Case Report

Successful treatment of refractory hypotension, noncardiogenic pulmonary edema and acute kidney injury after an overdose of amlodipine

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Abstract

Treatment of patients with amlodipine overdose remains challenging. We describe a case of successful treatment of refractory hypotension, noncardiogenic pulmonary edema and acute kidney injury after an intoxication with 250 mg of amlodipine. Marked improvement in all hemodynamic parameters was noted with combination of fluids, inotropes, low-dose calcium, low dose insulin, mechanical ventilation and hemodialysis. All available information on overdose of amlodipine is limited to case reports and series. Prospective trial on the use of these agents is required to define its role as the first-line treatment in amlodipine, a calcium channel blockers overdose.

Keywords: Amlodipine overdose, calcium, insulin, refractory hypotension

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Introduction

Calcium channel blockers (CCB) are leading cause of cardiovascular drug overdose and are responsible for 48% of deaths related to cardiovascular drug exposure.[1] Amlodipine is a dihydropyridine group of CCB having half life of 30-50 hours and a large volume of distribution (21L/kg).[1] Hemofiltration and dialysis may not be of help in CCB overdose because of high protein binding, extensive tissue distribution and rapid rate of metabolism of CCB.[2] Reports of CCB overdose are scarce in Indian literature.[3] We report a case of amlodipine overdose with non-cardiogenic pulmonary edema requiring hemodialysis due to acute kidney injury from profound hypotension.

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Case Report

A 28-year-old female with no past medical or psychiatric illness was brought with h/o suicidal ingestion of 50 tablets of Amlodipine (5 mg) expand almost 48 hours after ingestion. She received gastric lavage, intravenous (IV) fluids, dopamine and dexamethasone for BP of 70/50 mm of Hg, at a local hospital. She was transferred to our ICU for renal failure and hypotension. She complained of dizziness, cough with white sputum. On examination she was conscious but lethargic, pale with cold clammy extremities. Her pulse rate was 130/min, thready, regular and blood pressure was 80/60 mm of Hg (lying) and 70/50 mm of Hg (sitting). Her respiratory rate was 30/minute and JVP was normal. She was afebrile and had no cyanosis.

Investigations revealed hemoglobin 10.3 gm/dl, WBC 25,300/cmm with 88% neutrophils. Her liver function tests, calcium (1.1 mmol/L) and phosphorus (4.5 mg/dL) were normal. The glucose level was 128 mg/dL, creatinine was 3.2 mg\dl, and blood urea, 90 mg\dl. ECG showed sinus tachycardia with normal QRS interval and QTc 0.440 msec. Arterial blood gas (ABG)

showed PaO_2 48 mm of Hg, PCO_2 34 mm of Hg, pH 7.3 and bicarbonate 20 mmol/L, and oxygen saturation of 80%. X-ray chest (XRC) showed bilateral fluffy shadows without cardiomegaly. Portable echocardiogram revealed normal chamber size with normal LV function. Her central venous pressure (CVP) was 10 cm. Acute respiratory distress syndrome (ARDS) was diagnosed with the triad of an acute onset respiratory distress, bilateral pulmonary infiltrates on X-ray chest, and severe hypoxemia (PaO_2/FiO_2 ratio < 200) with no evidence of increased left atrial pressure (normal 2DECHO and CVP 10). Serum lactate level was 6.1 mmol/L (Normal reference range – 0.5 to 2.0 mmol/L). Her sputum culture and blood cultures were sterile. Intravenous normal saline with CVP monitoring and dopamine (10 μg/kg/min) were started and increased when the patient remained hypotensive despite an increase in the initial dopamine, norepinephrine infusion was initiated. Her tachycardia and tachypnea worsened and she had developed crepitations in scapular and infrascapular areas. She received oxygen, furosemide and broad spectrum antibiotics. Repeat ABG revealed worsening hypoxia on high flow oxygen mask (10L/min). Repeat XRC [Figure 1] showed typical batswing appearance without cardiomegaly. She was intubated under sedation and ventilated (initial settings, ACMV mode, FiO_2 =1.0, tidal volume 6-8 ml/kg, PEEP 5 cm H_2O rate 15/min) by intensivist. She received simultaneous infusion of 4 inotropes [dopamine (10-20 μ/kg/min), dobutamine (10-20 μ/kg/min), norepinephrine (10 μ/kg/min) and vasopressin (0.01–0.05 IU per min)] to maintain BP of 110/70 mm of Hg. In view of worsening oliguria, metabolic acidosis on repeat ABG, hyperkalemia (6.7 mEq/L) and fluid overload, hemodialysis was initiated and not just for therapeutic removal of amlodipine. She received sustained low efficiency dialysis (SLED) three times in 2 days, each time 8 hours with blood flow, 150 mL/min and dialysate flow, 250 mL/min. She received calcium gluconate 10%, 10 mL over 5-10 minutes and repeated boluses every 15 minutes, for a total of four doses, followed by an infusion of 5 mL/h with serum calcium ranging 1.2-1.95 mmol/L without any adverse events and normal ECG. Her BP was maintained 110/70 mm of Hg on 4 inotropes at maximum doses. She received glucagon (5 mg bolus and then 5 mg/hour for 3 hours) for worsening hypotension but that did not alter her hemodynamic status significantly. Glucagon was stopped because of lack of sustained significant hemodynamic improvement and its high cost. Dextrose–insulin infusion was initiated 12 hours after admission for worsening hypotension. She received 10 IU insulin IV bolus followed by an continuous infusion of 10 IU insulin in 100 mL 25% dextrose over 2-4 hour with careful monitor to avoid hypoglycemia and hypokalemia, BP increased to 130/80 mm of Hg and later urine output increased to 100 mL/h, allowing gradual discontinuation of inotropes. She was extubated on third day, inotropes were stopped on fourth day, and insulin-dextrose infusion was stopped on sixth day, her CXR showed complete clearance on eighth day. She improved gradually. She was discharged in good health after psychiatric consultation.

