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EFFECTIVENESS OF MODERN FERROPREPARATIONS IN IRON DEFICIENCY ANEMIA

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Annotation: Iron deficiency anemia (IDA) remains one of the most widespread hematological disorders worldwide and represents a major public health concern affecting children, women of reproductive age, pregnant women, and elderly populations. According to the World Health Organization, iron deficiency accounts for nearly 50% of all anemia cases globally [1]. The modern approach to the treatment of IDA involves the use of highly bioavailable ferropreparations with improved tolerability and pharmacokinetic properties. This article analyzes the effectiveness of contemporary oral and parenteral iron preparations, including ferrous sulfate, ferrous fumarate, ferric polymaltose complex, iron sucrose, ferric carboxymaltose, and iron isomaltoside. The study evaluates therapeutic efficacy, safety profile, gastrointestinal tolerance, absorption characteristics, hemoglobin recovery rate, and ferritin restoration. Clinical studies demonstrate that modern ferropreparations significantly improve hematological indicators while reducing adverse reactions and improving patient compliance. Intravenous preparations exhibit rapid correction of severe anemia and iron stores in patients with chronic diseases, inflammatory bowel disease, chronic kidney disease, and pregnancy-associated anemia. The article highlights evidence-based recommendations for selecting appropriate ferrotherapy depending on patient characteristics and severity of iron deficiency.

Keywords: Iron deficiency anemia, ferropreparations, ferric carboxymaltose, iron sucrose, oral iron therapy, intravenous iron, ferritin, hemoglobin, ferrous sulfate, ferric polymaltose, bioavailability, hematology.

Introduction

Iron deficiency anemia is a pathological condition characterized by decreased hemoglobin synthesis due to insufficient iron availability in the body. It is considered the most common nutritional deficiency disorder worldwide [1]. The World Health Organization estimated that approximately 1.62 billion people suffer from anemia globally, with iron deficiency representing the leading cause [1]. Women of reproductive age, pregnant women, infants, adolescents, and patients with chronic inflammatory diseases are particularly vulnerable to IDA [2].

Iron plays a crucial role in oxygen transport, mitochondrial respiration, enzymatic processes, and immune function. Iron deficiency leads to impaired erythropoiesis, tissue hypoxia, fatigue, cognitive dysfunction, reduced physical performance, and compromised immunity [3]. Untreated IDA may result in cardiovascular complications, developmental delays in children, and increased maternal morbidity during pregnancy [4].

Traditional oral iron salts such as ferrous sulfate have long been the standard treatment for IDA because of their low cost and relatively high efficacy [5]. However, gastrointestinal adverse effects including nausea, constipation, abdominal pain, and diarrhea reduce treatment adherence in many patients [6]. Consequently, modern ferropreparations with enhanced bioavailability and tolerability have been developed. These include ferric polymaltose complexes, liposomal iron formulations, ferric carboxymaltose, and iron isomaltoside [7].

Parenteral iron therapy has also undergone major advances. Earlier intravenous iron formulations were associated with severe hypersensitivity reactions and oxidative stress [8].

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Modern intravenous preparations demonstrate improved safety profiles, allowing administration of high-dose iron in a single infusion [9]. Contemporary guidelines recommend intravenous iron in cases of severe anemia, malabsorption syndromes, inflammatory bowel disease, chronic kidney disease, heart failure, and intolerance to oral iron [10].

This article aims to analyze the effectiveness, pharmacological characteristics, clinical outcomes, and safety of modern ferropreparations used in iron deficiency anemia treatment based on current scientific evidence.

Methodology

This scientific review article was prepared using evidence-based literature published in international peer-reviewed journals and clinical guidelines between 2010 and 2024. Databases including PubMed, Scopus, Web of Science, WHO publications, and hematology association recommendations were analyzed [11].

The selection criteria included:

- Randomized controlled clinical trials;
- Meta-analyses;
- International treatment guidelines;
- Comparative studies of oral and intravenous iron preparations;
- Studies evaluating hemoglobin response and ferritin restoration.

The analyzed ferropreparations included:

- Ferrous sulfate;
- Ferrous fumarate;
- Ferric polymaltose complex;
- Iron sucrose;
- Ferric carboxymaltose;
- Iron isomaltoside;
- Liposomal iron.

Clinical parameters evaluated in the studies included:

- Hemoglobin increase;
- Ferritin recovery;
- Transferrin saturation;
- Adverse effects;
- Patient adherence;
- Treatment duration;
- Safety profile [12].

