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Parenteral versus Oral Iron Therapy in Children with Iron Deficiency Anemia and the Safety Profile of Parenteral Iron Therapy

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ABSTRACT

OBJECTIVE: To assess the differences between parenteral and oral iron supplementation therapy for children with iron-deficient anemia.

METHODOLOGY: This prospective, randomized study was conducted at the Pediatric Healthcare Centre, Karachi, from January to December 2024. Pediatric patients aged 1-15 years diagnosed with anemia were randomly assigned to two groups: group A received oral iron therapy, and group B received parenteral iron therapy during the study period. SPSS 23 was used to analyze the data. Continuous variables were assessed as means and standard deviations, while categorical variables were analyzed as frequencies and percentages.

RESULTS: Total 82 patients were included in the study, mean age was reported as 4.2±1.6 years, the gender distribution was reported as 51(62.1%) male and 31(37.8%) females, Post treatment laboratory investigations indicated retics% of 3.63±1.22, hemoglobin as 7.48±0.89, MCV as 68.9±4.8 and serum iron level as 181.5±41.6 in group A oral therapy patients, while retics % of 9.17±2.33, Hemoglobin as 9.2±1.87, MCV as 70.2±5.61 and serum iron level as 214.2±70.9 in group B Parenteral therapy group respectively.

CONCLUSION: Parenteral therapy improves iron values more quickly and significantly.

KEYWORDS: Iron deficiency anemia, Iron therapy, Parenteral, pediatric

INTRODUCTION

One of the most prevalent dietary illnesses among children is iron deficiency anemia (IDA), which is a major cause of morbidity.
Worldwide. About half of all children under the age of five in developing nations like Pakistan are impacted, primarily as a result of socioeconomic inequalities, infections, and poor nutrition[1].
The main course of action for treating childhood IDA is iron supplementation, which can be given orally or parenterally, depending on the severity, tolerance, and adherence to therapy[2].
For children with mild to severe IDA, the World Health Organization advised utilizing oral iron therapy as the first line of treatment[3]. Iron is administered as ferrous fumarate, ferrous gluconate, or ferrous sulfate in liquid or tablet form. Oral therapy is non-invasive, simple to administer, economical, and does not require medical professionals to give the dosage[4]. When using oral iron supplements, gastrointestinal problems such as diarrhea, constipation, nausea, upset stomach, and abdominal discomfort are the most often reported side effects[5]. It is well recognized that delayed release formulations are kinder to the gastrointestinal tract, which lowers the likelihood of complications.
On the other hand, giving children iron supplements directly into their bloodstream is thought to be an aggressive approach to treating severe IDA, as waiting for delayed absorption of iron by oral supplementation may lead to negative consequences and serious difficulties. By bypassing the GI tract and delivering iron straight to the bloodstream, this technique eliminates GI-related iron therapy side effects while promoting a quick and effective increase in iron levels[6]. Although they are uncommon, complications from parenteral iron therapy can range from injection site infections to severe allergic reactions (such as anaphylaxis). Other non-medical factors related to parenteral iron therapy include the high cost of treatment, the requirement for a medical professional to administer it, the need for multiple consultations, and visits to a medical facility[7].
In developing nations like Pakistan, it can be challenging to identify a manageable and appropriate route of administration while keeping in mind the patient's circumstances and socioeconomic status. To understand the pattern of health-seeking behaviors and the obstacles to obtaining treatment routes, it is important to assess parental approval, hesitancy towards invasive therapies, financial barriers, and other related factors. The purpose of this study is to give a detailed examination of the differences between parenteral and oral iron supplementation therapy for children with iron-deficient anemia.

METHODOLOGY

This is a prospective, randomized study conducted at the Pediatric Healthcare Center, Karachi, from January to December 2024. A prior approval was taken from institutional review board, (ERC approval # CBC/HC.PH-II/No.61), Sample size was calculated with the help of WHO sample size calculator, keeping total registered number of pediatric patients visited out patient's department and diagnosed with Anemia in past 6 month (n=103), confidence interval as 95% and margin of error as 5%, the estimated minimum sample size was n=82. Pediatric patients aged 1-15 years diagnosed with anemia were allotted to two groups using a computer-generated randomization sequence, with an equal allocation ratio (1:1). Group A received oral iron therapy. In contrast, Group B received parenteral therapy to treat iron deficiency anemia during the study period.

Inclusion criteria

- Children aged 1–15 years
- Diagnosed with iron deficiency anemia
- Hb below age-specific cutoff
- Parental consent obtained

Exclusion criteria

- Hemoglobinopathy
- Chronic kidney disease
- Malignancy
- Recent blood transfusion
- Current iron therapy
- Severe systemic illness

Both genders were enrolled in the study. Informed consent was obtained in a language understood by the eligible patients' parents and/or guardians. After signing the consent form, all demographic details and medical history, including previous surgeries, hospital stays, daily activities, infection rates, morbidity, and antenatal diagnosis, were documented. Laboratory investigations, including Hemoglobin, MCV, and serum iron levels, were documented. (**Table I**)

Table I: Cut-off values of blood components according to age in pediatric population.

