

# Shock due to amlodipine overdose

Vimal Upreti, V. R. Ratheesh<sup>1</sup>, Pawan Dhull<sup>2</sup>, Ajay Handa<sup>3</sup>

## Abstract

Amlodipine is a commonly prescribed calcium channel blocker. Its toxicity is the leading cause of drug overdose seen in the practice of cardiovascular medicine. It can lead to profound hypotension and shock. Management involves early and aggressive supportive measures and calcium infusion in large doses to overcome competitive blockade. We report one such case that presented with amlodipine overdose and was successfully managed.

**Keywords:** Amlodipine, calcium channel blocker, hypotension

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## Introduction

Calcium channel blockers (CCB) are a leading cause (48%) of mortality resulting from drug overdose seen in cardiovascular medicine,<sup>[1]</sup> and amlodipine is a commonly prescribed long-acting CCB. A patient with amlodipine overdose may have profound refractory hypotension,<sup>[1]</sup> leading to tissue hypoperfusion and target organ damage. Its treatment involves aggressive supportive measures.<sup>[2]</sup> We present one such case of amlodipine overdose with a successful outcome.

## Case Report

A 28-years-old woman, with no significant past history, presented with giddiness, abdominal pain, vomiting, breathlessness, and reduced urine output 12 hours after consuming 50 tablets of amlodipine [of 5 mg strength]. She was rushed to a hospital near her home, found to have hypotension with hypoxemia; was intubated, given gastric lavage, inotropic support and 24 hours later, shifted to our hospital. At presentation she was found to have blood pressure (BP): 60/40 mmHg, heart rate: 128/min, respiratory rate: 32/min with spO<sub>2</sub>

on room air: 85%, raised central venous pressure [22 cm of saline], anasarca and crepitations in both interscapular area. She was admitted to the intensive care unit (ICU). Investigations revealed: Total leukocyte count: 18500/uL; neutrophils: 86%, serum creatinine: 1.8 mg/dl (normal range: 0.6-1.3 mg/dl), blood urea nitrogen 42 mg/dl (normal range: 10-20 mg/dl), and features of type -1 respiratory failure (pO<sub>2</sub>-48 mmHg, pCO<sub>2</sub>-26 mmHg, pH - 7.52, HCO<sub>3</sub>-22 mmHg). Ionized serum calcium (4.8 mg/dl; normal range: 4.6-5.6 mg/dl, serum albumin (3.9 mg/dl; range 3.5-5.5 mg/dl), and serum amylase (32 IU/L; range 18-108 IU/L) level at presentation were normal. X-ray of chest revealed bilateral reticulonodular opacities, upper lobar zone venous prominence, bilateral pleural effusion, and no cardiomegaly [Figure 1]. Her electrocardiogram was normal. Echocardiography revealed normal-sized chambers, valves, right and left atrial pressures, and left ventricular ejection fraction. Cultures of blood, urine, and tracheal aspirate were sterile. Intravenous inotropes were continued (dopamine: 10-15 µg/kg/min; noradrenaline: 10-12 µg/kg/min), systolic BP increased to 90-110 mmHg when iv frusemide was added. Two boluses of calcium gluconate were given (10 ml of 10% solution) 15 minutes apart, thereafter, low-dose infusion (at the rate 1 mg/kg of calcium) was started; ionized serum calcium level was maintained between 4.8-5.3 mg/dl. Thoracentesis was performed, 300 ml of exudative effusion (total count: 2800/cmm, leukocytes: 2400/cmm; predominantly lymphocytes; lactate

## From:

Department of Endocrinology, <sup>1</sup>Medicine, <sup>2</sup>Neurology, <sup>3</sup>Pulmonology, Command Hospital (Air Force), Bangalore, India

## Correspondence:

Dr. Vimal Upreti, Department of Medicine and Endocrinology, Command Hospital (Air Force), Bangalore - 560 007, India.  
E-mail: v\_upreti123@rediffmail.com



**Figure 1:** X-ray chest anteroposterior view showing pulmonary edema with bilateral pleural effusion

dehydrogenase – 698 U/L; protein – 3 g/dL) was drained from either side. She was ventilated initially invasively, later non-invasively; and empiric broad-spectrum antibiotics covering Gram-positive, Gram-negative organisms and *Pseudomonas aeruginosa* were started in view of prior hospitalization. Monitored parameters included clinical status, central venous pressure, urine output, fluid, and electrolytes including calcium levels and ECG every 4-6 hrs for first 48, thereafter every 12 hours. Her urine output improved after 24 hours. She was successfully weaned off ventilator after 48 hours; inotropes (noradrenaline after 18 hours, dopamine after 48 hours) and calcium infusion (after 48 hours) were gradually tapered off. She was shifted to a step-down ward from ICU after 72 hours and discharged after 5 days.

