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Original Research Article

COMPARISON OF FERROUS SULPHATE AND IRON POLYMALTOSE COMPLEX IN CHILDREN FOR THE TREATMENT OF IRON DEFICIENCY ANEMIA

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ABSTRACT

Background: *Iron deficiency anemia (IDA) is the most common nutritional deficiency in children worldwide. Oral iron therapy remains the cornerstone of treatment, with ferrous sulphate and iron polymaltose complex (IPC) commonly prescribed. However, their comparative efficacy remains a matter of debate.* ***Objective:*** *To compare the effectiveness of ferrous sulphate and iron polymaltose complex in children for the treatment of IDA.* ***Study Design:*** *Randomized controlled trial.* ***Setting:*** *Department of Pediatrics at Saidu Group of Teaching Hospitals, Swat, Pakistan.* ***Duration of Study:*** *21 July 2024 to 21 January 2025.* ***Methods:*** *A total of 72 children aged 2–10 years with confirmed IDA were enrolled and randomly allocated into two equal groups. Group A received oral ferrous sulphate at 6 mg/kg/day, while Group B was administered an equivalent dose of IPC. Treatment efficacy was defined as achieving a hemoglobin level of≥10.5 g/dL and a serum ferritin level of>15 ng/mL after four weeks of therapy. Data were analyzed using SPSS version 25, and the chi-square test was applied; $P < 0.05$ was considered statistically significant.* ***Results:*** *The mean age of children in Group A was 5.42 ± 2.51 years, while in Group B it was 6.47 ± 2.36 years. Treatment efficacy was achieved in 88.9% of children in the ferrous sulphate group compared to 63.9% in the IPC group ($P = 0.01$).* ***Conclusion:*** *Ferrous sulphate was significantly more effective than iron polymaltose complex in improving hematological parameters among children with IDA, supporting its role as the preferred first-line oral therapy.*

Keywords: Ferrous Sulphate, Iron Polymaltose Complex, Anemia, Serum Ferritin, Iron Deficiency Anemia

INTRODUCTION

Iron deficiency anemia (IDA) is the most prevalent hematological disorder in children, as well as the most prevalent form of anemia (1). The prevalence in developed nations is 20.1% among individuals aged 0-4 years and 5.9% among those aged 5-14 years, while prevalence rates in developing countries are considerably higher, at 48.1% (2). This condition is referred to as hypochromic microcytic anemia, characterized by hemoglobin levels that fall below the usual range for age, alongside reduced mean corpuscular volume and mean corpuscular hemoglobin. Iron is an essential mineral for the growth of the fetus as well as the child (3). The iron content of the body is dependent upon intake from food as well as absorption. The equilibrium between their uptake and release from cells determines the homeostasis of nutrients, where they are stored and recycled (4, 5).

Iron is released into circulation, delivered by plasma protein transferrin, and consumed in the duodenum by enterocytes. Additionally, it is recycled by macrophages from senescent erythrocytes and liver reserves. When iron levels in the body are insufficient, intestinal absorption increases (6). Conversely, when levels are high, iron is stored in enterocytes as ferritin and in the spleen, bone marrow, and the liver (7). Iron polymaltose complex and ferrous sulfate are often used as oral iron supplements for children with IDA. The debate concerning the evaluation of the benefits and side effects of both substances is ongoing (8, 9). Several studies indicate that there is no significant distinction in effectiveness or side effects between ferrous sulfate and iron polymaltose complex. While some research supports the beneficial effects of ferrous sulfate, others favor iron polymaltose complex. Traditionally, parenteral iron preparations have been linked with numerous adverse effects; however, contemporary formulations are typically well tolerated by patients (10, 11). A study indicated the efficacy of ferrous sulphate and iron polymaltose complex in treating IDA in children, with rates of 93.5% and 67.5%, respectively (12).

Various studies have reported variable findings regarding the efficacy of ferrous sulfate and IPC in the treatment of IDA in children. Moreover, the discrepancy also exists in the published literature, which creates a dispute over which therapy is more efficacious, as there is a paucity of literature on this topic at the local level. Therefore. The goal of this study is to compare the efficacy of ferrous sulfate and iron polymaltose complex in children for the treatment of iron deficiency anemia. The results of this study will help determine the evidence for a more beneficial and efficacious therapy. Moreover, the fast-acting nature will be fundamental in children, as they require prompt recovery from anemia to support their physical and cognitive development.

METHODOLOGY

The study was conducted as a randomized controlled trial in the Department of Pediatrics at Saidu Teaching Hospital, Swat. This research was conducted from July 21, 2024, to January 21, 2025, following ethical approval from the hospital.

The total sample consisted of 72 pediatric patients, with equal allocation into two intervention groups, each comprising 36 children. The sample size was calculated considering the anticipated efficacy of ferrous sulfate at 93.5% (12) and iron polymaltose complex at 67.5% (12), with a 95% confidence level and 80% power. The selection of participants followed a non-probability consecutive sampling technique. Eligibility criteria included children of either sex, aged 2–10 years, who were diagnosed with iron deficiency anemia, defined as hemoglobin levels below 10.5 g/dL and serum ferritin levels less than 15 ng/mL. Children with clinical evidence or documented history of malnutrition, bleeding disorders, or chronic systemic diseases such as cardiovascular, renal, or hepatic illness were omitted.

