

Liposomal SunActive versus conventional iron for treatment of iron-deficiency anemia in children aged 2–12 years: a prospective randomized controlled trial

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Background: Liposomal iron, a novel oral formulation of ferric pyrophosphate that demonstrates improved gastrointestinal absorption and bioavailability with fewer side effects than conventional iron, represents a significant advancement in the treatment of iron-deficiency anemia (IDA).

Purpose: To conduct an in-depth comparative study of liposomal SunActive and conventional iron supplements (iron polymaltose complex) for treating IDA in children aged 2–12 years

Methods: This prospective randomized controlled trial included 192 children who visited the outpatient clinic of the Pediatric Department at Menoufia University Hospital and were diagnosed with IDA. The patients were divided into group 1, 96 pediatric patients receiving oral liposomal SunActive iron; and group 2, 96 pediatric patients treated with conventional oral iron (iron polymaltose complex).

Results: After 1 month of oral iron therapy, group 1 exhibited higher hemoglobin, hematocrit, serum ferritin, and serum iron levels and greater transferrin saturation than group 2. After 6 months of oral iron therapy, hemoglobin level ($P < 0.001$), iron profile ($P < 0.001$), and growth-related anthropometric measurements were higher in group 1 versus group 2 ($P < 0.001$ for z score for weight).

Conclusion: Iron supplements effectively improve anthropometric measurements, complete blood count parameters, and iron profiles. However, orally administered liposomal SunActive iron exhibits better effects, reduced drug refusal rates, and improved compliance rates, thereby benefiting children's growth.

Key words: Liposomal SunActive iron, Conventional iron, Iron-deficiency anemia

Key message

Question: What is the best treatment for iron-deficiency anemia (IDA) in children?

Findings: This randomized controlled trial of 192 children assessed the impact of liposomal SunActive versus conventional oral iron for treating IDA. It also evaluated improvements in hemoglobin levels and iron profiles (primary outcome) as well as anthropometric measurements (secondary outcome).

Meaning: Children who received liposomal SunActive exhibited significant improvements in hemoglobin levels, iron profiles, and anthropometric measurements.

Introduction

Anemia constitutes a significant global health issue, affecting about 25% of the world's population. Iron deficiency, the leading cause, accounts for 50% of all anemia cases. The prevalence of iron deficiency is higher in developing nations; 9% of children between 12 and 36 months are iron-deficient, with one-third of these children developing anemia.¹⁾ Individuals with anemia experience fatigue, weakness, difficulty focusing, reduced cognitive abilities, and lower work productivity. Since roughly 80% of the iron required by the human body is used for hemoglobin production to generate 200 billion new red blood cells daily, anemia is often associated with iron deficiency.²⁾

An accurate diagnosis of iron-deficiency anemia (IDA) is crucial for safe treatment, yet it can sometimes be difficult to achieve. Importantly, the absence of anemia does not rule out IDA, as a healthy individual must deplete a significant portion of their iron reserves before hemoglobin (Hb) decreases to levels classified by the World

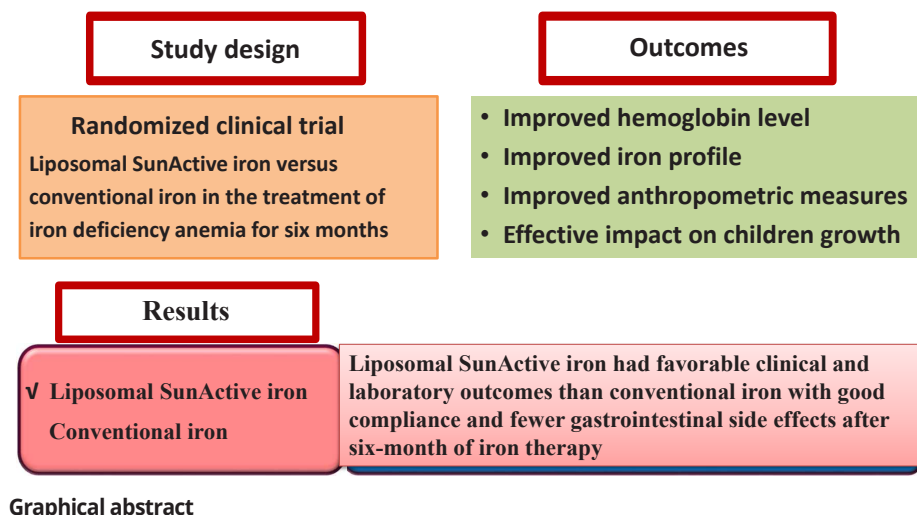
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Health Organization as anemia (Hb below 2 standard deviations from the average for the patient's age and sex).³⁾

