

Comparison of Ferrous Sulphate Versus Iron Polymaltose Complex in the Treatment of Iron Deficiency Anemia in Children

SAEED ZAMAN¹, MASUD MURAD KHAN², SAMINA TABUSSAM³, SADAF NAWAZ⁴, AMMARA AYUB⁵, SAJID ALI SHAH⁶

¹Associate Professor, Department of Paediatrics, Army Medical College, Rawalpindi.

²Senior Registrar, Department of Pediatrics, Combined Military Hospital (CMH), Kharian Medical College, Kharian.

³Assistant Professor, Combined Military Hospital (CMH) Institute of Medical Sciences, Bahawalpur.

⁴Consultant Child Specialist, Department of Pediatrics, Combined Military Hospital (CMH), Gilgit.

⁵Assistant Professor, Department of Paediatrics, Islamic International Medical College Trust, Rawalpindi.

⁶Consultant Child Specialist, Department of Pediatrics, Combined Military Hospital (CMH), Mardan.

Correspondence to: Saeed Zaman, Email: saeedzamankhattak@gmail.com

ABSTRACT

Objective: To compare the efficacy of ferrous sulphate versus iron Polymaltose complex (IPC) in the treatment of iron deficiency anemia (IDA) in children.

Study Design: Randomized controlled trial.

Place and Duration: Department of Pediatrics, Combined Military Hospital, Kharian Pakistan from Jan 2019 to Mar 2020.

Methodology: A total of 150 children with IDA were included. At baseline, blood sample was obtained for assessment of hemoglobin level. Then children were randomly divided in two groups. In Group-A (n=75), patients were given ferrous sulphate while in In Group-B (n=75), IPC was given. After 12-weeks of treatment, hemoglobin level was assessed. Efficacy was labeled as "yes" if there was 2 g/dl hemoglobin improvement.

Results: In a total of 150 children, the mean age in Group-A was 6.56±2.33 years and 6.05±2.78 years in Group-B. In group A, there were 37 (49.3%) males and 38 (50.7%) females while in Group-B there were 35 (46.7%) males and 40 (53.3%) females. At baseline in group A, the mean hemoglobin level was 6.07±1.12 g/dl while in group B, it was 6.16±1.14 g/dl. After 12-weeks, in Group-A the mean hemoglobin level was 9.44±1.61 g/dl whereas in Group-B, it was 8.83±2.01 g/dl (p=0.0420). There was insignificant difference observed for efficacy in both groups (p-value = 0.051).

Practical Implications: Both IPC and ferrous sulphate resulted in significant rise in hemoglobin levels but ferrous sulphate showed better results in comparison to IPC.

Conclusion: Although in comparison to IPC, ferrous sulphate resulted in significantly better rise in hemoglobin levels among children with IDA, but overall efficacy between the two studied drugs was relatively similar.

Keywords: Ferrous sulphate, iron Polymaltose complex, iron deficiency anemia.

INTRODUCTION

Globally, it has been considered that iron deficiency anemia (IDA) is the commonest nutritional anemia. The IDA affects developing countries more when compared to developed ones.¹ Most significantly, iron deficiency is exhibited through anemia, therefore, the terminologies "iron deficiency" and "iron deficiency anemia" are synonymously applied most of the time. However, if anemia is not present, iron deficiency might still develop.² Being a potential risk factor for the general health of the population, over one billion individuals of various age groups are affected by anemia worldwide.³ Every year, underdeveloped countries lose a lot of money treating IDA and its complications that further affects development programs in those programs.⁴ The "World Health Organization (WHO)" presented a statistical data collected from all over the world, according to which, the prevalence of IDA among pregnant women was around 40% and 43% among children.⁵ The prevalence of IDA in Pakistan is estimated to be around 29% among children.⁶ In Pakistan, females of child bearing age and children < 5 years of age are known to be most commonly affected groups by IDA.

The recommended route for iron therapy is oral but the bioavailability of oral preparation is not predictable. The absorption of iron depends on multiple factors. Also, it is not the recommended route where urgent iron replenishment is required. Both intramuscular (IM) and intravenous (IV) formulations are available to treat IDA.⁷ Historically, parenteral iron preparations were prone to induce variety of adverse events, however, new preparations are well tolerated.⁸

Literature has reported variable findings regarding the efficacy of iron Polymaltose complex (IPC) and ferrous sulphate for the treatment of IDA in children. Moreover, the discrepancy exists in local literature as well which creates a dispute that which therapy is more efficacious. So, we wanted to conduct this study to get the evidence about the more beneficial and efficacious therapy. Objective of this study was to compare the efficacy of ferrous sulphate versus IPC in the treatment of IDA in children.

