Review

Pediatric Oral Iron Therapy: Choosing the Right Product for Your Patient

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Review

Pediatric Oral Iron Therapy: Choosing the Right Product for Your Patient

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Abstract

In this narrative review, we address the prevention and therapy of iron deficiency anemia (IDA) with oral iron products in pediatric patients. Fortification of complementary foods with iron-containing micronutrient powders is the preferred method for the prevention of IDA in resource-limited settings. In developed countries, the prevention of sideropenia is through the consumption of iron-rich foods of animal origin. Regarding oral iron therapy, ferrous sulfate is the most widely used and cheapest product, but it is less well tolerated due to gastrointestinal side effects compared to complexes of ferric iron with polysaccharides, and complexes of iron with amino acids in casein, such as iron protein succinylate and iron acetyl aspartylate. These latter products are expensive and available only as single-dose vials with a fixed amount of elemental iron. Intermittent administration of ferrous sulfate, once or twice a week, is equally effective to daily therapy, with fewer side effects, and should be advocated. Oral carbonyl iron has excellent bioavailability and the additional advantage of a high safety margin in cases of accidental overdose compared to iron salts, an important consideration given the potentially lethal consequences of iron overdose. Newer liposomal and sucrosomial iron products appear to have better intestinal tolerance and similar efficacy in the treatment of IDA, but limited pediatric data exist. In conclusion, all oral medicinal iron products are effective when prescribed for the treatment of IDA, if well-absorbed and taken consistently for 3 to 6 months. Physicians should be prepared to use alternative oral agents with better tolerance in case of gastrointestinal side effects.

Keywords: ferrous sulfate; iron deficiency anemia (IDA); iron deficiency without anemia (IDWA); iron polymaltose complex; iron protein succinylate; liposomal iron; sucrosomial iron

1. Introduction

Anemia is a major public health problem, with the highest burden observed among young children, pregnant and postpartum women, and menstruating adolescent girls [1]. The World Health Organization (WHO) estimates that approximately 40% of children aged 6-59 months, corresponding to nearly 270 million children worldwide, are affected by anemia [2]. In developing countries, notably sub-Saharan Africa, the prevalence of anemia in children of the same age group is often > 60% [3]. As dietary iron deficiency (ID) is the most common cause of anemia in children <5 years of age, iron deficiency anemia (IDA) represents the most prevalent form of anemia in children worldwide. In addition, ID without anemia (IDWA) is at least twice as common [4]. In the United States, the overall prevalence of sideropenia for toddlers 12-23 months and for non-pregnant adolescent girls was 15.1% and 10.4%, respectively [5]. In a systematic review of European pediatric populations, which included 44 studies, ID prevalence among infants aged 6-12 months ranged from 2% to 25%, while in children aged 12 to 36 months between 3% and 48% [6]. Notably, the prevalence of IDA was typically <5% in Northern and Western Europe, but increased markedly in Eastern European countries, reaching levels of up to 40-50% in young children [6].

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2. Risk Factors for IDWA and IDA

Diets with low iron bioavailability are the main contributor to IDA in developing countries, where access to iron-rich meat-based foods is limited by high cost and availability [7]. In developed countries, the leading causes of IDWA and IDA in children are inappropriate feeding practices, as well as chronic blood loss from the gut or the genitourinary system [8]. Regarding infants and young children, inappropriate feeding practices include prolonged exclusive breastfeeding without iron supplementation, introduction of cow's milk before 12 months of age, excessive cow's milk intake (>24 ounces per day), and continued bottle use beyond the first birthday [5,9]. Other risk factors include prematurity, as birth iron stores are important in the prevention of early ID, low iron diet, obesity [10], heavy menstrual bleeding, inflammatory bowel diseases [11], and low socioeconomic status.

Early diagnosis and appropriate management of sideropenia are of paramount importance, given the critical role of iron in the development of the central nervous system in children and evidence that IDWA/IDA in infancy may be associated with long-term neurocognitive consequences, adverse psychomotor and socioemotional development, even after correction of the deficiency [12–14].

3. Prevention of IDWA and IDA

In settings where anemia prevalence among children < 5 years exceeds 20%, the WHO recommends adding iron-containing micronutrient powders (MNPs) for fortification of complementary foods in infants and young children aged 6 to 23 months [15]. In these formulations, iron is encapsulated within a lipid coating to minimize adverse effects (AE) on the taste and appearance of foods. MNPs are provided in single-dose sachets and are added to the child's meal after serving. The MNPs used should contain 12.5 mg of elemental iron per sachet, which corresponds to 37.5 mg of ferrous fumarate or 62.5 mg of ferrous sulfate ($FeSO_4$) heptahydrate, or equivalent amounts of other iron compounds [16]. De-Regil et al assessed the effects of point-of-use fortification of foods with iron-containing MNPs alone, or in combination with other vitamins and minerals, on nutrition, health, and development among preschoolers and children of school age, compared with no intervention, a placebo, or iron-containing supplements. They reviewed 13 studies involving 5,810 participants from Latin America, Africa, and Asia. MNPs containing iron were successful in reducing anemia and IDWA in preschool- and school-age children. However, information on developmental outcomes and AE was very limited [17]. The American Academy of Pediatrics (AAP) recommends supplementation of preterm neonates with 2 mg/kg/day of enteral iron, either as medicinal iron or in the form of iron-fortified formula. It is recommended that this start at one month of age and is continued until the first birthday. It is also recommended that exclusively breastfed term infants and those who receive more than one-half of their daily feedings as human milk and who are not receiving iron-containing complementary foods should obtain an iron supplementation of 1 mg/kg per day, starting at 4 months of age and continued until appropriate iron-containing complementary foods have been introduced [18].

Preventive oral iron supplementation is one of the strategies used to reduce the burden of IDWA/IDA in populations with high anemia prevalence (≥40%). According to the WHO, infants and young children aged 6-23 months should receive daily oral iron supplementation at doses of 10-12.5 mg administered for three consecutive months each year. [19].

4. Medicinal Products of Oral Iron

There are numerous oral iron formulations available in various dosage forms suitable for pediatric use, including drops, syrups, sublingual sprays, single-dose vials, capsules, and tablets. Many of these preparations belong to the category of ferrous salts, of which $FeSO_4$ is the most widely used and extensively studied, and which is considered the standard of care. Other types of oral iron include ferric (Fe^{3+}) iron complexes with polysaccharides, complexes of iron with amino acids in

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casein, including iron protein succinylate and iron acetyl aspartylate, as well as sucrosomial iron, carbonyl iron (CI), and heme iron polypeptides. Not all products are available in every market, but their large number is indicative of the absence of an ideal oral iron product. **Table 1** summarizes commercially available oral iron products.