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Upon obtaining informed consent from parents or legal guardians, demographic and baseline clinical information were recorded on a standardized pro forma. Data included age, gender, maternal education, maternal occupation, socioeconomic status, and residential setting. Block randomization was then applied to allocate the participants into one of two groups.

Children assigned to Group A received oral ferrous sulfate syrup at a dosage of 6 mg/kg/day, divided into appropriate doses, and administered daily over a four-week treatment period. Group B participants were administered iron polymaltose complex syrup containing an equivalent of 6 mg/kg/day of elemental iron, also provided once daily over the same duration. Clinical response was assessed at the conclusion of the four-week treatment period. Efficacy was defined as an increase in hemoglobin to ≥10.5 g/dl and serum ferritin to >15 ng/ml.

All clinical evaluations were conducted under the supervision of a senior consultant pediatrician with a minimum of five years of post-fellowship experience. Data was recorded on a designated proforma. The recorded data were analyzed using SPSS 25. Age, body mass index (BMI), hemoglobin, and serum ferritin were calculated as mean ± standard deviation. Gender, diarrhea, maternal occupation, socioeconomic status, residence, education, and efficacy were reported as frequencies and percentages. The primary comparative analysis of treatment efficacy between the two groups was carried out using the Chi-square test. A p-value of ≤ 0.05 was considered statistically significant. Stratifications were performed for diarrhea and demographics using the Chi-Square test with a P-value notable at ≤ 0.05.

RESULTS

The mean age of the children in Group A, treated with ferrous sulphate, was 5.42 ± 2.51 years, while those in Group B, receiving iron polymaltose complex, had a mean age of 6.47 ± 2.36 years. The average Body Mass Index was comparable between the cohorts, measuring 14.71 ± 0.60 kg/m² for Group A and 14.95 ± 0.60 kg/m² for Group B. With respect to gender, males constituted 58.3% (n = 21) of Group A and 55.6% (n = 20) of Group B (Table 1).

Following a four-week treatment period, an analysis of hematological parameters demonstrated a notable difference in outcomes. The mean hemoglobin level in Group A was measured at 13.20 ± 1.98 g/dl, which was higher than the mean of 11.16 ± 2.57 g/dl observed in Group B. Similarly, serum ferritin levels were greater in the ferrous sulphate group with a mean of 18.09 ± 3.37 ng/ml compared to 16.34 ± 3.76 ng/ml in the iron polymaltose group. Diarrhea was present in 16.7% (n=6) of children in group A and 8.3% (n=3) of those in group B.

The primary efficacy endpoint, defined as the achievement of both a hemoglobin level ≥10.5 g/dl and a serum ferritin level >15 ng/ml, was met by a notably larger proportion of children in Group A. Efficacy was confirmed in 88.9% (n=32) of participants treated with ferrous sulphate. In contrast, the efficacy rate in Group B was 63.9% (n = 23), indicating a considerable difference in treatment success between the two iron preparations (P = 0.01). Table 3 presents the stratifications.

Table 1: Demographic details of patients in both groups

Demographics		Groups			
		Group A		Group B	
		n	%	n	%
Gender	Male	21	58.3%	20	55.6%
	Female	15	41.7%	16	44.4%
Maternal education	Elementary	11	30.6%	9	25.0%
	Junior high school	16	44.4%	13	36.1%
	Senior high school	6	16.7%	10	27.8%
	University	3	8.3%	4	11.1%
Place of living	Rural	17	47.2%	20	55.6%
	Urban	19	52.8%	16	44.4%
Socioeconomic status	Lower class	9	25.0%	11	30.6%
	Middle class	24	66.7%	21	58.3%
	Upper class	3	8.3%	4	11.1%
Maternal occupation	Office job	7	19.4%	3	8.3%
	Housewife	23	63.9%	28	77.8%
	Other	6	16.7%	5	13.9%

Table 2: Comparison of efficacy between the two groups

Efficacy	Groups				P value
	Group A		Group B		
	n	%	n	%	
Yes	32	88.9%	23	63.9%	0.01
No	4	11.1%	13	36.1%	

Table 3: Stratification of comparison of efficacy between both groups with demographics and diarrhea

Demographics and diarrhea		Groups				P value
		Group A		Group B		
		n	%	n	%	
Age groups (Years)	2 to 6	25	69.4%	17	47.2%	0.05
	7 to 10	11	30.6%	19	52.8%	
BMI (Kg/m2)	13 to 14.5	19	52.8%	13	36.1%	0.15
	> 14.5	17	47.2%	23	63.9%	
Gender	Male	21	58.3%	20	55.6%	0.81
	Female	15	41.7%	16	44.4%	

