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COMPARATIVE EVALUATION OF CONTINUOUS AND INTERMITTENT IRON THERAPY IN CHILDREN AGED 6 MONTHS TO 5 YEARS WITH IRON DEFICIENCY ANEMIA.

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Abstract

Background: Iron deficiency anemia is one of the most common nutritional disorders affecting children worldwide, particularly in developing countries. Oral iron supplementation remains the cornerstone of treatment. Continuous daily iron therapy is widely practiced, whereas intermittent iron therapy has emerged as an alternative approach aimed at improving tolerability and adherence while maintaining therapeutic efficacy. ***Aims:*** To compare the efficacy, tolerability, and compliance of continuous versus intermittent oral iron therapy in children aged 6 months to 5 years diagnosed with iron deficiency anemia. ***Materials and Methods:*** This prospective comparative study was conducted over a period of 12 months in the Department of Paediatrics at Sree Mookambika Institute of Medical Sciences. A total of 54 children aged between 6 months and 5 years diagnosed with iron deficiency anemia were included in the study. Diagnosis was based on clinical features and laboratory parameters including hemoglobin concentration, peripheral smear findings, and serum ferritin levels. Children were randomly divided into two groups of 27 each. Group A received continuous daily oral iron supplementation, while Group B received intermittent iron therapy administered twice weekly. Patients were followed up periodically for assessment of hemoglobin improvement. Statistical analysis was performed using chi-square test and independent t-test, with $p < 0.05$ considered statistically significant. ***Results:*** The majority of children belonged to the age group of 1–3 years, accounting for 31 (57.4%) cases. Both groups were comparable with respect to age, gender, nutritional status, and baseline hemoglobin levels. At the end of therapy, the mean hemoglobin increase in Group A was 2.8 ± 0.7 g/dL compared to 2.4 ± 0.6 g/dL in Group B ($p = 0.04$). Improvement in serum ferritin levels was also higher in the continuous therapy group. However, gastrointestinal side effects were more common in Group A. Treatment compliance was significantly better in the intermittent therapy group, with good compliance noted in 24 (88.9%) children compared to 18 (66.7%) children receiving continuous therapy ($p = 0.04$). Weight gain and overall clinical improvement were observed in both groups. ***Conclusion:*** Continuous therapy demonstrated slightly superior hematological improvement, whereas intermittent therapy showed better compliance and fewer gastrointestinal adverse effects. Intermittent iron supplementation may therefore serve as an effective and better tolerated alternative in young children with iron deficiency anemia.

Keywords: Anemia; Childhood nutrition; Continuous therapy; Hemoglobin; Intermittent therapy; Iron deficiency anemia; Oral iron supplementation.

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INTRODUCTION

Iron deficiency anemia (IDA) is the most prevalent micronutrient deficiency disorder affecting children worldwide and remains a major public health problem, especially in developing countries.1 Young children between 6 months and 5 years are particularly vulnerable because of rapid growth, increased iron requirements, inadequate dietary intake, recurrent infections, and poor socioeconomic conditions.2 According to global health estimates, iron deficiency contributes significantly to childhood morbidity and adversely affects physical growth, cognitive development, behavior, and immune function. Early diagnosis and effective treatment are therefore essential to prevent long-term developmental consequences.3

Iron is an essential component of hemoglobin and plays a vital role in oxygen transport, cellular metabolism, enzymatic activity, and neurological development.4 During infancy and early childhood, iron requirements increase substantially due to rapid expansion of blood volume and tissue growth. Inadequate iron stores during this period can lead to impaired

psychomotor development, decreased learning capacity, reduced attention span, and increased susceptibility to infections. Persistent iron deficiency during early childhood may result in irreversible neurodevelopmental impairment even after correction of anemia.5,6

The common causes of iron deficiency anemia in children include poor dietary intake of iron-rich foods, prolonged exclusive breastfeeding without iron supplementation, early introduction of cow's milk, recurrent gastrointestinal infections, parasitic infestations, malabsorption disorders, and chronic blood loss.7 Socioeconomic deprivation, poor maternal nutrition, and lack of awareness regarding complementary feeding practices further contribute to the high prevalence of IDA in developing nations. Clinically, affected children may present with pallor, irritability, fatigue, poor appetite, delayed developmental milestones, recurrent infections, and reduced physical activity.8

