calcium channel blocker overdose

general

- Calcium channel blockers (CCBs) are commonly used in the treatment of angina and hypertension.
- Their use is complicated by adverse side effects, iatrogenic errors, and intentional overdoses.
- Significant morbidity and mortality can occur after accidental or intentional CCB poisoning.
- Sustained-release preparations can cause delayed-onset toxicity as late as 12 hours after ingestion

clinical manifestations

- The potentially life-threatening effects of CCB intoxication center on the cardiovascular system. The most common clinical manifestations are sinus bradycardia, hypotension, and shock.

cardiovascular effects

- Clinical effects may vary in mild to moderate poisoning, depending on the specific medication ingested. In massive overdose, specificity is lost, and all agents can cause bradycardia, depressed cardiac contractility, and cardiovascular collapse.
- Cardiovascular compromise may be compounded by ingestion of other cardiovascular toxins in addition to underlying patient comorbid illness.

respiratory effects

- Pulmonary toxicity from CCB poisoning includes both cardiogenic and noncardiogenic pulmonary edema secondary to:
(i) negative chronotropy,
(ii) excessive fluid resuscitation,
(iii) increased capillary permeability secondary to drug effect, and
(iv) increased sympathetic discharge in response to shock.

neurologic effects

- Neurologic manifestations include myoclonus, dizziness, syncope, focal neurologic deficits, and seizures. These are most likely related to central nervous system hypoperfusion.

GI effects

- GI symptoms caused by CCB ingestion are nonspecific and include nausea and vomiting.

renal effects

- CCB toxicity with ensuing shock can cause diffuse organ dysfunction, such as renal failure, secondary to poor tissue perfusion.

metabolic effects

- Metabolic derangements, including hypokalemia and mild hyperglycemia, may be found due to calcium channel blockade in the pancreatic beta islet cell that impairs insulin release.
- Metabolic acidosis can be caused by poor tissue perfusion and mitochondrial dehydrogenase inhibition.

differential diagnosis

- The most common agents in the differential diagnosis of CCB poisoning are ß-adrenergic antagonists, cardiac glycosides, imidazolines, class 1a and 1c antidysrhythmics, cyanide, organophosphates, and tricyclic antidepressants (late).
- Included in the differential diagnosis of CCB poisoning are nontoxicologic entities: acute coronary syndromes, hyperkalemia, myxedema coma, hypothermia, and sepsis.

diagnostic testing

- A 12-lead electrocardiogram should be obtained
- Arterial blood gas measurement offers a rapid assessment of oxygenation, tissue perfusion, and serum potassium.
- Chest radiography can demonstrate cardiac size and the presence of pulmonary edema
- Serum calcium levels generally are not affected by CCBs, but serial levels may be necessary if the patient is treated with parenteral calcium salts
- Serum levels of cardioactive medications with established therapeutic concentrations (e.g., digoxin , procainamide) should be obtained for patients with a suggestive history or physical examination.

monitoring

- Treatment of the patient poisoned by CCBs focuses on early recognition of shock and aggressive cardiovascular support.
- A low threshold should be maintained to initiate invasive monitoring techniques (arterial, central venous, and pulmonary catheters) for both administration of treatments and assessment of clinical responses.
- All patients should have a urinary bladder catheter to accurately monitor urinary output

treatment

overview

Drug	Dose	Goal
Activated charcoal	1-2 g/kg	Decreased systemic absorption (give within 1 hr after ingestion)
Whole bowel irrigation	500-2000 mL/hr until clear rectal effluent	Decreased system absorption
Intravenous fluids	2 L of normal saline solution or lactated Ringer's solution (limit intravenous fluids unless significantly dehydrated)	Increased BP
Calcium chloride	1 ampule i.v. over 2 min	Increased HR and SVR
Atropine	0.5-1 mg i.v. every 3 min (maximum dose is 3 mg)	Increased HR and CO
Glucagon	5-10 mg bolus, then 2-5 mg/hr infusion	Increased SVR (titrate for effect)
Isoproterenol	Initiate at 2 µg/min	Increased CO (titrate for effect)
Epinephrine	Initiate at 2 µg/min (consider weight-based dosing)	Increased SVR (titrate for effect)
Norepinephrine	Initiate at 0.5 µg/min (consider weight-based dosing)	Increased SVR (titrate for effect)
Ventricular pacing	Achieve ventricular capture at 50-60 bpm	Increased HR and CO (only if other interventions fail)
Intra-aortic balloon pump	Consult cardiologist	Only if refractory to all other interventions
Cardiopulmonary bypass	Consult cardiothoracic surgeon	Only if refractory to all other interventions

gastrointestinal decontamination:
- may have a role in very early presentation or in overdoses with sustained release formulations
- Patients who are obtunded, have poor airway protective mechanisms, are hypoxemic should undergo endotracheal intubation.

resuscitation

- Clinically significant CCB toxicity usually involves bradydysrhythmia or hypotension or both.
- Treatment of symptomatic bradycardia enlists an arsenal of therapies, including atropine, external or internal pacing, parenteral calcium salts, glucagon, vasopressors, and even extracorporeal hemodynamic support.
- None of the treatments has been studied in randomized, controlled human studies, and their use is based on animal studies, human case reports, and case series.

specific therapies

(i) iv fluids

- Intravenous fluids should be administered to hypotensive patients to improve blood pressure and tissue perfusion.
- Care should be maintained not to administer excessive volume to patients poisoned by CCBs because of the risk of pulmonary edema.

(ii) atropine

- Atropine has limited utility in reversing bradycardia, but it may be administered on an emergency basis while other therapies are being prepared.

(iii) pacing

- External or internal pacemaker therapy may be attempted in addition to intravenous fluids and atropine to improve symptomatic bradycardia.

(iv) calcium salts

- Administration of parenteral calcium salts may augment heart rate and blood pressure in the face of CCB poisoning
- Calcium chloride contains approximately three times the amount of calcium as the gluconate salt and is the preferred agent.
- Slow boluses of 1 to 3 g of calcium chloride may be given, and a continuous infusion of 2 to 6 g/hour may be initiated if a favorable hemodynamic response is noted.
- Serum ionized calcium levels should be monitored during parenteral calcium infusions and should be maintained at approximately 2 to 3 mmol/L.

(v) glucagon

- Although more commonly associated with ß-adrenergic antagonist poisoning, intravenous glucagon may offer another treatment modality by increasing cyclic adenosine monophosphate (cAMP) production to increase cardiac contractility and rate.
- Intravenous boluses of 2 to 10 mg may be administered, and resulting effects should be monitored. A beneficial response should be followed by a constant infusion of 2 to 5 mg/hour.

(vi) vasopressors

- Although several vasopressors have been used for the treatment of CCB toxicity, there is no optimal agent. Dopamine, epinephrine, isoproterenol, amrinone, and aminophylline all have demonstrated efficacy in animal models and humans series.
- In general, a patient with severe CCB poisoning should receive a pressor titrated to achieve a perfusing heart rate and blood pressure.

(vii) additional therapies

- Three investigational therapies are insulin/dextrose, hypertonic saline, and 4-aminopyridine.
- Patients who remain in cardiovascular collapse despite aggressive resuscitation may be candidates for extracorporeal blood pressure support in the form of cardiopulmonary bypass or an IABP.

medical clearance

- After resuscitation, an asymptomatic period of 24 hours is appropriate for medical clearance. A psychiatrist should evaluate all patients with a history or suspicion of intentional ingestion before ultimate disposition.