Clinical Pharmacology & Toxicology Pearl of the Week

~ Acute Iron Poisoning ~

Iron Pharmacology

- ✓ Iron is absorbed in its ferrous state (Fe^{2+}) within the proximal small bowel primarily via DMT-1 along the apical surface and via Ferroportin along the basolateral surface.
- ✓ The protein Hepcidin regulates transport protein expression and prevents excessive absorption of iron.
- ✓ Physiologic regulation of iron absorption becomes dysfunctional in massive ingestion
- ✓ There are no physiologic mechanisms for iron excretion

Iron Toxicity

- ✓ Iron exerts toxic effect through lipid peroxidation and free radical production culminating in caustic mucosal injury and "pseudo-uncoupling" of oxidative phosphorylation
- ✓ Life threatening toxicity may develop with doses greater than 60mg/kg of elemental iron
- ✓ A **Serum Iron Concentration (SIC)** at 4-6 hours post ingestion is prognostically relevant **(See Figure 2)**
- ✓ There are five classically described phases of toxicity:

Common sources of Iron (Figure 1)

- Ferrous Gluconate – 12% elemental iron
- Ferrous Sulfate – 20% elemental iron
- Ferrous Fumarate – 33% elemental iron

SIC Levels and associated morbidity (Figure 2)

- SIC < 63 umol/L – Minimal symptoms
- SIC 63 – 90 umol/L – Moderate toxicity
- SIC 90 – 180 umol/L – Serious toxicity
- SIC > 180 umol/L – Life-threatening toxicity

Gastrointestinal phase (~6 hours post-ingestion)
- Secondary to caustic mucosal injury
- Abdominal pain, nausea, vomiting

Latent phase (6-24 hours post-ingestion)
- Symptom resolution due to iron redistribution
- Often absent in severe toxicity however presence does not preclude deterioration

Shock and metabolic acidosis (12-48 hours post-ingestion)
- Anion gap metabolic acidosis with both distributive and cardiogenic shock
- Progressive multi-organ failure (ARDS, coagulopathy, renal failure)

Hepatotoxicity (24-96 hours post-ingestion)
- Massive hepatic iron deposition leads to acute hepatic necrosis

Bowel Obstruction (2-8 weeks post-ingestion)
- Secondary to caustic bowel injury and subsequent luminal scarring and stenosis

Management

- ✓ Obtain SIC 4-6 hours post ingestion and calculate the per-kilogram ingestion of elemental iron
- ✓ **Decontamination:** Whole bowel irrigation may play a role in large volume ingestion. Activated charcoal is **not** effective at binding iron
- ✓ **Antidote:** Deferoxamine is a chelating agent that binds ferric iron in the blood to form the water soluble compound ferrioxamine which can be renally excreted. Conventional dosing starts at 15 mg/kg/hr
- ✓ **Indications for deferoxamine include the following:** severe signs and symptoms including shock, metabolic acidosis, pills on abdominal x-ray, SIC > 90 umol/L, ingestion > 60 mg/kg elemental iron in remote areas unable to obtain a stat SIC

- ✓ Hypotension and ARDS may complicate administration of deferoxamine, especially if administration is continued for longer than 24 hours. Consultation with a medical toxicologist is recommended.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the Alberta Referral Directory (ARD) by searching "Pharmacology" from the ARD home page. Click HERE for more details about the service.

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. More CPT Pearls of the Week can be found HERE.

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