Oral iron is usually the first line of therapy in children with IDA due to the convenience and low cost of most oral formulations. Published evidence suggests that daily oral supplementation of iron alone, in combination with folic acid, or other vitamins or minerals, or both, may result in a significant reduction of IDA across various populations, with stool discoloration being the most common side effect [20]. Parenteral iron therapy should be used only when oral therapy has failed or when a quick resolution of the IDA is required. **Table 2** compares oral and intravenous iron therapy. For this manuscript, we will focus on oral iron therapy alone. We will not talk about ferric maltol and sodium ferric ethylenediaminetetraacetate, because both are not available in Greece.

Table 1. Commercially available oral iron products. Not all products are available in every market.

Ferrous iron salts	**Ferrous sulfate (gold standard), ferrous gluconate, ferrous fumarate, ferrous acetate, ferrous ascorbate. Available in many liquid and edible oral forms.**
Ferric iron salts	Ferric citrate (used mostly as an oral phosphate binder in patients with chronic kidney disease). Ferric Na_2EDTA (sodium feredetate).
Heme iron polypeptides	Available in many liquid and edible oral forms.
Carbonyl iron	Popular in the USA as stand-alone tablets or in combination with zinc, folic acid, vitamin C, and vitamin B12 in various combinations. Available as an oral suspension with MCT oil in some countries.
Ferrous glycine chelates (compounds of chelated iron with glycine)	Ferrous bisglycine chelate, ferric trisglycine chelate, ferrous bisglycinate hydrochloride, ferric glycinate
Ferric hydroxide polymaltose complex (iron polymaltose complex, IPC), ferric maltol	Available in drops, syrup, chewable tablets.
Iron succinylate	Complex of 5% ferric iron (Fe^{3+}) with succinylated casein or acetyl-aspartyl-casein.
Liposomal iron	Ferric pyrophosphate encapsulated in phospholipid vesicles.
Sucrosomial iron	Ferric pyrophosphate encapsulated within sucrosomes. It contains ascorbic acid (vitamin C) as a facilitator of iron absorption. The sucrosome is made by pregelatinized rice starch, sucrose esters of fatty acids, **s**unflower lecithin, glucose syrup, **t**ricalcium phosphate, and milk proteins.

Table 2. Comparison of oral and intravenous iron therapy for IDA in children.

	Oral iron therapy	**Intravenous iron therapy**
Cost	Low, but products of iron protein succinylate, liposomal, and sucrosomial iron can be expensive	High, but the limited need for laboratory work-up post-therapy reduces the total cost
Need for hospitalization	No	Yes, but with 3rd generation products, single or a few short IV infusions are required
Speed of anemia resolution	Slow	Fast

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Gastrointestinal side effects	Relatively common but depend on the product and the dose chosen. Ferric iron products are better tolerated	Absent
Risk of anaphylaxis	No	Minimal with 2nd and 3rd generation IV iron products
Need for frequent laboratory work-up to check for response	Yes	No

5. Oral Iron Therapy

Iron salts are commonly administered as oral supplements to prevent and treat sideropenia, despite their relatively poor bioavailability and frequent AE. Their use is frequently associated with gastrointestinal AE, which may compromise adherence to therapy. These include nausea, vomiting, epigastric discomfort, abdominal pain, constipation, diarrhea, black stools, teeth staining [21], and an unpleasant metallic aftertaste. Regarding the latter, in a prospective study to characterize barriers and facilitators of successful oral iron therapy in young children with IDA, poor taste was identified by the parents as a major barrier [22]. Although hemoglobin levels often respond rapidly to patients who adhere successfully to treatment, oral iron therapy requires 3 to 6 months to achieve resolution of the anemia, normalization of serum ferritin levels, and replenishment of body iron stores [23].

An ideal oral iron formulation should combine efficacy with optimal tolerability and ease of use, particularly in children. It should ideally be administered once daily or, at most, in two daily doses to improve compliance. Easy swallowing, an acceptable taste without a metallic aftertaste, and the absence of dental staining are important additional practical considerations. High bioavailability that is not diminished by food intake is highly desirable, along with a favorable safety profile characterized by minimal gastrointestinal side effects. In addition, the ideal oral iron formulation should have a long shelf life at room temperature after opening and remain affordable. Finally, minimal toxicity in the event of accidental overdose represents a critical safety feature, especially in children. Iron remains one of the most common causes of pediatric deaths reported to poison control centers [24]. Juurlink et al. demonstrated that 42% of iron poisonings occurred within one year of the birth of a sibling. In addition, they found a fourfold increase in the risk of iron poisoning in patients whose mothers were in the first postpartum month, a period when prenatal vitamins are more likely to be found at home [25]. **Table 3** summarizes the desirable properties of an ideal medicinal oral iron product.

Table 3. Desirable properties of an ideal oral iron product.

Available in both liquid and edible forms
Easy swallowing
Good taste, no metallic aftertaste
No or minimal discoloration of the teeth
Excellent bioavailability, unaffected by the type of food consumed
Easy administration schedule (once or twice daily)
Long shelf life after opening
Does not require a refrigerator for safe preservation
Low cost
No or minimal gastrointestinal side effects
Minimal systemic toxicity in case of overdose

Current treatment recommendations for iron-deficient children are not firmly evidence-based, and the recommended oral iron dose of 3-6 mg/kg/day is primarily based on empirical practice [23]. Clinical trials in children are relatively scarce and characterized by substantial heterogeneity in terms of iron formulations used, dosing strategies, and treatment duration. This lack of consistency and

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standardization significantly limits the comparability of findings and frequently complicates therapeutic decision-making. The practice of administering oral iron in two or three divided daily doses is being increasingly replaced by once-daily dosing, as studies have shown comparable therapeutic efficacy with improved compliance and lower costs [23]. Zlotkin et al. performed a randomized controlled clinical trial (RCT) in 557 anemic children. One group received $FeSO_4$ drops once daily, and the control group received $FeSO_4$ drops 3 times per day (total dose, 40 mg of elemental iron for both groups). They showed that the single versus the 3-times-daily dose of $FeSO_4$ drops over 2 months resulted in a similar rate of successful treatment of IDA, without side effects [26]. To reduce the burden of IDA, intermittent iron supplementation regimens have been studied. Investigators from Pakistan compared the results of once-weekly vs. daily oral iron supplementation in school children. For 2 months, $FeSO_4$ 200 mg was given daily to the first group and once weekly to the second. A significant and comparable improvement in hematologic parameters was observed in both groups. Moreover, weekly iron supplementation had few, if any, side effects [27]. Tavil et al randomized 94 children between the ages of 5 months and 6 years with IDA to receive $FeSO_4$ at 6 mg/kg daily or the same dose biweekly. Both treatment groups were reevaluated for hematological response at 2 months. Intermittent treatment was equally effective but better tolerated than daily treatment [28]. In a study from Jordan, 134 children, 2 to 6 years old, were randomly assigned to receive daily, weekly, or biweekly 5 mg/kg of elemental iron for three months as $FeSO_4$ drops along with parental nutritional counseling. Weekly and biweekly oral iron therapy was as effective as daily oral iron therapy in correcting IDA, as indicated by a similar rise in hemoglobin [29]. In a systematic review and meta-analysis of 129 RCTs providing ≥30 days of oral iron supplementation versus placebo or control to children and adolescents aged <20 years, the results suggest that frequent (3-7 times/week) and intermittent (1-2 times/week) iron supplementation are equally effective at decreasing IDWA and IDA [30]. Nevertheless, most available data relate to formulations of ferrous salts, which were used in approximately 70% of the included studies ($FeSO_4$ 60.7%, ferrous fumarate 10%) [30]. Consequently, the application of intermittent dosing regimens with other iron formulations should be approached with caution, as supporting evidence remains limited.

