RESEARCH PAPER

High-Dose Insulin Euglycaemic Therapy in Severe Calcium Channel Blocker Overdose Presenting as Refractory Shock: A Case Report

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ABSTRACT

Background: Shock refractory to standard resuscitative measures represents a medical emergency and should prompt evaluation for uncommon etiologies, including toxicological causes. Calcium channel blocker (CCB) overdose is associated with high morbidity and mortality due to severe myocardial depression, vasodilation, metabolic derangements, and multiorgan dysfunction. Early recognition and targeted therapy are crucial for survival.

Case Presentation: A 26-year-old female who presented with nausea, vomiting, and giddiness following intentional ingestion of large quantities of sustained-release diltiazem and amlodipine. On admission, she was profoundly hypotensive with metabolic acidosis, hyperglycemia, and new-onset atrial fibrillation. Despite aggressive initial management with intravenous fluids, calcium supplementation, glucagon, and maximal vasopressor support, the patient remained in refractory shock. Her clinical course was complicated by oliguria, respiratory compromise, pleural effusions, and worsening metabolic abnormalities. Two cycles of hemoperfusion were performed as adjunctive therapy. In view of persistent hemodynamic instability, high-dose insulin euglycaemic therapy (HIET) was initiated and titrated to high infusion rates with concurrent dextrose supplementation. Following initiation of HIET, the patient demonstrated sustained hemodynamic improvement, resolution of metabolic acidosis, and recovery of end-organ function. Vasopressors were successfully tapered, respiratory support was discontinued, and the patient was discharged with complete functional recovery. This case highlights the importance of considering CCB overdose in patients presenting with refractory shock and emphasizes the pivotal role of high-dose insulin euglycaemic therapy as an effective, life-saving treatment in severe CCB toxicity...

Keywords: Calcium channel blocker overdose; Refractory shock; High-dose insulin euglycaemic therapy; Amlodipine toxicity; Diltiazem toxicity; Toxicological shock; Cardiogenic shock; Metabolic acidosis; Hemoperfusion

How to cite this article: Haneef H, Udapudi SV, Pawar A, Ahmed AA, Hatti MA, TC A, M L, Unais A, KS J, Joji S; High-Dose Insulin Euglycaemic Therapy in Severe Calcium Channel Blocker Overdose Presenting As Refractory Shock: A Case Report, Int J Drug Deliv Technol. 2026; 16(6s): 217-221; DOI: 10.25258/ijddt.16.6s.28

Source of support: Nil.

Conflict of interest: Nil

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INTRODUCTION

Shock is a life-threatening clinical syndrome characterized by circulatory failure resulting in inadequate tissue perfusion and cellular hypoxia, ultimately leading to multiorgan dysfunction if not rapidly identified and treated [1]. It remains one of the most common and challenging emergencies encountered in critical care and emergency medicine. Conventionally, shock is classified into hypovolemic, cardiogenic, distributive, and obstructive types based on underlying pathophysiology [2]. However, in certain situations, patients may present with shock that is refractory to standard resuscitative measures, necessitating consideration of less common etiologies such as poisoning, envenomation, endocrine crises, or metabolic derangements. Toxicological shock, sometimes referred to as "type 5 shock," represents an important yet often underrecognized cause of refractory hypotension [3].

Among toxicological causes, calcium channel blocker (CCB) overdose is associated with particularly high morbidity and mortality [4]. CCBs are widely prescribed for hypertension, angina, arrhythmias, and other cardiovascular conditions. Their increasing availability has led to a rise in both accidental and intentional overdoses [5]. Dihydropyridine agents such as amlodipine predominantly cause peripheral vasodilation, while non-dihydropyridines like diltiazem exert additional negative inotropic and chronotropic effects. In massive overdoses, the pharmacological selectivity of these agents is lost, resulting in profound myocardial depression, severe hypotension, conduction abnormalities, and shock [6].

The pathophysiology of CCB toxicity is complex and multifactorial. By inhibiting L-type calcium channels, these agents impair calcium influx into cardiac myocytes and vascular smooth muscle cells, leading to decreased myocardial contractility, reduced cardiac output, and systemic vasodilation [7]. In addition, inhibition of calcium-dependent insulin release from pancreatic beta cells results in hypoinsulinemia and insulin resistance, causing hyperglycemia and impaired myocardial utilization of carbohydrates [8]. This metabolic shift further worsens cardiac performance and contributes to lactic acidosis, a hallmark of severe poisoning. As a result, CCB overdose often presents with shock that is resistant to conventional therapies such as fluids and vasopressors [3].

