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IRON DEFICIENCY ANEMIA;

COMPARISON OF EFFICACY OF FERROUS SULPHATE WITH IRON POLYMALTOSE COMPLEX FOR TREATMENT OF IRON DEFICIENCY ANEMIA.

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ABSTRACT… Objective: To compare the efficacy of Ferrous sulfate with iron polymaltose complex in treatment of iron deficiency anemia in children in terms of rise in hemoglobin. **Study design:** Randomized clinical trial. **Setting:** Department of Paediatric Medicine Unit I Allied Hospital Faisalabad. **Study duration:** 6 months. **Methodology:** All the children of age group 6 month to 12year with hemoglobin level <10g/dl, MCV<70fl corrected for age, MCHC<32%, serum ferritin<8μg/l were included. All other cases of anemia other than iron deficiency anemia such as thalassemia, sickle cell anemia, lead poisoning etc, patients with severe anemia (hb≤6g/dl) because they need blood transfusion to correct anemia, those with decompensated heart failure or acute infection were excluded. After enrolment patients were randomly divided into two groups by lottery method. Group A, patients were given ferrous sulphate. Group B, patients were given iron polymaltose complex (IPC). Both iron preparations were given in the dose of 5mg/kg/day of elemental iron in three divided dosage 30 minutes before meals. Patients were assessed at one month interval after the start of treatment and hemoglobin was checked at follow up visit by taking 2cc blood. **Results:** Sixty children were studied. Mean age was 2.5 ± 5.1 years, range 7 months to 12 years with 32 girls, 28 boys. The patients were evenly distributed between the two treatment groups (IPC, n = 30, 50%; ferrous sulfate, n = 30, 50%). All erythrocyte-related hematologic parameters after one month treatment showed a significant improvement from baseline with both treatments. A significant improvement in Hb was observed after one month treatment in the IPC group 9.5 ± 1.1g/dL to 10.6 ±1.0 g/dL and the ferrous sulfate group 9.4 ± 1.6 g/dL to 11.2 ± 0.9 g/dL which was statistically significant. **Conclusion:** From this randomized study, it is concluded that both ferrous sulphate and iron polymaltose complex have equal efficacy in treatment of iron deficiency anemia

Key words: Iron deficiency, Ferrous sulphate, iron polymaltose

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INTRODUCTION

There is worldwide prevalence of iron deficiency anemia especially effecting children and pregnant women.[1,2] Previous studies show an estimated prevalence of 65% in Pakistan about 40% in various under developed countries of Asia and Africa. The most common and preventable form of anemia is iron deficiency anemia. Prevalence rate of iron deficiency anemia worldwide is 43% and in Pakistan it is 29% as shown by statistics of World Health Organization.[3]

IDA (iron deficiency anemia) affects work capacity, immune function, neurological development and ability to learn in infants and children.[4] Causes of iron deficiency may include decrease dietary intake, increased requirement as occurs during pregnancy or chronic blood loss especially gastrointestinal. The most susceptible groups to develop iron deficiency anemia are infants and preschool age.[5]

In infants and toddlers blood loss is a very common cause of iron deficiency which may occur due to milk or other protein allergies, Mackle's diverticulum, polyp, worm infestations and in older children may be due to inflammatory bowel disease or infection with H pylori.[4]

Systemic, neurological and developmental

problems resulting from iron deficiency in infancy and childhood can be prevented by adequate iron supplementation that results from IDA (iron deficiency anemia) in infancy and childhood.[5] Soluble ferrous salt in aqueous solution such as ferrous sulphate or ferric complex such as Iron Polymaltose complex should be used as most practical iron supplement as recommended by joint UNICEF/USAID consultation as a first-line therapy.[5,2] IPC is an iron preparation with nonionic iron and Polymaltose in a stable complex [6].The bioavailability of IPC and Ferrous Sulphate is similar but IPC has better absorption due to more stable structure due to which bioavailability is similar to Ferrous sulphate but the structure is stable that ensures more controlled absorption of iron. A recent meta-analysis shows that rise in hemoglobin is 98.1% with ferrous Sulphate as compared to IPC in which rise is 71.7%.[7]

