



## EFFICACY AND SAFETY OF IV IRON SUCROSE IN CHILDREN TREATED FOR IRON DEFICIENCY ANEMIA

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### ABSTRACT

**Background and Aim:** Mostly cases of iron deficiency anemia caused by childhood malnutrition managed with oral iron supplements. However, intravenous (IV) iron is an option for those with severe Iron deficiency anemia who struggle with oral absorption of iron supplementation. Therefore, the present study aimed to investigate the efficacy and safety of intravenous (IV) iron sucrose in children treated for iron deficiency anemia.

**Patients and Methods:** Experimental research was conducted by giving intravenous iron sucrose to the patients between age of 3 months to 12 years, presented with iron deficiency anemia, within a control setting of Paediatrics intensive care unit CMH Peshawar. Routine blood screening including Hb, serum ferritin, MCV, MCHC, HCT, etc count and RBC count were done and results were recorded prior to IV iron therapy. IV iron sucrose was given with maximum dose of 7mg/kg every 3 to 7 days (not exceeding than 300mg/dose) until total dose is given. The patients were followed and relevant laboratory tests were repeated after one month of last dose of IV iron therapy. Demographics, baseline characteristics, and laboratory parameters such as hemoglobin levels, ferritin levels, and other associated variables were recorded for each patient. SPSS version 26 was used for descriptive statistics.

**Results:** The overall mean age was  $5.36 \pm 4.56$  years (age range 0-15 years). The Nutritional iron deprivation was the most prevalent cause of iron deficiency anemia. The mean value of hemoglobin (g/dL) at baseline and after 30 days was  $7.21 \pm 0.74$  and  $11.86 \pm 0.76$ , respectively. There were 41 (53.9%) male and 35 (45.1%) female. Prior to IV treatment, the mean corpuscular volume (MCV) was  $64.83 \pm 4.49$  fL, which increased to  $89.16 \pm 7.69$  fL after 30 days treatment. Similarly, there was significant difference observed in ferritin levels before ( $6.89 \pm 4.45$   $\mu$ g/L) and after ( $48.59 \pm 4.79$   $\mu$ g/L) the treatment.

**Conclusion:** Administration of IV sucrose for the treatment of iron deficiency anemia is effective, safe, and can significantly improve iron and hemoglobin levels.

**Keywords:** Iron deficiency anemia, Intravenous sucrose, Children, Efficacy

### INTRODUCTION

Iron deficiency anemia (IDA) is the most prevalent deficiency of nutrition in Pediatrics age group. Gastrointestinal bleeding, injury, low birth weight, rapid growth with insufficient intake, and

exclusive intake of cow's milk (Cow's milk is low in iron, and its iron is poorly absorbed are the most common contributing factors for iron deficiency anemia. Additionally, it decreases the absorption of iron from other dietary sources). To treat iron deficiency anemia, iron supplementation can be given both enterally and parenterally but majority cases of IDA administrated with oral iron preparations. Yet, severe IDA cases among children treated with intravenous (IV) iron. Low molecular weight (LMW) iron dextran (INFeD®, Watson g, Inc), the newest formulaton, ferumoxytol (Feraheme®, AMAG Pharmaceuticals), ferric gluconate (Ferrlecit®, Sanof-Avents), and iron sucrose (Venofer®, American Regent, Inc.) are various types of IV iron preparations available.

Iron deficiency due to nutrient deficiencies is the prevalent cause contributing to the 17% children (<5 years) suffering from IDA in developed countries [1, 2]. Blood loss, nutritional deficiencies, drugs consumption, and intestinal dysfunction are other predisposing factors for iron deficiency anemia in children. The incidence of IDA among Pakistani children aged  $\leq 5$  years varies from 40% to 70% [3, 4]. IDA has been shown to contribute to stunted growth, mental retardation, decreased interest in daily activities, and infant mortality. Oral iron therapy is not beneficial for these patients. In addition, young children are less likely to adhere to oral iron supplementation, thus necessitating alternative methods such as parenteral iron supplementation [5]. An earlier investigation suggested that intravenous iron is an alternative and effective treatment for renal failure children and those who are refractory to oral iron therapy. Iron dextran is another treatment option for children, which limit the use of iron supplement in pediatric age population [6].