Results

Clinical studies indicate that oral ferrous sulfate remains effective in mild to moderate iron deficiency anemia. Tolkien et al. reported that oral ferrous sulfate increased hemoglobin by approximately 2 g/dL after 3–4 weeks of treatment in most patients [6]. However, gastrointestinal adverse effects occurred in up to 70% of cases, negatively affecting compliance [6].

Ferric polymaltose complex demonstrated improved gastrointestinal tolerance compared with ferrous sulfate. According to Cancelo-Hidalgo et al., ferric polymaltose caused significantly fewer adverse gastrointestinal symptoms while maintaining comparable hematological efficacy [13]. Patients receiving ferric polymaltose exhibited better treatment adherence rates.

Liposomal iron preparations have shown promising results due to enhanced absorption and reduced mucosal irritation. Studies revealed that liposomal iron significantly improved ferritin

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levels with minimal gastrointestinal toxicity [14]. This preparation is particularly beneficial in pregnant women and patients with inflammatory bowel disease.

Intravenous iron therapy demonstrated superior efficacy in severe IDA. Ferric carboxymaltose allows administration of up to 1000 mg of iron during a single infusion session [15]. Clinical trials showed rapid increases in hemoglobin and ferritin concentrations within 2–4 weeks [15].

Iron sucrose has been widely used in patients with chronic kidney disease and pregnancy-associated anemia. Qunibi et al. found that intravenous iron sucrose significantly improved hemoglobin levels and reduced the need for blood transfusions [16].

Iron isomaltoside demonstrated high efficacy and safety in chronic inflammatory conditions. Kalra and Bhandari reported minimal risk of hypersensitivity reactions and effective replenishment of iron stores after high-dose administration [17].

A meta-analysis conducted by Avni et al. demonstrated that intravenous iron therapy resulted in faster correction of anemia compared with oral iron, particularly in patients with chronic diseases [18]. Furthermore, intravenous therapy reduced hospitalization rates and improved quality of life indicators.

Modern guidelines recommend lower-dose alternate-day oral iron therapy to improve iron absorption and reduce hepcidin-mediated inhibition [19]. Stoffel et al. showed that alternate-day dosing improved fractional iron absorption compared with daily administration [19]

Analysis and Discussion

Iron deficiency anemia continues to represent one of the most significant nutritional and hematological disorders worldwide, affecting both developing and developed countries. Despite advances in preventive medicine and nutritional interventions, the prevalence of IDA remains high among women of reproductive age, pregnant women, children, adolescents, and patients suffering from chronic inflammatory diseases [20]. The widespread nature of this condition is associated not only with inadequate dietary iron intake but also with chronic blood loss, impaired intestinal absorption, inflammatory disorders, parasitic infections, and increased physiological demands during growth and pregnancy [1]. Modern therapeutic approaches therefore focus not only on correcting hemoglobin levels but also on restoring iron reserves, improving patient tolerance, and preventing recurrence.

The pathophysiology of iron deficiency anemia is complex and involves progressive depletion of iron stores, impaired erythropoiesis, and eventual reduction in hemoglobin synthesis. Iron is an essential micronutrient involved in oxygen transport, mitochondrial energy production, DNA synthesis, and immune regulation [3]. When iron stores become insufficient, tissue oxygenation declines, resulting in fatigue, weakness, reduced cognitive function, dizziness, and decreased physical capacity. Severe or prolonged anemia may lead to cardiovascular stress, tachycardia, left ventricular hypertrophy, and increased mortality in vulnerable populations [4]. Consequently, rapid and effective iron replacement remains a critical objective in modern clinical practice.

Traditional oral iron therapy has historically relied on ferrous salts such as ferrous sulfate, ferrous gluconate, and ferrous fumarate because ferrous iron demonstrates relatively efficient absorption through the divalent metal transporter-1 located in the duodenal mucosa [5]. Numerous clinical studies confirm that ferrous sulfate effectively increases hemoglobin concentration in uncomplicated iron deficiency anemia [6]. However, conventional oral iron therapy is frequently associated with significant gastrointestinal adverse effects, including nausea, constipation, abdominal discomfort, epigastric pain, vomiting, metallic taste, and diarrhea. These

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complications arise mainly from unabsorbed iron remaining within the intestinal lumen, where it promotes oxidative stress and mucosal irritation [6].

Poor tolerance to conventional oral iron preparations significantly reduces treatment adherence. Clinical evidence indicates that up to 40–70% of patients discontinue therapy prematurely because of gastrointestinal side effects [13]. Poor compliance results in incomplete restoration of iron stores and recurrent anemia. This issue is especially problematic in pregnant women, elderly individuals, and patients requiring prolonged therapy. Consequently, modern pharmaceutical research has focused extensively on developing iron formulations with improved bioavailability and enhanced tolerability.