The rationale of this study is that anemia is very common in our society and iron deficiency is among one of the commonest and preventable cause, so by finding a drug which causes more rise in hemoglobin, IDA can be treated more effectively in our setup

METHODOLOGY

This study was carried out at the Department of Paediatric Medicine, Allied Hospital Faisalabad, Pakistan. IRB (Institutional review board) approval was obtained and informed written consent was taken from the parents. Treatment outcome and study purpose was explained to parents. Sixty patients in total met inclusion criteria and were enrolled in the study after taking complete history, thorough clinical and systemic examination.

BASELINE INVESTIGATION

To evaluate the extent and type of anemia following baseline investigations were performed; hemoglobin, Mean corpuscular volume, Mean corpuscular hemoglobin concentration and Serum ferritin level by taking 5 cc of blood to document iron deficiency as cause of the anemia. This Hemoglobin level before start of any treatment was recorded as baseline hemoglobin.

Randomization

According to the treatment plan patients were randomly divided into two groups by lottery method

Group A, patients were given ferrous sulphate

Group B, patients were given iron polymaltose complex

Randomization was maintained throughout study. It was single blind study which was maintained throughout study.

Dosage of Iron

Both iron preparations were given in the dose of 5mg/kg/day of elemental iron in three divided dosage 30 minutes before meals.

Data record

Demographic data and follow up record was maintained taking contact and address of every patient to ensure follow up by another investigator.

Follow up

Patients were assessed at 1 month interval after the start of treatment, compliance was ensured by direct question from parents. Details of any side effect were asked.

Outcome

Hemoglobin was checked at follow up visit by taking 5cc blood. All the observation were entered in preformed Performa

Statistical analysis

SPSS latest version was used to analyze quantitative variables. Mean and standard deviation were calculated for quantitative variables like age and dosage. Chi-square test was used to compare the mean rise in hemoglobin in both groups. P value < 0.05 was considered significant.

RESULTS

Sixty children were included in the study. 32 were girls and 28 boys. Mean age was 2.5 ± 5.1 years, range 7 months to 12 years. Patients were divided in two age groups, one ranging from 6 months to 5 years and second more than 5 years up to 12 years. Distribution of patient as per age ranges

were 40(67%) in age range 6 months to 5 years and 20(33%) in age range more than 5 years up to 12 years as shown in table I.

Age	Frequency	%age
6 months-5 years	40	67%
7-12	20	33%
Mean age	2.5±5.1 years	

Table-I. Age distribution

Age wise patient were evenly distributed between two groups as shown in Table-II.

Age	Group A	Group B
6 months-5 years	50%(20)	50%(20)
7-12 years	50%(10)	50%(10)

Table-II. Age distribution among groups

Variable	Group A N=30	Group B N=30	P-value
Age	2.5 ± 5.1 years	2.3 ± 5.3 years	Non-significant
Sex M/F	16/14	16/14	Non-significant
HB at baseline	9.4±1.10	9.5±1.5	Non-significant
HB at 1 month	10.5±1.0	11.3±1.0	P .001
Mean rise in HB	1.2±0.9	1.8±1.7	P .001

Demographic data between two groups was similar

Hemoglobin related parameters at month 1 showed a significant improvement from baseline in both groups. Improvement in Hb was significant in both groups at month 1 in the IPC group (9.5 ± 1.1g/dL to 10.6 ±1.0 g/dL) and the ferrous sulfate group (9.4 ± 1.6 g/dL to 11.2 ± 0.9 g/dL, P = 0.001)

DISCUSSION

This was a randomized clinical trial carried out in Pediatric unit 1 of Allied Hospital Faisalabad, comparing efficacy of ferrous Sulphate with iron Polymaltose complex for treating iron deficiency anemia. Sixty patients in total meeting inclusion criteria were enrolled in the study after IRB approval and taking informed written consent. Patients were equally divided in two groups on basis of non-probability consecutive sampling technique randomly. Group A patients were given ferrous Sulphate and Group B were given Iron Polymaltose Complex.