Liposomal iron represents a significant advancement in treating IDA that does not respond to traditional oral iron supplements. Liposomes serve as efficient drug delivery systems capable of targeting various therapeutic agents. Their compatibility with biological systems, ability to biodegrade, and minimal toxicity make them an appropriate choice for drug delivery.⁴⁾

Liposomal SunActive iron is an innovative oral iron formulation of ferric pyrophosphate encapsulated in a phospholipid and lecithin membrane, demonstrating excellent gastrointestinal absorption and bioavailability, along with fewer side effects. It utilizes advanced technology that employs liposomes as a transport medium, enabling iron to be absorbed directly in the intestine without interacting with the gastrointestinal mucosa. Ferric pyrophosphate's particle size is reduced through a method called micronization, which enhances iron solubility. Breaking the molecule into smaller particles increases its surface area, which in turn boosts its dissolution rate. Additionally, the micronized iron is surrounded by a lipid bilayer membrane similar to biological membranes via microencapsulation. This procedure ensures that liposomes inhibit the oxidation and degradation of the core's iron components while aiding in precise delivery.⁵⁾

The administration of alternative traditional iron supplements is associated with various side effects, such as nausea, vomiting, gas, stomach pain, diarrhea, constipation, indigestion, and dark or sticky stools. These adverse effects have been a major concern with oral iron treatment. Constraints linked to traditional iron salts have led to the development of several oral iron formulations, including carbonyl iron, iron polymaltose complex, ferrous ascorbate, sodium feredetate, and ferrous bisglycinate. Nevertheless, the effectiveness and adverse effects

remained similar among these standard iron formulations when administered to patients with iron IDA.^{6,7)}

The purpose of this study was to conduct a thorough comparative evaluation of liposomal SunActive iron and conventional iron supplements (iron polymaltose complex) in addressing IDA in children aged 2 to 12.

Methods

This randomized controlled trial (RCT) was conducted on 192 children diagnosed with IDA who visited the outpatient clinic in the Pediatric Department of Menoufia University Hospitals, a tertiary care facility, from September 2022 to September 2023.

1. Ethical considerations

The study received approval from the Ethical Committee at the Faculty of Medicine, Menoufia University, with approval ID number (4/2022 PEDI 20). Written consent from parents or caregivers was obtained from each subject after explaining the study's purpose to them. The trial has been registered with the Pan African Clinical Trial Registry (pactr.samrc.ac.za) under the identifier PACTR 202408587364621.

2. Inclusion criteria

Children aged 2 to 12 years with IDA and Hb levels below 11 g/dL were eligible. The initial serum ferritin levels ranged from 7.5 to 13 ng/mL. The participating children had no history of iron supplementation or blood transfusion in the 3 months prior to the start of the study. The underlying cause of IDA was inadequate dietary iron, combined with poor eating habits that diminish iron absorption.

3. Exclusion criteria

Children with different forms of anemia, acute or sub-acute illnesses, celiac disease, and those who declined to sign the informed consent were not included.

4. Data gathering

Each patient underwent evaluation via medical history, clinical examination, and anthropometric measurements, which were plotted on Egyptian z score charts. Laboratory tests included a complete blood count (CBC), serum iron levels, serum ferritin, and transferrin saturation.

5. Randomization

The patients were divided into 2 groups; group (1) consisted of 96 pediatric patients who received oral liposomal SunActive iron (FORTIFERRUM manufactured in A.E.I. 24, Spain) at a dosage of 1.4 mg/kg/day,⁸⁾ and group (2) comprised 96 pediatric patients who were administered oral conventional iron (iron polymaltose complex) (HYDROFER-RIN produced by Borg pharmaceutical industries, Egypt) at a dose of 6 mg/kg/day. Both treatments were given once daily following meals for 1 and 6 months. All included patients completed the analysis. Good compliance was noticed with oral liposomal SunActive iron.

Assessment of adherence and adverse effects involved abdominal discomfort, dark stools, or tooth discoloration. All patients adhered to the treatment without any observed side effects after oral liposomal iron. The assessment of hematological parameters and iron profiles, as well as anthropometric measurements, took place 1 and 6 months after treatment.