5.1. Ferrous Sulfate

$FeSO_4$ is available in syrup, tablets, and capsules. For better oral absorption, it is administered 30 minutes to two hours before or after meals along with orange juice, as an iron absorption facilitator [31]. Administration with food decreases bioavailability and thus should be consumed on an empty stomach. Twenty-one toddlers with mild to moderate IDA aged 6 to 17 months received an oral $FeSO_4$ heptahydrate solution at 2 mg/kg of elemental iron daily, and 19 were analyzed for hematologic response at three months. Hemoglobin and ferritin were normalized in 95% and 84% of the patients, respectively. Only one patient experienced upper abdominal pain [32]. An Indian study randomly assessed the clinical response and AE of $FeSO_4$ and iron polymaltose complex (IPC) in 118 children with IDA. All subjects were given elemental iron in three divided doses at 6 mg/kg/day, 30 minutes before meals, for 30 days. Children who received $FeSO_4$ had higher hemoglobin and fewer residual complaints at 30 days as compared to those who received IPC. However, gastrointestinal side effects were 2.5 times more common in those who received $FeSO_4$ [33]. Powers et al. randomized infants and children 9 to 48 months with IDA to receive low-dose $FeSO_4$ or IPC, i.e., 3 mg/kg of elemental iron once daily for 12 weeks. From baseline to the end of the study, mean hemoglobin increased from 7.9 to 11.9 g/dl ($FeSO_4$ group) vs 7.7 to 11.1 g/dl (IPC group), a greater difference of 1.0 g/dl ($P < .001$). Median serum ferritin level increased from 3 to 15.6 ng/ml ($FeSO_4$) vs 2.0 to 7.5 ng/mL (IPC), a greater difference of 10.2 ng/ml ($P < .001$) [34]. In an important Indonesian study, 50 infants, 12 to 18 months old with IDA, were randomly assigned to receive oral $FeSO_4$ 3 mg/kg/day or a placebo for 4 months. Similar treatment randomization was done among 29 infants with IDWA and 47 iron-sufficient infants. All infants underwent mental and motor assessment in the Bayley scales before enrollment and after intervention. Developmental delays were significantly more common among infants with IDA, and treatment with $FeSO_4$ reversed them, having no significant effects on the scores of the infants

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with IDWA and on the iron-sufficient infants. It should be noted that this study was underpowered to answer the question of whether IDWA affects mental and motor development [35]. In a systematic review of 111 studies on oral iron therapy, which included data on 10,695 patients, extended-release $FeSO_4$ with mucoproteose had the lowest incidence of AE (4.1% overall, 3.7% for gastrointestinal AE). Incidence rates of overall AE for the other supplements were 7.3% for iron protein succinylate, 23.5% for ferrous glycine sulfate, 30.9% for ferrous gluconate, 32.3% for $FeSO_4$ without mucoproteose, and 47 % for ferrous fumarate. The differences in incidence of AE between extended-release $FeSO_4$ with mucoproteose and all other supplements except iron protein succinylate were statistically significant [36].

5.2. Ferrous Ascorbate

Ferrous ascorbate is considered to have better tolerance compared to $FeSO_4$ [37]. Patil et al performed an RCT on 125 children aged 1 to 12 years with IDA. Both groups randomly received ferrous ascorbate or IPC at 6 mg/kg/day of elemental iron for 3 months. Both iron products used produced statistically significant improvements in the hematological parameters during the 3 months of intervention, but the improvement was significantly better with ferrous ascorbate [38]. Yewale and Dewan compared the efficacy of ferrous ascorbate and colloidal iron in the treatment of IDA in 73 children. The provided iron dose corresponded to elemental iron 3 mg/kg/day. The mean rise in hemoglobin at 12 weeks was significantly higher in the ferrous ascorbate group [3.59 ± 1.67 g/dl vs. 2.43 ± 1.73 g/dl; $P < 0.01$] [39].

5.3. Ferrous Fumarate

Ferrous fumarate is as well absorbed as $FeSO_4$ in non-anemic, iron-sufficient infants and young children, and can be recommended as a useful fortification compound for complementary foods designed to prevent ID [40]. The WHO recommended regimen for the prevention of IDA is one sachet of MNP powder daily containing 12 mg iron as encapsulated ferrous fumarate [15]. A hepcidin-guided screen-and-treat strategy of targeting iron administration in children aged 6 to 23 months succeeded in reducing the overall dose of iron used, but was considerably less effective in combating IDA than the above mentioned WHO's standard of care [41]. Zlotkin et al showed that the use of a single daily dose of microencapsulated ferrous fumarate sprinkles with ascorbic acid was equally effective to $FeSO_4$ drops in the management of IDA in anemic children aged 6 to 18 months without side effects [42]. Tchum et al. performed a population-based, randomized cluster trial of long-term prophylactic iron fortification on the risk of IDA in preschool children living in a malaria-endemic area. The intervention group received daily 12.5 mg of elemental iron, as ferrous fumarate, along with vitamin A, ascorbic acid, and zinc for 5 months. The placebo group received a similar MNP powder but without iron. The two groups had similar baseline anthropometric, demographic, dietary, and clinical characteristics. Of the 1,904 children who remained on study, the intervention group had significantly higher hemoglobin and serum ferritin than the placebo group [43]. However, in another study, iron absorption from ferrous fumarate was considerably lower than that of $FeSO_4$ in children 2 to 5 years old with IDA, questioning the preventive efficacy of ferrous fumarate in iron fortification programs [44].

5.4. Iron Polymaltose Complex

Ferric iron in the form of iron-hydroxide polymaltose complex has been shown in several clinical trials in infants, children, and adults to be effective in treating IDA [45]. Due to its pharmacokinetic properties, IPC is best administered with meals and in higher doses than those of classical ferrous iron salts, such as $FeSO_4$. Many studies have shown a lower rate of treatment interruption with IPC than with ferrous salts due to a lower incidence of AE from the upper gastrointestinal tract [46]. Jaber et al in Israel prospectively compared the efficacy and safety of sideropenia prophylaxis with iron gluconate (IG) or IPC in 105 healthy infants attending a community pediatric center. Participants

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were randomly assigned to receive one of the two iron formulations from the age of 4 to 6 months until the age of one year. Mean hemoglobin levels at study end were significantly higher in the IG group. However, gastrointestinal AE were considerably less common in the IPC group [47].

