Beta-Blocker/Calcium Channel Blocker Toxicity		
Medication	**Use**	**Dosing**
Immediate Therapy (within 1-2 hours of ingestion)		
Activated charcoal	Gastrointestinal decontamination	- Bolus: 1 g/kg - Repeat doses at 0.5 mg/kg q2-4h if positive bowel sounds or confirmation of no bowel obstruction
First-line agents - Used individually or simultaneously		
IV fluid resuscitation	Hypovolemia	- No explicit recommendations

IV Calcium Salts[a]	Positive inotropy, increases blood pressure and contractility	- Calcium chloride 10%
		  - Bolus: 1-2 grams q10-20 minutes over 5-10 minutes
		  - Continuous infusion 20-40 mg/kg/hr
		- Calcium gluconate 10%
		  - Bolus: 3-6 grams q10-20 min over 5-10 minutes
		  - Continuous Infusion: 60-120 mg/kg/hr

High-dose insulin[b]	Positive inotropy, Hyperglycemia, impaired insulin secretion	- Bolus: 1 unit/kg regular,short acting - Continuous infusion: 0.5 units/kg/hr regular,short acting (max 10 units/kg/hr)
Norepinephrine/ epinephrine	Initial hemodynamic support in the setting of shock	- Titrate to desired vitals
Atropine	Symptomatic bradycardia	- 0.5-1 mg q2-3 minutes (max 3 mg)
Other therapies		

Vasoactive medications	Hemodynamic support	- Dobutamine
		- Dopamine
		- Vasopressin
		- Methylene Blue (Vasoplegic shock)
		  - Bolus: 1-2 mg/kg over 20-60 minutes in 50-100 mL NS
		  - Continuous Infusion: 0.5-1 mg/kg/hr after bolus

Dextrose	Maintain Euglycemia	- Bolus: D50W - Continuous D5W, D10W infusion: 0.5-1 grams of dextrose/kg/hr
20% Lipid emulsion therapy[c]	Sequesters lipophilic drugs by creating a “lipid sink”	- Bolus: 0.125 mL/kg/hr - Continuous infusion: 0.025 mg/kg/min over 30 minutes
Glucagon	Increases cAMP	- Bolus: 1-10 mg IV - Continuous infusion: 3-6 mg/hr

There is no universally accepted treatment algorithm for the management of calcium channel blockage and beta blocker toxicity. Treatments are selected based on patient specific clinical factors, and medications can be initiated individually or simultaneously.

a) Calcium gluconate can be administered via peripheral or central venous access. Calcium chloride should always be given via central access. Calcium chloride contains 3 times more elemental calcium than calcium gluconate. Clinically significant hypercalcemia can occur from high-dose continuous infusion of calcium. Boluses can be repeated 3-4 times
b) Monitor for electrolyte abnormalities and hypoglycemia. Replenish as necessary
c) Monitor for hypertriglyceridemia, fat embolism, and infection

Beta-blocker / Calcium Channel Blocker Toxicity

Background

Mechanism of Toxicity

- Calcium channel blockers: both dihydropyridines and non-dihydropyridines target the L-type voltage gated calcium channels which are responsible for releasing calcium from the sarcoplasmic reticulum to trigger myocardial contraction. Calcium entry into the myocardial cells during the plateau phase of the action potential eventually leads to release calcium from the sarcoplasmic reticulum for use in the cytosol. Cytosolic calcium concentrations are primarily responsible for maintaining vascular smooth muscle tone. Maintenance of adequate stores of intracellular calcium are also responsible for the release of insulin, suggesting reasonable concern for profound hyperglycemia when L-type calcium channels are blocked. With significant overdoses, serum and tissue concentrations are so excessive that pharmacologic differences in affinity and action (between DHP and Non-DHP) are irrelevant. Furthermore, when overdosed these agents interfere with calcium-stimulated mitochondrial action and glucose catabolism resulting in lactic acid production, ATP hydrolysis and an acidemic state.
    - Pharmacokinetics/dynamics
        - Absorption: good oral absorption
        - Distribution: highly lipophilic, binding to plasma proteins, >2 L/kg Vd
        - Metabolism: extensive hepatic first-pass metabolism
        - Elimination: HD is ineffective due to high lipophilicity
- Beta-blockers: the mechanism of overdose is due to decrease of myocardial activity triggering bradycardia and decreased contractility. Normally, more lipophilic beta-blockers (e.g., propranolol) easily cross the blood brain barrier and cause CNS manifestations, whereas lipophobic/water-soluble beta-blockers (e.g., atenolol) are associated with tiredness and fatigue. However, receptor selectivity is lost in most cases of beta-blocker overdose.
    - Pharmacokinetics/dynamics
        - Absorption: good oral absorption
        - Distribution: degree of lipophilicity influences Vd
        - Metabolism: extensive hepatic first-pass metabolism
        - Elimination: liver excretion mainly

Clinical Presentation

- Hypotension, bradycardia, altered mental status
- ECG may reveal sinus bradycardia, AV block, QT prolongation

References

1. Barrueto, Fermin. “Calcium channel blocker poisoning”. UpToDate. May 18, 2022.
2. Chakraborty RK, Hamilton RJ. Calcium Channel Blocker Toxicity. [Updated 2022 Apr 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537147/
3. Khalid MM, Galuska MA, Hamilton RJ. Beta-Blocker Toxicity. [Updated 2022 Jul 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448097/
4. Krenz JR, Kaakeh Y. An Overview of Hyperinsulinemic-Euglycemic Therapy in Calcium Channel Blocker and β-blocker Overdose. *Pharmacotherapy*. 2018;38(11):1130-1142. doi:10.1002/phar.2177
5. St-Onge, Maude et al. “Experts Consensus Recommendations for the Management of Calcium Channel Blocker Poisoning in Adults.” Critical care medicine vol. 45,3 (2017): e306-e315. doi:10.1097/CCM.0000000000002087
6. ToxED.com