Clinical Pharmacology & Toxicology Pearl of the Week

~ Propofol-Related Infusion Syndrome (PRIS) ~

Mechanism of PRIS

- ✓ High doses of propofol (greater than 3mg/kg/h) lead to direct inhibition and uncoupling of mitochondrial electron transport chains, leading to greater reliance on anaerobic metabolism.
- ✓ Propofol also inhibits fatty acid metabolism, which leads to increased serum free fatty acids, hepatic steatosis & impaired lactate clearance.
- ✓ Muscle tissues are unable to metabolize fatty acids which leads to rhabdomyolysis

Clinical presentation

- ✓ Risk factors for the occurrence of PRIS include infusions rates ≥ 4mg/kg/h, prolonged continuous infusion ≥ 20-hours, carbohydrate depletion, catecholamine administration, severe stress, glucocorticoid use.
- ✓ The onset of PRIS can occur as early as following 20 hours of continuous propofol infusion
- ✓ The presence of metabolic acidosis is the most commonly reported initial sign of PRIS

Diagnosis

- ✓ Diagnosis is based on a constellation of clinical suspicion and biochemical signs including:
  - Hyperlactatemia
  - Metabolic acidosis
  - Rhabdomyolysis
  - Hepatomegaly
  - Hypertriglyceridemia
  - Hyperkalemia and renal failure

- ✓ Dysrhythmias can occur with a Brugada-pattern on ECG defined by coved-type ST segment elevations in the precordial leads

Management

- ✓ Early recognition is key to appropriate management
- ✓ Once PRIS is suspected, immediate discontinuation of propofol infusion is necessary
- ✓ Any additional administration of triglycerides (eg. TPN) should be discontinued
- ✓ Supportive management is the mainstay of treatment of PRIS

Prognosis

- ✓ PRIS mortality is 35% despite withdrawal of propofol and maximal supportive therapy
- ✓ The presence of hyperthermia is a very poor prognostic factor and is associated with an increased risk of heart failure and sudden death.

References:

1. Mirrakhimov AE, Voore P, Halytskyy O, Khan M, Ali AM. Propofol infusion syndrome in adults: a clinical update. *Crit Care Res Pract*. 2015;2015:260385

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.