IRON POISONING

ขอขอบคุณ รศ.พญ.จุฬธิดา โฉมฉาย
วิทยาลัยนานาชาติมหาวิทยาลัยมหิดล

- เด็กหญิงไทยอายุ 15 เดือน กินยาบำรุงเลือดของมารดามา ประมาน 20-30 เม็ด 3 ชั่วโมงก่อนมาโรงพยาบาล
- ผู้ป่วยเป็นบุตรคนที่ 4 มารดาเป็นคนงานก่อสร้าง ได้ออกไปทำงานและได้ทั้งผู้ป่วยและพี่อีก 3 คนไว้บ้านให้ป้าดูแล ก่อนเกิดเหตุ พี่ของผู้ป่วยได้หยิบขวดยา Haemovit ®ที่มียาเหลืออยู่ประมานครึ่งขวด มาจากหลังตู้เพื่อมาเล่น และผู้ป่วยได้กินไปจนหมด หลังกินมีอาเจียน 5-6 ครั้ง บ่นปวดท้องมาก และมีถ่ายเหลวสีดำ มารดาจึงได้พามาโรงพยาบาล

- Vital signs:
  - HR 119 bpm BP 80/60 RR 35/min
- Physical exam:
  - Alert active infant
  - Dry lips
  - Diffusely tender abdomen
    No guarding Decreased bowel sounds
  - Capillary refill <2 seconds

- แพทย์ที่โรงพยาบาลชุมชน ประเมินว่าเด็ก ดูดี หยุดอาเจียนแล้ว มี mild-moderate dehydration จึงให้ IVF และ consult ศูนย์พิษเพื่อปรึกษาว่าจะส่งต่อไปโรงพยาบาลจังหวัดหรือไม่?

- Baseline lab ที่โรงพยาบาลชุมชน
- CBC:
  - WBC 22,000
  - Platelet 450,000K
  - Hgb/HCT= 10.2/33
  - Blood glucose= 350
  - Elyte Na 135 K 4.2 Cl 101 Bicarb 13 Anion Gap=21

- Diagnosis: significant iron overdose with moderate dehydration
  - Symptomatic with vomiting and diarrhea
  - Acidosis
  - Leukocytosis with hyperglycemia

Iron preparations available in the market

Iron Formulation	*Elemental Iron (%)*
Ionic	
Ferrous chloride	28
Ferrous fumarate	33
Ferrous gluconate	12
Ferrous lactate	19
Ferrous sulfate	20
Nonionic	98[a]
Carbonyl iron	46[a]
Polysaccharide iron	

Pathophysiology of iron poisoning

- Iron is available in myoglobin, hemoglobin and cytochromes
- It can undergo redox reactions, changing from ferrous (Fe2+) to ferric (Fe3+)
- Normally iron is absorbed in the duodenum and is either stored as ferritin or transported to different organs via an iron-binding protein, transferrin
- Absorption, transport and utilization of iron is strictly regulated
- Absorption is usually limited at therapeutic dosing

Pathophysiology of Iron poisoning

- Quantity of elemental iron is the primary determinant of toxicity
- toxic effects occur at 10-20 mg/kg elemental iron
- GI epithelia damage promote iron absorption
- Upon absorption, ferrous iron (Fe2+) is converted to Ferric iron (Fe3+) and an unbuffered hydrogen ion is liberated
- Transferin is saturated
  - Increase in free iron
  - Increased distribution to organs

Pathophysiology

- Oxidative stress
  - Iron in mitochodria disrupts oxidative phosphorylation resulting in free radical formation and lipid peroxidation
  - Free iron also inhibits thrombin formation, resulting in coagulopathy not related to hepatic damage
    - Results in
      - Disruption of oxydative phosphorylation
      - Metabolic acidosis
      - Inhibition of thrombin leading to coagulopathy

Iron toxicity-clinical manifestation

- Iron toxicity occur in 5 stages
- Gastrointestinal damage (0-6 hours after ingestion)
  - Occur from local corrosive effects of iron
  - Permits excessive absorption of unbuffered iron ions into the systemic circulation
- Systemic absorption (6-24 hours after absorption)
  - Unbound irons can cause oxidative damage to tissues
  - Inhibit oxidative phosporylation process in the mitochondria causing lactic acidosis
  - Decreased thormbin formation leading to coagulopathy unrelated to hepatotoxicity

- Shock stage (12-24 hours after ingestion)
  - Hypovolemia, acidosis, poor cardiac output, iron-induced coagulopathy, lethargy, hypoventillation, coma
- Hepatic failure (2-3 days after ingestion)
- Gastric outlet obstruction (2-8 weeks) due to corrosive damage

Summary of clinical effects of iron toxicity

- Local corrosive effects
- Oxidative damage to GI mucosa
- Multiorgan damage including direct toxicity to liver, lungs and heart
- Increased proton formation from oxidized iron leads to metabolic acidosis
- Inhibition of thrombin formation