METHODOLOGY

This randomized controlled trial was carried out in The Outpatient Department of Pediatrics, Combined Military Hospital, Kharian, Pakistan from January 2019 to March 2020. Sample size of 150 children, 75 in each group was calculated with 80% power of study, 5% level of significance and taking expected percentage of efficacy i.e. 87.1% with ferrous sulphate and 70.6% with IPC for treatment of IDA.⁹ Sampling technique used was non-probability consecutive sampling. Approval from "Institutional Ethical Committee" was taken. Informed as well as written consents were sought from parents/caregivers.

Inclusion criteria were children of both genders aged between 2-10 years and presenting with IDA. Patients with liver disorders (ALT or AST>40IU, bilirubin >5mIU), renal diseases (creatinine>1.2mg/dl) and cardiac disease (on medical record), or those who already received iron therapy before inclusion (on medical record) were excluded. Children having megaloblastic anemia or severe anemia (requiring emergency blood transfusion), malnutrition (-2 Standard Deviation as per WHO definition) were also not included.

At the time of enrollment, demographic details were noted. At baseline, blood sample was obtained in a 3cc disposable syringe. All samples were stored and sent to the institutional laboratory of the hospital for assessment hemoglobin level. Adopting lottery method, children were randomly divided in 2 groups. In Group-A (n=75), ferrous sulphate in a dose of 6mg/kg/day of elemental iron once daily for 12 weeks orally in syrup form was advised. In Group-B, IPC in a dose of 6mg/kg/day of elemental iron once daily orally for 12 weeks was given. After 12-weeks, blood samples were again obtained in a 3cc disposable syringe for hemoglobin evaluation. If there was 2 g/dl hemoglobin improvement, then efficacy was labeled as "yes". Children losing in follow ups were replaced with a new enrollment in the same group.

Data was analyzed using "Statistical Package for Social Sciences (SPSS)", version 26.0. Quantitative variables were presented by Mean±standard deviation (SD). Qualitative data was shown as frequency and percentage. Both groups were compared

for various study variables including efficacy using chi-square test or independent sample t-test. P-value ≤ 0.05 was considered as significant.

RESULTS

In a total of 150 children, the mean age in Group-A was 6.56 ± 2.33 years whereas in Group-B, it was 6.05 ± 2.78 years ($p=0.2253$). In Group-A, there were 37 (49.3%) males and 38 (50.7%) females while in Group-B, there were 35 (46.7%) males and 40 (53.3%) females. The mean weight in Group-A was 18.28 ± 5.37 kg versus 17.5 ± 4.90 kg in Group-B ($p=0.3543$). The mean duration of IDA in Group-A and Group-B were 3.68 ± 1.73 months and 3.88 ± 1.64 months respectively ($p=0.4686$).

At baseline in Group-A, the mean Hb level was 6.07 ± 1.12 g/dl while in Group-B, it was 6.16 ± 1.14 g/dl ($p=0.6265$). After 4 weeks of treatment, mean Hb levels in Group-A was 9.44 ± 1.61 g/dl versus 8.83 ± 2.01 g/dl in group-B ($p=0.0420$). Efficacy was reported in 63 (84.0%) children in Group-A vs. 53 (70.7%) in Group-B ($p=0.051$).

In the age group of 2-5 years, there was no significant association between efficacy of treatment and treatment groups ($p=0.637$) whereas in the age group of 6-10 years there was significant association between efficacy of treatment and treatment groups ($p=0.002$). Among both males and females, there was no significant association between efficacy of treatment and treatment groups ($p>0.05$). There was no significant association between efficacy of treatment and treatment groups in all the weight categories ($p>0.05$). There was no significant association between efficacy of treatment and treatment groups regarding duration of IDA ($p>0.05$). Table-1 to 4 are showing efficacy of treatment of both iron preparations with respect to study variables.

