



Case Report

Management of Amlodipine overdose: A multi modal approach

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Abstract

Background

Calcium channel blockers (CCB) are among the first line medications recommended for the treatment of hypertension with amlodipine being a common choice [1]. Amlodipine is a dihydropyridine CCB with a primary vasodilatory effect on vascular smooth muscle cells via inhibition of calcium influx through L-gated calcium channels in cardiac and vascular smooth muscle cells [2]. Amlodipine overdose typically manifests as vasodilatory shock associated with reflex sinus tachycardia, metabolic acidosis, hyperglycemia, and pulmonary edema [3]. In contrast, non-dihydropyridine CCB medications such as verapamil and diltiazem have more direct effects on cardiac conduction and AV nodal activity, so overdose presents as bradycardia and heart block [2].

Among the cardiovascular drug overdose, the long-acting (30 -58 hours) Amlodipine overdose is very difficult to treat. They cause refractory hypotension demanding multi modal approach of critical treatment. Here we present a case of Amlodipine overdose, effectively managed in our ICU

Key words: Calcium channel blocker poisoning; CCB poisoning; Amlodipine overdose; Amlodipine toxicity; HIET; High dose Insulin; Glucagon; Intra lipid emulsion

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1. Case Presentation

A 43-year-old female, with no known comorbidities, consumed 25 tablets of Amlodipine 5 mg (total 125 mg) and 20 tablets of Vitamin B complex in an intentional overdose.

At the referring hospital, she underwent gastric lavage and had a central venous catheter (CVC) secured. Treatment was initiated with intravenous methylene blue, norepinephrine infusion at 20 ml/hour (55 mcg/min), and vasopressin infusion at 2 units/hour for profound hypotension, following which she was referred to our center for further management

On arrival to the Emergency Department, the patient was conscious and oriented, though she appeared drowsy and complained of giddiness. She was receiving ongoing

infusions of norepinephrine at 20 ml/hour and vasopressin at 2 units/hour at the time of presentation.

On examination, her vital signs revealed tachycardia with a pulse rate of 120/min and persistent hypotension with a blood pressure of 84/40 mmHg. She was tachypneic, with a respiratory rate of 26–28 breaths per minute, and hypoxemic, maintaining an SpO₂ of only 88% despite oxygen supplementation at 6 L/min via a simple face mask.

Her urine output was minimal and noted to be greenish in colour, likely attributable to Intravenous methylene blue treatment or the ingestion of vitamin B complex. Cardiovascular examination showed audible S1 and S2 with tachycardia, while respiratory examination revealed fine crepitations over bilateral basal lung zones, suggestive of pulmonary edema.

Her initial arterial blood gas (ABG) analysis revealed metabolic acidosis with pH 7.40, PaO₂ 67 mmHg, PaCO₂ 23 mmHg, bicarbonate 14.2 mmol/L, potassium 2.8 mmol/L, and lactate 1.1 mmol/L. Serial ABG monitoring was performed subsequently, which guided therapeutic interventions throughout her hospital stay

The patient's family was counselled about the anticipated risk of refractory hypotension associated with amlodipine overdose. In view of tachypnoea, oxygen desaturation, and lung ultrasound findings suggestive of pulmonary edema, non-invasive ventilation was initiated. An arterial line was secured, and invasive blood pressure monitoring was commenced for continuous hemodynamic assessment.

The primary therapeutic objectives in CCB poisoning are stabilization of blood pressure and prevention of pulmonary edema, and all treatment interventions in this case were aimed at achieving these goals. Her norepinephrine infusion was escalated to 25 ml/hour (66 mcg/min), and vasopressin was titrated up to its maximum dose of 2.4 units/hour

Following a 50 ml bolus injection of sodium bicarbonate administered over 30 minutes, an infusion was commenced at a rate of 10 ml/hour. A 20% lipid emulsion was initiated, with a 100 ml bolus administered over 30 minutes, followed by a continuous infusion at 10 ml/hour

