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Review article

Management Strategies for Iron Deficiency Anemia: A Clinical Review

Hammad Tufail Chaudhary

Taif University, Taif, Saudi Arabia
**Corresponding author`s email address:* h.hammad@tu.edu.sa

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Abstract: *Iron deficiency anemia (IDA) is a prevalent hematological disorder with multifactorial etiology, including inadequate dietary intake, malabsorption, and chronic blood loss. Among these, gastrointestinal pathologies contribute significantly to the development and persistence of IDA, necessitating targeted clinical strategies for effective management.* ***Objective:*** *To review the current diagnostic and therapeutic approaches to IDA, with an emphasis on gastrointestinal-related causes and their specific management challenges and strategies.* ***Methods:*** *This review article synthesizes evidence from recent literature regarding the pathophysiology, diagnosis, and treatment of IDA in various gastrointestinal conditions. Databases including PubMed, MEDLINE, and EMBASE were searched for relevant studies published in the last 10 years. The clinical contexts explored include bariatric surgery, inflammatory bowel disease (IBD), portal hypertensive gastropathy, gastric antral vascular ectasia (GAVE), celiac disease, and small-bowel angioectasias. Particular focus is placed on the role of ferritin as a diagnostic marker and the comparative efficacy of oral versus intravenous iron therapy.* ***Results:*** *Ferritin remains the principal biomarker for diagnosing IDA, though interpretation must be adjusted in the presence of inflammatory conditions. Oral iron supplementation is the first-line therapy due to its accessibility and cost-effectiveness. However, gastrointestinal side effects and poor absorption often compromise its efficacy, particularly in patients with underlying gastrointestinal disorders. In such cases, intravenous iron formulations offer a superior alternative with improved patient outcomes. A multidisciplinary approach is often required to address the complex etiologies and optimize treatment plans.* ***Conclusion:*** *Effective management of IDA, particularly in the setting of gastrointestinal pathology, requires individualized treatment strategies guided by the underlying disease process, ferritin thresholds, and patient tolerance. Intravenous iron therapy is recommended for patients with impaired absorption or intolerance to oral formulations. Further research is essential to improve therapeutic options, reduce healthcare costs, and enhance the overall quality of life in patients affected by IDA.*

Keywords: Anemia, Celiac Disease, Ferritins, Gastrointestinal Diseases, Inflammatory Bowel Diseases, Iron, Iron Deficiency Anemia, Iron-Dextran Complex, Malabsorption Syndromes, Parenteral Nutrition

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Introduction

One of the most prevalent nutritional deficiencies worldwide is Iron deficiency (ID). This fact can be understood by the fact that (1-4) % of men in the United States of America have ID, out of which 2 % suffer from iron-deficiency anemia (IDA) (2). Among women, at least 39% of those who are premenopausal and 8% of postmenopausal women are iron deficient, with overall IDA rates ranging from 4% to 17% (3). Ferritin is the most frequently used marker for diagnosing ID, although there is variation in recommended threshold levels. Recently, the American Gastroenterological Association (AGA) suggested a ferritin cut-off of 45 ng/mL for individuals with anemia, considering this value strikes an optimal balance between sensitivity and specificity (4). However, it is essential to note that patients with inflammatory conditions can still have ID or IDA, even with ferritin levels above 45 ng/mL, which is typically below 100 ng/mL. In such cases, additional tests, such as transferrin saturation, soluble transferrin receptor, or reticulocyte hemoglobin equivalent, can aid in diagnosis once ID is identified, with or without anemia, a thorough work-up should be performed, including assessment of dietary iron intake, menstrual blood loss in premenopausal women, and investigation of gastrointestinal causes such as poor absorption or blood loss, including Helicobacter pylori infection. Complex cases often require a multidisciplinary approach involving gastroenterologists, hematologists, and nutritionists. Nutritional counseling can help improve dietary iron intake, while a hematology consultation may be necessary for complicated anemia or if intravenous (IV) iron treatment is considered.
Restoring iron levels is crucial for enhancing the quality of life and reducing anemia-related complications. Oral iron supplements are typically the first treatment choice but are often poorly tolerated due to side effects like nausea, abdominal pain, and constipation (5). Moreover, because the intestines tightly regulate iron absorption, increasing absorption through oral supplementation can be challenging. This has led to the development and growing use of IV iron formulations. For patients with severe ID or conditions that limit oral iron absorption, IV iron may be used as the initial treatment. This Clinical Practice Update aims to review oral and IV iron therapy options and outline best management practices for ID in common gastrointestinal disorders. Previous AGA guidelines have detailed recommendations for the gastrointestinal evaluation of IDA. Although most gastrointestinal studies focus on IDA as an endpoint, similar principles apply to patients with ID who do not have anemia.