Table-1: Efficacy of Treatment in relation to age of children (N=150)

Age	Efficacy	Group-A (n=75)	Group-B (n=75)	p-value
2-5	Yes	20(69%)	26(74.3%)	0.637
	No	9(31%)	9(25.7%)	
6-10	Yes	43(93.5%)	27(67.5%)	0.002
	No	3(6.5%)	13(32.5%)	

Group-A: Ferrous Sulphate; Group-B: IPC

Table-2: Efficacy of Treatment in relation to Gender of children (N=150)

Gender	Efficacy	Group-A (n=75)	Group-B (n=75)	p-value
Male	Yes	31(83.8%)	25(71.4%)	0.208
	No	6(16.2%)	10(28.6%)	
Female	Yes	32(84.2%)	28(70%)	0.137
	No	6(15.8%)	12(30%)	

Group-A: Ferrous Sulphate; Group-B: IPC

Table-3: Efficacy of Treatment in relation to Weight of children (N=150)

Weight	Efficacy	Group-A (n=75)	Group-B (n=75)	p-value
9-15	Yes	22(88.0%)	20(76.9%)	0.30
	No	3(12.0%)	6(23.1%)	
16-22	Yes	22(81.5%)	21(67.7%)	0.23
	No	5(18.5%)	10(32.3%)	
23-29	Yes	19(82.6%)	12(66.7%)	0.24
	No	4(17.4%)	6(33.3%)	

Group-A: Ferrous Sulphate; Group-B: IPC

Table-4: Efficacy of Treatment in relation to duration of Iron deficiency Anemia (N=150)

Duration	Efficacy	Group-A (n=75)	Group-B (n=75)	p-value
1-3 months	Yes	27(84.4%)	21(63.6%)	0.057
	No	5(15.6%)	12(36.4%)	
4-6 months	Yes	36(83.7%)	32(76.2%)	0.386
	No	7(16.3%)	10(23.8%)	

Group-A: Ferrous Sulphate; Group-B: IPC

DISCUSSION

In the present study, 42.7% children were aged between 2-5 years while remaining 57.3% children were aged above 5 years to 10

years. Sheikh et al found major portion (60%) of the children with IDA to be aged less than 2 years and minor portion (40%) comprised of the children of the age between 2-6 years.⁹ According to another local study,¹⁰ the percentage of the children with IDA aged less than 3 years were 74% while remaining 26% were aged between 3-5 years. The higher occurrence rates of IDA during pediatric age groups could be due to the fact that the need of iron is higher among children as the body grows faster. There are some other prospects which contribute to the high proportion of IDA among children include underweight, poverty, high rates of ingestion of cow-milk and inadequate quantity of iron in additional foods given to the children.^{11,12}

The present findings showed that efficacy was noted in 84.0% children using ferrous sulphate vs. 70.7% using IPC. Our findings are contrary to what was observed by Sheikh et al describing the effectiveness of IPC as 91.4% versus 85.5% with ferrous sulphate ($p=0.45$).⁹ Another locally conducted study showed efficacy of ferrous sulphate in 97% cases versus 94% with IPC and these results are in accordance with our findings as our study did not find any significant difference regarding efficacy between IPC and ferrous sulphate groups ($p=0.051$).¹⁰ Bopche et al stated that children reported ferrous sulphate resulted in better increase in terms of Hb rise.¹³ Arvas et al¹⁴ and Geisser et al¹⁵ also presented the similar findings. But Sozmen et al reported that the rise in Hb and serum iron with ferrous sulphate and IPC was relatively similar.¹⁶

The literature reports the chances of gastrointestinal side effects to be higher among patients taking ferrous sulphate, yet the other side effects are more frequently reported in individuals taking IPC. Mahmood et al described that children who received ferrous sulphate, hemoglobin was increased in large proportion of children along with an increase in mean hemoglobin level of the children as well.¹⁸ According to our study results, in a comparison with IPC, a higher percentage of children (84%) were observed in the group who received ferrous sulphate and their levels of hemoglobin were increased, the results are in accordance with the above-mentioned study results.

