

# Survival Case Report of Adult with Severe Amlodipine Intoxication

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**Abstract:** *Amlodipine is a commonly prescribed calcium channel blocker (CCB), overdose of which results in profound shock and pulmonary edema [1]. A 40 years old male with severe Amlodipine toxicity presented with hypotension and pulmonary edema to our Hospital. Patient management involved early and aggressive supportive measures, calcium infusion in large doses to overcome competitive blockade and Insulin therapy for positive inotropic effect. A rise in Blood pressure was noted in 3 days and insulin infusion was stopped and patient was discharged after 10 days with psychiatric consultation. Positive inotropic effect of insulin therapy in our patient supports previous finding of its use as first line therapy in management of CCB overdose.*

**Keywords:** Amlodipine Toxicity, Calcium Channel Blocker, Insulin Infusion

## 1. Introduction

Amlodipine is dihydropyridine type of a Calcium channel blocker (CCB) used in the treatment of mainly hypertension, angina pectoris, cardiac arrhythmias, and other disorders. Amlodipine preferentially blocks the L - type calcium channels in the vasculature whereas non - dihydropyridines, such as verapamil and diltiazem selectively block L - type calcium channels in the myocardium. Thus amlodipine is potent vasodilator that has little negative effect upon cardiac contractility or conduction at standard doses.

Calcium channel blockers (CCB) are a leading cause (48%) of mortality resulting from drug overdose seen in cardiovascular medicine. Dihydropyridine intoxication generally results in arterial vasodilation and reflex tachycardia. However, as the dose is increased, this selectivity can be lost, and dihydropyridine CCBs may affect the myocardium and conducting system, resulting in decreased inotropy and bradycardia.

There are several cases of amlodipine overdoses reported worldwide with several of them having a lethal outcome. Here we report a survival case of 40 year old male patient in a severe amlodipine intoxication.

## 2. Case Report

A 40 years old male patient presented to Emergency room with complaints of 2 episodes of vomiting 7 hours after ingestion of 90 tablets of Amlodipine 5 mg (Total Dose 450 mg). On admission patient was conscious and oriented with Systolic Blood Pressure 80 mmHg. Other vitals including Pulse, Temperature and Respiratory rate were within normal range.

In the ER, patient received Gastric Lavage with activated Charcoal. He was started on IV Noradrenaline 4ml in 50 ml Normal Saline at rate of 8ml/hr, Normal saline at rate of 100ml/hr, Inj. Pantoprazole 40mg, Inj. Ondansetron 4ml and was transferred to Intensive Care Unit.

On Physical examination, The head and neck exams were unremarkable, The cardiac examination found normal heart

sounds without any murmurs, The lungs were clear to auscultation on admission but later developed crepitation, Abdominal examination was unremarkable and extremities showed no oedema or cyanosis. Hemogram showed white blood cell count of 15810/mm<sup>3</sup> with 85% Neutrophils, Haemoglobin 14.3 g/dl and Platelet count of 345000/mm<sup>3</sup>. Electrolytes value were unremarkable. LFT showed slightly increased direct bilirubin of 0.5 mg/dl with total bilirubin of 1.2 mg/dl and ALT 45 IU/L; Rest was unremarkable. RFT showed increase in S. Creatinine 1.73 mg/dl; Rest was unremarkable. Chest X - ray and ECG were unremarkable. Echocardiography was unremarkable.

Intravenous inotropes i. e. noradrenaline and dopamine were continued. Inj. Calcium gluconate was given at the rate of 10ml/hr for 2 days. Human insulin was started at the rate of 1 ml/hr intravenously which was increased upto 3ml/hr on third day. Inj. Potassium Chloride was given to replenish potassium. Broad spectrum antibiotic coverage is provided for first 5 days.

On 3rd day patient developed breathlessness and hypoxia. Upon investigation, he was diagnosed to have Pulmonary Edema for which he was treated with intravenous furosemide. Blood pressure was monitored every hour for 3 days and every 6 hourly thereafter. ECG, Arterial Blood Gas analysis and electrolytes were monitored daily.