6. Study outcome

The primary outcome was significant improvement in the hematological parameters and iron profile following 1 month of treatment. The secondary outcome was significant improvement in the clinical anthropometric measurements mainly z score of body weight with additional improvement in the hematological parameters and iron profile following 6 months of treatment.

7. Methodology

A total of 6 mL of venous blood was collected from each participant through a sterile puncture of the cubital vein and separated into 2 tubes. Tube 1: 4 mL of blood was drawn into plain vacutainer tubes and allowed to clot at 37°C for 30 minutes. Centrifugation separated the serum, which was used to assess the iron profile (serum iron, ferritin, total iron-binding capacity [TIBC], and transferrin saturation). Tube 2: A volume of 2 mL of blood was drawn into vacutainer tubes containing K3-EDTA, which was utilized for the CBC assay and for creating a peripheral

blood film. CBC was conducted using the Sysmex XN-1000 automated hematology analyzer (Sysmex Corp., Japan), employing fluorescent flow cytometry and hydrodynamic focusing techniques. Chemical analyses were performed using the ARCHITECT c 4000 analyzer (Abbott, USA). These assessments include serum iron, TIBC, and transferrin saturation. Serum ferritin was quantified with the ARCHITECT i1000SR analyzer (Abbott). All tests mentioned above were performed at the diagnosis of children with IDA, as well as during the first and sixth months following iron therapy, either oral conventional or oral liposomal SunActive iron.

8. Sample size calculation

According to an analysis of prior research,⁹⁾ the minimum sample size determined with the Statistics and Sample Size Pro program ver. 6 was 96 participants to achieve a study power of 80% and a confidence level of 90%.

9. Statistical analysis

Data were entered into the computer and analyzed using IBM SPSS Statistics ver. 20.0 (IBM Co., USA). Qualitative data were represented with numbers and percentages. Quantitative data were summarized by using the mean, standard deviation, and interquartile range. The Student *t* test was used to assess the relationship between 2 quantitative variables that are normally distributed. The Mann-Whitney *U* test was utilized to examine the relationship between 2 quantitative variables that are not normally distributed. A *P* value lower than 0.05 is considered statistically significant.

Results

One hundred ninety-two patients completed this 2-arm prospective RCT as detailed: 96 individuals received oral liposomal SunActive iron in group 1, while 96 patients were administered oral conventional iron (iron polymaltose complex) in group 2.

Regarding demographic characteristics of the studied groups, the mean age of group 1 was 4.67±2.62 years, and 4.82±2.98 years in group 2. There were 74 males and 22 females in group 1; while group 2 included 78 males and 18 females.

Regarding anthropometric measurements, there was no significant difference between the 2 groups concerning initial anthropometric values, as illustrated in Table 1. One month after therapy, group 1 showed a significant increase in body weight compared to group 2 (*P*=0.04). Furthermore, there was a significant increase in body mass index (BMI) in group 1 compared to group 2 (*P*=0.045), with no

Table 1. Patients' demographic characteristics and initial anthropometric measurements by study group

Variable	Group 1 (n=96)	Group 2 (n=96)	Test of significance	P value
Age (yr)			0.566 ^{a)}	0.572
Mean±SD	4.67±2.62	4.82±2.98		
Range	2–12	2.5–12		
Sex			0.505 ^{b)}	0.477
Male	74 (77.1)	78 (81.3)		
Female	22 (22.9)	18 (18.8)		
Weight (kg)			0.235 ^{a)}	0.814
Mean±SD	17.31±5.90	17.00±5.23		
Range	9–27	12–29		
Z score for weight			1.166 ^{a)}	0.243
Mean±SD	-0.73±1.27	-0.54±0.67		
Range	-2.5 – 0.7	-1.69 to 0.41		
Height (cm)			1.273 ^{c)}	0.205
Mean±SD	101.47±17.18	98.44±15.72		
Range	80–128	80–128		
Z score for height			0.339 ^{a)}	0.735
Mean±SD	-1.01±1.00	-1.00±1.00		
Range	(-2) – 1	-2.14 to 1.00		
BMI (kg/m ²)			1.093 ^{c)}	0.276
Mean±SD	17.00±1.90	16.68±1.71		
Range	14–19	14–19		
Z score for BMI			1.643 ^{a)}	0.100
Mean±SD	0.51±1.50	0.41±1.26		
Range	-2.0 to 2.5	-1.7 to 2.0		

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron; SD, standard deviation; BMI, body mass index.