5.5. Carbonyl Iron

A Brazilian study evaluated the efficacy of chewable CI tablets for the treatment of IDA in children <6 years old compared to $FeSO_4$. Seventy-three children were recruited. One group received chewable CI tablets, and the control group received a solution of $FeSO_4$ for 90 days, both at a dose of 5 mg/kg/day. Hemoglobin increased by 1.3 g/dl in the CI group and by 1.2 g/dl in the $FeSO_4$ group after 30 days of treatment. After 90 days of treatment, the CI group again had significantly higher hematocrit and ferritin concentration compared to the $FeSO_4$ group [48]. In a 3-week double-blind RCT involving 36 female blood donors with mild ID, high-dose CI (600 mg tid) was well tolerated compared to $FeSO_4$ 60 mg tid [49]. The 10-fold larger amount of CI resulted in a mean 1.5-fold increase in estimated iron absorption with similar gastrointestinal side effects. The major advantage of CI is its noticeably greater margin of safety when compared to $FeSO_4$. In humans, the estimated lethal dose of oral $FeSO_4$ is 200 mg Fe/kg body weight. On the other hand, human volunteers have taken doses of 10,000 mg of CI with no side effects [49]. Finally, no known case of corrosive gut injury from the consumption of CI has ever been reported to date [50].

5.6. Ferrous Bisglycinate

Ferrous bisglycinate is an amino acid iron chelate that is thought to be more bioavailable and associated with fewer gastrointestinal AE as compared with iron salts. A meta-analysis of 17 RCTs that reported hemoglobin or ferritin concentrations following at least 4 weeks' supplementation of ferrous bisglycinate compared with other iron supplements has been published. A non-significant trend for higher ferritin concentrations in pregnant women supplemented with ferrous bisglycinate was noted. No significant differences in hemoglobin or ferritin concentrations were detected among children. Hence, more trials are needed to assess its efficacy in children compared to cheaper iron salts [51]. Giancotti et al tested the efficacy of a new oral iron supplement combining ferrous bisglycinate chelate with sodium alginate in patients with celiac disease, an immunologically mediated disorder characterized by iron malabsorption. Twenty-six adults affected by IDA, of whom 14 were also affected by celiac disease, were enrolled. An oral iron absorption test was performed in each patient by administering the new oral iron supplement. Therapy was well tolerated, and a similar improvement in serum iron occurred in the two groups of patients (IDA plus celiac disease versus IDA alone) [52]. The Associazione Italiana di Ematologia ed. Oncologia Pediatrica prospectively recorded oral iron therapy in children, aged 3 months to 12 years with IDA, who were treated in one of 15 Italian centers. Of the 107 analyzed patients, 67 received ferrous bisglycinate iron 0.45 mg/kg, 18 received ferrous gluconate/sulfate 2 mg/kg (ferrous 2), 7 ferrous gluconate/sulfate 4 mg/kg (ferrous 4), 7 ferric iron salts 2 mg/kg, and 13 liposomal iron 0.7-1.4 mg/kg. A higher median increase was noted in the ferrous 2 and 4 groups at 2 and 8 weeks. Gastrointestinal side effects were reported in 16% (ferrous 2), 14% (ferrous 4), 6% (ferrous bisglycinate), and 0% (ferric and liposomal iron) of the patients. Hence, bisglycinate iron appears to have an excellent safety profile, but may be less effective than ferrous salts in rapidly increasing the hemoglobin of children with IDA [53].

5.7. Hydrogen-Reduced Iron (HR Fe)

At high temperatures, hydrogen gas reduces iron oxide into elemental iron powder, resulting in a pure, fine powder. This product, known as hydrogen-reduced iron (HR Fe), is used for public health fortification in cereal or other basic foods like flour to combat IDA, with low cost, and without affecting taste or color. However, its bioavailability is substantially lower than that of ferrous salts. Still, it can be improved if prepared into fine particles <45 μm, a process known as micronization, or if added post-baking [54].

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5.8. Iron Protein Succinylate

Iron protein succinylate contains ferric iron complexed with succinylated casein protein to form a compound with high-molecular-weight and improved oral bioavailability [55]. It resists stomach breakdown, allowing its intestinal dissolution, where iron release and absorption take place. In a study from Greece, 100 children, aged 1 to 9.4 years with IDWA or IDA were randomly assigned to receive 4 mg/kg of elemental iron with a maximum daily dose of 80 mg daily, for 2 months, as either iron succinylate or IPC. Side effects and efficacy were assessed after 30 and 60 days of therapy. Both drugs were well tolerated. Iron protein succinylate led to a faster increase in hemoglobin and ferritin than IPC, which was sustained after 2 months of treatment [56]. In a systematic review of iron protein succinylate that included 54 studies with a total of 8,454 subjects, including 960 children (premature infants to 14-year-old children), patients who received iron protein succinylate had the lowest rate of AE, proving it is an excellent choice to treat IDWA and IDA due to its superior tolerability [55]. However, due to its high cost, it should be used when cheaper first-line ferrous salts or IPC products have failed.

5.9. Liposomal Iron

In liposomal iron, ferric ions are encapsulated into liposomes. This bypasses the hepcidin-ferroportin axis, leading to absorption through the intestinal M-cells. Investigators from Egypt completed a prospective RCT in 192 children with IDA. Patients received liposomal iron (1.4 mg/kg/day) or ferric iron as IPC (6 mg/kg/day). Both medicinal irons were administered once daily. After one month of therapy, children receiving liposomal iron showed higher hemoglobin and serum ferritin levels. After 6 months of therapy, the hemoglobin and growth-related anthropometric measurements were significantly higher in patients who received liposomal iron. Moreover, liposomal iron use was associated with improved patient compliance [57]. Sharma et al compared the effects of oral liposomal iron with those of $FeSO_4$ as intermittent prophylaxis against IDA in children aged 6 to 59 months. Forty children in each group received 20 mg of elemental iron twice weekly for 3 months. The mean hemoglobin, serum iron, and transferrin saturation showed greater improvements in those who received liposomal iron, who also experienced fewer side effects and better compliance [58]. In a very recently published study, 433 children aged 6 to 59 months were screened for IDA and IDWA. This latter group was divided into two subgroups: One group that received a placebo, and another that received liposomal iron for four months. The IDA group also received liposomal iron for four months. Hematologic efficacy and tolerability, development, and growth were evaluated before and after treatment. The interventional group with IDWA showed significant improvement in total developmental scores compared to the placebo group. The final score was notably superior in the isolated sideropenia group that took liposomal iron compared to the IDA group ($P < 0.001$). Hence, liposomal iron, in addition to good efficacy and tolerability, improves the development and growth of iron-deficient children, with the best results obtained from early intervention before the establishment of anemia [59]. In another recent study, 60 pediatric patients with chronic kidney disease (CKD) were randomized equally to receive oral liposomal iron 30 mg/day for 3 months or intravenous iron dextran 50 mg three times/week for 3 months. Daily liposomal iron was equally or more effective than intravenous iron dextran for the treatment of these anemic children with CKD, with no reported AE during the study period [60].