Sozmen et al¹⁶ and Sheikh et al⁹ established that the rise in Hb and serum ferritin with both studied supplements were similar. Researchers have also revealed that the availability of iron by either from ferrous sulphate or IPC result in relatively similar efficacy when advised for a period of 12 weeks.¹⁹ In contrary, Bopche et al described that there was a notable rise in Hb when ferrous sulphate was given to a group of patients and followed up from baseline to the final visits.¹³ The drug was given in appropriate dosage, on regular basis for a period of 3 months to evaluate the effectiveness (increase in HB concentration by ≥ 2 g/dl). There was no significant finding regarding the effectiveness of the both study groups. According to Bopche et al, ferrous sulphate remained effective in 98.1% cases and the effectiveness of IPC was reported in 71.7% cases showing a remarkable difference between the groups. Another study revealed that IPC resulted in mean Hb after the treatment as 11.0 ± 0.77 g/dl whereas in ferrous sulphate group it was 10.9 ± 1.02 g/dl⁹ which is in contrast to our findings which showed the mean Hb after treatment in IPC group was 8.83 ± 2.01 g/dl and in ferrous sulphate group as 9.44 ± 1.61 g/dl.

CONCLUSION

Although in comparison to IPC, ferrous sulphate resulted in significantly better rise in hemoglobin levels among children with IDA, but overall efficacy between the two drugs was relatively similar.

REFERENCES

1. 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.
2. Soppi ET. Iron deficiency without anemia—a clinical challenge. Clin Case Rep. 2018;6(6):1082.

3. Sundararajan S, Rabe H. Prevention of iron deficiency anemia in infants and toddlers. *Pediatr Res*. 2021;89(1):63-73.
4. Luo D, Xu R, Ma J, Yan X, Hu P, Song Y, et al. The associations of economic growth and anaemia for school-aged children in China. *Matern Child Nutr*. 2020;16(2):e12936.
5. 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.
6. Khan SA, Khan J, Gul MS, Akbar K, Farid A, Adnan M. Iron deficiency associated with febrile seizures. *Rawal Med J*. 2021;46(3):530-2.
7. Perveen A, Raja NF, Khan IM, Shaheen H, Imran M, Ahmad RS. Comparison of conventional and newer iron preparations for the treatment of iron deficiency anaemia in children. *J Rawalpindi Med Coll*. 2020;24(2):112-6.
8. Drozd M, Jankowska EA, Banasiak W, Ponikowski P. Iron therapy in patients with heart failure and iron deficiency: review of iron preparations for practitioners. *Am J Cardiovasc Drugs*. 2017;17(3):183-201.
9. Sheikh A, Shah M, Shakir U. Comparison of efficacy of ferrous sulfate and iron Polymaltose complex in the treatment of childhood iron deficiency anemia. *Pak J Med Health Sci*. 2017;11(1):221-14.
10. Marwat IU, Hassan KA, Javed T, Chishti AL. Comparison of efficacy of Ferrous and Iron Polymaltose salts in the treatment of childhood Iron Deficiency Anemia. *Ann King Edward Med Uni*. 2013;19(4):322.
11. Roganović J, Starinac K. Iron deficiency Anemia in children. *Curr Topics Anemia*. 2018;47:47-71.
12. Yasa B, Agaoglu L, Unuvar E. Efficacy, tolerability, and acceptability of iron hydroxide polymaltose complex versus ferrous sulfate: a randomized trial in pediatric patients with iron deficiency anemia. *Int J Pediatr* 2011: 524520.
13. Bopche AV, Dwivedi R, Mishra R, Patel G. Ferrous sulfate versus iron polymaltose complex for treatment of iron deficiency anemia in children. *Indian Pediatrics* 2009;46(10):883-885.
14. Arvas A, Gür E. Are ferric compounds useful in treatment of iron deficiency anemia? *Türk J Pediatr*. 2000;42(4):352-3.
15. Geisser P. Safety and efficacy of iron (III)-hydroxide polymaltose complex. *Arzneimittelforschung* 2007;57(06):439-52.
16. Sözmen EY, Kavakli K, Çetinkaya B, Akçay YD, Yılmaz D, Aydinok Y. Effects of iron (II) salts and iron (III) complexes on trace element status in children with iron-deficiency anemia. *Biolog Trace Element Res*. 2003;94(1):79-85.
17. Ruiz-Argüelles GJ, Díaz-Hernández A, Manzano C, Ruiz-Delgado GJ. Ineffectiveness of oral iron hydroxide polymaltose in iron-deficiency anemia. *Hematology*. 2007;12(3):255-6.
18. Mahmood T. Comparison of ferrous sulphate with iron polymaltose in treating iron deficiency anaemia in children. *J Rawalpindi Med Coll*. 2017;21(4):376-9.
19. Jacobs P, Wood L, Bird AR. Better tolerance of iron polymaltose complex compared with ferrous sulphate in the treatment of anaemia. *Hematology*. 2000;5(1):77-83.