Clinical Question: What is the role of high-dose insulin euglycemia therapy (HIET) in the management of calcium channel blocker (CCB) overdose?

Calcium channel blockers (CCBs) are commonly prescribed for hypertension, arrhythmias, and angina, but overdose can cause life-threatening cardiovascular complications. In 2020, U.S. poison centers reported 6,132 single-substance CCB exposures, including 101 major adverse outcomes and 45 deaths (Alshaya et al., 2022). CCBs block L-type calcium channels in cardiac muscle, vascular smooth muscle, and pancreatic beta cells. Dihydropyridines, such as amlodipine, primarily cause vasodilation, while non-dihydropyridines, such as verapamil and diltiazem, decrease heart rate, atrioventricular (AV) conduction, and contractility. In overdose, this selectivity may be lost, causing cardiogenic shock, distributive shock, or both. Patients may experience dizziness, weakness, nausea, vomiting, or syncope. Clinical findings include hypotension (systolic blood pressure [SBP] <90 mmHg or mean arterial pressure [MAP] <65 mmHg), bradycardia (heart rate [HR] <60 beats/min), AV block, and hyperglycemia. Severe toxicity may cause altered mental status, metabolic acidosis, elevated lactate (>2 mmol/L), and decreased urine output, indicating poor tissue perfusion (Lavonas et al., 2023).

CCB overdose also decreases insulin secretion by blocking calcium entry into pancreatic beta cells, resulting in hyperglycemia and impaired myocardial glucose utilization. During shock, the heart increasingly relies on glucose for energy, so reduced glucose utilization further worsens contractility. HIET addresses this dysfunction by administering high doses of IV regular insulin to increase myocardial glucose uptake and adenosine triphosphate (ATP) production. Insulin also has positive inotropic effects independent of beta-adrenergic receptors, improving cardiac output and tissue perfusion. Unlike insulin used for diabetes, HIET aims to improve cardiac function rather than lower blood glucose. However, it does not directly reverse calcium channel blockade or significantly correct vasodilation, so vasopressors may still be needed (Krenz & Kaakeh, 2018; Mégarbane, 2023).

The recommended starting regimen is regular insulin 1 unit/kg IV bolus, followed by 1 unit/kg/hour. For a 70-kg patient, this equals 70 units IV followed by 70 units/hour. If hemodynamic improvement is inadequate after approximately 30 minutes, some protocols recommend increasing the infusion by 0.5 units/kg/hour every 10–15 minutes, with doses up to 10 units/kg/hour used in refractory cases. If initial blood glucose is below 200 mg/dL, a 25-g IV dextrose bolus may be administered. A dextrose infusion may start at approximately 0.5 g/kg/hour, adjusted to maintain glucose between 100 and 200 mg/dL; initially hyperglycemic patients may not require immediate dextrose. HIET may take 15–60 minutes to improve cardiac function, so other supportive treatments should not be delayed. Treatment continues until shock resolves, potentially requiring 24 hours or longer (University of Utah Poison Control Center, 2021; St-Onge et al., 2017).

The main adverse effects of HIET are hypoglycemia and hypokalemia, requiring close monitoring. Blood glucose should be checked every 15–30 minutes during initiation and titration, then approximately hourly once stable. Potassium should also be monitored frequently because insulin causes intracellular potassium shifts, potentially resulting in hypokalemia (K <3.5 mEq/L).

Replacement should be cautious because this primarily reflects redistribution rather than total-body depletion. Magnesium, phosphate, and fluid status should be monitored for electrolyte abnormalities and volume overload. Continuous ECG and blood pressure monitoring are necessary to assess treatment response. Therapeutic goals include MAP ≥65 mmHg, urine output ≥0.5 mL/kg/hour, improved mental status and contractility, decreasing lactate, and reduced vasopressor requirements, indicating improved organ perfusion. Glucose monitoring should continue after insulin discontinuation because hypoglycemia may occur as toxicity resolves (Krenz & Kaakeh, 2018; Mégarbane, 2023).

HIET is recommended for severe CCB poisoning with hypotension or shock, particularly with myocardial dysfunction, but is generally unnecessary in mild, hemodynamically stable cases. Vasopressors may be prioritized for predominantly vasodilatory shock with preserved contractility. In life-threatening CCB toxicity, the benefits of HIET generally outweigh its risks, with no established absolute contraindications specific to this use. However, several conditions warrant caution. Known insulin hypersensitivity may require an alternative preparation, while severe hypokalemia requires prompt correction and close monitoring. Renal impairment may prolong the risk of hypoglycemia due to reduced insulin clearance, and fluid overload may worsen with dextrose administration. Concentrated dextrose solutions may also require central venous access. HIET should be administered in a setting with frequent laboratory testing and continuous hemodynamic monitoring. Adjunctive therapies include IV calcium to improve contractility and conduction, norepinephrine or epinephrine for blood pressure support, and atropine for symptomatic bradycardia, although its effectiveness is limited. Venoarterial extracorporeal membrane oxygenation (VA-ECMO) may be considered for refractory cardiogenic shock (Krenz & Kaakeh, 2018; St-Onge et al., 2017; Lavonas et al., 2023).

The 2017 international expert consensus recommends HIET as a first-line treatment alongside IV calcium and vasopressors based on the patient's presentation (St-Onge et al., 2017). Similarly, the 2023 American Heart Association focused update recommends high-dose insulin for hypotension in life-threatening CCB poisoning (Lavonas et al., 2023). Although published clinical reports describe improvements in blood pressure and cardiac function following HIET, the evidence primarily consists of observational studies, case reports, animal studies, and expert consensus rather than randomized controlled trials. Therefore, its comparative benefit remains uncertain.

Overall, HIET is an important treatment for severe CCB overdose, particularly with hypotension and myocardial dysfunction. By improving myocardial glucose utilization and contractility, it helps restore cardiac output and tissue perfusion. HIET should be initiated early alongside IV calcium and vasopressors when indicated, with close glucose, potassium, and hemodynamic monitoring to minimize complications.

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