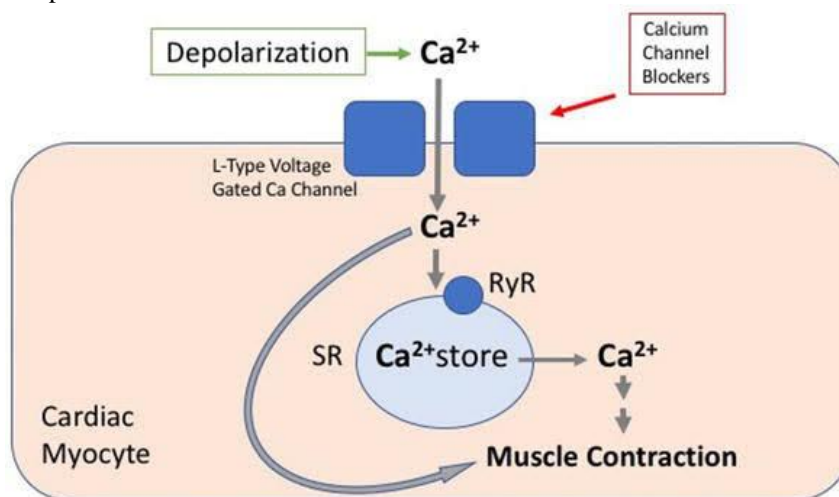
Patient started showing signs of clinical improvement and resolution of Acute Kidney Injury on Day 4. Inotropes and Insulin were gradually tapered off over a period of next 3 days. Patient recovered fully and was discharged after 10 days of hospital stay.

## 3. Discussion

Calcium channel blockers are one of the most commonly used group of anti - hypertensive agents. Amlodipine is a dihydropyridine type of CCB with long half - life (35 - 45hrs), large volume of distribution (21 L/Kg) and oral bioavailability of 60% - 75%. It is metabolised in Liver and excreted in urine.

Amlodipine primarily affects the smooth muscle in the arteries and due to its beneficial features, such as once - daily dosing and minimal effects on heart rate, amlodipine is commonly used in clinical practice.

Toxicity is seen in doses up to 5 - 10 times the therapeutic dose and sets within 30 - 60 minutes following ingestion.



The diagnosis of calcium channel blocker poisoning is made clinically on the basis of the history and clinical findings. Typically there is a history of overdose combined with hypotension. Dihydropyridines like Amlodipine intoxication results in arterial vasodilation and reflex tachycardia. This selectivity is lost when it is consumed at excessive doses, and the myocardium and conducting system gets disturbed, resulting in cardiac collapse and bradycardia that eventually results in Severe hypotension. [1, 2]

Although not present in our patient, ECG changes associated with CCB intoxication include PR interval prolongation and bradarrhythmias. In Amlodipine overdose, a finger stick blood glucose measurement may reveal hyperglycemia, caused by inhibition of calcium - mediated insulin release which in nondiabetic patient may help to distinguish CCB from beta blocker poisoning.

Amlodipine overdose treatment includes supportive care including maintenance of airway, breathing, and circulation (ABCs) with main focus on circulation. Hypotension can be profound and refractory even to maximal treatment with Intravenous (IV) fluids. Inotropes and vasopressors can be started among which norepinephrine is the initial vasopressor of choice as ideal vasopressor in CCB poisoning would be a direct - acting agent with positive inotropy, positive chronotropy, and vasoconstrictive effects. In patients who remain hypotensive at maximal doses of an initial vasopressor, a second vasopressor can be added. [3]

Gastrointestinal decontamination with gastric lavage and Activated charcoal has no definitive evidence of benefit of in CCB overdose but is recommended due to potential lethal nature of CCB overdose and lack of specific antidote. It can be a useful modalitie, especially in long - acting preparations as Gastric lavage can remove unabsorbed drug from the stomach for an extended time as CCBs reduce gastric motility. [4]

A high - dose continuous infusion of calcium has been used to overcome the competitive blockade of calcium channels. We treated our patient with parenteral calcium for 2 days

and monitored with clinical response, ECG, and serum calcium levels. [5, 6]

As per animal models and case reports High - dose insulin therapy has positive inotropic effects in patients with CCB toxicity. [7] Supplemental Dextrose is not given in all cases as CCB overdose often causes hyperglycemia. CCBs cause disruption of fatty acid metabolism and create relative insulin resistance within myocardium. Hyperinsulinemia - euglycemia therapy increases uptake of glucose in myocardial cells, cardiac contractility, and myocardial lactate oxidation. Calcium facilitates exocytosis of insulin from the beta - islet cells of the pancreas. CCBs also block the influx of calcium and prevent insulin release from the beta - islet cells of pancreas. High dose Insulin therapy can overcome carbohydrate dependence and relative insulin resistance in myocardium as well as overcome impaired insulin secretion from pancreas. [8]

Other treatment modalities that can be used include Glucagon which enhances calcium influx across the cardiac cell membrane and improves cardiac contractility, Methylene blue by reversing vasoplegia can help in Amlodipine poisoning and Lipid emulsion therapy. Invasive treatment like Extracorporeal membrane oxygenation (ECMO) and transvenous pacing should be used as last resort in patients with refractory cardiac arrest and multiorgan failure. ECMO has been demonstrated as effective in many reports. [9]

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