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

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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, Khanani 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 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 in 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, Khanani, 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>40U, bilirubin >5mlU), 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)

<table>
<thead>
<tr>
<th>Age</th>
<th>Efficacy</th>
<th>Group-A (n=75)</th>
<th>Group-B (n=75)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5</td>
<td>Yes</td>
<td>20(69%)</td>
<td>26(74.9%)</td>
<td>0.637</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>9(31%)</td>
<td>9(25.1%)</td>
<td></td>
</tr>
<tr>
<td>6-10</td>
<td>Yes</td>
<td>43(93.5%)</td>
<td>27(67.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>3(6.5%)</td>
<td>13(32.5%)</td>
<td></td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Gender</th>
<th>Efficacy</th>
<th>Group-A (n=75)</th>
<th>Group-B (n=75)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Yes</td>
<td>31(88.6%)</td>
<td>29(77.4%)</td>
<td>0.208</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6(16.2%)</td>
<td>10(28.6%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>Yes</td>
<td>32(84.2%)</td>
<td>28(70%)</td>
<td>0.137</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6(15.8%)</td>
<td>12(30%)</td>
<td></td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Weight</th>
<th>Efficacy</th>
<th>Group-A (n=75)</th>
<th>Group-B (n=75)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-15</td>
<td>Yes</td>
<td>22(88.0%)</td>
<td>20(76.9%)</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>3(12.0%)</td>
<td>6(23.1%)</td>
<td></td>
</tr>
<tr>
<td>16-22</td>
<td>Yes</td>
<td>22(81.5%)</td>
<td>21(67.7%)</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>5(18.5%)</td>
<td>10(32.3%)</td>
<td></td>
</tr>
<tr>
<td>23-29</td>
<td>Yes</td>
<td>19(82.2%)</td>
<td>12(66.7%)</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>4(17.4%)</td>
<td>6(33.3%)</td>
<td></td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Duration</th>
<th>Efficacy</th>
<th>Group-A (n=75)</th>
<th>Group-B (n=75)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 months</td>
<td>Yes</td>
<td>27(84.4%)</td>
<td>21(63.6%)</td>
<td>0.057</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>5(15.6%)</td>
<td>12(36.4%)</td>
<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>Yes</td>
<td>36(83.7%)</td>
<td>32(76.2%)</td>
<td>0.388</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7(16.3%)</td>
<td>10(23.8%)</td>
<td></td>
</tr>
</tbody>
</table>

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. According to another local study, 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 including underweight, poverty, high rates of ingestion of cow-milk and inadequate quantity of iron in additional foods given to the children.

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). 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). Bopche et al stated that children reported ferrous sulphate resulted in better increase in terms of Hb rise. 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.

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