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Maternal education	Elementary	11	30.6%	9	25.0%	0.64
	Junior high school	16	44.4%	13	36.1%	
	Senior high school	6	16.7%	10	27.8%	
	University	3	8.3%	4	11.1%	
Place of living	Rural	17	47.2%	20	55.6%	0.47
	Urban	19	52.8%	16	44.4%	
Socioeconomic status	Lower class	9	25.0%	11	30.6%	0.76
	Middle class	24	66.7%	21	58.3%	
	Upper class	3	8.3%	4	11.1%	
Maternal occupation	Office job	7	19.4%	3	8.3%	0.33
	Housewife	23	63.9%	28	77.8%	
	Other	6	16.7%	5	13.9%	
Diarrhea	Yes	6	16.7%	3	8.3%	0.28
	No	30	83.3%	33	91.7%	

DISCUSSION

The comparative analysis of the efficacy of ferrous sulphate and iron polymaltose complex (IPC) in the management of pediatric iron deficiency anemia (IDA) presents a compelling narrative. Our investigation encompassing 72 children equally distributed into two treatment groups reveals that ferrous sulphate outperforms IPC in elevating hemoglobin and serum ferritin levels.

Our findings align closely with the randomized controlled trial conducted by Bakht et al., where a greater mean increase in hemoglobin was observed in children treated with ferrous sulfate (1.35 ± 0.80 g/dL) compared to IPC (0.90 ± 1.00 g/dL), with statistical significance ($p = 0.003$). Ferritin level improvements echoed this trend, 1.62 ± 0.63 ng/ml for ferrous sulphate versus 0.82 ± 1.06 ng/ml for IPC ($p = 0.000$) (13). This parallels our own results, where Group A achieved a mean hemoglobin level of 13.20 ± 1.98 g/dL and a ferritin level of 18.09 ± 3.37 ng/mL, compared to Group B, which had a mean hemoglobin level of 11.16 ± 2.57 g/dL and a ferritin level of 16.34 ± 3.76 ng/mL, respectively.

A larger-scale study by Siraj et al. reinforces these observations. Although their design focused solely on ferrous sulfate, they recorded a substantial mean increase in hemoglobin of 3.11 g/dL and a gain in ferritin of 5.9 ng/mL over three months, demonstrating the sustained effectiveness of this formulation in pediatric settings (14). Notably, this change aligns directionally with the gains observed in our cohort treated with ferrous sulfate over a shorter four-week interval, suggesting even greater potential with more prolonged administration.

The Indian clinical trial by Bopche et al. similarly found superior hemoglobin elevation in the ferrous sulfate group (9.44 ± 0.67 g/dL) compared to the IPC group (8.67 ± 0.73 g/dL) after one month, along with fewer residual complaints and greater overall clinical improvement. While the IPC group reported fewer gastrointestinal side effects (7.6% vs. 17.0%), it still exhibited lower efficacy, with only 71.7% of IPC-treated children showing an increase in hemoglobin compared to 98.1% in the ferrous sulfate group (15). Our study also tracked side effects such as diarrhea reported in 16.7% of ferrous sulphate users versus 8.3% in the IPC group. This aligns with the study above, where ferrous sulfate is more commonly associated with gastrointestinal upset. Yet the trade-off appears justifiable given the superior hematological response and higher rate of treatment success (88.9% efficacy in our ferrous sulphate group vs. 63.9% for IPC).

In further confirmation, Mohd Rosli et al. aggregated data from eight randomized trials and found a notable mean difference favoring ferrous sulfate in hemoglobin (MD −0.81 g/dL) and ferritin levels (MD −21.24 ng/mL). The review concluded with moderate to high-certainty evidence that ferrous sulfate is clinically more efficacious than IPC for the treatment of IDA in children. Interestingly, the analysis revealed no statistically significant difference in gastrointestinal side effects between the two groups, contradicting the assumption that IPC is more tolerable (9).

The consistency of these results across geographically and demographically diverse populations underscores a strong trend. While IPC may offer slightly improved gastrointestinal tolerability, its therapeutic efficacy remains lower than that of ferrous sulphate.

In light of the collective evidence, our study reinforces the clinical recommendation that ferrous sulfate remains the superior first-line oral iron preparation in pediatric IDA. IPC, while potentially useful for children with a history of intolerance, does not achieve comparable hematologic correction within similar time frames. The broader implication is that public health policies should prioritize ferrous sulfate in national anemia control programs, especially where a rapid response is critical. For future research, our findings provide opportunities to explore dose adjustments, optimize treatment duration, and integrate dietary interventions.

CONCLUSION

We conclude that ferrous sulfate demonstrated notably better efficacy in improving hemoglobin and serum ferritin than iron polymaltose complex in children with iron deficiency anemia.

DECLARATIONS

Data Availability Statement

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

Ethics approval and consent to participate

Approved by the department Concerned. (IRB-140-ERB/023)

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTION

MUNEEB AMJAD (Postgraduate Resident)
Conception of Study, Data Collection Manuscript drafting., Manuscript revisions, and final approval of manuscript.

IHSAN UL HAQ (Professor)
Study Design, Critical Input, Supervision, Conception of Study, and final approval of manuscript.

Data entry, data analysis, and drafting articles.
QAISAR ALI (PGR Pulmonology)
Literature search, Critical Input

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