Age	Hb g/dL	MCV fL	Serum Iron µg/dL
New born	<13.2	<100	<63
6-24 months	<11.3	<68-72	<35
2-6 years	<11.5	<75	<22
6-12 years	<12	<77	<39
12-18 years	<13 (M)	<78	
	<12 (F)		

Source: Nathan and Oski's Hematology of Infancy and Childhood, Seventh edition, Elseviers, 2009.

Group A patients were prescribed oral ferrous sulphate (dose 5mg/kg/day) for the duration of 4 weeks. Group B patients were prescribed parenteral intramuscular iron sorbitol (Dose 1.5mg/kg/day) for 4 weeks as well. After 1 week, hemoglobin values were reassessed to

document changes, while after 4 weeks serum iron levels and clinical improvements were reported.
Statistical Package for the Social Sciences (SPSS) version 23 was used to enter, sort, and analyze the data. Normality of data was assessed with the help of the Shapiro-Wilk test; continuous variables were assessed as mean and standard deviation, while categorical variables were analyzed as frequency and percentages.

RESULTS

Total 82 patients were included in the study, mean age was reported as 4.2±1.6 years, the gender distribution was reported as 51(62.1%) male and 31(37.8%) females, age was categorized as 1-3, 3.1-6, 6.1-9, 9.1-12 and 12.1 – 15 years with patients reported as 12(14.6%), 19(23.1%), 26(31.7%), 19(23.1%) and 6(7.3%) respectively. (**Table II**)

Table II: Demographic variables in study participants

Variables		n (%)
Gender	Male	51(62.1%)
	Female	31(37.8%)
Age (Years)	1 to 3	12(14.6%)
	3.1 to 6	19(23.1%)
	6.1 to 9	26(31.7%)
	9.1 to 12	19(23.1%)
	12.1 to 15	6(7.3%)

Laboratory tests were divided into oral and parenteral groups. Group A patients receiving oral medication at baseline (before therapy initiation) had a serum iron value of 39.8±1.52, a hemoglobin level of 7.24±1.02, an MCV of 56.2±6.16, and a reticulocyte percentage of 0.81±0.34. At baseline, group B patients receiving parental therapy had a reticulocyte percentage of 1.03±0.13, hemoglobin levels of 6.12±0.99, MCV of 53.2±5.11, and serum iron levels of 40.1±0.93. For retics percentage, HB, MCV, and serum iron, the corresponding p-values were 0.23, 0.89, 0.44, and 0.21.
After treatment, the results showed that group A oral therapy patients had a reticulocyte percentage of 3.63±1.22, hemoglobin levels of 7.48±0.89, MCV of 68.9±4.8, and serum iron levels of 181.5±41.6, while reticulocytes
Post-treatment hematological parameters improved in both groups; however, parenteral therapy demonstrated significantly greater increases in hemoglobin and serum iron levels compared with oral therapy (**Table III**).

Table III: Comparison of laboratory investigations between oral versus parenteral group patients at baseline and post-treatment

Variables		Group A n=41	Group B n=41	P-Value
		Ferrous sulphate	Iron Sorbitol	
Pre treatment	Retics %	0.81±0.34	1.03±0.13	0.234
	HB g/dL	7.24±1.02	6.12±0.99	0.891
	MCV	56.2±6.16	53.2±5.11	0.441
	Serum Iron ug/dL	39.8±1.52	40.1±0.93	0.214
Post treatment	Retics %	3.63±1.22	9.17±2.33	<0.001
	HB g/dL	7.48±0.89	9.2±1.87	<0.001
	MCV	68.9±4.8	70.2±5.61	0.071
	Serum Iron ug/dL	181.5±41.6	214.2±70.9	0.031

The reported complications in oral therapy group were headache 1(1.2%), abdominal pain 13(15.8%), Transient mild hypotension 7(8.5%) and Vasovagal syncope 1(1.2%) respectively, while Parenteral therapy patients reported headache 3(3.6%), abdominal pain 2(2.4%), Transient mild hypotension 9(10.9%) and Vasovagal syncope 3(3.6%) respectively. The p-values were 0.04, <0.0001, 0.02 and 0.03 respectively. (**Table IV**)

Table IV: Reported complications of study participants within groups

Variables	Group A	Group B	P-Value
	Ferrous sulphate	Iron Sorbitol	
Headache	1(1.2%)	3(3.6%)	0.04
Abdominal pain	13(15.8%)	2(2.4%)	<0.0001
Transient mild hypotension	7(8.5%)	9(10.9%)	0.02
Vasovagal syncope	1(1.2%)	3(3.6%)	0.03

DISCUSSION

Iron deficiency anemia (IDA) continues to be a major contributor to pediatric morbidity worldwide, even though it is one of the most common nutritional illnesses in children [8–10]. Iron supplements administered orally or parenterally serve as the cornerstone of therapy. The current study compared the efficacy and safety of oral and parenteral iron therapy in children with IDA. The two groups' hematological values at baseline were comparable, indicating that they had a similar level of anemia before therapy. After treatment [11-12], both therapeutic strategies led to an increase in hematologic markers like serum iron levels, reticulocyte count, and hemoglobin. In contrast, children treated with parenteral iron showed a larger and faster increase in hemoglobin and iron markers compared to those who were given oral supplements[13].