Discussion

Our patient presented late to us, hence we did not do the gastrointestinal decontamination. Whole-bowel irrigation with polyethylene glycol along with activated charcoal was not effective in a patient who had treatment approximately 24 hours after CCB overdosel.[4] Our patient had refractory hypotension without cardiac conduction defects. Dihydropyridine CCBs have predominant effect on vascular smooth muscle cells with little effect on cardiac pacemaker cells or contractility.[5] Although non-cardiogenic pulmonary edema has been reported with other CCB overdose, it has been rarely reported with amlodipine.[6] Precapillary vasodilatation resulting in excessive pulmonary capillary transudation was suggested as the possible mechanism of non-cardiogenic pulmonary edema by Humbert *et al*.[7] CCB overdose is frequently complicated by renal failure, related to severe hypoperfusion and end-organ ischemia.[1] Similarly our patient had acute kidney injury from persistent hypotension and needed hemodialysis.

Efficacy of calcium in improving conduction, contractility and hypotension has varied. Treatment with calcium was successful in some patients with CCB overdose but had transient or no effects in others.[8] The optimum dosage of antidote, that is, intravenous calcium remains unclear.[8] Kenny *et al* has suggested 10 mL of 10% calcium chloride or 20-30 mL of calcium gluconate IV and depending on clinical response to be repeated 15-20 minutes up to four doses with monitoring of serum calcium.[2] We used low-dose calcium without adverse effects. It remains unclear which sympathomimetic agent is better for CCB poisoning.[9] We had to use a combination of sympathomimetics. Animal studies have demonstrated benefit of glucagon in CCB toxicity.[10]

Several case reports describe beneficial effect of treatment with hyperinsulinemic euglycemia in CCB overdose.[11-13] Insulin increases plasma levels of ionized calcium, improves the hyperglycemic acidotic state, improves myocardial utilization of carbohydrates and exerts its own independent

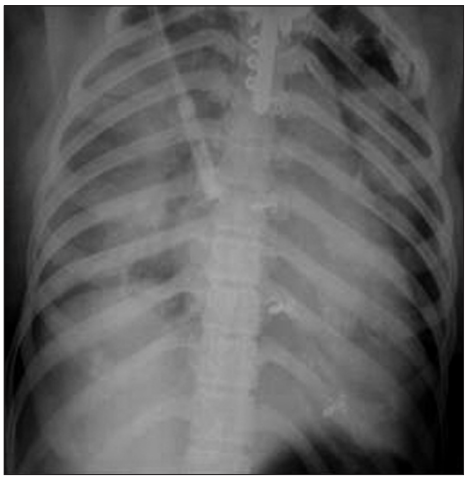

Figure 1: X-ray chest anteroposterior view showing pulmonary edema

inotropic effect.[8] Insulin was usually started after failure of treatment with calcium, glucagon and vasopressors. Marked improvement in all hemodynamic parameters was noted with low-dose insulin infusion (1-2IU/hour).[11] The dose and duration of dextrose-insulin therapy used in the reported cases varied, ranging from 0.1 to 1.0 U/kg per hour, with duration of 6-96 hours.[8,11-13] Due to the conflicting reports of efficacy and no standardization of dosage of calcium, and dextrose-insulin infusion, we used them in low doses to avoid the iatrogenic side effects like hypoglycemia, hypokalemia in dextrose-insulin therapy and hypercalcemia in calcium infusion.

Conclusions

Amlodipine overdose though near fatal, presenting with non-cardiogenic pulmonary edema, refractory shock leading to acute kidney injury requiring dialysis support, was salvaged effectively with combination of inotropes, low-dose calcium, low-dose insulin, mechanical ventilation and hemodialysis.

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