5.10. Sucrosomial Iron

Sucrosomial iron is a novel oral iron formulation in which ferric pyrophosphate is protected by a phospholipid bilayer, mainly from sunflower lecithin, plus a sucrester matrix (sucrosome), which is absorbed through paracellular and transcellular routes (M cells) [61]. In adults, high-dose oral sucrosomial iron (60 mg *per os* bid) was equally effective to intravenous ferric gluconate in patients refractory/intolerant to oral $FeSO_4$ [62]. Suva and Tirgar, in a retrospective observational study of 260 adults with IDA, showed that sucrosomial iron, compared to ferrous fumarate, ferrous ascorbate, and

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ferrous bisglycinate, was more effective in improving hemoglobin and iron indices and with a better safety profile [63]. In a single-center, retrospective, observational cohort study of children with newly diagnosed IBD, treatment with sucrosomial iron was effective in 88% of the patients at the end of follow-up, regardless of IDA severity at baseline, and with no serious AE [64]. The same conclusion was reached in a multi-center study in 52 adults with IBD-IDA, where 30 mg of sucrosomial iron daily for 12 weeks led to improved IDA symptoms, IBD activity, and patients' quality of life, with excellent adherence to the study medication [65]. However, in a cross-sectional, retrospective Turkish study, IDWA/IDA was observed at a significantly higher rate in children aged 9 to 13 months using sucrosomial and microencapsulated iron prophylaxis compared to children who received conventional ferrous or ferric iron salts [66].

6. Use of Oral Iron for Prevention and Treatment of IDA in Neonates

Iron supplementation in neonates should follow the guidelines of the AAP mentioned above [18]. Formula-fed infants up to 6 months of age should receive iron-fortified infant formula with an iron content of 4-8 mg/l of iron [9]. Slightly low-birth-weight infants (2000-2500 g) should receive iron supplements of 1-2 mg/kg/day. ESPHAGAN recommends the use of colloidal iron [67].

For premature and other high-risk infants at risk for IDWA/IDA, we recommend closely monitoring serum ferritin levels and supplementing iron up to 15 mg/kg/day to maintain iron adequacy [68]. Among ferrous iron salts, $FeSO_4$ and iron gluconate have been more extensively used in neonates; IPC and ferrous bisglycinate have also been successfully used, while studies are underway to assess the efficacy and safety of liposomal and sucrosomial iron in neonates.

Based on a systematic review of 27 articles, including 18 RCTs, long-term iron supplementation results in a reduction in IDA in preterm and low birth weight (LBW) infants [69]. Franz et al randomly assigned very low birth weight (VLBW) infants <1300 g to receive $FeSO_4$ 2 to 6 mg/kg/day as soon as enteral feedings of >100 ml/kg/day were tolerated (early group) or at 61 days of life (late group). The primary outcome was ferritin and the number of infants with ID. Ferritin at 61 days was not different between the two groups. However, infants in the late group received more blood transfusions after day 14 of life [70]. Supplementing VLBW infants with colloidal ferric hydroxide 3 mg/kg for infants 1000-1500g and 4 mg/kg for infants < 1000g starting at 2 weeks of age did not improve serum ferritin or hematological parameters at 2 months when compared to the standard practice of starting iron at 2 months [71]. However, a similar RCT with the same iron product at a dose of 2 mg/kg/day showed the opposite, with the early iron intervention at 2 weeks leading to improved serum ferritin and hemoglobin [72]. This study is in agreement with Arnon et al., who randomized infants <32 weeks gestational age to early or late iron supplementation (2 vs. 4 weeks) with IPC and found that the early group had better iron status than the late group [73].

7. Conclusions

In conclusion, the commercially available oral iron products are numerous and have different pharmacokinetic properties. Ferrous iron salts have better absorption than ferric iron products, at the expense of a higher rate of gastrointestinal side effects, when given in similar doses of elemental iron. We prefer to use therapeutically $FeSO_4$ up to 3 mg/kg once daily to improve gut tolerance. Moreover, since intermittent therapy wit once or twice weekly administrations of $FeSO_4$ is equally effective to daily administration and with substantially lower side effects, we advocate intermittent treatment with $FeSO_4$ for IDA in pediatric patients. In case of intolerance, IPC, ferrous bisglycinate, and CI are acceptable choices. In young infants who feed every 2 to 3 hours, we prefer to use IPC drops or syrup, because its absorption is enhanced by food consumption, but at higher doses compared to $FeSO_4$, i.e., 6 mg/kg/day, due to decreased bioavailability. For adolescents with IDA, we advocate the use of tablets or slow-release capsules of $FeSO_4$ with mucoproteose. In case of intolerance, iron protein succinylate, at a dose of 40 to 80 mg of elemental iron daily, and liposomal or sucrosomial iron at doses up to 30 mg once or twice daily are appropriate therapeutic choices. Finally, practitioners who

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treat children with IDWA/IDA should familiarize themselves with two to three oral iron products from the numerous options available to quickly and effectively treat patients in need.

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Abbreviations

The following abbreviations are used in this manuscript:

AAP	American Academy of Pediatrics
AE	Adverse Effects
CI	Carbonyl Iron
CKD	Chronic Kidney Disease
ESPHAGAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
$FeSO_4$	Ferrous Sulfate
IBD	Inflammatory Bowel Disease
ID	Iron Deficiency
IDA	Iron Deficiency Anemia
IDWA	Iron Deficiency Without Anemia
IPC	Iron Polymaltose Complex
LBW	Low Birth Weight
MCT	Medium-chain triglycerides
MNPs	Micronutrient Powders
RCT	Randomized Controlled Trial
VLBW	Very Low Birth Weight
WHO	World Health Organization