## Discussion

Calcium channel blockers [CCB] are one of the most widely used group of anti-hypertensive agents. Amlodipine is a dihydropyridines CCB with long half-life (30-58 hrs) and large volume of distribution (21 L/Kg).<sup>[2,3]</sup> Toxicity is seen in doses up to 5-10 times the therapeutic dose and sets within 30-60 minutes following ingestion.<sup>[2]</sup>

Our patient presented with giddiness caused by hypotension<sup>[2]</sup> attributable to generalized vasodilatation due to direct effect on vascular smooth muscle;<sup>[4]</sup> worsened by negative effect on the cardiac pacemaker and myocardial contractility.<sup>[1]</sup> Hyperglycemia due to reduced insulin release and lactic acidosis<sup>[5]</sup> seen in CCB overdose also contributes to reduced dromotropic effect. Abdominal pain and vomiting seen in our patient has been described<sup>[4]</sup> ascribed to reduced gastrointestinal motility and stasis of gastric contents. Oliguric renal

failure with features of fluid overload seen in our patient is well described;<sup>[2]</sup> and is attributable to prolonged hypotension and reduced effective circulatory volume.

An unusual finding in our case is bilateral exudative pleural effusion caused by amlodipine, that has not been reported earlier. We attribute this to capillary leak syndrome as a result of generalized vasodilatation. Several disorders may mimic systemic capillary leak syndrome [SCLS],<sup>[6]</sup> including severe sepsis, toxic shock syndrome, pancreatitis, ovarian hyperstimulation syndrome, anaphylaxis, and drug reactions including interleukin-2, granulocyte colony-stimulating factor, interferon alfa, gemcitabine, sirolimus, and acitretin. SCLS is an episodic disorder characterized by triad of hypotension, hemoconcentration, and hypoalbuminemia<sup>[6]</sup> associated with generalized edema, ascites, bilateral pleural effusion, pericardial effusion, cerebral edema, and encephalopathy. Exact mechanisms involved in pathogenesis are not clear, but it is believed to occur as a result of excess of vasodilators (histamine, prostaglandins, and bradykinins), proinflammatory cytokines (interleukin -6, tumor necrosis factor alpha), vascular endothelial growth factor, and altered immune response causing excess of CD25+ T cells.<sup>[6]</sup> SCLS is complicated by tissue hypoperfusion on the one hand and fluid overload due to overzealous fluid administration on the other. Other causes of secondary capillary leak were excluded by history and relevant investigations in our patient. The capillary leak syndrome, along with pleural effusions and acute lung injury attributable to the drug toxicity was complicated by renal failure and fluid overload.

Treatment includes supportive care including maintenance of airway, breathing, and circulation (ABCs). Hypotension is initially managed with volume loading; however, as our patient had signs of fluid overload, we did not continue to administer iv fluids. Inotropes (dopamine, norepinephrine, epinephrine) can be added<sup>[2,3]</sup> after normalization of CVP. Correction of acid-base disturbances and electrolyte abnormalities optimizes cardiac function. In refractory cases, glucagon (5-10 mg iv)<sup>[2,3]</sup> and hyperinsulinemic – euglycemia using dextrose and insulin infusion (with 0.5 IU/kg/hr) as inotropic agents;<sup>[7-9]</sup> cardiac pacing in third degree heart blocks, intra-aortic balloon pump are also reported to be useful.<sup>[2,3]</sup> Experimental modalities include extracorporeal membrane oxygenation and partial liquid ventilation.<sup>[2]</sup>

Gastric lavage with water or polyethylene glycol and activated charcoal (1 g/kg initially and to be continued for 24 through nasogastric tube) can be a useful

modalities, especially in long-acting preparations.<sup>[10]</sup> Gastric lavage can remove unabsorbed drug from the stomach for an extended time as CCB reduce gastric motility. Though definitive evidence of benefit of gastrointestinal decontamination in CCB overdose is lacking, it is still recommended due to potential lethal nature of CCB overdose and lack of specific antidote.<sup>[10]</sup> Cathartics may be added for gut decontamination.

Calcium gluconate or chloride in continuous infusion (Ca chloride 0.2 ml/kg/hr) or iv boluses (10 ml of 10% calcium chloride/20-30 ml of calcium gluconate, every 15-20 minutes; maximum: 30 g over 12 hours) is given to overcome the competitive blockade of calcium channels. We treated our patient with parenteral calcium and monitored with clinical response, ECG, and serum calcium levels.

The course of hospitalization was complicated by oliguric acute renal failure that was managed conservatively though renal replacement therapy may be needed.<sup>[9]</sup>

## Conclusion

Amlodipine overdose can be potentially fatal owing to non - cardiogenic pulmonary edema, refractory shock, and acute renal failure, and its management can be challenging. Outcome can be improved by early and

aggressive intensive care, inotropic support, calcium infusion and other supportive measures.

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