^{a)}Mann-Whitney test. ^{b)}Chi-square test. ^{c)}Student *t* test.

notable variation in height between the 2 groups, as in Table 2.

Six months after therapy, group 1 exhibited a significant increase in body weight, weight z score, height, height z score, BMI, and BMI z score compared to group 2 ($P=0.045$, $P<0.001$, $P=0.043$, $P=0.042$, $P=0.014$, and $P=0.038$, respectively), as in Table 3.

Regarding laboratory results, there was no significant difference between the 2 groups in terms of initial blood picture parameters and iron profiles, as illustrated in Table 4. A month after therapy, group 1 showed a significant increase in Hb, hematocrit, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) when compared to group 2 ($P<0.001$, $P=0.015$, $P<0.001$, and $P=0.006$, respectively), whereas red blood cell distribution width (RDW) and platelet count were significantly lower in group 1 than in group 2 ($P=0.003$ and $P=0.038$, respectively). Group 1 demonstrated a significant increase in serum iron, serum ferritin, and transferrin saturation, along with a substantial decrease in TIBC when compared to group 2 ($P<0.001$), as illustrated in Table 5.

Six months after therapy, group 1 showed a significant

Table 2. One-month posttherapeutic anthropometric measurements by study group

Variable	Group 1 (n=96)	Group 2 (n=96)	Test of significance	P value
Weight (kg)			2.003 ^{b)}	0.047
Mean±SD	18.66±5.00	17.19±5.15		
Range	14–29	12–29		
Z score for weight			2.040 ^{a)}	0.04
Mean±SD	0.09±0.99	-0.18±0.68		
Range	-1.4 to 2.0	-1.4 to 8.0		
Height (cm)			1.789 ^{b)}	0.075
Mean±SD	102.70±15.56	98.29±13.50		
Range	85–130	80–128		
Z score for height			0.297 ^{a)}	0.767
Mean±SD	-0.56±1.46	-0.9±1.1		
Range	-2.26 to 2.00	-2.5 to 1.0		
BMI (kg/m ²)			2.021 ^{b)}	0.045
Mean±SD	17.83±1.70	17.35±1.53		
Range	15–20	15–19		
Z score for BMI			0.08 ^{a)}	0.936
Mean±SD	1.19±0.79	1.13±0.88		
Range	-0.23 to 2.5	-0.23 to 2.5		

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron; SD, standard deviation; BMI, body mass index.

^{a)}Mann-Whitney test. ^{b)}Student *t* test.

Boldface indicates a statistically significant difference with $P<0.05$.

Table 3. Six-month posttherapeutic anthropometric measurements by study group

Variable	Group 1 (n=96)	Group 2 (n=96)	Test of significance	P value
Weight (kg)			20.019 ^{b)}	0.045
Mean±SD	20.5±4.3	19.13±4.90		
Range	16–30	12–26		
Z score for weight			3.582 ^{a)}	<0.001
Mean±SD	0.49±1.02	0.2±0.78		
Range	-1.19 to 2.00	-1.4 to 2.00		
Height (cm)			2.040 ^{b)}	0.043
Mean±SD	105.17±15.11	101.00±13.13		
Range	86–132	80–128		
Z score for height			2.029 ^{a)}	0.042
Mean±SD	-0.21±1.41	-0.56±1.70		
Range	-1.5 to 2.5	-2.5 to 1.0		
BMI (kg/m ²)			2.475 ^{b)}	0.014
Mean±SD	18.56±1.68	17.97±1.63		
Range	15.7–21.0	15.0–19.1		
Z score for BMI			2.073 ^{a)}	0.038
Mean±SD	1.67±0.73	1.24±1.12		
Range	-1.0 to 2.4	-2.33 to 2.40		

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron; SD, standard deviation; BMI, body mass index.

^{a)}Mann-Whitney test. ^{b)}Student *t* test.

Boldface indicates a statistically significant difference with $P<0.05$.