References

1. Subramaniam G, Girish M. Iron deficiency anemia in children. *Indian J Pediatr*. **2015**, 82, 558-64. https://doi.org/10.1007/s12098-014-1643-9
2. Gardner WM, Razo C, McHugh TA, Hagins H, Vilchis-Tella VM, Hennessy C, et al. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990–2021: findings from the Global Burden of Disease Study 2021. *Lancet Haematol*. **2023**, 10, e713-34. https://doi.org/10.1016/S2352-3026(23)00160-6
3. Lemoine A, Tounian P. Childhood anemia and iron deficiency in sub-Saharan Africa – risk factors and prevention: A review. *Archives de Pédiatrie*. **2020**, 27, 490-6. https://doi.org/10.1016/j.arcped.2020.08.004
4. Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anemia burden from 1990 to 2010. *Blood*. **2014**, 123, 615-24. https://doi.org/10.1182/blood-2013-06-508325
5. Gupta PM, Hamner HC, Suchdev PS, Flores-Ayala R, Mei Z. Iron status of toddlers, nonpregnant females, and pregnant females in the United States. *Am J Clin Nutr*. **2017**, 106, 1640S-6S. https://doi.org/10.3945/ajcn.117.155978

 doi:10.20944/preprints202601.1156.v1

6. Eussen S, Alles M, Uijterschout L, Brus F, Van Der Horst-Graat J. Iron Intake and Status of Children Aged 6-36 Months in Europe: A Systematic Review. *Ann Nutr Metab*. **2015**, 66, 80-92. https://doi.org/10.1159/000371357
7. Al-Naseem A, Sallam A, Choudhury S, Thachil J. Iron deficiency without anaemia: a diagnosis that matters. *Clin Med (Lond).* **2021**, 21, 107-13. https://doi.org/10.7861/clinmed.2020-0582
8. Mantadakis E. Iron deficiency anemia in children residing in high and low-income countries: Risk factors, prevention, diagnosis and therapy. *Mediterr J Hematol Infect Dis*. **2020**, 12, e2020041. https://doi.org/10.4084/mjhid.2020.041
9. Domellöf M, Braegger C, Campoy C, Colomb V, Decsi T, Fewtrell M, et al. Iron Requirements of Infants and Toddlers. *J Pediatr Gastroenterol Nutr*. **2014**, 58, 119-29. https://doi.org/10.1097/MPG.0000000000000206
10. Aigner E, Feldman A, Datz C. Obesity as an Emerging Risk Factor for Iron Deficiency. *Nutrients.* **2014**, 6, 3587-600. https://doi.org/10.3390/nu6093587
11. Tharu R, Kushwaha S, Srivastava R, et al. Burden of anemia in inflammatory bowel disease: A systematic review and meta-analysis. *Clin Epidemiol Glob Health.* **2026**, 37, 102262. https://doi.org/10.1016/j.cegh.2025.102262
12. Lozoff B. Iron Deficiency and Child Development. *Food Nutr Bull*. **2007**, 28, S560-71. https://doi.org/10.1177/15648265070284S409
13. Lozoff B, Smith JB, Kaciroti N, Clark KM, Guevara S, Jimenez E. Functional Significance of Early-Life Iron Deficiency: Outcomes at 25 Years. *J Pediatr*. **2013**, 163, 1260-6. https://doi.org/10.1016/j.jpeds.2013.05.015
14. Beard J. Iron deficiency alters brain development and functioning. *J Nutr.* **2003**, 133, 1468S-72S. https://doi.org/10.1093/jn/133.5.1468S
15. WHO Guideline: Use of Multiple Micronutrient Powders for Point-of-Use Fortification of Foods Consumed by Infants and Young Children Aged 6–23 Months and Children Aged 2-12 Years. Geneva: World Health Organization; **2016** (WHO Guidelines Approved by the Guidelines Review Committee).
16. Pasricha SR, Drakesmith H, Black J, Hipgrave D, Biggs BA. Control of iron deficiency anemia in low- and middle-income countries. *Blood*. **2013**, 121, 2607-17. https://doi.org/10.1182/blood-2012-09-453522
17. De-Regil LM, Jefferds MED, Peña-Rosas JP. Point-of-use fortification of foods with micronutrient powders containing iron in children of preschool and school-age. Cochrane Developmental, Psychosocial and Learning Problems Group, editor. *Cochrane Database Syst Rev.* **2017**, 2017. https://doi.org/10.1002/14651858.CD009666.pub2
18. Baker RD, Greer FR, The Committee on Nutrition. Diagnosis and Prevention of Iron Deficiency and Iron-Deficiency Anemia in Infants and Young Children (0–3 Years of Age). *Pediatrics.* **2010**, 126, 1040-50. https://doi.org/10.1542/peds.2010-2576
19. WHO Guideline: Daily iron supplementation in infants and children. Geneva: World Health Organization; **2016** (WHO Guidelines Approved by the Guidelines Review Committee).
20. Laine LA, Bentley E, Chandrasoma P. Effect of oral iron therapy on the upper gastrointestinal tract. A prospective evaluation. *Dig Dis Sci.* **1988**, 33, 172-7. https://doi.org/10.1007/BF01535729
21. Vahedi P, Bagheri N, Khoramian Tusi S, Mohammadian M. Comparative evaluation of the effects of four types of iron supplements on primary teeth discoloration: an in vitro study. *BMC Oral Health.* **2025**, 25, 1428. https://doi.org/10.1186/s12903-025-06846-x
22. Powers JM, Nagel M, Raphael JL, Mahoney DH, Buchanan GR, Thompson DI. Barriers to and Facilitators of Iron Therapy in Children with Iron Deficiency Anemia. *J Pediatr.* **2020**, 219, 202-8. https://doi.org/10.1016/j.jpeds.2019.12.040
23. Powers JM, Buchanan GR. Diagnosis and management of iron deficiency anemia. *Hematol Oncol Clin North Am.* **2014**, 28, 729-45, vi–vii. https://doi.org/10.1016/j.hoc.2014.04.007
24. Litovitz TL, Holm KC, Bailey KM, Schmitz BF. 1991 annual report of the American Association of Poison Control Centers National Data Collection System. *Am J Emerg Med.* **1992**, 10, 452-505. https://doi.org/10.1016/0735-6757(92)90075-9
25. Juurlink DN, Tenenbein M, Koren G, Redelmeier DA. Iron poisoning in young children: association with the birth of a sibling. *CMAJ*. **2003**, 168, 1539-42.