Methodology

This review article aimed to summarize current information about the diagnosis and management of iron deficiency and IDA. Gastrointestinal and systemic disorders were specifically taken into consideration. Literature was reviewed by searching electronic sources like PubMed and MEDLINE using keywords like "iron deficiency," "iron-deficiency anemia," "oral iron," "intravenous iron," "inflammatory bowel disease," "celiac disease," "bariatric surgery," "portal hypertensive gastropathy," "GAVE," and "angioectasia." Clinical guidelines, meta-analyses, review articles, and systematic reviews were preferred from 2000 to 2025. Specific inclusion and exclusion criteria were not considered because of the narrative nature of the article.

Review of literature:

Oral supplementation of Iron:

Different types of IV iron are available, varying in the amount required and the frequency of administration. Most work about the same and are equally safe, so doctors usually pick the ones that can fill up your iron stores with just one or two treatments. Real allergic reactions to IV iron rarely happen. Most adverse reactions are false allergic reactions that occur when your immune system becomes overactive, and they can't be predicted when they'll happen. These reactions appear to be allergies, but they aren't. If you experience a mild reaction, the doctor can temporarily stop the IV and restart it at a slower rate after approximately 15 minutes. Stronger reactions might need steroids. Don't use Benadryl because its side effects—dry mouth, racing heart, sweating, sleepiness, and low blood pressure—can make it seem like your allergic reaction is getting worse. Mild reactions occur in approximately 1 out of 200 treatments, while serious ones are extremely rare, at about 1 in 200,000.(5,6)

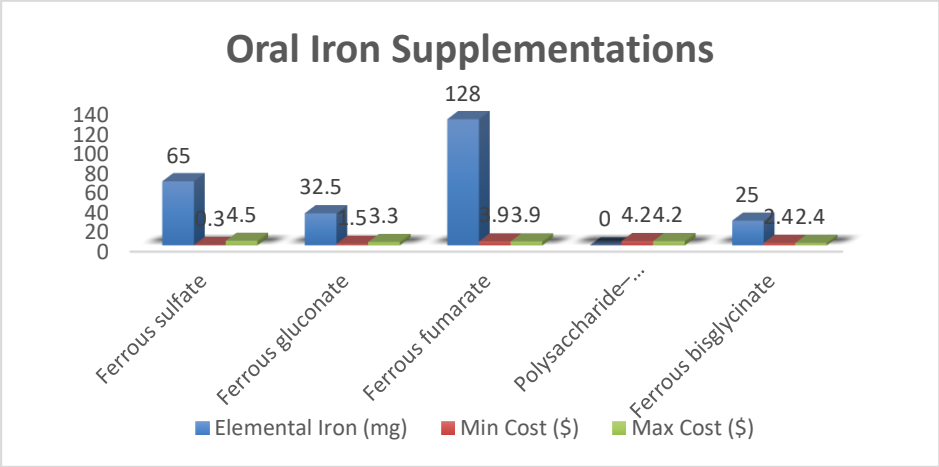

Figure 1: Oral Iron Supplementations

Intravenous (IV) iron formulations:

All IV iron products can cause side effects, but none are considered the safest. Two types need special attention, though. Ferumoxytol (Feraheme) is coated with sugar and contains magnetic iron particles that are also used for MRI scans. If you receive this iron, please ensure that your doctor and radiologist are aware of it, especially if you plan to undergo an MRI within the next three months. Iron carboxymaltose (Injectafer) can cause low phosphate levels in your blood, especially if you get multiple doses. This can persist for a long time, causing fatigue and weakened bones. Doctors are careful when using this type in people who don't eat well or have trouble absorbing nutrients.

