Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

ToxTidbits: Antidote Facts

1-800-222-1222

High-Dose Insulin (HDI)

Calcium channel blocker (CCB) and beta blocker (BB) overdose can result in life-threatening cardiovascular collapse. There are several pharmaceutical therapeutic interventions that can be initiated to provide cardiovascular support in the setting of bradycardia and hypotension. These include calcium, glucagon, vasopressors (e.g. norepinephrine and epinephrine) and HDI therapy.

Mechanism/Indications: The proposed mechanisms of action of HDI include: 1. increased inotropy, 2. increased glucose metabolism, 3. vascular dilatation. Cardiac tissues preferentially utilize fatty acid as an energy source during normal conditions; under stressed conditions (hypotension or drug-induced toxicity) cardiac tissues rely on glucose metabolism as their primary energy source. CCB overdose decreases insulin release from the pancreas by blocking L-type Ca channels, which can further inhibit glucose metabolism in cardiac tissues. Severe CCB or BB overdose may result in cardiogenic shock that is refractory to initial interventions such as calcium, glucagon or vasopressor infusion. High-dose insulin therapy has demonstrated improvement in CCB- or BB-induced hypotension in both animal and human studies. Insulin has a positive inotropic effect on the heart by improving metabolic support of cardiac tissues during hypotensive shock. Some studies have also demonstrated that high doses of insulin can induce endothelial nitric oxide synthase activity and improve microvascular dysfunction by a vasodilatory effect in cardiac and pulmonary vasculature.

High-dose insulin therapy should be initiated in severe CCB and BB overdoses with refractory hypotension. Clinical effect may be delayed up to 15 to 60 minutes. Thus, vasopressor support and/or glucagon should be initiated in conjunction with HDI and titrated down as tolerated. Further intervention (e.g. intravenous lipid emulsion) should be considered if the patient is refractory to HDI.

Insulin Dosing:

- Insulin (regular) 1 unit/kg IV bolus, then 0.5 – 1 unit/kg/hr continuous infusion.
- Titrate HDI infusion by 1 unit/kg/hr every 30 – 45 minutes to achieve desired hemodynamic status.
- Up to 10 units/kg/hr has been infused in case reports.
- If glucose is <250 mg/dL, give 50mL of D50 IV bolus, then initiate dextrose infusion 0.5 gm/kg/hr.
    - Consider D20/D25 solutions (vs. D5/D10 solutions) to minimize infusion volume.
- Potassium supplementation may be needed.

Adverse Effects: Adverse effects associated with administration of high-dose insulin are primarily hypoglycemia and hypokalemia. Dextrose infusion and potassium supplementation may be required.

High-Dose Insulin (continued)

For more on high-dose insulin:

- *Engebretsen KM et al. High-dose insulin therapy in beta-blocker and calcium channel-blocker poisoning. Clin Toxicol 2011:49;277-283.*
- *Hoffman RS, Howland MA, Lewin NA, Nelson LS, Goldfrank, LR. Goldfrank's Toxicologic Emergencies. 10th ed. New York: McGraw Hill Medical; 2015. Antidotes in Depth: High-Dose Insulin Euglycemia; p.851-855.*
- *St-Onge M et al. Treatment for calcium channel blocker poisoning: a systematic review. Clin Toxicol 2014:52:926-944.*
- *Jang DH et al. Toxin-induced cardiovascular failure. Emerge Med Clin North Am 2014;32:79-102.*
- *DeWitt CR, Waksman JC. Pharmacology, pathophysiology and management of calcium channel blocker and beta-blocker toxicity. Toxicol Rev 2004:23;223-38.*

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