Pregnant Patient with Intentional Iron Overdose

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Target Audience: Emergency Medicine, Medical Students

Primary Learning Objectives:

- 1. Immediate management of the acutely unstable patient.
- 2. Identification of pregnancy as a risk factor for overdose/suicidal intent.
- 3. Obtain good history including collateral to identify prenatal vitamin overdose.
- 4. Manage iron toxicity with deferoxamine.
- 5. Consider whole bowel irrigation for the multiple iron tablets noted on the abdominal x-ray.

Secondary Learning Objectives: detailed technical/behavioral goals, didactic points

- 1. Describe the pathophysiology of iron toxicity
- 2. Calculate elemental iron and determine toxicity in mg/kg prior to the iron concentration returning.
- 3. Describe the management priorities for the emergent stabilization of the pregnant patient with an iron overdose including management of GI bleed and the antidote, deferoxamine.
- 4. Discuss safety of deferoxamine in pregnancy.
- 5. Explain how deferoxamine helps eliminate iron.
- 6. Monitor the patient on the deferoxamine infusion, discuss anaphylactoid reaction, and the management of this reaction.

Critical actions checklist:

- 1. Obtain IVs, monitor, recognize abnormal vital signs
- 2. Initiate IV fluid resuscitation for hypotension, tachycardia
- 3. Obtain a sitter and place on suicide precautions
- 4. Obtain investigatory studies: CBC, CMP, acetaminophen level, salicylate level, PT/INR/PTT, lactate, type and screen, pregnancy test, beta hcg, iron level
- Evaluate for fetal complications (ask LMP, assess fetal heart tones, vaginal bleeding, abdominal pain)
- 6. Obtain EKG
- 7. Transfuse pRBCs
- 8. Identify iron toxicity via pill count, labs, and iron concentration
- 9. Consult toxicology/poison control center
- 10. Treat with deferoxamine and monitor closely on the infusion for any complications including anaphylactoid reaction.
- 11. Treat the anaphylactoid reaction. Then continue the infusion at slower rate.
- 12. Once the patient is more stable, discuss safety at home, and consider social worker consult.
- 13. Consult obstetrics and psychiatry; admit to MICU.

Environment:

- 1. Room Set Up ED critical care area
 - a. Manikin Set up: wig and dress to make manikin female. Burgundy vomit around mouth, blood in basin (small amount)
 - b. Props: Standard ED equipment
 - c. Props: Iron pills: Ferrous fumarate 324 mg tabs, will need 40 tabs missing
 - d. Props: Prenatal vitamins without iron

CASE SUMMARY

SYNOPSIS OF HISTORY/ Scenario Background

33-yr-old female with no significant PMH will present with nausea, bloody emesis, abdominal pain. Will have been vomiting blood at home. Pt will be hypotensive, tachycardic. Labs will reveal a metabolic acidosis and positive pregnancy. Pt initially denies pregnancy and denies any ingestion; she refuses to speak with staff. Later, she states she is 15 weeks pregnant once positive pregnancy test comes back. She has an OB, no complications. G2P1. No prior miscarriages, ectopic pregnancy, abortions. An Xray will show iron pills in her GI tract. Further history will reveal that she overdosed on her iron supplements in a suicide attempt, unknown time of ingestion. She will need treatment with deferoxamine, pRBC transfusion, supportive care, consult toxicology/poison control center and MICU admission.

PMH: Refuses to answer. When she eventually answers, no PMH

PSH: Refuses to answer. When she eventually answers, no PSH.

Medications: Refuses to answer. When she eventually answers, she says her prenatal vitamins

Allergies: Refuses to answer. When she eventually answers, NKDA.

Social history: Refuses to answer. When she eventually answers, she denies smoking, alcohol or drug use.

Patient is sent to the critical care area of the ED.

EMS provides a pill bottle upon request by the emergency medicine physician.

40 tablets of ferrous fumarate 324 mg missing from her pill bottle.

SYNOPSIS OF PHYSICAL

Patient is awake, but depressed. She has a flat affect and does not want to answer questions. Nauseated with occasional vomiting.