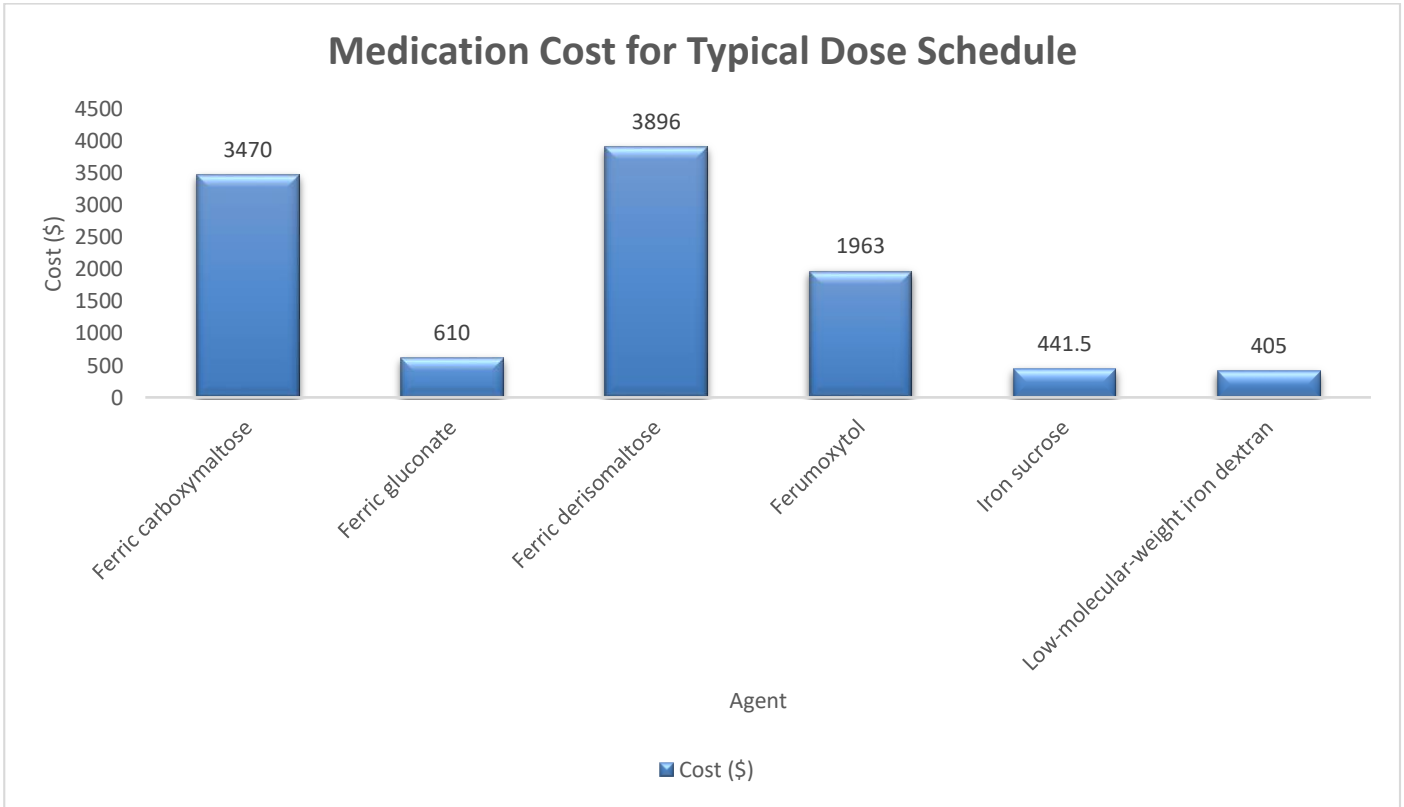

Figure 2: Intravenous Iron Supplementations

Iron-Deficiency Anemia After Weight Loss Surgery:

Iron-deficiency anemia occurs frequently after weight loss surgery, especially after procedures like gastric bypass that disrupt the normal absorption of iron in the first part of the small intestine (9,10). Other weight loss surgeries, such as gastric bands and sleeve surgery, as well as some non-weight loss surgeries that affect iron absorption, can also cause this problem. While there are usually several reasons why people develop iron-deficiency anemia after surgery, the primary one is that they are unable to absorb iron properly. This occurs because iron is absorbed most efficiently in the duodenum and the beginning of the small intestine, parts that are often bypassed or altered during many weight loss surgeries (9,10). Additionally, your stomach produces less acid after surgery, and stomach acid helps extract iron from food, making it easier for your body to absorb. Another problem is that people often develop ulcers where the surgeon connected parts of the intestine, and these ulcers can cause bleeding that you might not even notice. Due to this bleeding risk, patients who develop iron-deficiency anemia after weight loss surgery should undergo an upper endoscopy to check for ulcers. (9,10)

Treating iron-deficiency anemia after weight loss surgery involves addressing both the anemia and the absorption issues. Iron supplement plans vary significantly for these patients, and many don't provide enough iron to prevent or treat the anemia. Because of the changes made during surgery, IV iron usually works better, especially for individuals with severe anemia or those who don't respond to iron pills. For example, one study examined women with iron deficiency after gastric bypass and found that a single IV iron treatment was more effective and caused fewer side effects than iron pills. If it takes too long to build up iron stores, doctors may need to check for other vitamin deficiencies or ongoing bleeding (9,10).