Earlier research indicates that parenteral iron therapy leads to a faster replenishment of iron stores[14] because it overcomes gastrointestinal absorption barriers and has superior bioavailability. This trend is consistent with the larger body of research on pediatric IDA. A large pediatric systematic review of 4,010 children revealed that the pooled hemoglobin increase was somewhat in favor of intravenous (IV) iron over oral iron (26.7 vs. 22.1 g/L), with a trend toward quicker correction [15]. Similarly, numerous reviews and editorials stress that intravenous iron is more effective than oral iron, especially in cases when quick remedy is required [16-17]. In pediatric IV iron groups, there is typically a 3-4 g/dL rise in Hb and noticeable changes in MCV and ferritin within a few weeks [18]. Additionally, several comparative trials and meta-analyses of adults and mixed-age IDA have revealed that IV iron therapy results in significantly greater and faster hemoglobin increases, as well as greater iron reserves, than oral iron treatment [19]. Consequently, the superior post-treatment indices seen in the parenteral group are not only plausible but also consistent with the established pattern: parenteral iron bypasses intestinal constraints and adherence concerns, resulting in rapid erythropoiesis (high reticulocytes) and higher Hb, MCV, and serum iron over the same interval as oral therapy[17].

Even though both treatments were effective, there were differences in their safety profiles. Gastrointestinal issues, particularly abdominal discomfort, a common adverse consequence of oral supplementation, were more frequently reported by patients who underwent oral iron therapy. In contrast, parenteral treatment was associated with a somewhat higher incidence of vasovagal responses and transient hypotension, probably because injectable therapy is intrusive [18-20]. With proper clinical monitoring, most adverse effects were minor and manageable, even in light of these 18 occurrences. A targeted pediatric review concludes that, for the most part, modern parenteral iron seems safe and only causes minor, treatable adverse effects. Several pediatric IV iron series (ferric carboxymaltose, iron sucrose, dextran derivatives) indicate a minimal incidence of negative events (about 2–6%), with only a few minor infusion responses and a low rate of anaphylaxis [17]. Compared to oral treatment (3.7% vs 77.9%), IV iron had significantly fewer adverse effects in a retrospective pediatric IDA cohort [21]. When comparing IV, oral, and transfusion administration, a comprehensive systematic review of pediatric IDA revealed that IV iron had comparable or even somewhat reduced pooled adverse event rates (7.3%) to oral iron (8.4%) [22]. This positive profile is reflected in meta-analyses of adults and pregnancies, which demonstrate that IV iron raises Hb levels more quickly and is associated with fewer gastrointestinal adverse effects and fewer general adverse events than oral iron. In this way, parenteral iron is well supported as both more effective and acceptably safe, particularly when oral therapy is restricted by adherence, intolerance, malabsorption, or severity.

According to the findings of this study, which corroborate existing clinical recommendations [23-24], oral iron therapy is still a recommended first-line treatment for mild to moderate pediatric IDA because of its simplicity of use, affordability, and acceptable safety profile[25]. Parenteral iron therapy may be a helpful choice when anemia must be treated right away or when oral treatment is ineffective or not well tolerated [26]. According to pediatric evaluations and guidance, IV iron is acceptable when oral treatment is ineffective, intolerable, or too slow for clinical needs. To prevent transfusion or reduce the neurocognitive hazards associated with persistent IDA, rapid replenishment of iron and Hb reserves is necessary [27]. In these cases, parenteral administration may help to restore iron reserves and hematological health more quickly [28].

This study has several limitations that must be taken into account when interpreting the results. The findings may not be widely applicable since the study was conducted at just one location with a small sample size. Additionally, it was impossible to assess the treatment's long-term results or the recurrence of anemia because the follow-up period lasted only four weeks. Future multicenter studies with larger sample sizes and longer follow-up times are recommended to evaluate better the relative efficacy and long-term safety of different iron supplementation regimens in children.

CONCLUSION

By comparing oral and parenteral iron therapy for the treatment of pediatric iron deficiency anemia (IDA), this study contributes to the growing body of knowledge. Although both methods work, parenteral iron causes iron levels to rise more quickly and noticeably. Clinicians should take into account the severity of the anemia, the patient's tolerance, and any underlying diseases that can affect iron metabolism or absorption when choosing a therapy plan. The long-term implications of each therapy, including their impact on quality of life and overall cost-effectiveness, require more investigation.

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AUTHOR CONTRIBUTION

Rehman EU: Objective, consultation, write-up
Nuzhat M: Data collection, consultation
Raza MS: Ethical consideration, data collection
Rafique M: Data entry, data interpretation, final approval
Mumtaz H: Data analysis, ethical consideration
Tariq S: Data Analysis, data entry

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