Patient is tachycardic, hypotensive and in mild distress actively vomiting but protecting her airway.

HEENT: PERRLA, vomit around mouth is bloody

Chest: clear bilateral, no respiratory distress

Abdomen is diffusely tender, +bowel sounds. No rebound. No palpable uterus.

Neuro: Intact. AAOx4. GCS 15. Skin: no jaundice, no abnormalities

CRITICAL ACTIONS

1. Obtain IVs, monitor, recognize abnormal vital signs

Pt is ill appearing, vomiting blood. Place on monitor and obtain vital signs, 2 large bore IVs. o Cueing Guideline: Nurse asks if the patient should be placed on the monitor as the patient appears sick.

<u>Cueing Guideline</u>: Nurse asks if the patient should be placed on the monitor as the patient appears sick.

2. Start managing abnormal vitals, IVF for hypotension, tachycardia. Give antiemetics.

Pt starts responding to IVF with slight improvement in HR and eventually BP. Can consider pressors. Can consider sepsis workup as well. Give antiemetics.

Cueing Guideline: Nurse asks if she can repeat the vital signs after the IVF.

3. Obtain a sitter and place on suicide precautions.

More collateral info and empty bottles of iron suggest an overdose. Pt does not want to be in the ED and requests to go home.

<u>Cueing Guideline</u>: Nurse states she is calling for a sitter and to be placed on suicide precautions. Pt wants to talk to her family. Call family for collateral.

4. Obtain investigatory studies: CBC, CMP, acetaminophen level, salicylate level, PT/INR/PTT, lactate, type and screen, pregnancy test, beta hcg, iron level

Order a broad array of tests in this acutely ill pregnant patient including an iron level. Cueing Guideline: The nurse can ask the doctor if he wants any labs sent.

5. Discuss OB history, ask if vaginal bleeding, abdominal pain.

Ask more about OB history once pt stops vomiting and is feeling better. Ask if she is safe at home and if there has been any trauma.

Cueing Guideline: Nurse asks if the doctor thinks this is pregnancy related.

6. Obtain EKG

Order an EKG and discuss the read.

<u>Cueing Guideline</u>: Nurse notes patient is tachycardic with empty bottles, and asks if the medications may be affecting the patient's heart.

7. Administer pRBCs and PPI such as pantoprazole for hemorrhagic gastritis

H/H returns low and patient is symptomatic and vomiting blood.

<u>Cueing Guideline</u>: Nurse can ask doctor if they want to do anything about the patient's low hemoglobin.

8. Identify iron toxicity via pill count, labs, and iron concentration

Pt has missing ferrous fumarate tablets. Elemental iron can be calculated from this. Discussion of toxicity based on mg/kg ingestion.

<u>Cueing Guideline</u>: Nurse asks if there any way for us to figure out how much iron she took. If further cuing is needed, nurse suggests using the pill bottles to get an idea of how much iron she took.

9. Treat with deferoxamine, monitor closely on infusion.

Deferoxamine started and an anaphylactoid reaction occurs. Treat this with diphenhydramine, ranitidine, steroids, and IVF. Continue infusion at slower rate. Discuss what is happening with the patient who is agitated and upset.

<u>Cueing Guideline</u>: Nurse notes patient's trouble breathing, hives, and insists something be done.

10. Admit to MICU. Consider consulting GI, obstetrics and psychiatry.

Admit to MICU. MICU asks if GI, obstetrics and psychiatry have been notified. Discuss what is happening with the patient who is agitated and upset.