Management of severe CCB poisoning is challenging due to the absence of a specific antidote. Initial treatment strategies include aggressive fluid resuscitation, administration of calcium salts to overcome channel blockade, glucagon to enhance intracellular cyclic AMP, and vasopressor support to maintain perfusion [4]. Despite these measures, many patients continue to deteriorate, highlighting the need for advanced and targeted therapies. Over the past two decades, high-dose insulin euglycaemic therapy (HIET) has emerged as a key treatment modality for severe CCB toxicity. Insulin improves myocardial contractility by facilitating glucose uptake and utilization by cardiac cells, enhancing energy production, and exerting direct positive inotropic effects independent of catecholamine pathways [9].

Early recognition of CCB overdose and prompt initiation of HIET can be life-saving, particularly in patients presenting with refractory shock and metabolic acidosis [10]. This case report illustrates a severe mixed CCB overdose presenting as refractory shock in a young female and highlights the critical role of high-dose insulin therapy and multimodal supportive management in achieving complete clinical recovery [11].

CASE PRESENTATION

Patient Information: A 26-year-old female was brought to the emergency department of a tertiary care hospital at approximately 5:15 am with acute onset gastrointestinal and neurological symptoms. The patient was previously apparently healthy and had no known chronic medical illnesses. She was residing with her parents and was not on any long-term medications. There was no prior history of psychiatric illness documented; however, family members reported recent behavioral changes.

Presenting Complaints: The patient presented with complaints of nausea, multiple episodes of vomiting (approximately six episodes), and giddiness of 30 minutes duration prior to arrival. The vomiting was non-bilious and non-blood-stained. There was no history of loose stools, abdominal pain, fever, chest pain, palpitations, dyspnea, seizures, or loss of consciousness. No history suggestive of food poisoning or infectious illness was elicited.

History of Present Illness: According to the patient and corroborated by her parents, she had been experiencing reduced appetite and disturbed sleep for the preceding 10–12 days. On further probing in a nonjudgmental environment, the patient disclosed intentional ingestion of medications at her residence around 12:30 am on the same day of presentation. She admitted to consuming approximately 20 tablets of sustained-release diltiazem 120 mg and 30 tablets of amlodipine 10 mg. There was no co-ingestion of alcohol, sedatives, or other drugs. No medical attention was sought immediately after ingestion, and she was brought to the hospital only after the onset of symptoms.

Past Medical and Personal History: The patient had no known history of hypertension, diabetes mellitus, coronary artery disease, arrhythmias, or renal disease. There was no past surgical history. Family history was non-contributory. She consumed a mixed diet and denied use of tobacco, alcohol, or illicit substances. There were no known drug allergies.

Clinical Examination at Presentation: On arrival at the emergency department, the patient was conscious, alert, and oriented to time, place, and person. She appeared anxious but was cooperative. Vital signs revealed tachycardia with a pulse rate of 110 beats per minute and severe hypotension with a systolic blood pressure of 70 mmHg. Diastolic blood pressure was not recordable initially. Respiratory rate was 16 breaths per minute, and oxygen saturation was 99% on room air. She was afebrile. Random blood glucose at presentation was 170 mg/dL. Glasgow Coma Scale score was 15/15. Pupils were bilaterally equal in size and reactive to light.

Systemic examination revealed warm peripheries with delayed capillary refill. Cardiovascular examination showed tachycardia with no murmurs. Respiratory system examination revealed normal breath sounds with no added sounds initially. Abdominal examination was soft and non-tender with no organomegaly. Neurological examination showed no focal deficits.

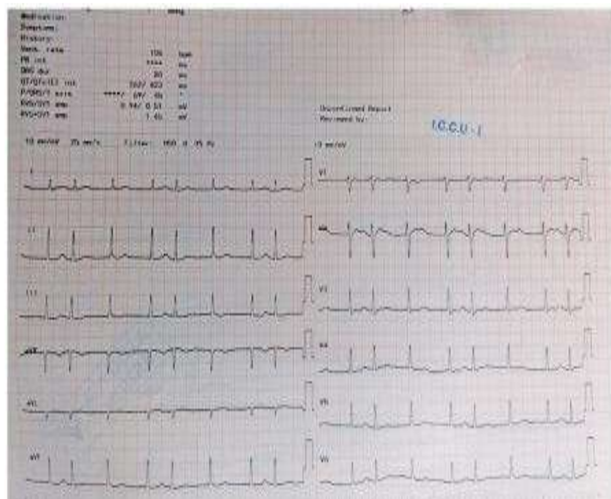

Figure 1: Twelve-lead electrocardiogram showing new-onset atrial fibrillation characterized by an irregularly irregular rhythm, absence of P waves, and controlled ventricular rate in a patient with severe calcium channel blocker overdose.

