Comparison of efficacy of Ferrous and Iron Polymaltose salts in the treatment of childhood Iron Deficiency Anemia

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ABSTRACT
Background
Iron deficiency of anemia (IDA) is defined as reduced number of red blood cells, and / or reduced concentration hemoglobin (Hb) due to deficiency of iron. Treatment involves dietary modifications and inorganic iron salt supplements like ferrous sulfate (FS) or Iron polymaltose complex (IPC). The decision to select either drug rests on therapeutic efficacy, untoward side effects; cost of complete course, patient's compliance and discretion of physician. Both drugs can be prescribed in oral form.

This study aimed at comparing the efficacy of two iron preparations (ferrous sulphate and iron polymaltose complex salts) in childhood iron deficiency anemia.

Objective
To compare the efficacy of Ferrous Sulphate and Iron Polymaltose Complex salts in the treatment of childhood Iron Deficiency Anemia.

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Methodology
This randomized controlled trial was conducted at Department of Pediatric Medicine Unit-II Mayo Hospital, Lahore, for a period of 6 months. One hundred and fifty children aged 6 months to 5 years suffering from iron deficiency anemia were selected and randomly divided into two groups of 75 each (Group A and B prescribed FS and IPC respectively). Results were analyzed in terms of rise in Hb from the baseline after three months. Increase in Hb level $\geq$2gm/dl after three months of treatment was considered as effective. Results were analyzed by SPSS version 17. Efficacy of both the drugs, was compared by chi square test. P value $\leq$0.05 was accepted as significant.

Results
There were 34 cases (22.7%) in 6-12 months age, 77 cases (51.3%) between 1-3 years age and 39 cases (26%) between 3-5 years age. The number of male and female children was 82 (54.7%) and 68 (45.3%) respectively.

The baseline hemoglobin of all study cases was 6.64±1.08gm/dl (6.59±1.13gm/dl in Group A and 6.69±1.04gm/dl in Group B). At completion of therapy, the mean hemoglobin of all study cases was 9.15±1.21gm/dl (9.20±1.17gm/dl in Group A and 9.11±1.25gm/dl in Group B). The difference between both groups was insignificant on statistical analysis. The observed rise in hemoglobin of all cases was 2.52±0.67gm/dl (2.62±0.61gm/dl in group A and 2.42±0.71gm/dl in group B). The difference between both groups was statistically insignificant. The observed efficacy among all study cases was seen in 96% cases (97.33% in

group A and 94.67% in group B) with insignificant statistical difference.

Conclusion

It was concluded that there was no significant difference in the efficacy of two drugs given for iron deficiency anemia in children. Ferrous sulphate salts are economical compared to iron polymaltose complex (IPC) and have equal efficacy without compromising untoward effects.

Key words: *Iron deficiency anemia, ferrous sulphate, iron polymaltose complex, hemoglobin*

INTRODUCTION

The World Health Organization (WHO) defines nutritional anemia as low hemoglobin level due to deficiency of one or more essential nutrients.[1] Iron deficiency anemia occurs due to insufficient iron stores in body.[2] The magnitude of iron deficiency anemia (IDA) in Pakistan is immense and incurs a health care burden as high as 65% of general population including children and adults.[3] According to WHO, 43% children worldwide and 29% children in Pakistan are affected by iron deficiency.[3] Children below 2 years, especially at start of complementary feeding are at higher risk because of rapid growth and increased demand. The situation is further complicated due to factors like diet, socioeconomics and biology.[4] Iron deficiency anemia and malnutrition go side by side, rather interconnected in a vicious cycle. Anorexia, apathy and irritability, being consequences of iron deficiency anemia, further reduce food intake, thus aggravating the situation.[3]

Iron deficiency anemia has marked influence on wellbeing of small children. It affects working capacity, neurologic development and learning abilities of a child.[5] Deficiency of iron in childhood may increase the risk of psychiatric illness in later life.[6] It is a significant risk factor for developing of febrile fits and breath holding spells during childhood and stroke in later life.[7] Iron deficiency state leads to poor school performance despite normal IQ. It not only affects the children but also the parents, exposing them to anxiety, agony and economic burden. Treatment of childhood iron deficiency anemia is simple. World public health authorities recommend the use of aqueous solution of ferrous salts like ferrous sulphate

(FS) and Iron polymaltose complex (IPC).[8] Ferrous sulphate is a time tested drug therapy but its use is limited by low and variable gut absorption, chelation with food particles and free radical mediated mucosal damage. Iron polymaltose complex was introduced to overcome these problems.[9]

The bioavailability and efficacy of FS has been compared with IPC in various studies. The comparison of two drugs in some studies suggest Iron polymaltose complex being as effective or even superior to ferrous sulphates.[10, 11] However other regional studies have not supported these observations.[3, 8] A study conducted in 2009 showed expected percentage of efficacy (in terms of 1gm/dl increase in HB from baseline) as 71.7% in IPC versus 98.1 % in FS group in children with iron deficiency anemia.