Cueing Guideline: Nurse asks who they should call for admission

Critical Actions Checklist¹

Resident										
Name										
Case										
Descri	ption									
Skills										
Core compe Patient care, knowledge, I and commur Professional based learning improvement	measured Core competencies: PC Patient care, MK Medical		Very Unacceptable		Very Unacceptable Acceptable Acceptab			y able		
Data A	cquisit	ion								
(D) PC MK I	[1	2	3	4	5	6	7	8
Proble	m Solv	ing								
(S) PC MK 1	PB	,	1	2	3	4	5	6	7	8
Patient	ţ									
Manag	ement		1	2	3	4	5	6	7	8
(M)	(M)		_							
PC MK IC P PB SB										
Resource Utilization (R)		1	2	3	4	5	6	7	8	
PC PB S										
	Health Care Provided (H) PC SB		1	2	3	4	5	6	7	8
Interpersonal Relations (I) IC P		1	2	3	4	5	6	7	8	
Comprehension of Pathophysiology (P) MK PB			1	2	3	4	5	6	7	8
Compe	Clinical Competence (C) PC MK IC P PB SB		1	2	3	4	5	6	7	8
				Critic	cal Act	ions	•	•	-	
Yes	No					mment	٠ <u>٠</u>			
		Obtai	n IVs and vital	signs	CO					
		Admi	nister initial fl	ister initial fluid resuscit						
	Orde		r a sitter/suicide precautions							
Obtai APAF		n investigatory , pregnancy te n EKG	y studies: C	BC,						
Admi		inister pRBCs								
Ident		ify iron toxicity	y and dosag	ge						
Const		ult poison control/toxicology								
		nister deferox	amine							

HISTORY

You are called to see a new patient (33-year-old female) who was transported by EMS.

Onset of Symptoms: Today

Background Info: Name: Isabelle Porter

Method of of transportation: EMS

Person giving information: Patient. Doctor can call family for

collateral.

Chief Complaint: Nausea and vomiting

Past Medical Hx: None

Past Surgical Hx: None

Habits: none

Family Med Hx: HTN

Social Hx: No recent alcohol use, no tobacco use, no

recreational drug use. She is married.

Medications: EMS brought a bag of her meds: prenatal vitamins and iron supplements (ferrous

fumarate)

PLAY OF CASE GUIDELINES

This is a case of a 33-year-old female with no PMH who presents with nausea and intermittent vomiting. Pt is able to talk the entire time. She is protecting her airway.

Pt is on bed. MUST say: "I don't want to talk to you" then "I've been throwing up." "I've been throwing up blood." "I want to die." "Just leave me alone." Pt appears depressed.

- 1. Pt is unstable with hypotension and tachycardia on arrival. Brought in by EMS. No family with her.
- 2. Iron is the primary toxicant in the case.
- 3. The patient presents with nausea and vomiting. On further questioning, she wants to die. Appears depressed, flat affect.
- 4. The participant must obtain a thorough history and physical, generate a broad differential for her abnormal vitals, low hemoglobin, metabolic acidosis, and elevated LFTs. A pregnancy test must be obtained as well as an iron concentration.
- 5. Aggressive supportive care, antiemetics, IV pantoprazole bolus and consider a pantoprazole infusion, transfuse pRBCs and administer deferoxamine infusion (can ask pharmacy for dosing of deferoxamine).
- 6. Deferoxamine anaphylactoid reaction must be identified and treated.
- 7. Consultation with the Poison Center/Toxicologist, obstetrics, gastroenterology; and the MICU for admission is required.

PHYSICAL EXAM

General Appearance: Awake, but depressed, so will not talk much, flat voice. Nauseated with occasional vomiting. Vomit has notable bright red blood.

Vital Signs: BP: 85/60 mmHg P: 130/minute R: 18/minute T: 37C (98.6F) POx: 99%

HEENT: Atraumatic. EOMI. PERRLA. No scleral icterus. Vomit around mouth.

Lungs: Clear to auscultation. No wheezes, rales, or rhonchi.

CV: Tachycardic rate and regular rhythm. No murmurs. Normal perfusion.

Abdomen: soft, but epigastric abdomen is mildly tender. Normal bowel sounds. Not palpably gravid.

Extremities: Atraumatic. No edema. Normal strength.

Rectal: +guaiac but no visible melena or hematochezia.

Pelvic: Obtain chaperone. No blood noted in vaginal vault. No dc. No adnexal ttp or CMT. No genital sores or signs of bruising or trauma.