Oral iron supplementation remains the standard treatment for iron deficiency anemia because of its effectiveness, affordability, and easy availability.9 Continuous daily iron therapy has traditionally been recommended for replenishment of iron stores and correction of hemoglobin levels.10 However, daily administration is frequently associated with gastrointestinal adverse effects such as nausea, abdominal discomfort, constipation, diarrhea, and vomiting. These side effects often reduce treatment adherence, especially in young children, resulting in poor therapeutic outcomes.11

To overcome these limitations, intermittent iron therapy has been proposed as an alternative strategy. Intermittent supplementation involves administering iron at spaced intervals, commonly once or twice weekly, rather than daily. This approach is based on the physiological turnover of intestinal mucosal cells and may improve iron absorption while reducing gastrointestinal intolerance.12

Several studies have evaluated intermittent iron therapy in comparison with continuous daily supplementation, with varying conclusions regarding efficacy and tolerability. While daily therapy may achieve slightly greater hematological improvement, intermittent therapy has been associated with fewer side effects and better compliance. In resource-limited settings, where adherence to prolonged therapy is often difficult, intermittent regimens may offer practical advantages.

AIMS AND OBJECTIVES

- To compare the efficacy, tolerability, and compliance of continuous versus intermittent oral iron therapy in children aged 6 months to 5 years diagnosed with iron deficiency anemia.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Paediatrics at Sree Mookambika Institute of Medical Sciences over a period of 12 months from April 2025 to March 2026. The study included 54 children aged between 6 months and 5 years who were diagnosed with iron deficiency anemia based on clinical evaluation and laboratory investigations. written informed consent was obtained from parents or guardians of all participating children.

Children aged 6 months to 5 years with hemoglobin levels below the age-appropriate reference range and laboratory findings suggestive of iron deficiency anemia, including microcytic hypochromic peripheral smear and reduced serum ferritin levels, were included in the study. Children presenting with pallor, poor appetite, fatigue, irritability, recurrent infections, delayed growth, or nutritional deficiency were clinically evaluated and screened for eligibility. Patients were randomly allocated into two equal groups comprising 27 children each. Group A received continuous daily oral iron therapy, while Group B received intermittent oral iron therapy administered twice weekly.

Children with severe anemia requiring immediate blood transfusion, hemolytic anemia, thalassemia, aplastic anemia, anemia secondary to chronic kidney disease or malignancy, congenital hematological disorders, severe acute malnutrition requiring intensive nutritional rehabilitation, malabsorption syndromes, chronic liver disease, active tuberculosis, or severe systemic illness were excluded from the study. Children who had received iron supplementation within the previous three months, those with known hypersensitivity to oral iron preparations, and children whose parents were unwilling to participate were also excluded.

Detailed demographic data including age, gender, socioeconomic status, dietary history, feeding practices, immunization status, and past medical history were recorded in a structured proforma. Thorough clinical examination including assessment of pallor, anthropometric measurements, nutritional status, developmental milestones, and systemic examination was performed in all children. Baseline laboratory investigations included complete blood count, peripheral smear examination, mean corpuscular volume, mean corpuscular hemoglobin, serum ferritin levels, and stool examination for parasitic infestation when indicated.

Children in Group A received oral elemental iron supplementation daily according to standard pediatric dosing guidelines, while children in Group B received the same calculated dose divided into intermittent administration twice weekly. Parents were counseled regarding correct administration of iron therapy, dietary modifications, iron-rich foods, and adherence to treatment. Compliance was assessed during follow-up visits by reviewing parental reports and remaining medication quantity. All children were followed up regularly at monthly intervals for clinical and laboratory assessment.

Parameters evaluated during follow-up included improvement in hemoglobin concentration, serum ferritin levels, weight gain, appetite, activity level, and resolution of clinical symptoms. Adverse effects such as nausea, vomiting, abdominal pain, constipation, diarrhea, black discoloration of stools, and refusal of medication were documented. Treatment compliance and tolerability were compared between the two groups throughout the study period.

All collected data were entered into a master chart and analyzed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Statistical analysis was performed using chi-square test and independent t-test. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 54 children aged between 6 months and 5 years diagnosed with iron deficiency anemia were included in the study. Patients were equally divided into Group A (continuous daily iron therapy) and Group B (intermittent twice-weekly iron therapy), with 27 children in each group.