Hb was measured before start of any therapy in both groups A & B with mean Hb 9.4 ± 1.10 in group A and 9.5 ± 1.5 in group B respectively. Hb was measured after one month of treatment with iron supplements with ferrous Sulphate in group A and iron Polymaltose complex in group B respectively. Mean Hb after one month treatment was 10.5 ± 1.0 and 11.3 ± 1.0 in groups A and B respectively. Mean rise in Hb from baseline was 1.2 ± 0.9 and 1.8 ± 1.7 in groups A & B respectively. P- Value was significant, which was 0.001.

Results of this randomized study showed that mean rise in hemoglobin concentration is significant and almost same in children treated with either Iron Polymaltose complex or ferrous Sulphate for iron deficiency anemia after one-month and both ferrous sulphate and iron Polymaltose complex have compare able efficacy, though mean Hb rise with iron Polymaltose complex was higher than with ferrous sulphate. Some previous studies show superiority of Iron Polymaltose complex as treatment of iron deficiency anemia achieving a significant increase in Hb levels in children with IDA.[8-12] In a randomized trail of 49 iron deficiency anemic infants, Murahovschi et al. found that with ferrous sulfate there was faster increase in Hb during the first month of treatment which then became slower after 1 month compared to those given Iron Polymaltose complex, both at a dose of 4mg/kg/day.

Abdominal cramps, constipation, gastrointestinal intolerability in the form of nausea, vomiting and diarrhea is very common with use of iron preparation. This is particularly common with ferrous Sulphate as evidenced from studies.[13-14] This is also evidenced from studies in adults showing better tolerability and lesser GI related side effects with Iron Polymaltose Complex than Ferrous Sulphate. Less gastrointestinal adverse events and less frequent tooth staining with iron polymaltose complex was noted in children as compared to those given ferrous sulfate.[9] This difference in safety profiles between the two preparations is probably related to more stable

nature of Iron Polymaltose complex molecule releasing iron more slowly[15]. While opposite occurs with ferrous sulfate causing rapid iron release overloading uptake mechanisms and causing local gut irritation leading to gastrointestinal intolerability[16], So there is an increase in non-transferrin bond iron (NTBI). Non-transferrin bond iron is known to induce oxidative stress and increased oxidative stress leading to GI disturbances.[16-18]

Meal affects bioavailability of iron. Meals though reduce bioavailability of ferrous salts but this reduction improves GI tolerability, in contrast Iron Polymaltose complex can be taken with meals without affecting its bioavailability[19] or effectiveness. This better bioavailability of IPC is confirmed in a randomized trial of 105 healthy infants comparing efficacy and tolerability of IPC versus ferrous gluconate in the prevention of anemia[20] showing gastrointestinal intolerability and teeth discoloration significantly less frequently in the IPC treatment group.

Due to these adverse events, compliance becomes an important issue with ferrous salts[21]which becomes a barrier towards long term use of these preparations. Studies have shown that compliance and adherence with a ferrous sulfate regimen may reduce to as low as 30–40% over a one-week period.[22,23]

CONCLUSION

From this randomized study, it is concluded that both ferrous sulphate and iron polymaltose complex have equal efficacy in treatment of iron deficiency anemia, but limitations to this study include small patient cohort, short follow up, need to study safety profile of both formulations.

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CORRECTION

The amendment of the Professional Vol: 25, No.03 (Prof-4402) titled: "Upper complete denture; Location of vibrating line with reference to fovea palatinae in determining posterior border" on page 419 is as under;

INCORRECT	CORRECT
Shabbir Ahmed	Shabir Ahmed

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Jawaria Khalid	Main Author	
2	M. Mehboob Ahmed	Manuscript Writing	
3	Misbah Khalid	Data collection and write up	
4	M. Asghar Butt	Supervising the research	
5	Khalid Mahmood Akhtar	Proof reading and discussion	