Back: Normal. No CVA tenderness.

Neurological: Awake, alert. Not interactive. +lightheaded, near syncope if ambulation is attempted. Normal motor function. Normal sensation. AAOx4.

Skin: No track marks. No jaundice or rashes.

Required Actions within the First Two Minutes

- Perform primary survey.
- Start patient interview.
- Perform problem-based physical exam.
- Peripheral IV access established, and diagnostics should be ordered.
- Antiemetics administered and IVF started.

Branch Points

- Recheck vitals after IVF 1 or 2 L NS.
- Transition point 1 after IVF: Vital signs HR 120 BP 95/70, RR18, Sat 98% RA sinus tach on monitor
- Exam: Unchanged.
- Family member will be available on the phone (if they still have not hit diagnosis)
- Recheck patient nausea and vomiting after antiemetics.
- Pt nausea and vomiting improved after antiemetics
- If activated charcoal is ordered, patient gets worse, more vomiting, more hypotension and tachycardia.

Required Actions over the Next Four Minutes

- Diagnostics should be returned as ordered.
- Consider differential.
- Low hemoglobin/hematocrit should be recognized be treated.
- Administration of 2 units of pRBCs→ HR 110, BP 100/70, RR 18 Sat 98% RA
- Elevated iron concentration should be recognized and treated.
- Transition point 2: Triggered by administration of DEFEROXAMINE
- Vital signs HR 135 BP 75/55, RR 22, Sat 95%
- Recognize deferoxamine anaphylactoid reaction
- Stopping infusion→HR 100 BP 100/70 RR 18, Sat 99%

Branch Points

- If iron level has not been ordered by this time, nurse can show doctor empty bottle of iron.
- Pt continues to state she does not want to live and continues to have bloody emesis.
- If deferoxamine ordered, pt improves but then develops an anaphylactoid reaction which also needs to be treated.
- If KUB ordered, consider whole bowel irrigation with polyethylene glycol if patient is not vomiting. Can give PO or via nasogastric tube.

#10

STIMULUS INVENTORY

EKG #1 #2 Chest Xray #3 KUB #4 CBC #5 CMP #6 Venous blood gas #7 Lactate #8 Acetaminophen and salicylate levels #9 Urine Pregnancy Test

Serum Iron Level

LAB DATA & IMAGING RESULTS

Stimulus #1			
EKG	Sinus tachycardia		
Stimulus #2			
Chest Xray	Normal with small radioopaque foreign bodies in the GI tract		
Stimulus #3			
KUB	Normal with small radioopaque foreign bodies in the GI tract		
Stimulus #4			
Complete Blood C	Count (CBC)		
WBC	13,600/mm ³		
Hemoglobin	5.4 g/dL		
Hematocrit	28.3%		
Platelets	170,000/mm ³		
Stimulus #5			
CMP			
Sodium	137 mEq/L		
Potassium	4.5 mEq/L		
Chloride	93 mEq/L		
Bicarbonate	11 mEq/L		
Glucose	70 mg/dL		
BUN	18 mg/dL		
Creatinine	1.0 mg/dL		
AST	125 U/L		