Intravenous iron and oral supplement are the main factors for improving the nutritional status in treating iron deficiency anemia. Iron sucrose, iron dextran, and gluconate are the other available alternatives for treating IDA. The adoption of intravenous sucrose improve the iron restoration and elevate hemoglobin levels [7]. The iron dextran uses are adversely affecting the children in terms of anaphylactic reactions among treated patients. Additionally, ferritin levels and serum iron increased significantly after the administration of iron dextran [8, 9]. Iron gluconate and iron sucrose have comparatively few side effects. Indeed, iron gluconate has been successfully administered to patients with previous severe reactions, including anaphylaxis, to iron dextran [10].

A community-based study found that intravenous iron sucrose was safe and effective in the treatment of iron deficiency anemia. The study found that the hemoglobin level before intravenous iron sucrose was  $7.85 \pm 0.78$  g/dL, which increased to  $10.29 \pm 0.89$  g/dL ( $p < 0.001$ ) after three months of treatment [11]. Although, intravenous (IV) iron sucrose was approved in 2000 by FDA and had shown effective results in treating iron deficiency anemia among adults but knowledge about use of IV iron, its efficacy and safety in Pedriatces patient is extremely limited we attempt to determine the efficacy and safety of IV iron sucrose in treating iron deficiency anemia among children at CMH Peshawar.

## METHODOLOGY

Experimental research was conducted by giving intravenous iron sucrose to the patents between age of 3 months to 12 years, presented with iron deficiency anemia, within a control setting of Paediatrics intensive care unit CMH Peshawar. Routine blood screening including Hb, serum ferritin, MCV, MCHC, HCT, etc count and RBC count were done and results were recorded prior to IV iron therapy. IV iron sucrose was given with maximum dose of 7mg/kg every 3 to 7 days (not exceeding than 300mg/dose) until total dose is given. The patients were followed and relevant laboratory tests were repeated after one month of last dose of IV iron therapy. Mean Change in Hb, serum ferritn, MCV, MCHC, HCT, etc. and RBC count were compared with Pre Iv records. Doses of IV iron sucrose was calculated based on the Iron-deficit equation:

**Total cumulatve dose (mg) = [Target Hb – Actual6 Hb] × weight (kg) × 0.24 + [15 × weight (kg)]**

The product named venofer was used, diluted in normal saline to 1mg/mL concentraton administered over 2 hours. Strict monitoring of vitals (BP, oxygen saturaton, pulse, temperature) was done every 30 minutes. Patients were also observed for possible side effects during or immediately after the therapy. Different laboratory parameters were measured at day 1 and after 30<sup>th</sup> days.

SPSS version 26 was used for descriptive statistics. Qualitative variables such as gender cause of anemia, and age groups were expressed as numbers and percentages whereas quantitative variables such as age, hemoglobin, ferritin level, and red blood count were expressed as mean and standard deviation. Variations in iron levels and red blood cell indices before and after the IV sucrose treatment were compared using Paired t-test by taking 5% level of significance and 95% confidence interval.

## RESULTS

The overall mean age was  $5.36 \pm 4.56$  years (age range 0-15 years). The mean value of hemoglobin (g/dL) at baseline and after 30 days was  $7.21 \pm 0.74$  and  $11.86 \pm 0.76$ , respectively. There were 41 (53.9%) male and 35 (45.1%) female. Prior to IV treatment, the mean corpuscular volume (MCV) was  $64.83 \pm 4.49$  fL, which increased to  $89.16 \pm 7.69$  fL after 30 days treatment. Similarly, there was significant difference observed in ferritin levels before ( $6.89 \pm 4.45$   $\mu\text{g/L}$ ) and after ( $48.59 \pm 4.79$   $\mu\text{g/L}$ ) the treatment. One patient experienced a severe side effect, exhibiting cough and wheezing during the infusion. Distribution of patients based on their age groups are illustrated in Figure-1. Table-I represents the baseline details of patients. Table-II compares the different laboratory parameters associated with iron indices measured at baseline and 30<sup>th</sup> days. The Nutritional iron deprivation was the most prevalent cause of iron deficiency anemia followed by Gastritis due to *Helicobacter pylori*, Celiac disease, and Stool parasites (recurrent giardia lamblia) as depicted in Figure-2.