 doi:10.20944/preprints202601.1156.v1

26. Zlotkin S, Arthur P, Antwi KY, Yeung G. Randomized, Controlled Trial of Single Versus 3-Times-Daily Ferrous Sulfate Drops for Treatment of Anemia. *Pediatrics.* **2001**, 108, 613-6. https://doi.org/10.1542/peds.108.3.613
27. Siddiqui IA, Rahman MA, Jaleel A. Efficacy of daily vs. weekly supplementation of iron in schoolchildren with low iron status. *J Trop Pediatr.* **2004**, 50, 276-8. https://doi.org/10.1093/tropej/50.5.276
28. Tavil B, Sipahi T, Gökçe H, Akar N. Effect of twice weekly versus daily iron treatment in Turkish children with iron deficiency anemia. *Pediatr Hematol Oncol.* **2003**, 20, 319-26.
29. Faqih AM, Kakish SB, Izzat M. Effectiveness of Intermittent Iron Treatment of Two- to Six-Year-Old Jordanian Children with Iron-Deficiency Anemia. *Food Nutr Bull.* **2006**, 27, 220-7. https://doi.org/10.1177/156482650602700304
30. Andersen CT, Marsden DM, Duggan CP, Liu E, Mozaffarian D, Fawzi WW. Oral iron supplementation and anaemia in children according to schedule, duration, dose and cosupplementation: a systematic review and meta-analysis of 129 randomised trials. *BMJ Glob Health.* **2023**, 8, e010745. https://doi.org/10.1136/bmjgh-2022-010745
31. on behalf of the SPOG Pediatric Hematology Working Group, Mattiello V, Schmugge M, Hengartner H, von der Weid N, Renella R. Diagnosis and management of iron deficiency in children with or without anemia: consensus recommendations of the SPOG Pediatric Hematology Working Group. *Eur J Pediatr*. **2020**, 179, 527-45. https://doi.org/10.1007/s00431-020-03597-5
32. Pachuta Węgier L, Kubiak M, Liebert A, Clavel T, Montagne A, Stennevin A, et al. Ferrous sulfate oral solution in young children with iron deficiency anemia: An open-label trial of efficacy, safety, and acceptability. *Pediatr Int*. **2020**, 62, 820-7. https://doi.org/10.1111/ped.14237
33. Bopche AV, Dwivedi R, Mishra R, Patel GS. Ferrous sulfate versus iron polymaltose complex for treatment of iron deficiency anemia in children. *Indian Pediatr*. **2009**, 46, 883-5.
34. Powers JM, Buchanan GR, Adix L, Zhang S, Gao A, McCavit TL. Effect of Low-Dose Ferrous Sulfate vs Iron Polysaccharide Complex on Hemoglobin Concentration in Young Children With Nutritional Iron-Deficiency Anemia: A Randomized Clinical Trial. *JAMA.* **2017**, 317, 2297-304. https://doi.org/10.1001/jama.2017.6846
35. Idjradinata P, Pollitt E. Reversal of developmental delays in iron-deficient anaemic infants treated with iron. *Lancet.* **1993**, 341, 1-4. https://doi.org/10.1016/0140-6736(93)92477-b
36. Cancelo-Hidalgo MJ, Castelo-Branco C, Palacios S, Haya-Palazuelos J, Ciria-Recasens M, Manasanch J, et al. Tolerability of different oral iron supplements: a systematic review. *Curr Med Res Opin.* **2013**, 29, 291-303. https://doi.org/10.1185/03007995.2012.761599
37. Chandra J. Treating Iron Deficiency Anemia. *Indian J Pediatr.* **2019**, 86, 1085-6. https://doi.org/10.1007/s12098-019-03107-y
38. Patil P, Geevarghese P, Khaire P, Joshi T, Suryawanshi A, Mundada S, et al. Comparison of Therapeutic Efficacy of Ferrous Ascorbate and Iron Polymaltose Complex in Iron Deficiency Anemia in Children: A Randomized Controlled Trial. *Indian J Pediatr*. **2019**, 86, 1112-7. https://doi.org/10.1007/s12098-019-03068-2
39. Yewale VN, Dewan B. Treatment of Iron Deficiency Anemia in Children: A Comparative Study of Ferrous Ascorbate and Colloidal Iron. *Indian J Pediatr*. **2013**, 80, 385-90. https://doi.org/10.1007/s12098-012-0906-6
40. Harrington M, Hotz C, Zeder C, Polvo GO, Villalpando S, Zimmermann MB, et al. A comparison of the bioavailability of ferrous fumarate and ferrous sulfate in non-anemic Mexican women and children consuming a sweetened maize and milk drink. *Eur J Clin Nutr.* **2011**, 65, 20-5. https://doi.org/10.1038/ejcn.2010.185
41. Wegmüller R, Bah A, Kendall L, et al. Hepcidin-guided screen-and-treat interventions for young children with iron-deficiency anaemia in The Gambia: an individually randomised, three-arm, double-blind, controlled, proof-of-concept, non-inferiority trial. *Lancet Glob Health*. **2023**, 11, e105–16. https://doi.org/10.1016/S2214-109X(22)00449-1
42. Zlotkin S, Arthur P, Antwi KY, Yeung G. Treatment of anemia with microencapsulated ferrous fumarate plus ascorbic acid supplied as sprinkles to complementary (weaning) foods. *Am J Clin Nutr*. **2001**, 74, 791-5. https://doi.org/10.1093/ajcn/74.6.791

 doi:10.20944/preprints202601.1156.v1

43. Tchum SK, Arthur FK, Adu B, Sakyi SA, Abubakar LA, Atibilla D, et al. Impact of iron fortification on anaemia and iron deficiency among pre-school children living in Rural Ghana. *PLoS One*. **2021**, 16, e0246362. https://doi.org/10.1371/journal.pone.0246362
44. Sarker SA, Davidsson L, Mahmud H, Walczyk T, Hurrell RF, Gyr N, et al. Helicobacter pylori infection, iron absorption, and gastric acid secretion in Bangladeshi children. *Am J Clin Nutr*. **2004**, 80, 149-53. https://doi.org/10.1093/ajcn/80.1.149
45. Mohd Rosli RR, Norhayati MN, Ismail SB. Effectiveness of iron polymaltose complex in treatment and prevention of iron deficiency anemia in children: a systematic review and meta-analysis. *PeerJ* **2021**, 9, e10527. https://doi.org/10.7717/peerj.10527
46. Geisser P. Safety and Efficacy of Iron(III)-hydroxide Polymaltose Complex. *Arzneimittelforschung*. **2011**, 57, 439–52. https://doi.org/10.1055/s-0031-1296693
47. Jaber L, Rigler S, Taya A, Tebi F, Baloum M, Yaniv I, et al. Iron Polymaltose Versus Ferrous Gluconate in the Prevention of Iron Deficiency Anemia of Infancy. *J Pediatr Hematol Oncol.* **2010**, 32, 585-8. https://doi.org/10.1097/MPH.0b013e3181ec0f2c

a. Farias ILG, Colpo E, Botton SR, Silveira RB, Fleig A, Schimitz CAA, et al. Carbonyl iron reduces anemia and improves effectiveness of treatment in under six-year-old children. *Rev Bras Hematol Hemoter*. **2009**, 31, 125-31. https://doi.org/10.1590/S1516-84842009005000041

