Acute iron intoxication in pregnancy: case report

INTRODUCTION

Acute ironing poisoning is a common and potentially lethal condition often observed in the pediatric population, usually in the context of unintentional ingestion. Intentional overdose is more common among females and is associated with higher mortality. Consequences of iron ingestion depend on the amount of ingested elemental iron. Symptoms are usually absent for doses under 20mg/Kg. Between 20 and 60mg/Kg, severe toxicity may develop. Death from iron toxicity has been reported with doses from 60 to 300mg/Kg.

The toxic effects of iron become apparent throughout five stages: gastrointestinal stage, latent stage, shock and metabolic acidosis, hepatotoxicity and bowel obstruction.

Gastrointestinal phase is the result of mucosal damage, occurring 30 minutes to 6 hours after ingestion. Symptoms include abdominal pain, vomiting, diarrhea, hematemesis, melena, lethargy, metabolic acidosis and shock. Latent stage may not become apparent in all patients and it represents a period of stability that might correspond to true recovery or to anticipation of clinical deterioration. Shock and metabolic acidosis usually occur from 6 to 72 hours after ingestion. Patients may present signs of gastrointestinal hemorrhage, bowel perforation, pulmonary dysfunction, hypo/hyperglycemia, iron induced coagulopathy and renal and neurologic dysfunction. Hepatotoxicity, usually occurs within two days of intoxication. Nonetheless it may develop between 12 to 96h after pills ingestion.

We present an unusual clinical case of a 30-week pregnant woman with potential severe iron intoxication in the context of a suicide attempt.
CASE REPORT

A 27-year old, 3 Gest 2 Para woman was transferred from a secondary hospital to our Unit after an intentional ingestion of 50-60 tablets of extended release ferrous sulfate (329.7mg corresponding to 105mg of elemental iron– Ferro Gradumet® each). She had an ongoing pregnancy of 30 weeks6 days with no complications so far. From her medical past, we could register two unremarkable pregnancies with vaginal deliveries at term and two untreated depressive episodes in the past year. This woman belonged to a low income family and she was unemployed from her job as a factory worker. Her first husband died during her first pregnancy, and she had moved to an inner village losing her family and social supports.

At the admission in the secondary hospital emergency department, she presented with vomits and abdominal pain. She was hemodinamically stable and her physical examination was normal. Initial therapy included intravenous hydration, gastric lavage and betamethasone to induce fetal lung maturation. Laboratory testing five hours after ingestion revealed serum iron concentration of 516mcg/dL with no other abnormalities.

At our institution, she presented with persistent abdominal pain and vomiting. Vital signs were stable and besides hematic drainage through nasogastric tube physical examination was normal. We estimated an iron ingestion of 53-66.9mg/Kg of elemental iron. Eight hours after ingestion seric iron was 452mcg/dL, and complete blood count, coagulation, glucose, electrolytes and liver enzymes were within the normal range. Supportive care with fluids and ion replacement, gastric protectors, prokinetic agents and analgesics was started. Specific treatment with deferoxamine infusion was initiated at a rate of 15mg/Kg/hour. Fetal well-being was confirmed at admission and periodically during hospitalization.

Twenty-four hours after ingestion, in spite of worsening abdominal pain and hematic nasogastric tube drainage, her vital signs were normal, with good peripheral perfusion and normal diuresis. Urine had orange-red discoloration. Laboratory tests showed compensated metabolic acidosis with normal anion gap, seric iron of 140 mcg/dL and no other abnormalities. She was transferred to the Intermediate Care Unit.

The patient had a favorable evolution, with progressive symptoms resolution and only a mild transient bilirubin elevation. Treatment with deferoxamine was suspended 24hours after initial perfusion and corticotherapy cycle was completed.

Psychiatric evaluation diagnosed a moderate depressive disorder and the patient was discharged from hospital nine days after admission, under Sertraline 50mg/day and Lorazepam 2.5mg at night.

She kept pregnancy and psychiatric surveillance at our institution and labor was induced at 40weeks1 day due to oligoamnios diagnosed at term. An apparently healthy female newborn was delivered with 3540g, Apgar score 10/10. No puerperal or neonatal complications were registered. Patients didn't attend pediatric and puerperal visits so we lost them for follow-up.

DISCUSSION

Our patient had an increased risk for systemic toxicity because she had an ingestion of possibly more than 60mg/Kg of elemental iron, peak serum iron concentration greater than 500mcg/dL at 4-6hours after ingestion and persistent vomiting2 (the most sensitive symptom for severe ingestions3). On the other hand, eight hours after ingestion (the best time to evaluate peak serum iron concentration for slow-release iron formulations1 such as Ferro Gradumet®) iron concentration was 452 mcg/dL, and there were no signs suggesting an evolution to the latent phase such has lethargy, tachycardia, tachypnea, abdominal tenderness or diarrhea1.