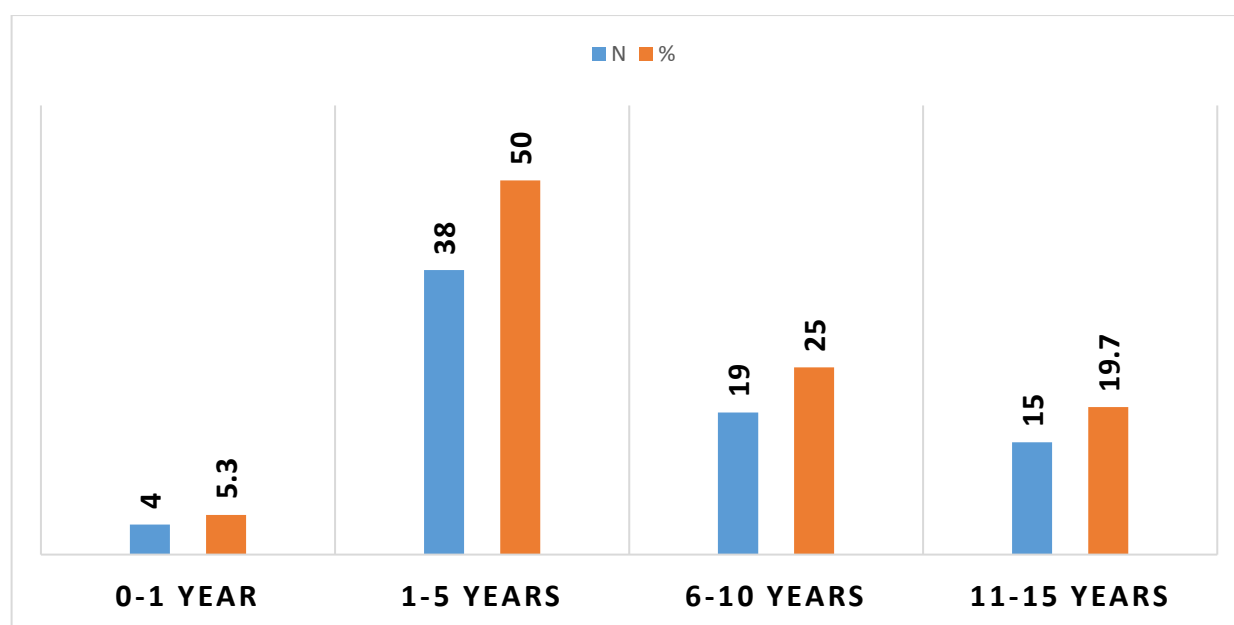


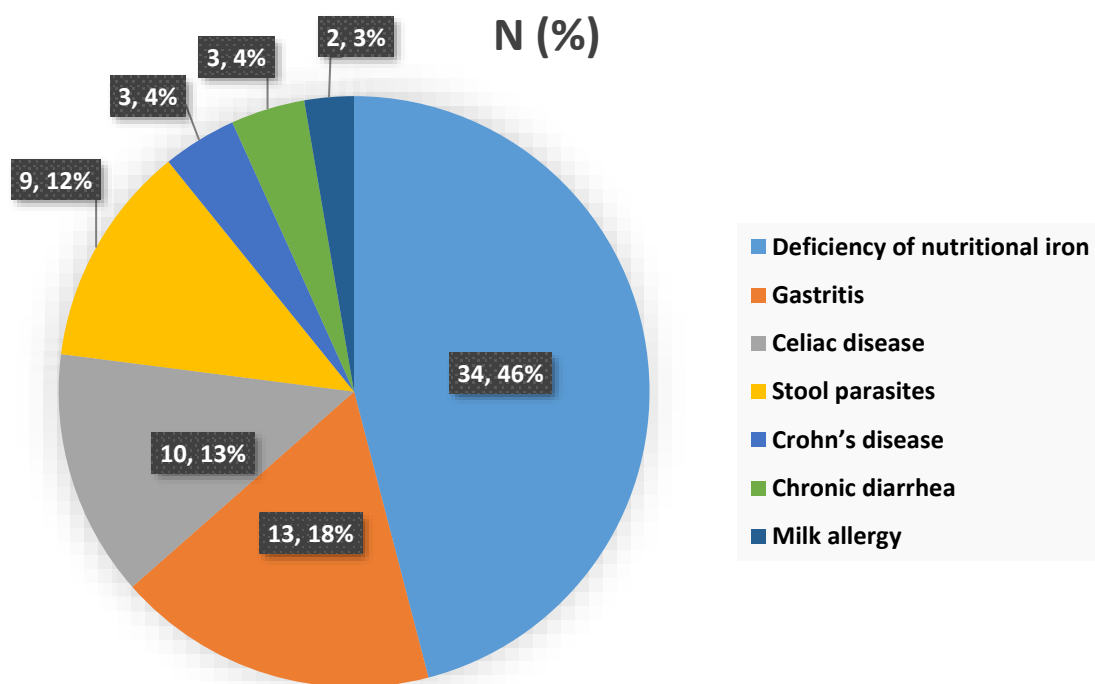
Figure-1 Distribution of patients based on their age groups (N=76)