Table 4. Initial complete blood count and iron profiles by study group

Variable	Group 1 (n=96)	Group 2 (n=96)	Test of significance	P value
Hb (gm/dL)			1.819 ^{a)}	0.071
Mean±SD	9.4±1.07	9.6±0.57		
Range	7.4–10.7	8.2–10.5		
Hematocrit (%)			0.645 ^{a)}	0.520
Mean±SD	28.68±3.57	28.41±1.85		
Range	21.7–35.4	25–31		
MCV (fL)			0.809 ^{a)}	0.420
Mean±SD	65.6±5.48	65.06±3.56		
Range	57–80	58.5–69		
MCH (pg)			1.964 ^{a)}	0.053
Mean±SD	19.99±1.92	19.52±1.41		
Range	17–25	17.3–21.5		
RDW%			1.021 ^{a)}	0.306
Mean±SD	15.16±0.73	15.25±0.59		
Range	14–16	14–16		
Platelet count (×10 ⁹ /L)			0.617 ^{a)}	0.538
Mean±SD	355.02±91.59	363.35±95.49		
Range	231–508	200–511		
TLC (× 10 ⁹ /L)			0.056 ^{a)}	0.955
Mean±SD	8.18±1.55	8.19±1.55		
Range	6–11.2	6–11		
Serum iron (µg/dL)			1.758 ^{a)}	0.08
Mean±SD	32.97±9.64	30.88±6.6		
Range	22–56.7	21–50		
Serum ferritin (ng/mL)			1.198 ^{a)}	0.232
Mean±SD	11.7±63.42	12.24±2.64		
Range	7.5–12	7.9–13		
TIBC (µg/dL)			0.39 ^{a)}	0.693
Mean±SD	425.95±37.4	424.04±29.28		
Range	372–480	391–470		
Transferrin saturation %			1.338 ^{a)}	0.183
Mean±SD	0.13±0.03	0.14±0.01		
Range	0.11–0.18	0.11–0.16		

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron; Hb, hemoglobin; SD, standard deviation; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red blood cell distribution width; TLC, total leukocyte count; TIBC, total iron-binding capacity.

^{a)}Student *t* test.

Boldface indicates a statistically significant difference with *P*<0.05.

increase in Hb, hematocrit, MCV, and MCH compared to group 2 (*P*<0.001), whereas RDW and platelet count significantly decreased in group 1 relative to group 2 (*P*<0.001 and *P*=0.015). Group 1 exhibited a notable rise in serum iron, serum ferritin, and transferrin saturation, along with a marked decrease in TIBC compared to group 2 (*P*<0.001), as illustrated in Table 6.

Regarding adverse effects of iron therapy; constipation, black stools, teeth staining and abdominal pain were more prevalent in patients in group 2 than in those in group 1 (*P*<0.001), as illustrated Table 7.

Discussion

Table 5. One-month posttherapeutic complete blood count and iron profile by study group

Variable	Group 1 (n=96)	Group 2 (n=96)	Test of significance	P value
Hb (gm/dL)			3.834 ^{a)}	<0.001
Mean±SD	12.12±0.95	11.9±0.57		
Range	10.8–14	10.2–12.9		
Hematocrit (%)			2.46 ^{a)}	0.015
Mean±SD	34.73±3.06	33.87±1.46		
Range	31–40	31–37		
MCV (fL)			7.083 ^{a)}	<0.001
Mean±SD	80.43±6.1	75.58±2.69		
Range	73–92	70.6–82		
MCH (pg)			2.766 ^{a)}	0.006
Mean±SD	27.89±2.74	26.93±2.08		
Range	23.9–43	23–31		
RDW%			2.958 ^{a)}	0.003
Mean±SD	12.57±0.86	12.88±0.51		
Range	11–14	12–14		
Platelet count (×10 ⁹ /L)			2.091 ^{a)}	0.038
Mean±SD	331.52±94.53	385±80.78		
Range	199–462	176–492		
TLC (× 10 ⁹ /L)			1.067 ^{a)}	0.287
Mean±SD	7.87±1.2	8.08±1.45		
Range	6.5–10.0	6.7–11.0		
Serum iron (µg/dL)			10.732 ^{a)}	<0.001
Mean±SD	73.4±6.56	64.32±5.07		
Range	65–83	57–73		
Serum ferritin (ng/mL)			5.314 ^{a)}	<0.001
Mean±SD	29.52±11.65	23.05±2.62		
Range	16–51	19–29		
TIBC (µg/dL)			4.444 ^{a)}	<0.001
Mean±SD	333.08±51.33	359.6±27.99		
Range	250–450	324–410		
Transferrin saturation %			5.564 ^{a)}	<0.001
Mean±SD	0.26±0.05	0.23±0.03		
Range	0.18–0.35	0.17–0.29		

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron; Hb, hemoglobin; SD, standard deviation; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red blood cell distribution width; TLC, total leukocyte count; TIBC, total iron-binding capacity.