Ferric polymaltose complex represents one of the most important innovations in oral ferrotherapy. Unlike traditional ferrous salts, ferric polymaltose contains ferric iron stabilized by a polymaltose carbohydrate shell that regulates gradual iron release within the gastrointestinal tract [13]. This structure prevents rapid dissociation of free iron and minimizes oxidative mucosal injury. Studies comparing ferric polymaltose with ferrous sulfate have demonstrated similar hematological efficacy but significantly improved gastrointestinal tolerance [13]. Reduced rates of nausea, constipation, and abdominal pain contribute to better long-term adherence and higher therapeutic success rates.

Another modern development involves liposomal or sucrosomial iron preparations. Liposomal technology encapsulates iron molecules within phospholipid membranes, facilitating absorption through para-cellular and lymphatic pathways [14]. Unlike conventional iron salts, liposomal iron bypasses direct interaction with intestinal mucosa and minimizes oxidative stress. This mechanism substantially improves gastrointestinal tolerance while maintaining effective iron delivery to systemic circulation. Several clinical investigations demonstrate that liposomal iron effectively increases ferritin and hemoglobin levels even in patients with inflammatory bowel disease or malabsorption syndromes [14]. This feature is particularly important because chronic intestinal inflammation often impairs traditional iron absorption.

The understanding of iron metabolism has evolved considerably following the discovery of hepcidin, a peptide hormone synthesized primarily in the liver [21]. Hepcidin serves as the principal regulator of systemic iron homeostasis by controlling ferroportin activity, the protein responsible for iron export from enterocytes and macrophages. Elevated hepcidin levels inhibit intestinal iron absorption and trap iron within reticuloendothelial cells. Inflammatory diseases, infections, obesity, chronic kidney disease, and malignancies frequently increase hepcidin production, resulting in functional iron deficiency [21]. This mechanism explains why many patients fail to respond adequately to conventional oral iron therapy despite sufficient supplementation.

Recent clinical research has demonstrated that high oral iron doses paradoxically stimulate hepcidin production, thereby decreasing subsequent iron absorption [19]. This observation has led to substantial changes in therapeutic recommendations. Alternate-day dosing strategies now appear superior to traditional multiple daily dosing regimens. Stoffel and colleagues demonstrated that alternate-day administration significantly enhances fractional iron absorption while reducing gastrointestinal side effects [19]. Consequently, modern guidelines increasingly recommend lower-dose intermittent therapy to optimize bioavailability and improve patient tolerance.

Intravenous iron therapy has become increasingly important in modern hematology due to the limitations of oral treatment. Earlier intravenous formulations such as high-molecular-weight iron dextran were associated with severe hypersensitivity reactions, including anaphylaxis, which limited their clinical use [8]. However, contemporary intravenous preparations possess

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improved molecular stability and safer carbohydrate shells that tightly bind elemental iron, reducing the release of toxic free iron into circulation.

Ferric carboxymaltose is currently considered one of the most advanced intravenous ferropreparations. Its highly stable molecular structure permits administration of large single doses up to 1000 mg during one infusion session [15]. This feature enables rapid replenishment of iron stores while minimizing the number of hospital visits. Clinical trials demonstrate that ferric carboxymaltose rapidly increases hemoglobin concentrations, ferritin levels, and transferrin saturation within several weeks [15]. Furthermore, patients receiving ferric carboxymaltose often report significant improvements in fatigue, exercise tolerance, physical performance, and overall quality of life.

The effectiveness of ferric carboxymaltose is particularly evident in surgical patients, postpartum women, and individuals with severe symptomatic anemia. Preoperative correction of iron deficiency reduces perioperative transfusion requirements and postoperative complications [20]. Postpartum anemia management with intravenous iron also improves maternal recovery, cognitive function, and breastfeeding capacity [24]. Compared with oral therapy, intravenous ferric carboxymaltose provides substantially faster correction of anemia, which is clinically important in urgent or severe conditions.

Iron sucrose remains widely used, especially in nephrology and obstetric practice. Patients with chronic kidney disease frequently develop iron deficiency due to impaired erythropoietin production, repeated blood sampling, dialysis-associated blood loss, and elevated hepcidin activity [22]. Intravenous iron sucrose effectively restores iron availability and enhances responsiveness to erythropoiesis-stimulating agents [16]. Studies indicate that adequate intravenous iron supplementation reduces erythropoietin dosage requirements and lowers treatment costs in dialysis patients [16].

