IV IRON USE IN PREGNANCY

SUMMARY: Iron deficiency anemia during pregnancy has been associated with an increased risk of adverse outcomes. When a patient fails oral iron replacement therapy, IV iron can be considered as a therapeutic alternative.

RATIONALE: Iron deficiency anemia (IDA) refers to the condition when stored, transport and functional iron are all low. Iron deficiency anemia during pregnancy has been associated with an increased risk of adverse outcomes including low birth weight, preterm delivery, and perinatal mortality. In addition, there may be an association between maternal iron deficiency anemia and postpartum depression. Children born to iron deficient mothers demonstrate lower cognitive function as well as memory and motor deficits. Therefore, all pregnant women should be screened for anemia during pregnancy. All women should receive iron supplementation in prenatal vitamins. Those with iron deficiency anemia should be treated with additional supplemental iron.

Screening

The primary screening test for IDA is a hemoglobin concentration. If Hemoglobin is low, indicating anemia, further testing is warranted to ensure iron deficiency is the cause of anemia with serum iron, TIBC and serum ferritin. Measurement of ferritin levels has the highest sensitivity and specificity for diagnosing iron deficiency. Levels < 10–15 micrograms/L confirm iron-deficiency anemia.

Treatment

Oral iron therapy is considered first line treatment of iron deficiency in pregnancy. Parenteral (IV) iron use is typically reserved for situations where absorption is impaired or oral therapy is not tolerated or has failed.

The three preparations of IV iron that have been evaluated for use in pregnancy include: LMW iron dextran (ID, INFED), iron sucrose (IS, VENOFER), and ferric carboxymaltose (FCM, INJECTAFER). All show similar efficacy and very low risk of serious adverse events (SAEs).

Infusion reaction and premedication

If an infusion reaction occurs, it is usually mild and not anaphylactic. Until recently, iron dextran (ID) was avoided due to higher occurrences of SAEs. A retrospective analysis of over 30 million doses of IV iron as well as other recent retrospective and prospective data showed the large majority of SAEs with ID were due to the older, HMW formulations. When these formulations are excluded, the LMW formulations (such as INFED) are safe with a SAE rate of less than 1:200,000 administrations.

Premedication, while commonly used, is not recommended in the absence of multiple drug allergies or known asthma. If premedication is indicated, steroids are the preferred choice. Antihistamines are more likely than the iron infusion to cause side effects and may exacerbate an adverse reaction. Test dose is required for ID but slow infusion at the outset is recommended for all formulations to observe for adverse reactions.
Eligible patients:

1. Confirmed iron deficiency anemia [Hgb (g/dL) levels < 11 in the first trimester; 10.5 in the second trimester; and 11 in the third trimester] AND one of the following:
   a. No response to oral iron therapy after 2-4 weeks of treatment.
   b. Inability to tolerate oral therapy due to gastrointestinal side effects
   c. Malabsorption disorder, including prior gastric bypass surgery, that would effect efficacy of oral therapy.
2. Severe iron deficiency anemia (Hgb < 7 mg/dL)

Contraindications:

- Acute hypersensitivity reaction including wheezing, stridor, hypotension, tachycardia, tachypnea or periorbital/angioedema in response to IV iron infusion.

Technique:

1. All pregnant women should be screened for anemia with Hgb or CBC. If anemia is found, red blood cell indices, serum iron levels, and ferritin levels can be utilized to confirm IDA and hemoglobin electrophoresis may be indicated based on ethnic background.
2. In some cases, when other causes of anemia do not pose a high risk, oral iron therapy may be initiated empirically. Reticulocyte response is expected in 7-10 days and response in Hgb is typically noted in 3-4 weeks.
3. If no response is noted, confirmation of iron deficiency is recommended before increasing oral dose or moving to IV replacement.
5. Three IV iron formulations are included in the SECU outpatient infusion protocol (see attached protocol) and all can be used in pregnancy. These have been approved by the FDA at the following doses:
   a. Iron dextran (INFED): 100 mg IV bolus over 20 minutes
      i. Multiple studies including in pregnant women demonstrating safety and efficacy of 1000 mg IV infusion over 4 hours
      ii. Test dose is necessary for ID
   b. Iron sucrose (VENOFER): 200-400mg IV over 2-90 minutes.
   c. Ferric carboxymaltose (INJECTAFER): 750 mg IV over 15 minutes. 2 doses are recommended.

Special Considerations:

1. For African-American adults, IOM recommends lowering the Hgb cutoff levels listed above by 0.8.
2. If premedication is performed due to multiple drug allergies or asthma, steroids are recommended prior to iron infusion including: methylprednisolone 40-100 mg IV or hydrocortisone 50-100 mg IV.

3. Patients are generally observed for 15 minutes after IV ID test dose. If no infusion reaction occurs, it is unlikely to occur during remainder of infusion.

4. If a minor infusion reaction including myalgias, arthralgias, hand swelling, nausea, or flushing (without other hypersensitivity symptoms) occurs, observation until resolution of symptoms is recommended prior to continuing infusion.

5. ID and FCM have the benefit that fewer infusions are required to replace the iron deficit and often, only one infusion is necessary.

Reference(s):


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