Stages of iron poisoning and pathophysiology

Clinical stage	Symptoms	Pathophysiology
I-local effects (within 6 hrs)	Nausea, vomiting, abdominal pain	Direct oxidative damage to gastric mucosal
II- latent phase (latent 6-24 hrs)	Gi symptoms resolved, metabolic acidosis ensued	On going free radical damage
III- shock stage	Hypovolemic shock, coagulopathy, acidosis	Inhibition of cellular respiration On going oxidative damage
IV (2-3 days)	Hepatic failure	Direct uptake of iron into reticuloendothelial system
V	Gastric outlet obstruction	Stricture and scaring from corrosive injury

Management

- Initial approach
  - ABC
  - Hemodynamic stability
- Limiting absorption
  - Whole bowel irrigation with Colyte®
- Giving antidote
  - deferoxamine

Predicting iron toxicity

- Iron level
  - Peak level occur 4-6 hours after ingestion
  - Level > 300mcg/dL – gastrointestinal symptoms
  - Level > 300-500 mcg/dL- gastrointestinal with systemic
  - Level > 500 mcg/dL- significant morbidity/mortality
- Abdominal radiographs
- follow efficacy of WBI in removing iron tablets
- CBC + serum glucose
  - WBC > 15,000 mm3 and serum glucose of 150 mg/dl
- Elyte
  - acidosis secondary to dehydration and as a direct toxic effect of iron on cellular respiration

Laboratory studies

- Labs used as surrogate marker of toxicity
- Serum glucose > 150 mg/dL and WBC > 15,000 (unreliable when negative)
- Serum iron > 300 µg/dL (interpret with care depending on absorption time)
- TIBC > [serum iron] but TIBC can be elevated as an acute phase reactant ----no value in predicting toxicity

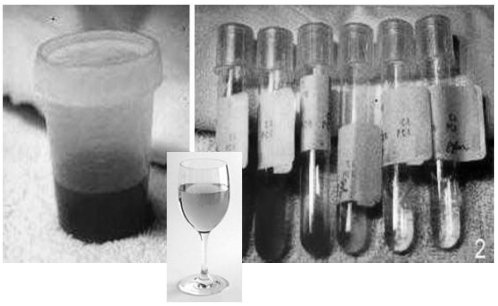
How reliable is the radiograph?

- Adult formulation with high iron contents are more likely to be radiopague
- liquid and chewable vitamins with iron are less likely to be radiopague
- Careful clinical observation is required with or without x-ray findings
  - patients with significant history of ingestion and/ or significant symptoms should be worked up and decontaminated

Deferoxamine in acute iron poisoning

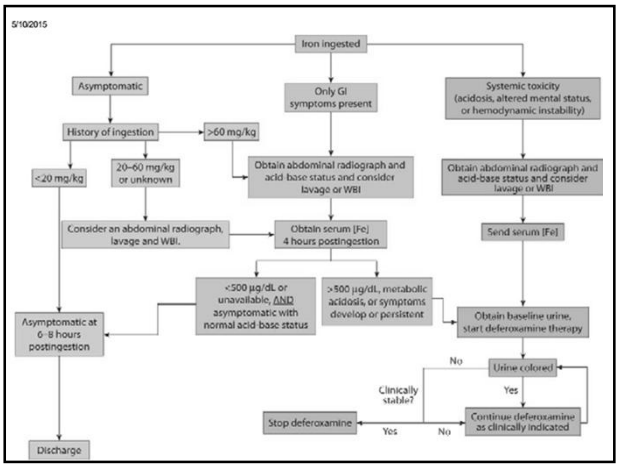
- Binds Fe 3+ ions in cytoplasm and mitochondria
- Effective in decreasing toxicity to cellular respiration
- Effective at preventing complications of iron poisoning
  - when administered early and in conjunction with whole bowel irrigation
- adverse effects occur when given as RAPID intravenous infusion
  - tachycardia, hypotension, shock, erythema and urticaria
- Prolonged use > 24 hours have been associated with ARDS(ALI)
- DFO-iron complex enhances growth of *Yersinia* and *Aeromonas*

Vin Rose Urine after chelation with deferoxamine



Progress

- ผู้ป่วยได้รับการ refer ไป รพ จังหวัด ที่นั่นไม่มี polyethylene glycol จึง refer ผู้ป่วยต่อไปยัง รพ. ศูนย์
- ได้รับการทำ whole bowel irrigation ที่ 18 ชม หลังกิน
- Serum iron 170
- Plan discharge หลังทำ whole bowel irrigatioin
- ที่ 72 ชม หลังกิน ผู้ป่วยมี massive gastrointestinal bleeding และ DIC
- ให้ blood products และ supportive care
- Discharge ที่ day 6



Prevention

- Keep medication in a locked cabinet
- Never say medicine is candy
- Pick up medicines when they are dropped on the floor
- Never store medication or chemicals in containers that used to contain food