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).

Starting Treatment

1. Continue conventional resuscitation and advanced cardiac life support measures.

2. Measure potassium and glucose prior to initiation of HDIG treatment.
    a. Supplement potassium and dextrose as needed.
    b. Do not initiate HDIG treatment until glucose is greater than 4.0 mmol/L and potassium is greater than 2.8 mmol/L.

3. To start HDIG treatment, administer insulin regular (i.e., HumuLIN R) 1 unit/kg IV bolus.

4. After the insulin bolus, immediately start an infusion of insulin regular 1 unit/kg/hour IV.

5. If glucose is less than 13.0 mmol/L prior to insulin bolus:
    a. Adult: Administer 50% dextrose (D50) 25 g IV bolus.
    b. Pediatric: Administer 25% dextrose (D25) 0.25 g/kg bolus.

6. For all patients, start a continuous infusion of 10% dextrose (D10) at 80% of the patient's maintenance fluids rate (assuming a 150 mL/hour maintenance rate for adults).

7. It may take up to 30-60 minutes to start seeing improvement after initiation of HDIG treatment. Other therapies including vasopressors should be continued.

Ongoing Treatment and Monitoring

1. Monitor glucose every 15 to 30 minutes until consistently 5 to 11 mmol/L for 4 hours.
    a. CCB poisoned patients can be hyperglycemic and may not require supplemental dextrose. Continue to monitor glucose even if no supplementation required.
    b. Titrate dextrose infusion rate to target blood glucose between 5 to 11 mmol/L.
    c. If glucose is less than 4.0 mmol, administer dextrose bolus and increase dextrose infusion rate. Do NOT stop the insulin infusion.
    d. Once blood glucose has been within the target range for 4 hours, transition to monitoring blood glucose once every hour.

2. If requiring a rate of more than maintenance on D10, a more concentrated dextrose infusion should be started to avoid volume overload. Dextrose concentrations greater than or equal to 20% (e.g., D25) require a central line for use as a continuous infusion.

3. Assess for signs of improvement with HDIG therapy by monitoring for signs of improved organ perfusion including blood pressure, urine output, mental status, skin perfusion and serum lactate level. Note that HR may not improve with HDIG.
    a. If no improvement, titrate the insulin infusion up to a maximum infusion rate of 10 units/kg/hour.
    b. Assessment of cardiac contractility with point-of-care or formal echocardiogram may also guide response to treatment.
        i. If ongoing poor contractility, continue to titrate up the insulin infusion.
        ii. Once contractility has been maximized, if hypotension and/or hypoperfusion persist, other therapies should be pursued.

4. Monitor serum potassium every hour while initiating or titrating the insulin infusion, followed by every 4 hours once the insulin infusion rate is stable.
    a. Replace potassium with IV and/or oral supplementation as required to maintain serum potassium level between 3.0 to 4.0 mmol/L.

5. If the patient has continued signs of shock or increased vasopressor requirements despite HDIG treatment, consult PADIS to review additional treatment options with the Medical Toxicologist.

Discontinuation of Treatment

1. Once improvement in systolic blood pressure and perfusion is achieved and maintained, begin to wean vasopressors.

2. When the patient is requiring no vasopressors, begin to titrate down the insulin infusion.

3. After HDIG treatment, the effects of insulin can be prolonged. Blood glucose and potassium should continue to be monitored for 24 hours after insulin is discontinued.

References

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4. Laskey D. 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.

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8. Baruetto F. Calcium channel blocker poisoning. In: UpToDate, Stolbach A (Ed), Wolters Kluwer. (Accessed on June 8, 2024).

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The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in Alberta Referral Directory (ARD) by searching "Toxicology" from the ARD home page.

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