/hr) were then infused.

Table 1: Laboratory results

Lab parameter	ICU admission	Pre-ECLS*	12 hrs after ECLS
Lactate (mmol/L)	4.3	9.0	2.7
pH	7.32	7.26	7.34
pCO_2 (mmHg)	25	21	36
PaO_2 (mmHg)	107	127	92
Base excess (mEq/L)	-11	-18	-4.8
BUN (mg/dL)	10	11	9*
Creatinine (mg/dL)	1.0	1.1	0.7*
Glucose (mg/dL)	161	207	130

Pre-ECLS: three hours after ICU admission

Due to evidence of decreased end organ perfusion and persistent refractory hypotension, which was expected to last at least 48 hrs after the ingestion of amlodipine, the patient was electively placed on veno-arterial extracorporeal life support (VA ECLS) 15 hrs after the ingestion and 9 hrs after presentation to the ED. The patient was induced with fentanyl 10 mcg/kg IV, paralyzed with rocuronium and intubated A 17 French (Fr) arterial cannula was placed in the right femoral artery. A 12 Fr arterial cannula was placed distal to this site to maintain perfusion to the right lower extremity. A Goretex graft was used during the insertion of the arterial cannulas to facilitate subsequent decannulation. A 21 Fr venous cannula was inserted in the left femoral vein. ECLS flow was initiated slowly and increased to 70 cc/kg/min as tolerated. Heparin was infused to maintain the activated clotting time 160-180 seconds.

Over the subsequent 24 hrs, the epinephrine and norepinephrine infusions were weaned off. The serum lactate and creatinine declined [Table 1]. The patient was alert and followed commands. The ECLS flows were decreased and the patient was successfully decannulated after 57 hrs on ECLS. She was extubated later that day and was neurologically intact. She was discharged from the PICU to an inpatient psychiatric unit two days later.

Discussion

The cardiovascular symptoms of CCB overdose are hypotension, due to peripheral vasodilation, myocardial depression, and bradycardia. Intentional CCB overdose is often exacerbated by the ingestion of other drugs, e.g., tricyclic antidepressants, or β- blockers, which exacerbate CCB toxicity. In the case presented, the co-ingestion of barbiturates contributed to the patient's hypotension.

Treatment of CCB overdose includes initial stabilization and resuscitation. Gastric decontamination with activated charcoal and polyethylene glycol is indicated if the patient presents within two hours of ingestion or if a delayed release preparation has been ingested,[2] Supportive therapy initially includes the administration of IV crystalloid. Patients often require one or more vasoactive agents for hemodynamic support. Dopamine, Epinephrine, and Norepinephrine may be administered. The antidote for CCB overdose is IV calcium chloride (20 mg/kg, up to 1 gram) or IV calcium gluconate (50 mg/kg, up to 1 gram) in an attempt to increase circulating calcium and overcome blockade of calcium channels.

Insulin administration may ameliorate the effects of CCB overdose. Insulin resistance occurs after CCB overdose and decreases intracellular glucose stores and increases fatty acid oxidation. Insulin activates calcium and potassium channels and increases intracellular ATP, which improves myocardial contractility, and inhibits the release of pro-inflammatory mediators.[3] In our patient, there was no hemodynamic improvement within two hours of starting insulin therefore the patient was placed on ECLS.

Glucagon has been used to treat CCB overdose, although this is an unlabelled use of the medication. Glucagon bolus followed by an infusion has been used with favorable response by Doyon *et al* and helps to improve the metabolism of cardiac myocytes and thus improves contractility.[4]

Levosimendan is a relatively new inotropic agent that may be beneficial in CCB overdose. Levosimendan sensitizes myocytes to calcium by binding to troponin C and increasing the availability of calcium to actin and myosin fibers. Cardiac contractility is increased. Varpula *et al*, reported the administration of levosimendan in two patients with CCB toxicity and refractory hypotension. Both patients had in improvement in their mean arterial pressure within 60 to 90 minutes and were weaned off inotropic support within 12 hours.[5]

ECLS has been reported twice in cases of refractory CCB overdose, once due to diltiazem overdose and once due to verapamil and propranolol overdose.[6,7] Both cases involved 16 yr old females with CCB overdoses who were emergently cannulated onto ECLS due to cardiac arrest and subsequently decannulated with no evidence of neurologic deficit. The patient outlined in this report was electively cannulated and subsequently decannulated in less than 72 hrs. Elective cannulation possibly resulted in decreased ICU and hospital Length of stay. Our patient also had no deficits after decannulation. ECLS is useful because it restores end organ perfusion and allows metabolism and excretion of the CCB.

Conclusion

CCB overdose is associated with profound refractory hypotension and can be lethal. Treatment is primarily supportive via the use of IV fluids and inotropes. Experimental therapies such as the administration of glucagon, insulin and levosimendan, have also been reported. ECLS may be indicated if a patient with CCB overdose continues to have refractory and severe hypotension despite conventional and experimental therapies.

References

1. Lexicomp-toxicology [Internet] Calcium channel blockers. Available from: http://www.erlonline.com. [last accessed on 2010 Sep 10].
2. Salhanick SD, Shannon MW. Management of calcium channel antagonist overdose. Drug Safety 2003;26:65-79.
3. Shephard G, Klein-Schwartz W. High dose insulin therapy for calcium channel blocker overdose. Ann Pharmacother 2005;39:923-30.
4. Doyon S, Roberts JR. Use of glucagon in a case of calcium channel blocker overdose. Ann Emerg Med 1993;22:1229-33.
5. Varpula T, Rapola J, Sallisalmi M, Kurola J. Treatment of serious calcium channel blocker overdose with Levosimendan, a calcium sensitizer. Anesth Anal 2009;108:790-2.
6. Kolcz J, Pietrzyk J, Januszewska K, Procelewska M, Mroczek T, Malec E. Extarcorporeal Life support in severe propranolol and verapamil intoxication. J Intensive Care Med 2007;22:381-4.
7. Durward A, Guerguerian A, Lefebvre M, Shemie SD. Massive diltiazem overdose treated with Extracorporeal Membrane Oxygenation. Pediatr Crit Care Med 2003;4:372-6.

How to cite this article: Persad EA, Raman L, Thompson MT, Sheeran PW. The use of extracorporeal life support in adolescent amlodipine overdose. Indian J Crit Care Med 2012;16:204-6.

Source of Support: Nil, **Conflict of Interest:** None declared.