Stimulus #6		
VBG		
рН	7.27	
pCO ₂	25 mm Hg	
pO ₂	100 mm Hg	
HCO ₃	10 mEq/L	

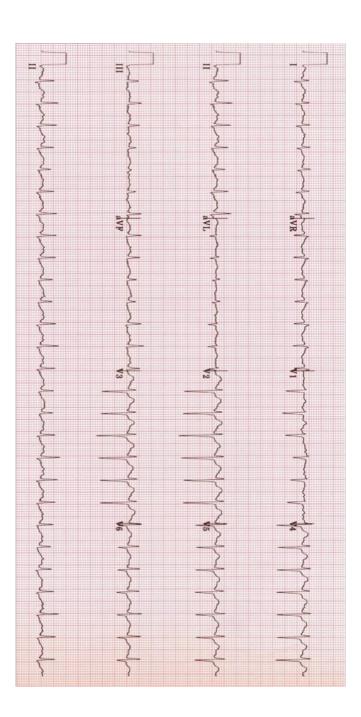
Stimulus #7	
Lactate	5.9 mmol/L

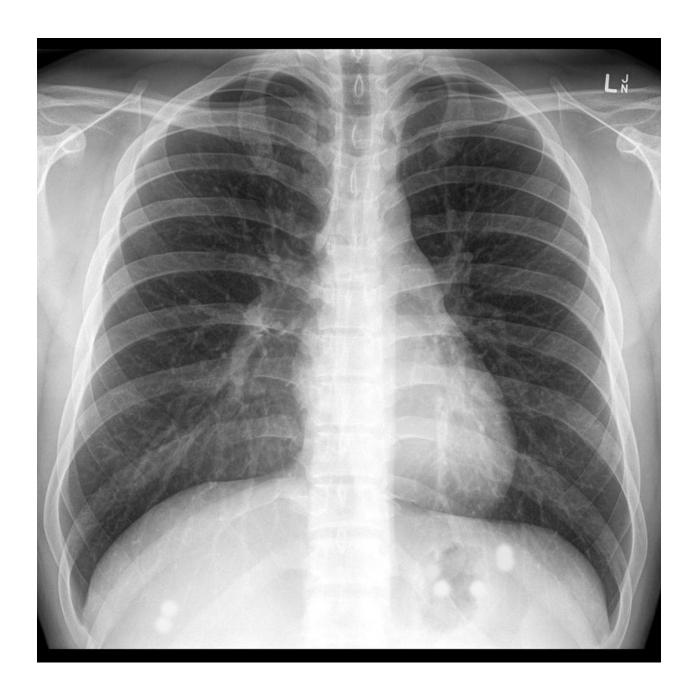
Stimulus #8	
Toxicology	
Salicylate	< 4 mg/dL
Acetaminophen	undetectable

Stimulus #9	
POC Urine Pregnancy	Positive

Stimulus #10	
Serum Iron Level	510 mcg/dL

Stimulus #1 EKG







Debriefing Materials

Exposure:

- The 3 most common oral iron preparations include:
 - Ferrous fumarate
 - Ferrous sulfate
 - Ferrous gluconate
- The amount of ingested elemental iron determines toxicity.
- Ferrous fumarate, ferrous sulfate and ferrous gluconate are the most common forms of iron exposures.

To calculate the amount of elemental iron ingested.

- Ferrous fumarate: divide dose in mg by 3
 - o Ferrous fumarate is 33% elemental iron
- o Ferrous sulfate: divide dose in mg by 5
 - Ferrous sulfate is 20% elemental iron
- o Ferrous gluconate: divide dose in mg by 9
 - Ferrous gluconate is 12% elemental iron
- Our case: The patient ingested 40 tablets of 324 mg ferrous fumarate. Each tablet contains 33% elemental iron. Total elemental iron ingested is (324 mg x 40 tablets) / 3 = 4,320 mg
- o Or calculate (324 mg x 40 tablets) x 0.33 = 4276.80 mg
- Patient weight is 65 kg. To calculate mg/kg.
- \circ 4300 mg/65 kg is > 60 mg/kg.
- Dose Related Toxicity:
 - < 20 mg/kg: typically, asymptomatic</p>
 - o 20-60 mg/kg: GI symptoms
 - o 60-120 mg/kg: potential for systemic toxicity
 - >120 mg/kg: potentially lethal
- Serum iron concentration (always ask time of ingestion):
 - Peaks at 4-6 hours post-ingestion
 - o After 6 hours, there is an intracellular shift, so levels fall
 - Levels do not clearly correlate with toxicity
- Classic stages of iron poisoning with time course of toxicity:
 - o STAGE I
 - 0-6 hours post-ingestion: Local toxicity. GI symptoms and concern for GI bleed, can lead to hypovolemia
 - STAGE II
 - 6-24 hours post-ingestion: Pt appears to be getting better as gastrointestinal symptoms improve. However, despite symptoms improving, the iron continues to shift intracellularly from the circulation. This stage is not truly quiescent as cellular toxicity continues.
 - STAGE III
 - 12-48 hours post-ingestion: Cellular toxicity can occur with third-spacing and vasodilatory shock, high anion gap metabolic acidosis, elevated lactate levels, and

hepatorenal failure. CNS effects include lethargy, seizures, and coma. Iron-induced coagulopathy worsens bleeding and hypovolemia.