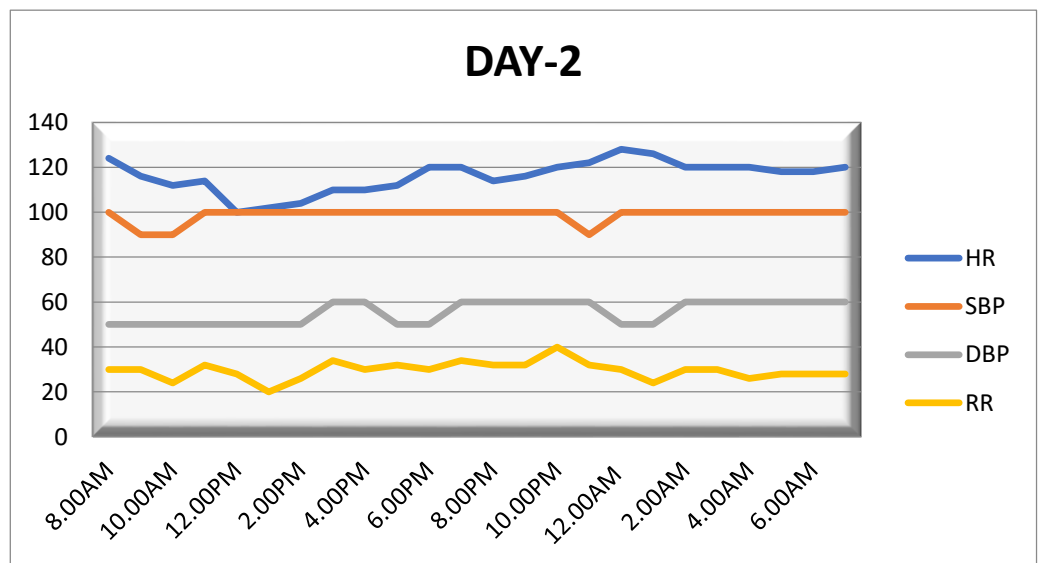
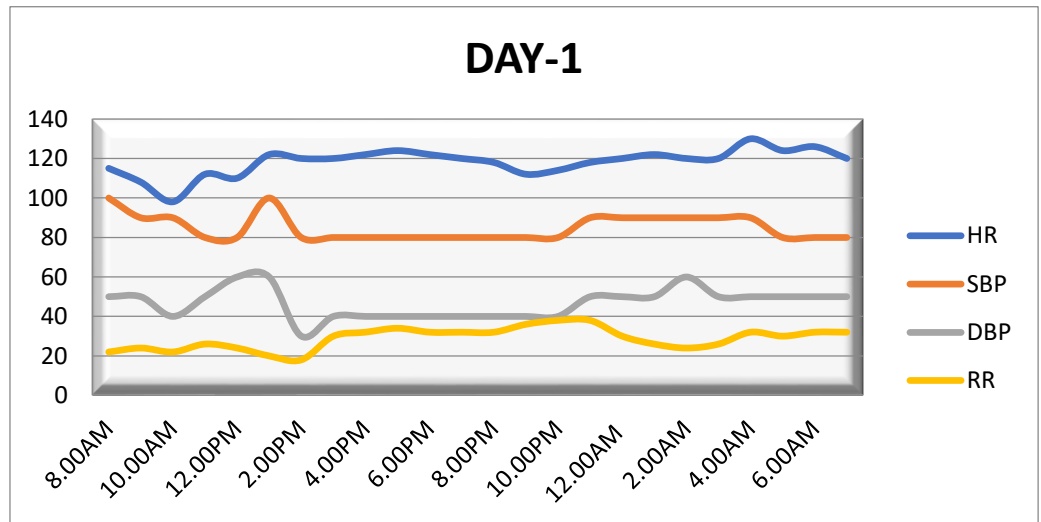
A 3-gram bolus of calcium gluconate was administered, followed by a continuous infusion. The infusion rate was titrated to maintain serum ionised calcium levels around 2 mmol/L. A slow intravenous bolus of Glucagon 3 mg was administered, following which a continuous infusion was initiated at a rate of 0.5–2 mg/hour

