Clinical Pharmacology & Toxicology Pearl of the Week

~ High Dose Insulin and Glucose ~

Background

- ✓ Overdose of calcium channel blockers may cause hypotension, bradycardia, and hyperglycemia.
- ✓ During shock, the heart becomes dependent on carbohydrates for energy.
- ✓ Administration of insulin permits maximal myocardial utilization of carbohydrates during shock and improves myocardial function without increasing oxygen consumption (i.e. myocardial work).
- ✓ Evidence for use of HIE therapy is greatest in calcium channel blocker poisoning but may also be used for beta blockers.

Indications

- ✓ Hemodynamic instability secondary to either calcium channel blockers or beta blockers which is unresponsive to conventional resuscitation and advanced cardiac life support therapies (e.g. fluid boluses, atropine, calcium, glucagon, vasopressors).

Dosing

Insulin:

- ✓ Continue conventional resuscitation and advanced cardiac life support therapies.
- ✓ Administer 1 unit/kg intravenous bolus of regular insulin (e.g. Humulin R).
- ✓ Follow the bolus with an insulin infusion of 0.5-1 units/kg/hour. Infusion can be titrated beyond 1 unit/kg/hour if needed to a maximum of 10 units/kg/hr.
    - o For concentration of 1 unit/mL, prepare infusion by adding 100 units (1 mL) of regular insulin to 100 mL normal saline for final concentration of 100 units/100 mL.
    - o If fluid overload is a concern, a more concentrated infusion (16 units/mL) can be used. To prepare the concentrated infusion, remove 40 mL from 250 mL normal saline bag. Add 4000 units (40 mL) of regular insulin for final concentration of 4000 units/250 mL.
- ✓ A blood pressure (BP) response to HIE is typically seen within 30-60 minutes of starting therapy. Target systolic BP is > 100 mm Hg.
- ✓ Target heart rate (HR) is > 50 BPM. Note that HR may not improve with HIE therapy.
- ✓ Improvements in urine output, mental status, and skin perfusion are also useful indicators of HIE effectiveness.
- ✓ Once improvement in SBP has been established and maintained, wean vasopressors as tolerated.

Glucose:

- ✓ Because calcium channel blocker poisoned patients are often hyperglycemic, supplemental glucose may not be required.
- ✓ Administer dextrose bolus to patients with initial blood glucose of less than 13 mmol/L.
    - o For adults, give 50 mL of dextrose 50% (1 amp of D50W, which is 25 g dextrose).
    - o For children, give 0.25 g/kg of dextrose 25% (most easily performed by adding 50 cc of D50W to a 50cc minibag of NS).
- ✓ Follow with a dextrose infusion of D10NS at 80% of maintenance (assume maintenance = 150 cc/hr in adults). Patients who have initially low blood glucose may need higher infusions of dextrose (0.5 to 1.0 g/kg/hr of dextrose). Given the potentially high fluid rates needed for less concentrated solutions such as D10NS, consider utilizing central venous access for administration of higher glucose solutions at higher rates.
- ✓ Supplement the infusion as needed with repeat dextrose boluses as described above if hypoglycemia develops.
- ✓ Monitor blood glucose every 15 to 30 minutes until consistently 5 to 11 mmol/L for 4 hours, then monitor every hour. Titrate dextrose infusion to maintain blood glucose in the range of 5 to 11 mmol/L.
- ✓ Once cardiovascular stability is achieved, the insulin infusion can be slowly titrated off. Continue the dextrose infusion and monitoring the serum glucose after the insulin infusion is off, as the effects of insulin can be prolonged.

Potassium:

- ✓ Administer supplemental potassium initially if patient is hypokalemic. Several doses of potassium orally or via oro/nasogastric tube and even intravenous potassium may be required. Maintain the serum potassium above 3.5 mmol/L.
- ✓ Monitor serum potassium every hour while actively titrating the insulin infusion, then every 4 hours once the infusion is stabilized.
- ✓ Continue to monitor the serum potassium after the cessation of the insulin infusion as the effects of insulin can be prolonged.

References

1. Megarbane et al. The Role of Insulin and Glucose (Hyperinsulinaemia/Euglycaemia) Therapy in Acute Calcium Channel Antagonist and β-Blocker Poisoning. Toxicol Rev 2004;23(4) 215-222.
2. Kerns W. Management of Beta Adrenergic Blocker and Calcium Channel Blocker Toxicity. Emerg Med Clin NA 2007;25:309-331
3. Boyer et al. Hyperinsulinemia/euglycemia therapy for calcium channel blocker poisoning. Ped Emerg Care 2002.18(1);36-7.
4. Laskey D et al. Stability of high-dose insulin in normal saline bags for treatment of calcium channel blocker and beta blocker overdose. Clin Tox 2016. 54(9):829-32.
5. Alberta Children's Hospital – Pediatric Intensive Care Unit: Drug and Dosing Guidelines 2005
6. Page CB, Ryan NM, Isbister GK. The safety of high-dose insulin euglycaemia therapy in toxin-induced cardiac toxicity. Clin Tox 2017 October 26:1-8.

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click HERE for clinical issues the CP service can assist with.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.