Inflammatory Bowel Disease with Iron-Deficiency Anemia:

90% of people with inflammatory bowel diseases, such as Crohn's disease or ulcerative colitis, have Iron deficiency. The reasons are complex and involve several factors: bleeding from the gut (which may or may not be visible), difficulty absorbing iron, and inadequate iron intake from food. Those who have a current disease or have undergone intestinal surgery. (11,12)

Because there are many causes, treatment typically begins by controlling the inflammation that causes ulcers and bleeding, as well as making it difficult for the body to absorb iron. Doctors need to optimize medications for inflammation and help patients with their diet. All IBD patients with iron-deficiency anemia should take iron supplements (11,12).

There is no consensus on the matter of administering IV iron to individuals with IBD. IV works better than iron pills according to several studies. A comprehensive review of five studies involving 694 adults with IBD found that IV iron was more likely to increase hemoglobin levels by at least 2.0 g/dL compared to oral iron supplements. IV iron also caused fewer side effects, resulting in fewer patients needing to discontinue treatment. While iron pills are generally safe and commonly used, IV iron is more effective and easier to tolerate for these patients. Current guidelines from European IBD experts recommend IV iron as the first choice if the hemoglobin is below 10 g/dL. Still, iron pills may be effective for some patients with mild anemia, inactive disease, and good tolerance to oral iron; however, these patients require close monitoring to ensure the treatment is both effective and safe. (11,12)

Portal Hypertensive Gastropathy with Iron-Deficiency Anemia:

Mostly in patients with cirrhosis and portal hypertension, portal hypertensive gastropathy can occur. It often causes iron-deficiency anemia and occurs due to high pressure in the portal vein. The exact cause is complex and not fully understood. It is suggested that specific changes in the stomach lining can be observed under a microscope. While you need portal hypertension for this condition to develop, having portal hypertension doesn't guarantee you'll get it. It is diagnosed with endoscopy (7).

Treating iron-deficiency anemia in patients with this condition commences with treatment of the underlying cirrhosis and portal hypertension, primarily by lowering the portal pressure. Beta-blockers, such as propranolol, can reduce portal pressure, and clinical studies have shown that they improve outcomes in patients with both bleeding and non-bleeding cases compared to a placebo. More definitive treatments to lower portal pressure include TIPS procedures and liver transplantation. Endoscopic treatment rarely helps because the bleeding originates from widespread areas rather than specific spots.

During the treatment of portal hypertension, all patients with iron-deficiency anemia associated with this condition should be given iron supplements, either orally or intravenously, depending on the severity of the iron deficiency. Since this condition doesn't interfere with iron absorption, iron pills usually work fine. However, IV iron can be used safely and may be better for patients with severe anemia.

Gastric Antral Vascular Ectasia with Iron-Deficiency Anemia:

Gastric antral vascular ectasia (GAVE) is associated with several long-term conditions like scleroderma, cirrhosis, and chronic kidney disease. While it's a relatively rare cause of chronic gut bleeding, GAVE can be tough to manage. There are no established medications for GAVE, but endoscopic treatments like band ligation or heat treatments have been shown to reduce bleeding and decrease the need for blood transfusions (13).

Studies comparing band ligation to heat treatments show that both methods work well with endoscopy; however, band ligation tends to reduce transfusion needs more effectively and improve hemoglobin levels better. Specifically, patients treated with band ligation required fewer transfusions on average and experienced greater increases in hemoglobin. Additionally, band ligation typically requires fewer treatment sessions (approximately 2.6 versus nearly 3.8 sessions) to eliminate GAVE, with comparable safety.

All patients with iron-deficiency anemia due to GAVE should receive iron replacement therapy, with the choice between oral and IV iron depending on the severity of the iron deficiency and the patient's tolerance.

Celiac Disease with Iron-Deficiency Anemia:

2% to 6% of people with iron-deficiency anemia who don't have other symptoms have Celiac disease. Patients with celiac disease who are anemic usually have higher tissue transglutaminase antibody levels and more severe damage to their small intestine lining compared to those without anemia. Iron deficiency in celiac disease occurs due to damage to the intestinal lining, particularly in the duodenum, which hinders iron absorption. However, doctors should also consider other possible causes of iron deficiency. (14,15)

In most patients without other explanations for their iron deficiency, a strict gluten-free diet can improve anemia, even without iron supplements, although this is not true in 20% of cases. Typically, iron levels improve as the small intestine lining heals. (14,15)

Guidelines for iron supplementation in celiac disease aren't clearly defined and usually depend on how bad the symptoms are, how well the patient tolerates iron pills, and whether there are other sources of bleeding. Iron pills, along with a gluten-free diet, may be recommended for patients with symptoms of iron deficiency; however, they are less effective in cases of severe intestinal damage, where IV iron may be necessary, especially if symptoms are severe and persistent. IV iron is also an option for those whose iron levels don't improve enough with iron pills and a strict gluten-free diet. For patients whose iron stores take too long to recover, doctors need to check for other nutrient deficiencies, ongoing bleeding, or anemia from chronic inflammation (14,15).