Table-I Baseline details of patients

Parameters	Value
Age (years)	$5.36 \pm 4.56$ years
<b>Gender N (%)</b>	
Male	41 (53.9%)
Female	35 (45.1%)
<b>Maternal education N (%)</b>	
Illiterate	21 (27.6%)
Primary	35 (46.1%)
Secondary	9 (11.8%)
Graduate and above	11 (14.5%)
<b>Father's occupation N (%)</b>	
Employed	58 (76.3%)
Unemployed	18 (23.7%)

**Table-II Comparison of the different laboratory parameters associated with iron indices measured at baseline and 30<sup>th</sup> days (N=76)**

Lab. Parameters	Baseline	30 <sup>th</sup> Day	P-value
Hemoglobin (g/dL)	7.21 ± 0.74	11.86 ± 0.76	<0.001
MCV (fL)	64.83 ± 4.49	89.16 ± 7.69	<0.001
MCH (pg)	22.87 ± 2.9	35.64 ± 7.75	<0.001
Ferritin (µg/L)	6.89 ± 4.45	48.59 ± 4.79	<0.001
RBC (x106 cells.mm3)	3.49 ± 0.39	5.58 ± 0.41	<0.001

**Figure-2 Causes of iron deficiency anemia (N=76)**

## DISCUSSION

The present study mainly investigated the effectiveness of intravenous sucrose in treating iron deficiency anemia children and reported that use of intravenous iron sucrose is safe, resulting in a significant improvement in iron and hemoglobin levels. Iron deficiency generally affects physical and neurological function, and early recognition and management in early childhood is essential [12]. Oral iron therapies have been developed and shown strong safety with few adverse effects [13].

The present study found that intravenous iron sucrose significantly increased the levels of hemoglobin, MCV, MCH, and RBC. These data are consistent with an earlier study in which hemoglobin levels increased from 7.39 g/dL at baseline to 9.30 g/dL to 11.94 g/dL after 14<sup>th</sup> day and six months though that initial hemoglobin level was elevated in their examination (7.39 g/dL). dL) was slightly increased than in our study (7.21 ± 0.74 g/dL), however, the correlation between treatment and increased hemoglobin was evident. Increased hemoglobin levels after treatment indicate successful erythropoietic capacity by intravenous iron sucrose [14].

Serum ferritin levels were a reliable marker of iron Storage, increases rapidly initially after treatment and decreased after few months [15]. Ferritin levels has no association with hemoglobin levels, which explain the effect. Erythropoietic recovery on one side, followed by reactive. The response in mRNA levels leads to a decrease in ferritin [16, 17].

In the current investigation, the efficacy of IV sucrose was evident as the iron supplement from day 1 significantly increased to day 30 after treatment. Earlier investigations reported that treating IDA children might reduce the symptoms. Similar findings were reported by an earlier studies, which

concluded that IV iron sucrose was safe for iron-deficient children and increased hemoglobin levels and improved iron metabolism [18, 19].

Gómez et al. found that nausea and vomiting after implantation were common side effects of treatment [20]. Another study demonstrated intravenous iron as an effective alternative to sorbitol administration in pediatric patients [21]. Intravenous iron sucrose has been previously shown to be very beneficial in replenishing iron supplement in children suffering from IDA [22]. The current investigation observed that IDA children treated with IV iron significantly improve the symptoms and flow of RBC. Iron sucrose supplementation has been found to be a safe treatment with few adverse effects, short duration, and modifiable, even in young children.

## CONCLUSION

Administration of IV sucrose for the treatment of iron deficiency anemia is effective, safe, and can significantly improve iron and hemoglobin levels. No side effects were observed in IDA children treated with IV iron sucrose.