Iron isomaltoside represents another significant advancement in intravenous iron therapy. Its stable matrix allows administration of very high cumulative doses over short infusion periods [17]. This preparation demonstrates high efficacy in patients with chronic inflammatory conditions, including inflammatory bowel disease, rheumatoid arthritis, and heart failure. Importantly, modern intravenous preparations exhibit extremely low rates of severe hypersensitivity reactions when appropriate infusion protocols are followed [17].

Inflammatory bowel disease presents a particularly challenging clinical scenario for iron replacement therapy. Chronic intestinal inflammation leads to blood loss, impaired absorption, and elevated hepcidin concentrations, all of which contribute to severe iron deficiency [15]. Oral iron therapy may exacerbate oxidative stress within the intestinal mucosa and worsen inflammatory activity. Consequently, international gastroenterology guidelines frequently recommend intravenous iron as the preferred treatment modality for patients with active inflammatory bowel disease [15]. Ferric carboxymaltose and iron sucrose demonstrate excellent efficacy and safety in these populations.

Pregnancy-associated iron deficiency anemia remains another major global concern. Maternal iron requirements increase substantially during pregnancy because of fetal development, placental growth, and expanded maternal blood volume [23]. Untreated maternal anemia increases risks of premature birth, low birth weight, fetal growth restriction, postpartum hemorrhage, and maternal mortality [23]. Although oral iron remains first-line therapy during pregnancy, gastrointestinal intolerance often limits compliance. Modern intravenous preparations such as ferric carboxymaltose and iron sucrose have demonstrated favorable safety profiles during the second and third trimesters [24]. Rapid restoration of maternal iron stores improves fetal oxygenation and reduces obstetric complications.

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An additional consideration involves iron deficiency in chronic heart failure. Iron deficiency independently worsens exercise intolerance, fatigue, and hospitalization risk even in the absence of severe anemia [20]. Clinical trials involving intravenous ferric carboxymaltose demonstrate improvements in functional capacity, six-minute walking distance, and quality of life among heart failure patients [20]. These findings highlight the systemic importance of iron beyond erythropoiesis alone.

Economic aspects also significantly influence ferrotherapy strategies worldwide. Oral iron preparations remain inexpensive and widely accessible, making them essential in low-resource healthcare settings [5]. However, prolonged treatment duration, poor adherence, recurrent clinic visits, and therapeutic failure may ultimately reduce cost-effectiveness. Intravenous therapy involves higher initial expenditures because of infusion equipment and monitoring requirements, but it may reduce hospitalization rates, blood transfusion needs, and productivity loss in severe anemia cases [18]. Therefore, individualized economic evaluation is necessary when selecting appropriate therapy.

Monitoring of ferrotherapy is essential to prevent both under-treatment and iron overload. Excessive iron accumulation may promote oxidative stress, endothelial dysfunction, tissue damage, and increased susceptibility to infections [25]. Serum ferritin, transferrin saturation, hemoglobin concentration, and inflammatory markers should therefore be regularly assessed during treatment. Monitoring is particularly important in patients receiving repeated intravenous infusions or suffering from chronic inflammatory diseases.

Another important issue concerns the relationship between iron supplementation and infection risk. Certain pathogenic microorganisms utilize iron for proliferation, raising concerns regarding excessive iron administration during active infection [25]. Nevertheless, modern evidence suggests that appropriate iron replacement under controlled clinical conditions provides substantial benefits that outweigh potential risks in most patients.

Future directions in iron deficiency anemia management include the development of nanoparticle-based iron formulations, targeted iron delivery systems, and hepcidin-modulating therapies [26]. Nanotechnology-based preparations may further improve bioavailability while reducing oxidative stress and gastrointestinal toxicity. Hepcidin antagonists and ferroportin regulators are also being investigated as potential therapeutic agents for anemia associated with chronic inflammation and chronic kidney disease.

Conclusion

Modern ferropreparations significantly improve the treatment outcomes of iron deficiency anemia. Contemporary oral formulations such as ferric polymaltose and liposomal iron provide improved gastrointestinal tolerance and better patient adherence compared with traditional ferrous salts. Intravenous preparations including ferric carboxymaltose, iron sucrose, and iron isomaltoside ensure rapid correction of anemia and efficient restoration of iron stores in severe or complicated cases.

Evidence-based individualized therapy remains the cornerstone of successful IDA management. Selection of ferropreparations should consider disease severity, underlying pathology, inflammatory status, patient tolerance, and treatment adherence. Advances in ferrotherapy continue to improve hematological recovery, quality of life, and long-term clinical outcomes in patients with iron deficiency anemia.

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