Majority of children in both groups belonged to the 1–3 years age group, reflecting the higher prevalence of iron deficiency anemia during early childhood. Both groups were comparable with respect to age and gender distribution, with no statistically significant difference observed ($p > 0.05$). (Table 1)

Table 1: Age and Gender Distribution of Study Population (n = 54)

Variable	Category	Group A n (%)	Group B n (%)	p-value
Age Group	6 months–1 year	5 (18.5%)	4 (14.8%)	0.89
	1–3 years	16 (59.3%)	15 (55.6%)	
	3–5 years	6 (22.2%)	8 (29.6%)	
Gender	Male	15 (55.6%)	14 (51.9%)	0.79
	Female	12 (44.4%)	13 (48.1%)	

Baseline hematological and anthropometric parameters were comparable between the two study groups. Both groups demonstrated moderate iron deficiency anemia with reduced hemoglobin and serum ferritin levels at the time of enrollment. (Table 2)

Table 2: Baseline Clinical and Hematological Parameters.

Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Hemoglobin (g/dL)	8.1 ± 0.9	8.3 ± 1.0	0.47
Serum ferritin (ng/mL)	10.8 ± 2.6	11.1 ± 2.4	0.65
Weight (kg)	10.9 ± 2.1	11.2 ± 2.4	0.61
Mean corpuscular volume (fL)	68.4 ± 4.8	69.1 ± 5.2	0.58

Children receiving continuous daily iron therapy demonstrated significantly greater improvement in hemoglobin concentration and serum ferritin levels compared to the intermittent therapy group. However, weight gain was observed in both groups without statistically significant difference. (Table 3)

Table 3: Hematological Improvement After Therapy (n = 54)

Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Hemoglobin increase (g/dL)	2.8 ± 0.7	2.4 ± 0.6	0.04*
Serum ferritin improvement (ng/mL)	8.6 ± 2.1	6.9 ± 1.8	0.01*
Weight gain (kg)	1.3 ± 0.5	1.1 ± 0.4	0.12

Intermittent iron therapy was associated with significantly better treatment compliance and fewer gastrointestinal adverse effects compared to continuous therapy. Medication refusal was also less frequent in the intermittent therapy group. (Table 4)

Table 4: Treatment Compliance and Adverse Effects (n = 54)

Variable	Category	Group A n (%)	Group B n (%)	p-value
Good compliance	Present	18 (66.7%)	24 (88.9%)	0.04*
	Absent	9 (33.3%)	3 (11.1%)	
Gastrointestinal side effects	Present	10 (37.0%)	4 (14.8%)	0.03*
	Absent	17 (63.0%)	23 (85.2%)	
Medication refusal	Present	6 (22.2%)	2 (7.4%)	0.12
	Absent	21 (77.8%)	25 (92.6%)	

Both treatment regimens resulted in considerable clinical improvement in pallor, appetite, and activity levels. The overall symptomatic improvement was comparable between the two groups, indicating clinical effectiveness of both continuous and intermittent iron supplementation. (Table 5)

Table 5: Clinical Improvement Following Therapy (n = 54)

Clinical Parameter	Improved n (%) Group A	Improved n (%) Group B	p-value
Pallor	24 (88.9%)	22 (81.5%)	0.44
Appetite	21 (77.8%)	20 (74.1%)	0.75
Activity level	23 (85.2%)	21 (77.8%)	0.48
Recurrent infections	6 (22.2%)	8 (29.6%)	0.53

Poor treatment compliance showed significant association with gastrointestinal adverse effects and continuous daily iron therapy ($p < 0.05$). Children receiving intermittent therapy demonstrated better tolerability and adherence to treatment. (Table 6)

Table 6: Correlation of Clinical Variables with Poor Treatment Compliance (n = 54)

Variable	Category	Poor Compliance n (%)	Good Compliance n (%)	p-value
Age Group	≤3 years	7 (20.6%)	27 (79.4%)	0.21
	>3 years	5 (25.0%)	15 (75.0%)	
Gastrointestinal side effects	Present	9 (64.3%)	5 (35.7%)	<0.01*
	Absent	3 (7.5%)	37 (92.5%)	
Type of therapy	Continuous	9 (33.3%)	18 (66.7%)	0.04*
	Intermittent	3 (11.1%)	24 (88.9%)	

