OVERVIEW OF THE CAUSES AND TREATMENT OF IRON-DEFICIENCY ANEMIA

Iron is essential for many biologic processes such as breathing and the production of energy, DNA, and cells. Although the body possesses various mechanisms to maintain iron within normal ranges, modifications to iron homeostasis can result in iron deficiency. Iron deficiency and iron-deficiency anemia are universal health complications. Even though the prevalence of iron deficiency anemia has declined, it is still commonly encountered in clinical practice. Iron deficiency is the main cause of anemia worldwide and has a significant effect on certain populations. Those most commonly affected are young children and premenopausal women in both high-income and developing countries. Iron deficiency is characterized by a decrease in iron stores that precedes iron-deficiency anemia or continues without progression, whereas iron-deficiency anemia is a more severe condition that consists of low iron levels and anemia characterized by microcytic hypochromic red blood cells. This issue of CLIPs briefly summarizes an article that considers iron deficiency and its associated anemia in the context of systemic iron homeostasis and assesses causes, pathophysiological features, and iron supplementation in adults. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


A Global Health Problem
- Iron deficiency affects more than 2 billion people globally and is the top cause of anemia.
- Prevention programs have reduced prevalence rates globally. Currently the highest prevalence is in Central and West Africa and South Asia.
- Preschool children, menstruating females, and pregnant women are most commonly affected by iron deficiency in areas where dietary fortification is lacking.
- These findings are indicative of increased physiological need for dietary iron during particular stages of life and according to sex.

Causes of Iron-deficiency Anemia
- In developing countries, poverty, malnutrition, and famine are some of the more evident reasons for iron deficiency.
- Grain in cereal based diets decreases iron absorption, thereby, decreasing the amount of iron reaching the systemic circulation.
- Another common cause is chronic blood loss due to hookworm infections and schistosomiasis.
- In developed countries, typical causes include certain diets (e.g., vegan and vegetarian), malabsorption, and chronic blood loss due to heavy menstruation.
- Some patients, especially males and the elderly, can have chronic blood loss from the gastrointestinal tract.
- People who frequently donate blood are at increased risk of iron deficiency and should have their iron levels monitored.
- Some drug-related causes of iron-deficiency are potential blood loss due to NSAIDs and anticoagulants and reduced iron absorption due to proton-pump inhibitors.
- Multiple causes of iron deficiency may coexist at once. In elderly patients, anemia is associated with old age, iron deficiency, inflammatory conditions, reduced red blood cell production, and cancer.

Iron-refractory Iron-deficiency Anemia
- Iron-refractory iron-deficiency anemia (IRIDA) is a rare autosomal recessive disorder caused by a gene mutation. This mutation leads to overproduction of hepcidin, a hormone synthesized in the liver, which blocks the intestinal absorption of iron.
- An increase of less than 1 g of hemoglobin after 4 to 6 weeks of treatment with oral iron can be classified as IRIDA.

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Iron-refractory Iron-deficiency Anemia (continued)

- IRIDA encompasses less than 1% of the cases of iron-deficiency anemia and is characterized by an intensified severity in children and resistance to oral iron treatment.
- Usually iron resistance is due to a gastrointestinal tract disorder or surgery. Some recognized causes are Helicobacter pylori infection, celiac disease, autoimmune atrophic gastritis, inflammatory bowel disease, partial or total gastrectomy, and bariatric surgery.

Clinical Findings

- Iron-deficiency anemia is a chronic, often asymptomatic condition and can go undiagnosed in many patients.
- Common symptoms associated with iron-deficiency anemia are weakness, fatigue, reduced concentration, and diminished work productivity. In children, reduced cognitive performance and delayed mental and motor development have been reported.
- In pregnancy, severe iron-deficiency anemia is related to increased risk of preterm labor, decreased neonatal weight, and increased newborn and maternal death.
- Iron deficiency may cause patients to be more susceptible to infections, heart failure, and restless leg syndrome.

Determination of Iron Status

- Serum ferritin is the most useful lab measurement for the identification of iron deficiency.
- A serum ferritin level of less than 30 mcg is indicative of iron deficiency and levels are even lower in patients with iron-deficiency anemia. A transferrin saturation of less than 16% represents an iron supply that is inadequate to support normal red blood cell production.
- However, it is important to consider the entire picture because significantly higher cut off levels for ferritin and transferrin saturation are used to determine iron-deficiency anemia in the presence of certain comorbidities.

Therapy

- Patients with iron-deficiency anemia should be treated with iron supplementation.
- Because iron deficiency is protective against malaria, caution should be exercised when considering iron supplementation for patients who live in malaria-endemic regions.
- Oral iron therapy is a convenient, cheap, and effective way to supplement iron in stable patients. There are numerous oral iron preparations available. Iron sulfate is the most commonly used, but gluconate and fumarate are also effective iron salts.
- 100 to 200 mg of elemental iron for adults or 3 to 6 mg/kg of a liquid preparation for children administered in divided doses without food is the daily recommendation. The addition of vitamin C may enhance absorption.
- Three to six months of oral iron therapy is necessary to replenish iron stores and serum ferritin levels.
- Nausea, vomiting, constipation, and metallic taste are frequent side effects of oral iron that limit long term use.
- In the past, the possibility of hypersensitivity reactions deterred the use of IV iron; however, due to the recent availability of safer preparations, clinical practice is changing.
- IV iron is more effective and rapid at elevating hemoglobin levels than oral iron. Also, the total dose needed (up to 1000 mg) by a patient can sometimes be given in a single infusion.
- While the cost of IV iron therapy is expensive, it greatly reduces patients’ hospital and clinic visits.
- IV iron supplementation may be required for the following conditions: malabsorption and genetic IRIDA, the need for a rapid increase in hemoglobin, iron-deficiency anemia caused by chronic blood loss in which oral iron is insufficient, active inflammatory bowel disease, and anemia in patients with chronic kidney disease who are receiving dialysis and treatment with erythropoiesis – stimulating agents.
- Temporary side effects of parenteral iron administration include nausea, vomiting, itching, headache, flushing, muscle and joint pain, and chest and back pain. Hypersensitivity reactions, including severe or life-threatening reactions, are rare.
- Because of a lack of safety data, IV iron should not be used in the first trimester of pregnancy; it has a tolerable side effect profile later in pregnancy.
- Clinical trials support the efficacy and safety of parenteral iron, however there has been some concern regarding the long-term effects of iron. Until randomized controlled clinical trials can confirm the long-term effects, parenteral iron should only be used when the benefits exceed the risks.

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