^{a)}Student *t* test.

Boldface indicates a statistically significant difference with *P*<0.05.

Iron is a crucial heavy metal for human nutrition and serves as an essential component of human life. It plays vital roles in oxygen and electron transport, cell division, differentiation, and the control of gene expression.¹⁰⁾ IDA is a commonly encountered health issue seen in routine medical practice. Iron deficiency occurs when the body's requirement for iron cannot be fulfilled due to several physiological factors, such as blood loss and insufficient dietary intake.¹¹⁾

Over a hundred randomized studies have examined the positive impact of oral iron supplements on hematological

Table 6. Six-month complete blood counts and iron profiles by study group

Variable	Group 1 (n=96)	Group 2 (n=96)	Test of significance	P value
Hb (gm/dL)			7.258 ^{a)}	<0.001
Mean±SD	13.32±1.5	12.13±0.59		
Range	11–16	10.5 – 13.1		
Hematocrit (%)			4.490 ^{a)}	<0.001
Mean±SD	39.24±4.86	36.88±1.7		
Range	31–47	33–40		
MCV (fL)			12.511 ^{a)}	<0.001
Mean±SD	89.21±7.72	78.79±2.62		
Range	73–100	71–85		
MCH (pg)			4.863 ^{a)}	<0.001
Mean±SD	30.74±3.84	28.61±1.93		
Range	23.9–37	24–33		
RDW%			8.907 ^{a)}	<0.001
Mean±SD	11.66±0.66	12.4±0.54		
Range	11–13	11–14		
Platelet count (×10 ⁹ /L)			2.466 ^{a)}	0.015
Mean±SD	316.5±97.48	347.08±72.56		
Range	199–500	176–485		
TLC (× 10 ⁹ /L)			4.080 ^{a)}	<0.001
Mean±SD	8.52±1.70	7.64±1.23		
Range	6–11	6–11		
Serum iron (µg/dL)			10.914 ^{a)}	<0.001
Mean±SD	86.68±15.00	68.6±6.20		
Range	68–113	58–84		
Serum ferritin (ng/mL)			8.042 ^{a)}	<0.001
Mean±SD	39.62±16.55	25.86±2.62		
Range	26–65	21–31		
TIBC (µg/dL)			5.277 ^{a)}	<0.001
Mean±SD	312.85±56.16	346.60±27.79		
Range	220–413	302–400		
Transferrin saturation %			7.577 ^{a)}	<0.001
Mean±SD	0.37±0.12	0.27±0.04		
Range	0.18–0.55	0.19–0.35		

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron; Hb, hemoglobin; SD, standard deviation; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red blood cell distribution width; TLC, total leukocyte count; TIBC, total iron-binding capacity.

^{a)}Student t test.

Boldface indicates a statistically significant difference with $P<0.05$.

Table 7. Side effects of iron therapy by study group

	Group 1 (n=96)	Group 2 (n=96)	P value
Side effects of iron therapy			<0.001
No	91 (94.8)	72 (75)	
Constipation	3 (3.1)	8 (8.3)	
Black stool	2 (2.1)	6 (6.3)	
Abdominal pain	0 (0)	3 (3.1)	
Teeth staining	0 (0)	3 (3.1)	
Constipation and black stool	0 (0)	4 (4.2)	

Group 1, pediatric patients treated with oral liposomal SunActive iron; group 2, pediatric patients treated with conventional oral iron.

Boldface indicates a statistically significant difference with $P<0.05$.

factors associated with IDA.¹²⁾ There is a lack of targeted clinical trials to assess different iron formulations, dosages, and treatment durations.⁸⁾

In this RCT, the response to 2 oral iron formulations was evaluated by studying 192 patients with IDA aged 2 to 12 years. The present study revealed no significant difference between the 2 groups concerning baseline anthropometric measurements. After 6 months of therapy, group 1 showed a notable increase in weight, z scores for weight and height, BMI, and z scores for BMI when compared to group 2. Kiliç et al.¹³⁾ conducted a study with 137 children treated with the iron hydroxide-polymaltose complex and 174 children treated with liposomal ferric pyrophosphate; no significant difference was noted between the groups regarding initial anthropometric measurements.