Pakistan, being a resource limited country with a large population of low socioeconomic status, cannot accept and promote the wide scale use of new high cost compounds for treatment of iron deficiency anemia. The issue of efficacy between two therapies remains unsettled yet. If effectiveness of two therapies is comparable, then cost effective drug should be preferred in children of iron deficiency anemia especially at community level. This study has a rationale to explore the issue of efficacy of two iron drug therapies in the treatment of children with iron deficient anemia, along with their compliance, cost and untoward effects.

OBJECTIVE

To Comparison of efficacy of Ferrous and Iron Polymaltose salts in the treatment of childhood Iron Deficiency Anemia

OPERATIONAL DEFINITIONS
EFFICACY

This was defined as the increase in Hemoglobin (Hb) concentration by ≥ 2 gm/dl from baseline and assessed after regular use of prescribed drug in adequate dosage for three months.

MATERIALS AND METHODS
SETTING

This Randomized controlled trial was conducted at department of Pediatric medicine, King Edward Medical University/Mayo Hospital, Lahore from 1st Sept 2011 to 29th Feb 2012 9(6 months)

Sample size of 150 cases (75 in each group) was calculated with 80% power, 5% level of significance and expected percentage of efficacy in both groups i.e. 71.7% in iron polymaltose complex group versus 98.1% ferrous sulphate group in children with iron deficiency anemia. Cases were selected by non-probability purposive sampling technique.

One hundred and fifty children age 6 months to 5 years with hemoglobin less than 8g/dl or Serum ferritin less than 12 mcg/l having microcytic hypochromic anemia on peripheral blood smear were included in the study after obtaining informed written consent.

Children having received any form of iron therapy before enrolment, having anemia of prematurity (assessed from gestational age), megaloblastic anemia (MCV > 95 fl, dysmaturity of RBC's, hyper segmented neutrophils), severe anemia requiring emergency blood transfusion, systemic disorders like renal failure, or liver diseases and those with hemoglobinopathies were excluded.

DATA COLLECTION AND PROCEDURE:
Based on inclusion and exclusion criterion, patients were selected and written informed consent was obtained. One hundred and fifty cases of children (from outdoor and emergency section) were enrolled when baseline Hb was below 8gm/dl. They were randomized in two groups with the help of computer generated tables (75 in each group). Group A was given ferrous sulphate salt (6 mg/kg/ day for three months orally). Group B was given Iron polymaltose complex (3 mg/kg/day for three months orally). Results were analyzed in terms of rise in Hb from the baseline after three months. Increase in Hb concentration ≥2gm/dl assessed after three months of start of treatment was considered as effective. Patients with irregular follow up, and those not completing the course of therapy were labeled as dropouts, and not included in data analysis.

DATA ANALYSIS:
Results were analyzed by SPSS version 17. Quantitative variables like age were presented in the form of mean ±S.D. Qualitative variables like efficacy were presented in form of frequency and percentages. Efficacy of both drugs was compared by using chi square test. P value less than 0.05 was accepted as significant.

RESULTS
A total of 150 cases were enrolled and randomized into two treatment groups. There were 34 (22.7%) cases in 6-12 months of age, 77 (51.3%) were in 1-3 years of age and 39 (26%) were in 3-5 years of age. (**Table-1).** In this study, 54.7% patients were male and 45.3% patients were female with M: F ratio 1.2:1. (**Table-2**)

Initially the mean hemoglobin of all study cases was 6.64±1.08gm/dl (range 3.10-7.90gm/dl). The baseline mean Hb in group A was 6.59±1.13gm/dl and that in group B was 6.69±1.04gm/dl. The difference between both groups was insignificant for initial Hb level. (P-value = 0.553). (**Table-3**)

The mean hemoglobin of all study cases at completion of therapy was 9.15±1.21gm/dl (range 4.50-11.60gm/d). The mean post-treatment Hb in group A was 9.20±1.17gm/dl and 9.11±1.25gm/dl in group B. The difference between both groups was insignificant (P-value = 0.618). (**Table-4**)

The mean rise in hemoglobin of all children was 2.52±0.67gm/dl (range 0.67-0.70gm/dl). The mean rise in Hb in group A was 2.62±0.61gm/dl. The mean rise in Hb in group B was 2.42±0.71gm/dl (range 0.70-4.70gm/dl). The difference between both groups was insignificant (P-value = 0.618). (**Table-5**)