- STAGE IV
 - 2-5 days post-ingestion: acute hepatic failure (periportal)
- STAGE V
 - 2-8 weeks post-ingestion: chronic sequelae occur in survivors including GI scarring and strictures such as gastric outlet obstruction and small bowel obstruction.

Pathophysiology:

- Local corrosive effects: gastrointestinal injury resulting in vomiting, diarrhea, and gastrointestinal bleed.
- Systemic effects:
 - Increased absorption due to membrane breakdown
 - Inducer of oxidative stress
 - Gastrointestinal loss and increased capillary permeability can cause hypotension, hypovolemia, and venodilation
 - o Coagulopathy: thrombin formation inhibition and protease malfunction
 - o Iron engages in redox reactions, forming free radicals and causing cell death
 - o Direct hepatic, CNS and cardiac toxicity
- Iron leads to metabolic acidosis through several mechanisms:
 - o Iron toxicity causes hypovolemia and hypotension so lactic acidosis occurs.
 - Iron induces oxidative stress.
 - Oxidative damage to the gastrointestinal epithelium produced by iron-induced reactive oxygen species permits iron ions to enter systemic circulation.
 - o Iron uncouples oxidative phosphorylation. Thus, anaerobic metabolism is promoted. Lactic acidosis occurs.
 - o Iron from the gastrointestinal tract leads to the conversion of ferrous iron to ferric iron. As ferrous iron is converted to ferric iron, hydrogen ions are released.
 - Iron toxicity causes reduced cardiac output and myocardial contractility which leads to shock.
- Iron Toxicity in Pregnancy
 - Maternal resuscitation should be the primary objective.
 - Fetal demise results from maternal iron toxicity and not from direct iron toxicity to the fetus
 - Fetal toxicity is related to maternal hemodynamic and physiologic status, not fetal poisoning.
 - Deferoxamine should be used to treat serious maternal iron poisoning.
 - Neither iron nor deferoxamine is transferred to the fetus in appreciable quantities.

Diagnostic Testing:

- Measure serum iron concentration at 4 hours after ingestion if possible.
- Peak iron concentration:
 - < 300 mcg/dL typically lacks significant clinical effect.
 - 300-500 mcg/dL mild to moderate toxicity with nausea, vomiting, diarrhea, mild systemic symptoms
 - >500 mcg/dL generally predictive of systemic toxicity
 - >1000 mcg/dL has significant morbidity and mortality
- Blood gas/serum chemistry

- The presence of an elevated anion gap metabolic acidosis is a useful marker of systemic toxicity.
- In the absence of serum iron levels, a serum bicarbonate level can be used as a surrogate marker. Our patient was in shock with metabolic acidosis with an iron ingestion. No need to wait for serum iron concentration prior to starting deferoxamine.
- Liver function tests and coagulation studies can be used to evaluate for hepatic failure.
- Lactate levels
- Abdominal x-ray can evaluate for pill fragments in the gastrointestinal tract.
 - o Iron in pill form can be radiopaque.
 - Radiographs are not helpful in chewable vitamins and liquid iron formulations.
 - Finding radiopaque pills on abdominal radiograph is helping in guiding and evaluating the success of GI decontamination.
 - The absence of radiographic evidence of pills is not a reliable indicator to exclude potential toxicity.
- Bedside echocardiogram to evaluate the fetus and fetal heart, as well as the patient's cardiac contractility (cardiogenic shock in iron toxicity) and free fluid in cases of an ectopic pregnancy, trauma, etc.