Initial Laboratory and Radiological Investigations: Baseline hematological investigations showed hemoglobin of 12.2 g/dL, total leukocyte count of 27,300/mm³, and platelet count of 116,000/mm³. Biochemical parameters revealed hyperglycemia with serum glucose of 366 mg/dL. Renal function tests showed urea of 78.5 mg/dL and serum creatinine of 0.99 mg/dL, which later demonstrated a rising trend. Serum electrolytes revealed mild hyponatremia and borderline hypokalemia. Cardiac biomarkers showed elevated troponin I and creatine kinase- MB levels.

Arterial blood gas analysis revealed severe metabolic acidosis with pH 7.18, bicarbonate 8.7 mmol/L, partial pressure of carbon dioxide 23.8 mmHg, and elevated lactate level of 6.95 mmol/L. Electrocardiogram showed new-onset atrial fibrillation with a controlled ventricular rate. Chest radiograph was initially unremarkable but later showed bilateral diffuse non- homogeneous opacities suggestive of pleural effusion. Ultrasonography of the abdomen revealed bilateral mild pleural effusion with basal lung collapse and moderate ascites. Two- dimensional echocardiography showed normal cardiac structure and function. Toxicological screening by thin-layer chromatography detected amlodipine.

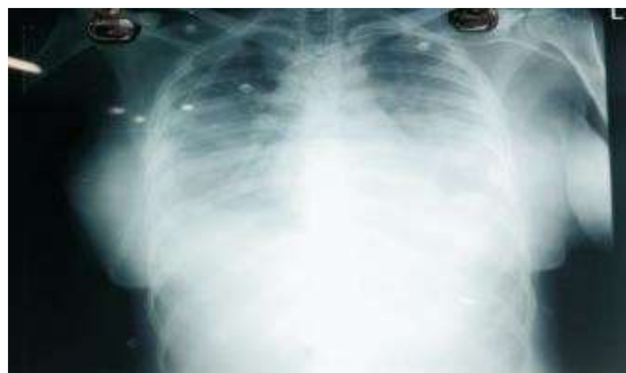

Figure 2: Bilateral pleural effusion with underlying basal lung collapse/consolidation, consistent with fluid overload and respiratory compromise in the setting of severe shock.

Hospital Course and Clinical Progression: The patient was admitted to the intensive care unit with a diagnosis of refractory shock secondary to calcium channel blocker overdose. She was initiated on aggressive fluid resuscitation and multiple vasopressors, including noradrenaline, vasopressin, and dopamine. Despite maximal inotropic and vasopressor support,
she remained hypotensive. During the ICU stay, the patient developed atrial fibrillation, which was managed with electrical cardioversion and initiation of antiarrhythmic therapy.

Approximately 23 hours after ingestion, two cycles of hemoperfusion were performed using a HA330 cartridge. On the second day of hospitalization, the patient showed clinical deterioration with reduced urine output, abdominal distension, bilateral pedal edema, and worsening breathlessness. She developed hypoxemia and was initiated on non-invasive ventilation with continuous positive airway pressure. Chest physiotherapy was instituted.

Therapeutic Interventions and Outcome: In view of persistent refractory shock and metabolic derangements, high-dose insulin euglycaemic therapy was initiated. The patient received an initial insulin bolus followed by continuous intravenous insulin infusion, which was gradually titrated up to 300 units per hour, with concurrent dextrose infusion to maintain euglycemia. Close monitoring of blood glucose and electrolytes was performed.

Following initiation of high-dose insulin therapy, the patient demonstrated gradual but sustained hemodynamic improvement over the next 48 hours. Vasopressor requirements decreased and were subsequently tapered off. Renal function parameters stabilized and showed improving trends. Oxygen requirements decreased, and the patient was weaned off non- invasive ventilation to supplemental oxygen via face mask. She was transferred to the general ward on day eight of hospitalization and discharged on day ten in a stable condition with complete functional recovery.

DISCUSSION

Calcium channel blocker (CCB) overdose represents one of the most severe and challenging forms of cardiovascular drug toxicity encountered in emergency and critical care

practice [10]. Although relatively uncommon compared to other poisonings, CCB toxicity is associated with disproportionately high morbidity and mortality due to profound myocardial depression, vasodilation, and metabolic disturbances leading to refractory shock. This case highlights the importance of early recognition of CCB overdose as a cause of unexplained or refractory shock and underscores the pivotal role of high-dose insulin euglycaemic therapy (HIET) as a life- saving intervention.

