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Settling Controversies in the Management of Hyperkalemia: Focus on Calcium and Insulin

Session overview

Hyperkalemia is a common, life-threatening electrolyte emergency, yet several controversies exist related to its management including administration of calcium in the absence of ECG changes, which calcium salt is best, and co-administration of dextrose plus insulin. This session will explore practical issues associated with hyperkalemia pharmacotherapy and associated patient-oriented outcomes.

Objectives

- Evaluate recommendations for dosing and administration of parenteral calcium.
- Apply practical methods for co-administration of insulin and dextrose.

Calcium

- Why we give it
    - Elevated calcium concentration decreases the depolarization effect of an elevated K+. IV calcium antagonizes cardiac membrane excitability thereby protecting the heart against dysrhythmias. (Am J Physiol 1956; UK Renal Association Guidelines 2014)
- When we give it
    - Life-threatening ECG changes, dysrhythmias, & cardiac arrest - YES
    - Peaked T waves - PROBABLY
    - Normal ECG - PROBABLY NOT
        - ECG can be normal, but in some cases is an insensitive marker for assessing severity (Tex Heart Inst J 2006; Am J Kidney Dis 1986; Int J Clin Pract 2001)
- How to dose it
    - Optimal dose unclear; start with at least 1 gm $CaCl_2$ or 2 gm calcium gluconate IV
    - Onset ~3 minutes; redose in 5-10 minutes if no effect seen from first dose
    - Effects last 30-60 minutes (may need to redose if further treatment needed while awaiting emergent HD)
- Which salt to give
    - Calcium gluconate does not act slower than $CaCl_2$ because it needs hepatic activation!
        - Serum ionized calcium levels were measured in 15 hypocalcemic patients during the anhepatic stage of liver transplantation (before and up to 10 min after calcium therapy). Half received $CaCl_2$ 10 mg/kg, the other half received calcium gluconate 30 mg/kg. Equally rapid increases in calcium concentration after administration of $CaCl_2$ and gluconate were observed, suggesting that calcium gluconate does not require hepatic metabolism for the release of calcium and is as effective as $CaCl_2$ in treating hypocalcemia in the absence of hepatic function. (Martin, Anesthesiology 1990)
        - Same result in another study of children and dogs (Cote, Anesthesiology 1987)
        - Same result in a study of ferrets and in vitro human blood (Heining, Anaesthesia 1984)

Insulin and Dextrose

- How insulin works
    - Temporarily shifts potassium intracellularly through a complex process of activating Na+-K+ ATPase and by recruitment of intracellular pump components into the plasma membrane. Insulin binding to specific membrane receptors results in extrusion of Na+ and cellular uptake of K+. (Hundal, J Biol Chem 1992)
- The right insulin dose
    - 5 unit boluses up to 20 unit/hr infusions have been used (Am J Med 1988). Most common dose studied is 10 units IV regular insulin bolus (lowers K+ ~ 0.5-1 mEq/L).
- Preventing hypoglycemia
    - Hypoglycemia when treating hyperkalemia is such an important problem, The Institute for Safe Medication Practices highlighted it in a February 2018 Safety Alert
    - Incidence of hypoglycemia
        - A 10 unit dose of IV regular insulin has an onset of action ~5-10 minutes, peaks at 25-30 minutes, and lasts 2-3 hours. IV dextrose only lasts about an hour.
        - Overall incidence of hypoglycemia appears to be ~10%, but could be higher (Kidney Int 1990; J Hosp Med 2012; Apel, Clin Kidney J 2014)
    - Risk factors for developing hypoglycemia (Apel, Clin Kidney J 2014)
        - No prior diagnosis of diabetes
        - No use of diabetes medication prior to admission
        - Lower pretreatment glucose (104 ± 12 mg/dL vs 162 ± 11 mg/dL, P = 0.04)
        - Renal dysfunction (insulin may be partially renally metabolized) (Nutrition 2011)
        - Higher insulin dose (LaRue, Pharmacother 2017)
    - Strategies for avoiding hypoglycemia
        - Here is a suggested strategy for administering enough dextrose to counter the initial insulin bolus of 10 or 20 units. It is loosely based on the Rush University protocol. (Apel, Clin Kidney J 2014)