48. Gordeuk VR, Brittenham GM, Hughes M, Keating LJ, Opplt JJ. High-dose carbonyl iron for iron deficiency anemia: a randomized double-blind trial. *Am J Clin Nutr.* **1987**, 46, 1029-34. https://doi.org/10.1093/ajcn/46.6.1029
49. Manoguerra AS, Erdman AR, Booze LL, et al. Iron Ingestion: an Evidence-Based Consensus Guideline for Out-of-Hospital Management. *Clin Toxicol (Phila).* **2005**, 43, 553–70. https://doi.org/10.1081/CLT-200068842
50. Fischer JAJ, Cherian AM, Bone JN, Karakochuk CD. The effects of oral ferrous bisglycinate supplementation on hemoglobin and ferritin concentrations in adults and children: a systematic review and meta-analysis of randomized controlled trials. *Nutr Rev.* **2023**, 81, 904-20. https://doi.org/10.1093/nutrit/nuac106
51. Giancotti L, Talarico V, Mazza GA, Marrazzo S, Gangemi P, Miniero R, et al. Feralgine™ a New Approach for Iron Deficiency Anemia in Celiac Patients. *Nutrients.* **2019**, 11, 887. https://doi.org/10.3390/nu11040887
52. Russo G, Guardabasso V, Romano F, Corti P, Samperi P, Condorelli A, et al. Monitoring oral iron therapy in children with iron deficiency anemia: an observational, prospective, multicenter study of AIEOP patients (Associazione Italiana Emato-Oncologia Pediatrica). *Ann Hematol*. **2020**, 99, 413-20. https://doi.org/10.1007/s00277-020-03906-w
53. Shamah-Levy T, Villalpando S, Rivera-Dommarco JA, Mundo-Rosas V, Cuevas-Nasu L, Jiménez-Aguilar A. Ferrous Gluconate and Ferrous Sulfate Added to a Complementary Food Distributed by the Mexican Nutrition Program Oportunidades Have a Comparable Efficacy to Reduce Iron Deficiency in Toddlers. *J Pediatr Gastroenterol Nutr*. **2008**, 47, 660-6. https://doi.org/10.1097/MPG.0b013e318167b03b
54. Martínez Francés A, Leal Martínez-Bujanda J. Efficacy and tolerability of oral iron protein succinylate: a systematic review of three decades of research. *Curr Med Res Opin*. **2020**, 36, 613-23. https://doi.org/10.1080/03007995.2020.1716702
55. Haliotis FA, Papanastasiou DA. Comparative study of tolerability and efficacy of iron protein succinylate versus iron hydroxide polymaltose complex in the treatment of iron deficiency in children. *Int J Clin Pharmacol Ther*. **1998**, 36, 320-5.
56. Bahbah WA, Omar ZA, El-Shafie AM, Mahrous KS, El Zefzaf HMS. Interventional impact of liposomal iron on iron-deficient children developmental outcome: randomized, double-blind, placebo-controlled trial. *Pediatr Res.* **2025**. https://doi.org/10.1038/s41390-025-04204-9
57. Sharma A, Bellad RM, Charantimath US. Effectiveness and Safety of Liposomal Ferric Pyrophosphate vs. Ferrous Sulfate for Intermittent Iron Prophylaxis in Children Aged 6-59 months: A Randomized Controlled Trial. *Indian J Pediatr*. **2025**, 92, 423. https://doi.org/10.1007/s12098-025-05436-7
58. Bahbah WA, Younis YAHS, Elbelouny HS, Mahmoud AA. Liposomal SunActive versus conventional iron for treatment of iron-deficiency anemia in children aged 2-12 years: a prospective randomized controlled trial. *Clin Exp Pediatr.* **2025**, 68, 608-15. https://doi.org/10.3345/cep.2025.00262

59. Hegazy SK, Koura MSED, Elharoun MS. Liposomal iron dramatic effect on chronic kidney disease pediatric anemia: a randomized clinical trial. *Pediatr Res*. **2025** https://doi.org/10.1038/s41390-025-04418-x
60. Gómez-Ramírez S, Brilli E, Tarantino G, Girelli D, Muñoz M. Sucrosomial® Iron: An Updated Review of Its Clinical Efficacy for the Treatment of Iron Deficiency. *Pharmaceuticals*. **2023**, 16, 847. https://doi.org/10.3390/ph16060847
61. Giordano G, Napolitano M, Di Battista V, Lucchesi A. Oral high-dose sucrosomial iron vs intravenous iron in sideropenic anemia patients intolerant/refractory to iron sulfate: a multicentric randomized study. *Ann Hematol*. **2021**, 100, 2173-9. https://doi.org/10.1007/s00277-020-04361-3
62. Suva MA, Tirgar PR. Comparative evaluation of different oral iron salts in the management of iron deficiency anemia. *Daru*. **2024**, 32, 485-94. https://doi.org/10.1007/s40199-024-00517-y
63. D'Arcangelo G, Distante M, Veraldi S, Tarani F, Musto F, Aloi M. Natural History of Anemia and Efficacy and Safety of Oral Iron Therapy in Children Newly Diagnosed With Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. **2023**, 76, 771-5. https://doi.org/10.1097/MPG.0000000000003764
64. Bastida G, Herrera-de Guise C, Algaba A, Ber Nieto Y, Soares JM, Robles V, et al. Sucrosomial Iron Supplementation for the Treatment of Iron Deficiency Anemia in Inflammatory Bowel Disease Patients Refractory to Oral Iron Treatment. *Nutrients*. **2021**, 13, 1770. https://doi.org/10.3390/nu13061770
65. Tosyalı M, Demirçelik Y, Bağ Ö, Karaarslan U, Gökçe Ş, Koç F. Use of Different Iron Preparations for Prophylaxis and Effects on Iron Status in Infancy. *Healthcare (Basel)*. **2024**, 12, 1043. https://doi.org/10.3390/healthcare12101043
66. Agostoni C, Buonocore G, Carnielli V, et al. Enteral Nutrient Supply for Preterm Infants: Commentary From the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr*. **2010**, 50, 85-91. https://doi.org/10.1097/MPG.0b013e3181adaee0
67. Juul S, German K. Iron supplementation for infants in the NICU: What preparation, how much, and how long is optimal? *Semin Fetal Neonatal Med*. **2025**, 30, 101612. https://doi.org/10.1016/j.siny.2025.101612
68. McCarthy EK, Dempsey EM, Kiely ME. Iron supplementation in preterm and low-birth-weight infants: a systematic review of intervention studies. *Nutr Rev*. **2019**, 77, 865-77. https://doi.org/10.1093/nutrit/nuz051
69. Franz AR, Mihatsch WA, Sander S, Kron M, Pohlandt F. Prospective Randomized Trial of Early Versus Late Enteral Iron Supplementation in Infants With a Birth Weight of Less Than 1301 Grams. *Pediatrics*. **2000**, 106, 700-6. https://doi.org/10.1542/peds.106.4.700
70. Sankar MJ, Saxena R, Mani K, Agarwal R, Deorari AK, Paul VK. Early iron supplementation in very low birth weight infants--a randomized controlled trial. *Acta Paediatr*. **2009**, 98, 953-8. https://doi.org/10.1111/j.1651-2227.2009.01267.x
71. Joy R, Krishnamurthy S, Bethou A, Rajappa M, Ananthanarayanan PH, Bhat BV. Early versus late enteral prophylactic iron supplementation in preterm very low birth weight infants: a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed*. **2014**, 99, F105-9. https://doi.org/10.1136/archdischild-2013-304650
72. Arnon S, Shiff Y, Litmanovitz I, et al. The Efficacy and Safety of Early Supplementation of Iron Polymaltose Complex in Preterm Infants. *Am J Perinatol*. **2007**, 24, 95-100. https://doi.org/10.1055/s-2007-970179