Additionally, they indicated that the group taking liposomal iron supplements showed greater weight and length, expressed as percentiles for weight and height according to age. Tosyalı et al.¹⁴⁾ discovered that the average weight was 9.8 kg in the conventional oral iron therapy group and 9.927 kg in the liposomal iron group.

The current study revealed no notable difference between the 2 groups concerning baseline CBC parameters and iron profile. Tosyalı et al.¹⁴⁾ indicated that there was no significant difference in initial blood count parameters among the study groups. Moreover, Helal et al.¹⁵⁾ discovered no significant difference in initial CBC parameters between group I (which received ferrous bisglycinate supplementation) and group II (which underwent sucrosomial iron therapy).

In this study, 6 months after treatment, group 1 showed a notable increase in Hb, hematocrit, MCV, and MCH compared to group 2, whereas RDW and platelet count were significantly lower in group 1 relative to group 2. In group 1, there was a notable rise in serum iron, serum ferritin, and transferrin saturation, along with a considerable decline in TIBC compared to group 2. Gastrointestinal adverse effects in the form of constipation, black stools, teeth staining and abdominal pain were more prevalent in patients in group 2 than in those in group 1.

Srivastav et al.¹⁶⁾ reported a notable increase in serum iron and serum ferritin following 30 days of liposomal iron therapy. In addition, Ibrahim et al.¹⁷⁾ discovered a statistically significant increase in serum iron, serum ferritin, and serum transferrin following iron therapy for IDA using ferrous sulfate.

Cesarano et al.¹⁸⁾ discovered that oral liposomal iron raised the achievement of transferrin saturation goals from 11.8% at the start to 50.0%, along with elevated Hb levels after a 6-month period.

Helal et al.¹⁵⁾ discovered a notable rise in serum ferritin and iron, as well as a reduction in TIBC in group II, in

contrast to group I, during the evaluation period of 8 weeks. Tosyalı et al.¹⁴⁾ found that serum iron and ferritin levels were reduced in the group taking sucrosomial iron compared to those using Fe + 2 and Fe + 3 salts. An initial study suggested that individuals with IDA and inflammatory bowel disease (IBD) receiving liposomal iron experienced a greater rise in Hb levels than those taking ferrous sulfate. An elevation of Hb >2 gm/dL was more common in patients receiving liposomal iron compared to those without iron supplementation. Liposomal iron was effectively tolerated by patients with IDA and IBD.¹⁹⁾ In a comparable study, one-third of the IBD patients administered liposomal iron showed normalization within 12 weeks, with an average Hb rise from 11.1 to 11.8 gm/dL.²⁰⁾ Oral liposomal iron treatment effectively enhances mild IDA and quality of life, while also reducing fatigue in patients with inactive or mildly active IBD.²¹⁾ Oral liposomal SunActive has demonstrated superior effectiveness, with improved Hb recovery and enhanced tolerance, resulting in fewer gastrointestinal adverse effects.²²⁾ Liposomal iron offers improved gastrointestinal absorption and bioavailability compared to conventional ferrous salts. In the former case, amino acids bind to iron to create chemically inert complexes that are absorbed in an unaltered state through specialized active transporters across the mucosal membrane. This active uptake leads to increased bioavailability when contrasted with the limited passive absorption of iron salts. Liposomal iron is absorbed directly by the M cells in the small intestine and, through the lymphatic system, reaches the liver where the iron is released. The bioavailability is higher, and the free iron does not chemically interact with the gastrointestinal membrane.²³⁾ It is 4 times better absorbed compared to conventional iron. Additionally, it is stable against heat, salt, pH, and oxidation.²¹⁾

Oral liposomal iron, in contrast to intravenous iron, demonstrated a significant rise in Hb levels and transferrin saturation, normalization of serum ferritin, and a significant reduction in erythropoietin use among individuals with chronic kidney disease.^{23,24)} In young patients with advanced-stage Hodgkin lymphoma, the addition of oral liposomal iron was well tolerated and kept Hb levels elevated above those needing additional supportive care.²⁵⁾

Small sample size and the information regarding these formulations in pediatrics remains scarce.

In conclusion, iron formulations are effective in improving anthropometric measurements, complete blood picture parameters and iron profile but liposomal SunActive iron has better effects as being available in oral form, decreasing drug refusal, better compliance with effective impact on children growth.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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