Small-Bowel Angioectasias with Iron-Deficiency Anemia:

Iron deficiency can develop in patients with gut angioectasias due to episodes of bleeding. Studies show that angioectasias are found in 20% to 40% of patients getting small-bowel evaluation for iron-deficiency anemia. Diagnosing and managing angioectasias is challenging because they tend to bleed again even after treatment. For example, one analysis of 14 studies with 623 patients found an overall rebleeding rate of 34% and a higher rate of 45% specifically for small-bowel angioectasias. (16,17,18)

Endoscopic treatment usually involves the destruction of the lesions, with argon plasma coagulation being the most commonly used method. Other techniques, such as clips and injections, have some evidence of effectiveness. Radiofrequency ablation resulted in a 20% rebleeding rate over six months. (16,17,18)

Despite the frequent use of destruction techniques, endoscopic treatment alone often isn't enough, which may explain the high rebleeding rates, especially for small-bowel angioectasias. One reason might be that doctors can't see the entire small bowel completely. Some small studies have found that using attachments on the end of the endoscope, such as clear caps, can significantly improve the detection and treatment of angioectasias in the small bowel. However, further research is needed to determine the role of such devices and the most effective treatment approaches (16,17,18).

Additional medical treatments, including iron supplementation and hormone-like medications, may help improve hemoglobin levels, reduce the need for transfusions, and lower the risk of hospital admissions due to rebleeding. The choice between oral and IV iron therapy depends on the severity of the iron deficiency, the symptoms the patient is experiencing, and their tolerance level. Research reviews suggest that somatostatin analogues can reduce transfusion requirements and rebleeding rates, with octreotide appearing more effective than lanreotide (16,17,18).

Two controlled studies have examined anti-angiogenesis therapy, particularly thalidomide. One study found that thalidomide significantly reduced transfusion needs and rehospitalizations compared to iron therapy alone. Another study showed a dose-related decrease in rebleeding at one year in patients treated with thalidomide compared to those treated with a placebo. However, thalidomide causes significant side effects like nerve damage, constipation, and bowel perforation. Therefore, anti-blood vessel growth therapy should be reserved for patients who don't respond to other treatments and should be administered by experienced doctors. (16,17,18)

IDA is a condition that is affected by various factors and has a wide range of implications for patients. Oral iron supplementation is the primary treatment modality; however, gastrointestinal side effects and poor absorption in certain conditions limit its efficacy. Intravenous (IV) treatment is a suitable alternative, particularly for patients who are intolerant to oral treatment due to side effects or inflammation. Conditions with blood loss, such as portal hypertensive gastropathy, gastric antral vascular ectasia, and small-bowel angioectasias, need additional therapeutic and pharmacological care with iron therapy. IDA treatment is often complicated and requires a multidisciplinary approach involving gastroenterologists, hematologists, and nutritionists.

A significant amount of research has been conducted and is ongoing to establish therapeutic protocols; however, gaps remain in achieving optimal treatment strategies. Future research is needed to refine the treatment options and explore further therapies. Effective treatment of Ida will ultimately lead to improved quality of life for patients and to effective healthcare utilization.

Conclusion

Iron-deficiency anemia management involves addressing the underlying cause and replenishing iron stores. Iron replacement can be administered as pills or through IV, with the choice depending on the cause and severity of iron deficiency, the patient's tolerance for iron pills, and the likelihood that oral supplements will be effective. While iron pills often restore iron levels effectively, one of the safe and effective options for patients with severe deficiency or those unlikely to respond to oral treatment is IV iron. More research is needed to identify the most effective iron types and delivery methods, as well as to determine which patients may benefit from earlier use of IV iron. Additionally, further studies are necessary to develop the most effective gut treatment strategies for complex conditions such as portal hypertensive gastropathy, gastric antral vascular ectasia, and small-bowel angioectasias.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned.

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

HTC (Assistant Professor)

Manuscript drafting, Study Design, Review of Literature, Data entry, and drafting articles.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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