High-Dose Insulin (HDI) Therapy

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 high-dose insulin (HDI) therapy.

**Mechanism/Indications:** The proposed mechanism of action of HDI includes: 1. increased inotropy, 2. increased glucose metabolism, 3. vascular dilatation. Cardiac tissues preferentially utilize fatty acid as an energy source during normal condition; 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 calcium 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 overdose with refractory hypotension. Clinical effect may be delayed up to 15 to 60 minutes; therefore, vasopressor support 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:**
- Starting dose: 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.
- Response to insulin infusion may take 15 – 60 minutes; therefore, vasopressor support should also be initiated and titrated down as needed/tolerated.
- Up to 10 units/kg/hr has been infused in case reports.
- If glucose is < 250 mg/dL, give D50 50mL IV bolus, then initiate dextrose infusion 0.5 gm/kg/hr.
- Potassium supplementation may be needed.

**Contraindications:**
- None
High-dose insulin therapy (continued)

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

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For more on HDI:


March 2016