

HYPERINSULINEMIA EUGLYCEMIA THERAPY (HIET) FOR BETA BLOCKER (BB) AND CALCIUM CHANNEL BLOCKER (CCB) TOXICITY

Background

- Under normal physiologic conditions the heart prefers to use free fatty acids as its primary energy source. In a stressed state the heart turns to prefer carbohydrate and insulin appears to facilitate this preference.
- Insulin increases myocardial glucose uptake resulting in positive inotropic and chronotropic effects.
- Insulin bolus and infusion can take 20-30 minutes to induce clinical inotropic/chronotropic effect.
- HIET has been shown to be a safe and effective treatment for BB and CCB toxicity.
- Hypoglycemia and hypokalemia are potential adverse events when using HIET. Glucose and electrolytes should be closely monitored while using this therapy.

Monitoring

- Contact the Poison Center and follow their recommendation including indication for need of gastric lavage.
- Check baseline creatinine, glucose, and potassium.
- Blood glucose every 30 minutes for 1-2 hours until stable. It should be maintained between 150-250 mg/dL and checked prior to every titration.
- Monitor serum potassium every hour during titration, then every 4-6 hours once steady state is reached. Maintain serum potassium ≥ 2.8 mEq/L.
- Monitor calcium, magnesium and phosphorus every 4-6 hours and replace as needed.
- Obtain central venous access for safe infusion of concentrated glucose. Concentrate all fluids to avoid volume overload and pulmonary edema.
- Obtain a bedside echocardiogram upon arrival to estimate the patient's LV function. Consider repeat after 1-2 days of insulin therapy. An improvement in LV function is a good sign that therapy is working.

Management

- Traditional management includes fluid resuscitation, atropine, cardiac pacing, calcium, +/- glucagon and vasopressors. When these fail, care may escalate to ECMO.
- Vasopressors IV infusions will usually include combinations of norepinephrine, epinephrine, and vasopressin along with balanced crystalloids targeting MAP >65 mmHg or SBP >90 mmHg and UO >0.5 mL/Kg/h.
- Glucagon: 1 mg IV over 5 min and start infusion at 5-15 mcg/min if needed.

HIET initiation:

- 1 U/kg of regular insulin IV push.
- If serum glucose <250 mg/dL, concurrently administer a bolus of dextrose 25-50 g (or 0.5-1 g/kg) IV.

HIET Continuous Infusion:

A wide range of continuous maintenance infusion of insulin for inotropic/chronotropic support have been reported with apparent safe use in the range of 3-10 Units/kg/hr.

- Begin infusion of 1 U/kg/hr of regular insulin along with an infusion of dextrose; use D20 via a peripheral IV line until central access has been obtained, then start D50 at 25 g/hr.
- Increase insulin infusion 1-2 U/kg/hr every 10-15 minutes to a maximum of 10 U/kg/hr until shock improves (similar to administration of a pressor to maintain a desired hemodynamic effect). Titrate to maintain glucose 150 - 250 mg/dL.
- If the fluid overload is a concern, the insulin can be concentrated to 10 U/mL.

- If hypoglycemia does occur, bolus with dextrose and/or increase dextrose infusion first before considering a decrease or cessation of insulin infusion. For every hypoglycemic reading, give 25 g of D50 as a bolus and increase the dextrose infusion by 25 g/hr.

Therapeutic end points:

Use balanced crystalloids and combination of norepinephrine, epinephrine, and vasopressin.

- SBP >90 mmHg
- HR >60/min
- UO >0.5 mL/kg/h, improve mentation and resolution of acidemia with normal lactate value
- Once stable, wean vasopressors before HIET.
- HIET is weaned after withdrawal of other vasopressors. Contact the Poison Center regarding weaning of HIET once stability has been reached.