Gastric lavage with a large-bore orogastric tube is particularly indicated for patients with a significant number of radiopaque pills identified on the abdominal X-ray1,7. Our patient was not evaluated with this exam but the amount of tablets ingested would also justify this approach4. Pregnancy should not preclude X-ray study if it helps determining the risk for high iron ingestion since no single X-ray study is likely to adversely affect the fetus6. Whole bowel irrigation would be also an effective tool for gastrointestinal decontamination1,6.

Deferoxamine is the treatment of choice for severe iron intoxication1, as it is associated to lower morbidity and mortality8. It’s indicated if there are severe symptoms1, anion gap metabolic acidosis1, peak serum iron concentration greater than 500mcg/dL1,9 or a significant number of pills in the X-ray1. It’s contraindicat-

ed in the setting of anuria or severe chronic renal disease4.
However there are some concerns about its safety and the criteria for therapy cessation. Deferoxamine is associated with urticaria, rash, hypotension and acute respiratory syndrome. This syndrome has been reported for perfusions longer than 32 hours.

Several criteria have been proposed to stop deferoxamine. Manufacturer suggests stopping therapy once the patient starts to improve, which is a subjective criterion. The return to normal urine coloration (during chelation therapy urine acquires a "vin rosé" discoloration indicating iron chelating products) is another subjective criterion proposed to guide the end of therapy. Serum or urine iron concentration is modified by deferoxamine use, limiting its value in therapy monitoring. Our patient exhibited seric iron within the normal range 16h after initial therapy, however this could have also reflected the rapid clearance of serum iron from plasma. More sensitive methods, such as atomic absorption and plasma emission spectrographic methodologies, are not affected by deferoxamine, but they are expensive and not easily available. Yatscoff, proposed measuring ferruresis by first cleaving the iron from the chelating agent and then determining the iron concentration. These authors proposed stopping therapy when urine iron to creatinine ratio is 12.5 (97.5th centile for non-trographic methodologies, are not affected by deferroxamine). Serum or urine iron concentration is modified by deferoxamine use, limiting its value in therapy monitoring. Our patient exhibited seric iron within the normal range 16h after initial therapy, however this could have also reflected the rapid clearance of serum iron from plasma. More sensitive methods, such as atomic absorption and plasma emission spectrographic methodologies, are not affected by deferoxamine, but they are expensive and not easily available. Yatscoff, proposed measuring ferruresis by first cleaving the iron from the chelating agent and then determining the iron concentration. These authors proposed stopping therapy when urine iron to creatinine ratio is 12.5 (97.5th centile for non iron poisoned individuals). Another criterion to stop therapy is when serum iron becomes inferior to iron-binding capacity. The typical duration of therapy is 24h and so it was with our patient. No adverse effects were noted.

Concerns about fetus safety during deferoxamine treatment might also be an issue. Although animal studies have associated deferoxamine to fetal wastage and skeletal anomalies, these haven’t been described in humans. In one series of 25 pregnant women treated with deferoxamine (one during organogenesis) all outcomes were normal. In the context of iron poisoning (but no cases during organogenesis) there were no fetal anomalies as well. In a series of 24 pregnant women in organogenesis period treated with deferoxamine for iron overload secondary to transfusion dependent beta-thalassemia, just one case of spontaneous abortion was reported. One case report involves the delivery of an infant within the period of treatment with deferoxamine; this newborn presented with low seric iron, possibly due to in utero chelating action, but iron supplementation reversed this deficit. Once the fetal outcome is strongly associated to maternal outcome, if chelating use is indicated no fetal concerns should delay its use. This case report represents a successful case of deferoxamine use in pregnancy with both maternal and fetal favorable outcomes.

Currently iron intoxication is the second most common overdose in pregnancy, with potentially devastating consequences. Literature review shows that poor maternal and fetal outcomes in the context of iron poisoning are related to delay or absence of treatment with deferoxamine. So it’s important for physicians taking care of pregnant women to be familiar with acute iron overdose in pregnancy and its current management since iron is prescribed regularly in pregnancy and is an easy access medication. As Paracelsus noted, “Poison is in everything, and nothing is without poison. The dosage makes it either a poison or a remedy”.

DECLARATION OF INTERESTS
The authors don’t have any conflict of interests to declare. There was no involvement of any pharmaceutical company or other sponsor funding our work, nor any assistance by medical writing or editorial company.

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