## REFERENCES

1. Orhan MF, Büyükavci M. Intravenous iron therapy for children with iron deficiency anemia. *Journal of Pediatric Hematology/Oncology*. 2023 Jan 1;45(1):e56-9.
2. Butragueño-Laiseca L, de la Mata Navazo S, Sánchez Galindo AC, Santiago Lozano MJ. Intravenous iron for critically ill children. Comparison of three dose regimens. *Pediatric blood & cancer*. 2024 Jan;71(1):e30734.
3. Malik NA, Shah SA, Mashhadi SF. Evaluation of injectable iron sucrose therapy in children with iron deficiency anemia. *Pak Armed Forces Med J* 2016; 66(5): 680-83.
4. Khan MS, Khan A, Hussain U, Khan A, Tahir M, Afnan B, Abbas K. Effectiveness and Safety of Intravenous Iron Sucrose Therapy in Children with Iron Deficiency Anemia. *Education*. 2022;21:13-8.
5. Korczowski B, Farrell C, Falone M, Blackman N, Rodgers T. Safety, pharmacokinetics, and pharmacodynamics of intravenous ferric carboxymaltose in children with iron deficiency anemia. *Pediatric Research*. 2023 Oct;94(4):1547-54.
6. Lepus CA, Samela K, Mokha JS. Efficacy and safety of intravenous iron sucrose in children younger than 2 years with intestinal failure. *Nutrition in Clinical Practice*. 2023 Aug;38(4):899-903.
7. Namjoshi SS, Muradian S, Bechtold H, et al. Nutrition deficiencies in children with intestinal failure receiving chronic parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2018; 42(2): 427-435.
8. Stein RE, Plantz K, Maxwell EC, Mamula P, Baldassano RN. Intravenous iron sucrose for treatment of iron deficiency anemia in pediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2018; 66(2): e51-e55.
9. Kaneva K, Chow E, Rosenfield CG, Kelly MJ. Intravenous iron sucrose for children with iron deficiency anemia. *J Pediatr Hematol Oncol*. 2017; 39(5): e259-e262.
10. Nawaz A, Aslam A, Ain Q. Oral versus parenteral iron supplements: which is better in postpartum iron deficiency anemia? *Asian J Res Med Pharm Sci* 2018; 3(2): 1-6.
11. Zaman S, Shah SA, Jehanzeb K, Sabir S, Rashid HU, Haq ZU. Effect of intravenous iron therapy on serum ferritin and haemoglobin levels in children reporting with iron deficiency anaemia. *Pak Armed Forces Med J* 2020; 70(5): 1344-48.
12. Sillis R. Iron-Deficiency Anemia. In: Kliegman R, Stanton B, St Geme J, Schor N, Eds. *Nelson Textbook of Pediatrics*, 20th ed. Canada: Elsevier 2016: 2323-6.
13. Kazancı EG, Korkmaz MF, Orhaner B. Efficacy and safety of intravenous iron sucrose treatment in children with iron deficiency anemia. *Med Sci Discov* 2019; 6(10): 278-83.
14. Nazir F, Khurshid A, Talib MA. Intravenous iron sucrose in malnourished children with iron deficiency anemia. *Prof Med J* 2020; 27(09): 1867-71.

15. Mantadakis E, Tsouvala E, Xanthopoulou V, Chatzimichael A. Intravenous iron sucrose for children with iron deficiency anemia: a single institution study. *World J Pediatr* 2016; 12(1): 109-13.
16. Papadopoulos M, Patel D, Korologou-Linden R, Goto E, Soondrum K, Fell JM, et al. Safety and efficacy of parenteral iron in children with inflammatory bowel disease. *Br J Clin Pharmacol* 2018; 84(4): 694-9.
17. Hussain S, Ahmad TM, Sabir MU, Tarar SH. Comparison of efficacy of oral and intramuscular iron supplementation for treatment of iron deficiency anemia in children. *Pak Armed Forces Med J* 2015; 65(1): 153-9.
18. Crary SE, Hall K, Buchanan GR. Intravenous iron sucrose for children with iron deficiency failing to respond to oral iron therapy. *Pediatr Blood Cancer* 2011; 56(4): 615-9.
19. Karadaş N, Töret E, Karadaş U. Is intravenous iron treatment in pediatric patients safe and effective enough?. *GUNCEL PEDIATRI*. 2022;20(2).
20. 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 Jun 6;16(6):847.
21. Auerbach M, Gafter-Gvili A, Macdougall IC. Intravenous iron: a framework for changing the management of iron deficiency. *The Lancet Haematology*. 2020 Apr 1;7(4):e342-50.
22. Kondrakunta DR. Study of efficacy and compliance of iron sucrose in iron deficiency anaemia in pregnancy. *Int J Clin Obstet Gynaecol*. 2021;5(5):170-4.