Efficacy was assessed as rise in Hb concentration by ≥1 gm/dl from baseline and assessed at completion of therapy. Efficacy was shown in 144 (96%) cases, 97.33% cases in group A and 94.67% cases in group B. The difference between both groups was insignificant. (P-value = 0.405). (**Table-6**)

Table – 1
Distribution of patients in different age groups

Age range	Frequency	Percentage
6-12 months	34	22.7%
1-3 years	77	51.3%
3-5 years	39	26.0%
Total	150	100.0%

Table – 2
Distribution of gender of the patients

		Frequency	Percentage
Gender	Male	82	54.7%
	Female	68	45.3%
	Total	150	100.0%

Table – 3
Comparison of initial hemoglobin in study groups

Group		Group A	Group B	Total
Initial Hb (gm/dl)	N	75	75	150
	Mean	6.59	6.69	6.64
	SD	1.13	1.04	1.08
	Minimum	3.10	3.10	3.10
	Maximum	7.90	7.90	7.90
	Range	4.80	4.80	4.80

T-test = 0.595
P-value = 0.553 NS

Table – 4
Comparison of Hemoglobin at completion of therapy in study groups

Group		Group A	Group B	Total
Post treatment Hb (gm/dl)	N	75	75	150
	Mean	9.20	9.11	9.15
	SD	1.17	1.25	1.21
	Minimum	4.50	5.40	4.50
	Maximum	11.50	11.60	11.60
	Range	7.00	6.20	7.10

T-test = 0.500
P-value = 0.618 NS

Table – 5
Comparison of rise in hemoglobin in study groups

Group		Group A	Group B	Total
Rise in Hb (gm/dl)	N	75	75	150
	Mean	2.62	2.42	2.52
	SD	0.61	0.71	0.67
	Minimum	0.90	0.70	0.70
	Maximum	4.10	4.70	4.70
	Range	3.20	4.00	4.00

T-test = 1.862
P-value = 0.065 NS

Table – 6
Comparison of efficacy in study groups

		Group		Total
		Group A	Group B	
Efficacy	Yes	73(97.33%)	71 (94.67%)	144 (96.0%)
	No	2 (2.67%)	4 (5.33%)	6 (4.0%)
Total		75 (100%)	75 (100%)	150 (100%)

Chi-square = 0.694
P-value = 0.405 NS

Table: 7

Adverse drug reactions (ADR)		
ADR	Group A	Group B
Nausea & vomiting	15	10
Abdominal pain	7	6
Diarrhea	13	12
Teeth staining	35	40

DISCUSSION:

Childhood IDA is a common disorder of undeveloped countries, with a prevalence of 4-8% between 12 and 36 months of age.[12-14]In this study, 150 children of IDA were enrolled and randomized them into two treatment groups; FS and IPC. The age and sex distribution of study cases as shown in Table 1 & 2 were comparable. In Afzal et al study, the male-to-female ratio was 2:1 suggesting male predisposition compared to female children.[3]

The efficacy and rise in hemoglobin in both groups was comparable. (Table 3, 4, 5). In another study, Sozmen, et al., showed that both preparations induced comparable rise of hemoglobin and serum iron levels. Some studies concluded that equal amount of iron is available from ferrous sulphate or iron polymaltose complex in correcting hemoglobin levels over a twelve weeks observation period. There was no difference whichever drug is given.[11, 15, 16]

But Bopche et al., showed that FS group had significant increase in Hb level from baseline to final follow-up. Their results were same as those reported by Arvas and Langstaff.[8, 17, 18]

Efficacy (rise in Hb concentration by ≥ 2 gm/dl) after regular use of prescribed drug in adequate dosage for three months was assessed. Regarding efficacy the difference between both groups was insignificant. Bopche et al., showed that efficacy of FS was 98.1% and IPC showed efficacy of 71.7% with significant difference between both groups.[8] But results of some studies are contradictory.[10, 11] The type and frequency of adverse drug reactions are shown in **Table 7**; they are comparable in both groups with no significant difference. According to one study, the overall untoward effects were more common in the FS than in IPC group (78% vs 31%). The compliance on the other hand was significantly higher for the IPC (91%) group than for the FS (87%) group. The tolerance of IPC was clearly better than that of FS; the differences were also significant for the adverse reactions. This probably reflected a better risk/benefit ratio of IPC. The newly marketed IPC preparations are more expensive than time-tested ferrous salts; the total cost of complete drug therapy may be almost double. Properly conducted, multiple randomized controlled trials

in pediatric population are needed to reach final conclusion.[10]

CONCLUSION

The results clearly show that no significant differences in the efficacy of both drugs were noted in the treatment of iron deficiency anemia. Ferrous salts can be prescribed confidently in place of iron polymaltose complex as these are comparatively more expensive but have equal efficacy without compromising adverse effects.

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