Treatment:

- Decontamination:
 - Charcoal does not adsorb iron. There is no indication for charcoal.
 - Orogastric lavage is not helpful because of the iron pills large size and poor solubility of tablets. They can form adherent masses.
 - Consider whole bowel irrigation if pills are noted on the radiograph and the patient is severely toxic, 2L/hr in adults or 500 mL/hr in children of PEG-ELS. Consider placing a nasogastric tube if the patient is awake, alert and not actively vomiting. If the airway is an issue, the physician should be intubated prior to placing NGT.
 - However, no controlled studies support the efficacy of whole bowel irrigation so individual risks and benefits shoulder be considered.
 - For patients with persistent iron in the gastrointestinal tract despite whole bowel irrigation, upper endoscopy and surgical removal of iron tablets adherent to the gastric mucosa may be necessary.
- Volume resuscitation with crystalloid to prevent shock from gastrointestinal losses, vasodilation and third spacing.
- Transfuse blood as needed for hemorrhagic gastritis.
- Consider pantoprazole bolus with or without infusion for hemorrhagic gastritis.
- Ongoing reassessment of perfusion status, airway, and supportive care.
- Consult the regional poison center or consult your local medical toxicologist.
- Antidote: Deferoxamine
 - Dosage: start at 5 mg/kg/hr and gradually increase to 15 mg/kg/hr as patient tolerates.
 - Therapy duration is no more than 24 hours.
 - Indications for deferoxamine are not well defined:
 - Hypotension/shock
 - Lethargy/coma
 - Anion gap metabolic acidosis
 - Serum iron concentrations > 500 mcg/dL
 - Deferoxamine can be given to pregnant women with iron poisonings; it does not cross the

placenta in appreciable quantities.

- O Deferoxamine + Ferric iron (Fe^{3+}) = ferrioxamine (causes vin rose colored urine)
 - Ferrioxamine is renally eliminated.
 - Also used for aluminum toxicity.
- Deferoxamine adverse effects to consider:
 - 4 toxicities are associated with Deferoxamine
 - Anaphylactoid reaction: Rate-related Hypotension and shock (associated with rapid infusion).
 - Likely multifactorial, including volume depletion from iron with histamine release from deferoxamine.
 - Acute kidney injury
 - Recommend volume expansion prior to deferoxamine to decrease the risk of renal injury.
 - Pulmonary syndrome / acute lung injury: fever, noncardiogenic pulmonary edema, increased respiratory rate, and increased eosinophils.
 - Primarily with prolonged infusion > 24 hours
 - Infectious complications Yersinia entercolitica, Aeromonas hydrophilia, Zygomycetes spp (Mucormycosis) infections. Iron is a required growth factor for certain bacteria. Deferoxamine acts as a siderophore from Streptomyces pilosus, thereby facilitating bacterial growth and infection.

Disposition:

- Iron poisoning is a clinical diagnosis.
- Concentrations over 500 mcg/dL can be associated with profound toxicity and shock. These patients need ICU admission.
- For iron levels < 300 mcg/dL, you may observe for 6 hours. If repeat level is down trending and patient is completely asymptomatic with normal vital signs, the patient may be discharged.

Consultations:

- Consult the regional poison center or local toxicologist for recommendations.
- Psychiatry consultation for intentional ingestions.
- Once the patient is stabilized, consult obstetrics.
- Consider gastroenterology consultation for the iron corrosive effects.

Take Home Points:

- Immediate management of the unstable patient.
- Identification of pregnancy as a risk factor for suicidal ideation and overdose.
- Obtain collaborative information about time of ingestion, preparation of iron, dosage, intent, prior history via family, EMS, etc. Ask family and EMS for pill bottles if possible.
- Identify and manage iron toxicity.
- Iron preparations have varying toxicities based on the amount of ingested elemental iron.
- Aggressive volume resuscitation is important as gastrointestinal symptoms occur early.
- Call poison control center and/or consult the local toxicologist for management.
- Deferoxamine can be used for iron toxicity including pregnant patients.
- Monitor for deferoxamine adverse effects and treat appropriately.

References:

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