DISCUSSION

A total of 54 children aged between 6 months and 5 years with iron deficiency anemia were included in the present study. Patients were equally divided into Group A receiving continuous daily iron therapy and Group B receiving intermittent twice-weekly iron therapy, with 27 (50.0%) children in each group. Majority of children belonged to the age group of 1–3 years, accounting for 31 (57.4%) cases, reflecting the increased vulnerability to iron deficiency during early childhood because of rapid growth and increased nutritional requirements. Male children constituted 29 (53.7%) of the study population. Similar male predominance and nutritional association were reported by Ravi Kanth K et al.13 who observed that nutritional deficiency was the most common cause of anemia among children and that iron deficiency anemia accounted for majority of cases.

At enrollment, both groups demonstrated moderate iron deficiency anemia with reduced hemoglobin levels, low serum ferritin, and microcytic hypochromic peripheral smear findings. The mean baseline hemoglobin was 8.1 ± 0.9 g/dL in the continuous therapy group and 8.3 ± 1.0 g/dL in the intermittent therapy group, indicating similar disease severity at the beginning of treatment. Nutritional deficiency and inadequate dietary iron intake were common associated factors observed among the study population. Algül M et al.14 also demonstrated comparable baseline characteristics among children receiving different iron regimens and reported low baseline hemoglobin and ferritin levels in all treatment groups.

Following treatment, both regimens resulted in significant hematological and clinical improvement. However, children receiving continuous daily iron therapy showed comparatively greater improvement in hemoglobin concentration and serum ferritin levels. The mean hemoglobin increase in Group A was 2.8 ± 0.7 g/dL compared to 2.4 ± 0.6 g/dL in Group B. Similarly, serum ferritin improvement was higher among children receiving continuous therapy, suggesting better replenishment of body iron stores. Comparable findings were reported by Alblewi SM et al.15 who concluded that daily iron supplementation produced greater improvement in hemoglobin compared to intermittent regimens among children

with iron deficiency anemia. Likewise, Algül M et al.14 observed that anemia resolution and ferritin improvement were highest among children receiving daily iron therapy.
Despite slightly superior hematological response with continuous therapy, both groups demonstrated satisfactory clinical recovery with improvement in pallor, appetite, weight gain, and activity levels. Similar observations were made by Pasupathy E et al.16 who found significant hematological improvement in both alternate-day and daily therapy groups without major difference in secondary clinical outcomes. Saylık S et al.17 also reported that although daily therapy produced faster initial hemoglobin improvement, long-term hematological outcomes became comparable between the groups.

Treatment compliance differed significantly between the two groups. Good compliance was observed in 24 (88.9%) children receiving intermittent therapy compared to 18 (66.7%) children receiving continuous therapy. Gastrointestinal adverse effects were more common in the continuous therapy group, affecting 10 (37.0%) children, whereas only 4 (14.8%) children in the intermittent group developed similar side effects. Common adverse effects included nausea, abdominal discomfort, constipation, and diarrhoea, which contributed to poor acceptance of therapy and medication refusal among some children. Similar findings were reported by Gautam M et al.18 who observed significantly higher gastrointestinal side effects with continuous iron therapy compared to intermittent therapy. Grover P et al.19 also demonstrated fewer gastrointestinal adverse effects and better compliance with alternate-day oral iron therapy.

The present study additionally demonstrated that intermittent therapy was better tolerated and associated with improved adherence among young children. Thirathanaboon P et al.20 similarly suggested that intermittent or alternate-day iron administration may be considered in patients experiencing significant adverse effects with daily therapy. Aly SM et al.21 also reported effective anemia resolution with lower-dose iron regimens and highlighted the importance of balancing efficacy with tolerability.

CONCLUSION

Both continuous and intermittent oral iron therapy were effective in improving hematological parameters and clinical symptoms in children aged 6 months to 5 years with iron deficiency anemia. Continuous daily therapy produced slightly greater improvement in hemoglobin concentration and serum ferritin levels, whereas intermittent therapy demonstrated better compliance and fewer gastrointestinal adverse effects. Improved tolerability associated with intermittent supplementation contributed to better adherence among young children. Intermittent iron therapy may therefore be considered a safe, practical, and effective alternative to continuous daily therapy, particularly in children with poor tolerance or compliance to prolonged oral iron supplementation.

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CONFLICTS OF INTEREST
There are no conflicts of interest.

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