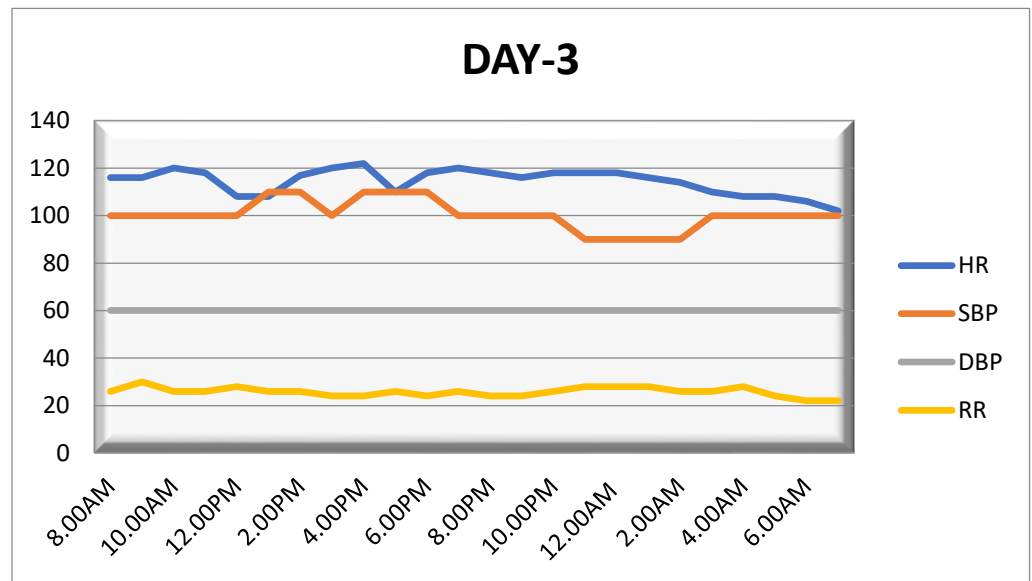
In view of persistent hypotension (BP 80/40 mmHg, MAP 55), she was initiated on an epinephrine infusion at 0.8 mg/hour (approximately 130–135 mcg/min)

High-dose Insulin Euglycemic Therapy (HIET) was initiated with an insulin infusion at a rate of 0.5–1 unit/kg/hour, along with 15–20 g/hour of dextrose (equivalent to 1 ml/kg of 25% dextrose). Hourly blood glucose monitoring was performed to ensure that blood glucose levels were maintained within the target range of 140–200 mg/dL. Potassium levels were also monitored and correction was given as per the observed values, the values were more of hypokalemic.

Following 200mg IV bolus of Hydrocortisone, 50mg Q6th hourly IV was continued for 48 hours. Antibiotic Cefuroxime was also started as there was a doubt of aspiration pneumonitis. Patient required NIV support for the first 72 hours and was gradually weaned intermittently

From the third day onwards, the requirement for epinephrine, norepinephrine, and vasopressin gradually decreased as blood pressure improved. High-dose insulin euglycemia therapy (HIET) was tapered off on day 3 in view of stabilizing hemodynamics. Intralipid emulsion was aggressively weaned. Oral intake was initiated with clear liquids, followed by semi-solid diet. Non-invasive ventilation (NIV) was continued intermittently, with progressive extension of non-NIV periods. Her hemodynamics are charted as follows.





*Patient’s hemodynamics improved gradually over 72 hours of treatment

By the morning of Day 4, all vasopressors, intravenous calcium, and intralipid emulsion were gradually tapered and subsequently discontinued. The patient’s blood pressure remained stable for over 12 hours, allowing for the safe removal of the arterial line. Urine output was well maintained and appropriate for her body weight. NIV was weaned off by morning, and the patient was transitioned to oxygen via face mask. By evening, oxygen was withdrawn, and she was comfortably maintaining respiration on room air. Bedside lung ultrasound and echocardiography revealed normal findings. A psychiatry consultation was obtained, and counselling was provided to both the patient and her family members. She was shifted to room

On Day 5 of hospitalization, the patient was asymptomatic, tolerating a normal oral diet, and ambulating well.

Patient was discharged in a stable condition on day 6.

