Near-Fatal Amlodipine Poisoning

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Abstract
Amlodipine poisoning is very rare and only few cases have been reported in English literature. We report here a case of severe amlodipine poisoning with non-cardiogenic pulmonary edema.

INTRODUCTION
Calcium channel blockers (CCB) are the leading cause of overdose death among all cardiovascular medicines. Clinical toxicity of calcium channel blockers usually begins within 30-60 minutes of ingestion of an overdose of 5-10 times the therapeutic dose. It may be delayed in sustained release (SR) preparations. Complications like hypotension, pulmonary oedema both cardiogenic and non-cardiogenic, conduction blocks are responsible for major morbidity. Central nervous effects like drowsiness, confusion, and rarely seizures may be seen.

Metabolic acidosis and hyperglycemia are the rare metabolic abnormalities. Serum calcium is usually normal. Amlodipine is a newer dihydropyridine CCB with half-life of 30-58 hours, several times longer than other CCB.

CASE REPORT
A 20 years male student with no past medical or psychiatric illness was brought with h/o suicidal ingestion of 40 tablets of Amlodipine (10 mg) almost 10 hours after ingestion. He had received gastric lavage at a local hospital four hours after ingestion. The BP recorded there was 70/50 mm of Hg. He was administered dexamethasone, dopamine, mephentine and was referred to our hospital. While being shifted, he had vomited and developed upper abdominal pain. There was no history of chest pain, palpitation, dyspnoea, cough, loss of consciousness or convulsions. On examination he was alert. His pulse rate was 108/min, thready. Blood pressure recorded on admission was 90/60 mm (lying) and 70/50 mm (standing), respiratory rate was 22/minute and JVP was normal. He was afebrile and had no cyanosis. Systemic examination was unremarkable. ECG showed sinus tachycardia with QRS interval 80 msec and QTc 0.430 msec. Chest X-ray (CXR) was normal. Arterial blood gas (ABG) showed paO2 95 mm of Hg, pCO2 33 mm Hg, pH 7.31, bicarbonate 22 mmol/L, oxygen saturation 99%. Investigations revealed normal haemoglobin, counts of 15,300/cmm with 88% neutrophils and normal ESR. His liver function tests, renal functions, calcium and phosphorus were normal. Portable echocardiogram facility was not available to us. Gastric lavage was given. IV fluids and dopamine at 10 µg/kg/min were started. 10% calcium gluconate 10 ml was given intravenously. His BP was maintained on inotropes. Next day he developed cough with white sputum and was febrile. His tachycardia and tachypnoea worsened and had developed crepitations in infra-axillary and infra-scapular area. ABG revealed type 1 respiratory failure. CXR showed bilateral fluffy shadows without cardiomegaly. Repeat counts showed WBC count of 19,600/cmm with 94% neutrophils. He was given oxygen, furosemide and broad-spectrum antibiotics. He continued to worsen had pink frothy sputum, with increasing hypoxia and required mechanical ventilation. Repeat CXR on day 3 showed typical batwing appearance without cardiomegaly (Fig. 1). Central venous pressure was 16 mm of Hg, however

Fig. 1 : X-ray chest posteroanterior view showing batwing appearance without cardiomegaly
pulmonary capillary pressure measurement could not be done. A probable diagnosis of non-cardiogenic pulmonary oedema was made. He was continued on inotropes, furosemide, and intermittent calcium gluconate with broad-spectrum antibiotic. His sputum culture and blood cultures were sterile. He improved gradually over the next four days; inotropes were stopped and was extubated on Day 8. His CXR showed complete clearance. He was discharged in good health after psychiatric consultation.

**DISCUSSION**

Treatment of calcium channel blockers overdose involves gastrointestinal decontamination in the form of gastric lavage with activated charcoal and in slow release (SR) preparations total gut lavage with polyethylene glycol. The specific antidote is calcium gluconate or chloride. 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. Continuous calcium infusion of Ca chloride 0.2 ml/kg/hr is another option. However, Buckley et al recommend higher doses to overcome the competitive blockade with ECG monitoring rather than serum calcium levels. Maximum dose used by him was 30 g over 12 hours, and highest serum calcium level was 23.8 mg/dl without any adverse events. Glucagon 5-10 mg IV is another inotropic drug. Insulin has been found to be a very good inotrope in CCB poisonings and hyperinsulinemia euglycemia technique has been used with remarkable success recently. Other inotropes like dopamine, dobutamine, adrenaline, isoprenaline, amrinone are used as adjuncts. Cardiac pacing in third degree heart blocks and intraaortic balloon pump are useful in refractory cases. Newer agents like 4-aminopyridine, extracorporeal membrane oxygenation, partial liquid ventilation have been tried. Extracorporeal removal techniques are not helpful.

There are few cases of amlodipine poisoning reported in the English literature. A case of inadvertent ingestion of 100 mg of amlodipine with haemodynamic abnormality lasting for 10 days was treated with calcium, glucagon and vasoactive medicines which the patient survived but succumbed to other complication of intensive care. In another case of survival the dose ingested was small being 50-100 mg. Fatality is reported due to irreversible shock with 70 mg of amlodipine plus an unknown amount of oxazepam. In another case with combination of amlodipine ingestion of 6.7 mg/kg with atenolol 33.3 mg/kg, and alprazolam 1 mg/kg with severe hypotension and third degree heart block, the authors had administered glucose-insulin infusion for 49 hours as an adjunct with very good result. Hyperinsulinemia euglycemia therapy with 0.5 IU/kg/hr of insulin has been shown to be very effective for hypotension in another case of amlodipine poisoning with ingested dose of 30 mg. As our patient came almost 10 hours after ingestion the valuable observations of initial few hours were not possible, including early charcoal administration. Though non-cardiogenic pulmonary oedema has been reported with other calcium channel blocker overdose, it has not been reported with amlodipine. We suppose our patient had non-cardiogenic pulmonary oedema as he had no cardiomegaly with batwing appearance on chest X-ray, although we could not prove the same with echocardiography and pulmonary capillary pressures. The echocardiography was not done before discharge, as we did not expect to find any abnormality when he was stable. The leukocytosis which was present initially which further increased has been just our observation, which has not been found in other reports of CCB overdose excepting in one case. We conclude that by aggressive early decontamination, calcium, insulin and other supportive measures like inotropes and ventilation we can successfully treat amlodipine overdose, though it is a therapeutic challenge.

**REFERENCES**