The clinical manifestations of CCB toxicity depend on the specific agent, dose, and formulation ingested. Dihydropyridine CCBs such as amlodipine primarily cause peripheral vasodilation, resulting in distributive shock, while non-dihydropyridine agents like diltiazem exert significant negative inotropic and chronotropic effects, leading to cardiogenic shock and conduction abnormalities [12]. In massive ingestions, particularly with sustained-release formulations, the pharmacological selectivity of these drugs is lost, and patients often present with a mixed shock state. In the present case, combined ingestion of amlodipine and sustained- release diltiazem resulted in severe hypotension, atrial fibrillation, metabolic acidosis, and end- organ dysfunction, reflecting both vasodilatory and cardiodepressant effects.

A distinctive feature of severe CCB poisoning is the development of hyperglycemia and lactic acidosis. By inhibiting calcium-dependent insulin release from pancreatic beta cells, CCBs induce hypoinsulinemia and insulin resistance, impairing cellular glucose uptake [8]. The myocardium, under conditions of stress, preferentially utilizes carbohydrates as its primary energy source [13]. In the absence of adequate insulin-mediated glucose transport, myocardial energy failure ensues, further compromising cardiac output. This metabolic derangement explains why conventional therapies such as fluids and vasopressors often fail to reverse shock in severe CCB toxicity, as seen in this patient [11].

Initial management of CCB overdose focuses on supportive care and hemodynamic stabilization [7]. Calcium salts are administered to overcome calcium channel blockade, glucagon is used to enhance intracellular cyclic adenosine monophosphate, and vasopressors such as norepinephrine or epinephrine are employed to counteract hypotension. However, these interventions alone are frequently insufficient in severe cases [6]. In the present case, despite aggressive fluid resuscitation, calcium infusion, glucagon, and multiple vasopressors, the patient remained profoundly hypotensive, necessitating escalation of therapy [11].

High-dose insulin euglycaemic therapy has emerged as a cornerstone in the management of severe CCB poisoning [9]. Insulin exerts its beneficial effects through multiple mechanisms, including improved myocardial glucose uptake, enhanced intracellular calcium handling, and direct positive inotropic effects independent of catecholamine pathways [11]. HIET also improves systemic vascular resistance and corrects metabolic acidosis by restoring aerobic metabolism. In this patient, initiation and titration of insulin infusion up to 300 units per hour resulted in marked hemodynamic improvement, allowing gradual withdrawal of vasopressor support and reversal of end-organ dysfunction.

Extracorporeal therapies such as hemoperfusion and hemodialysis have a limited but evolving role in CCB toxicity [14]. While most CCBs are highly protein-bound and have large volumes of distribution, hemoperfusion may offer benefit in selected cases, particularly with sustained- release preparations and severe toxicity [15]. In this case, hemoperfusion was performed as an adjunctive measure, although the most significant clinical improvement was observed following initiation of HIET [16].

This case emphasizes several key clinical lessons. First, toxicological causes must be actively considered in young patients presenting with unexplained refractory shock. Second, early initiation of HIET can be life-saving and should not be delayed until all conventional therapies fail. Finally, successful outcomes in severe CCB poisoning require a multimodal approach, close monitoring, and early intensive care involvement. Prompt recognition and timely escalation of therapy can result in complete recovery even in critically ill patients, as demonstrated in this case.

CONCLUSION

Calcium channel blocker overdose is a potentially fatal condition that can present with profound, refractory shock and severe metabolic derangements. Early recognition of toxicological causes in patients with unexplained hypotension is crucial, particularly in young individuals without underlying comorbidities. This case highlights the limitations of conventional therapies such as fluid resuscitation, calcium supplementation, glucagon, and vasopressors in severe calcium channel blocker toxicity. High-dose insulin euglycaemic therapy played a decisive role in reversing myocardial dysfunction, correcting metabolic abnormalities, and restoring hemodynamic stability. Adjunctive therapies, including hemoperfusion and advanced respiratory support, may provide additional benefit in selected cases. A structured, aggressive, and multidisciplinary approach is essential for optimal outcomes. Timely initiation of high-dose insulin therapy should be strongly considered in patients with calcium channel blocker overdose presenting with refractory shock, as it can significantly improve survival and lead to complete functional recovery..

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