Drug infusions / Respiration status / Intake & Output																
	Day 1				Day 2				Day 3				Day 4			
	8.00AM	2.00PM	8.00PM	2.00AM	8.00AM	2.00PM	8.00PM	2.00AM	8.00AM	2.00PM	8.00PM	2.00AM	8.00AM	2.00PM	8.00PM	2.00AM
Norepinephrine (8 mg in 50 ml) ml/hour	15	10	25	25	25	20	20	17	10	8	6	5	2	1		
Epinephrine (4 mg in 50 ml) ml/hour		5	10	10	10	5	3	3	3	3	3	2				
Vasopressin Units / hour	1.2	1.2	2.4	2.4	2.4	2.4	2.4	2.4	2.5	1.4	1					
7.5% Soda bicarboante ml/hour	10	10	10	10	10	10	10									
25 % Dextrose ml / hour	60	60	60	80	80	80	80	80	80	40	50	50				
20 % Lipid emulsion ml/hour	100 (30MINS)	10	10	10	10	10	10	10	10	10	10	10				
Glucagon mg/hour	1	2	5	5	5	5	5	5	5	5	5	3	3			
Insulin Units / hour	30	30	30	30	30	30	20	15	15	20	20	20				
NIV / O2 / Room air	NIV (40%)		NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	NIV (40%)	4 L O2	Room air	Room air	Room air
IV fluid	100ML	100ML	100ML	100ML	100ML	100ML	100ML	100ML	100ML	75ML	75ML	75ML	50ML	50ML	50ML	50ML
Urine output	5ML	15ML	25ML	25ML	30ML	20ML	45ML	15ML	45ML	35ML	40ML	150ML	250ML	250ML	100ML	70ML

ABG / other investigations																
INVESTIGATION	Day 1				Day 2				Day 3				Day 4			
	8.00AM	2.00PM	8.00PM	2.00AM	8.00AM	2.00PM	8.00PM	2.00AM	8.00AM	2.00PM	8.00PM	2.00AM	8.00AM	2.00PM	8.00PM	2.00AM
pH	7.4		7.47		7.4		7.4		7.44		7.44		7.48			
PO2	67		182		138		89		116		112		92			
PCO2	23		22		33		33		35		33		35			
HCO3	14.2		16		22.4		23.5		22.2		22.4		24.1			
Sodium	141		135		143		142		140		136		137			
Potassium	2.8		4.2		2.9		4.1		3.4		3.65		3.6			
Calcium	0.99		1.14		1.33		1.23		1.27		1.31		1.35			
Lactate	1.1		4.6		1.5		1.5		1.9		1.1		1.2			
Urea	74.9				96.3								74.2			
Creatinine	2.12				1.9								1.06			
Total Bilirubin	0.87												0.68			
SGOT	62												50			
SGPT	37												62.7			



CCB overdose patient
 - On NIV and multiple infusions
 - Continuous hemodynamic monitoring

2. Discussion

Toxicity of amlodipine presents similar to distributive shock as both are due to marked peripheral vasodilation. There are numerous interventions in the management of amlodipine overdose, despite which many patients continue to suffer life-threatening shock.

Calcium channel blockers (CCBs) can be divided into two major categories based upon their predominant physiologic effects: dihydropyridines, such as nifedipine, amlodipine etc, which preferentially block the L-type calcium channels in the vasculature; and non-dihydropyridines, such as verapamil and diltiazem, which selectively block L-type calcium channels in the myocardium [4, 5].

L-type calcium channels are responsible for myocardial contractility and vascular smooth muscle contractility; they also affect conducting and pacemaker cells. Dihydropyridines are potent vasodilators that have little negative effect upon cardiac contractility or conduction at standard doses. In contrast, verapamil and diltiazem are relatively weak vasodilators but have a depressive effect on cardiac conduction and contractility [5]

Dihydropyridine intoxication generally results in arterial vasodilation and reflex tachycardia, whereas diltiazem and verapamil toxicity cause peripheral vasodilation, decreased cardiac inotropy, and bradycardia [6]

The therapeutic plasma level of amlodipine ranges from 5 to 18 mg/L. Amlodipine has the longest plasma half-life of 30–50 h compared to all calcium channel blockers [7,8], as well as a large volume of distribution (21 L/kg), strong binding to albumin (90–95%), and a relative lack of negative inotropy [9]. Hypotension and other signs of amlodipine toxicity may appear or last up to 7 days due to the long drug half-life, making it clinically prudent to monitor patients following amlodipine overdose for 24–36 hours. Hemodialysis is not used since these drugs are highly protein bound, require large volume of distribution (21 L/kg) and have rapid metabolism

The diagnosis of calcium channel blocker (CCB) poisoning is made clinically on the basis of the history, hypotension coupled with reflex tachycardia, although severe toxicity may result in hypotension and bradycardia, may include signs of heart failure (pulmonary crackles, distended IJV, etc). CCB-poisoned patients may maintain a surprisingly clear mental status in the setting of hypotension throughout their hospital stay.

Central venous access and invasive arterial BP monitoring is mandatory in severe CCB poisoning. Serial monitoring of Blood pressure, preferably invasive BP, guided by serial monitoring of calcium, blood glucose, urea, creatinine, potassium, ABG to assess the severity of metabolic acidosis & lactate, continuous ECG to diagnose heart blocks or sinus arrest with nodal rhythm, lung ultrasound or Chest X-ray to assess pulmonary edema, bedside ECHO to assess cardiac contractility are the mainstay in treatment journey of a CCB poisoning.

Severe CCB poisoning consists of multiple simultaneous treatment options

- Gastric decontamination and activated charcoal via NG tube
- Stabilization of the airway and breathing as necessary
- Additional IV boluses of isotonic crystalloid
- IV calcium salts
- IV glucagon

- IV high-dose insulin and glucose- HIET
- IV vasopressor (eg, epinephrine, norepinephrine, vasopressin,)
- IV lipid emulsion therapy
- IV methylene blue
- Extra Corporeal Membrane Oxygenation

The desired outcome for CCB poisoning is revival of hypotension & prevention of pulmonary edema, and all treatment interventions are directed toward achieving this goal. Detailing and dosing for each of these therapies is provided below

1. Nasogastric tube shall be placed and stomach wash is given and 1g/kg of activated charcoal is administered via NG tube, stomach wash and activated charcoal is considered within 2 hours of ingestion, beyond which it is not effective. Whole bowel irrigation is another option when extended-release preparation is used
2. Stabilisation of airway and breathing with endotracheal intubation and ventilatory support is indicated if the patient develops severe hemodynamic instability
3. Administer IV bolus followed by maintenance crystalloids to support hemodynamics and ensure adequate urine output
4. Calcium chloride/gluconate helps to overcome the competitive blockade of calcium channels. It improves hypotension, contractility, and conduction abnormalities. IV calcium, bolus therapy – 10 to 20 ml of 10% calcium chloride or 30 to 40 ml of 10% calcium gluconate over one hour followed by infusion of 0.5meq/kg per hour to achieve a calcium around 2.0 meq/L. Serial monitoring of calcium and ECG is needed to avoid complications due to hypercalcemia
5. Glucagon stimulates adenylate cyclase and increases intracellular cyclic adenosine monophosphate (cAMP). This improves cardiac contractility and heart rate. An initial 3 to 5 mg IV bolus over 30 minutes is a reasonable start. A glucagon infusion can be started at the total dose at which a response is noted, may be 0.5 mg to 2 mg per hour infusion. Nausea and vomiting are common side effects of glucagon administration.
6. HIET, High dose Insulin Euglycemic therapy – early initiation of HIET is recommended which helps in increasing ionized calcium levels, improving cardiac contractility. Bolus therapy – Regular Insulin 1unit/kg IV with simultaneous Dextrose infusion of 25 to 40 grams/ hour, take care of glucose levels and potassium. Maintenance therapy - Regular insulin at 0.5 Units/kg per hour IV; titrate upwards until hypotension is corrected up to a dose of 1 Units/kg per hour with simultaneous infusion of Dextrose: 0.5 grams/kg per hour; titrate to euglycemia. Monitor blood glucose and serum potassium hourly or depending upon the levels. Potassium correction with supplemental magnesium may be needed.
7. IV vasopressors, nor epinephrine infusion to start with and add up vasopressin and epinephrine infusion if needed, not exceeding maximal dose level
8. IV lipid emulsion (20% solution), Bolus therapy – 1 to 1.5ml/kg over one minute, Maintenance therapy – 0.25 ml to 1 ml /minute infusion continued for 2 to 3 days, maximum dose being 10 mL/kg over 24 hours
9. IV methylene blue, 1-2mg/kg IV infusion over 10 to 15 minutes as a single dose.

10. If the patient fails to improve with above interventions, he or she may require trans-venous cardiac pacing, intra-aortic balloon pump or ECMO.

3. Conclusion

Ingestions of calcium channel blockers result in severe, and even fatal, consequences. A CCB overdose can cause severe refractory hypotension, shock, cardiovascular instability, and metabolic acidosis that may not respond to vasopressor agents with high doses. So, this life-threatening condition requires a multimodal approach and coordination across multiple specialties. Effective teamwork, timely administration of appropriate antidotes, and meticulous execution of treatment can significantly improve outcomes. Finally, psychiatric counselling and follow-up play a crucial role in addressing the social and psychological aspects of recovery.

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