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ORIGINAL ARTICLE

Iron Supplementation in Anemic Pregnant Women: A Comparison of Different Prescription Options in Pakistan

ASMA KAZI[1], AISHA AZIZ[2], SHOAIB AHMED[3], SABEENA UMER[4], SHAZIA ROMAN[5], FAIZA IRSHAD[6]
[1]*Associate Professor, Department Medicine Rashid Latif Medical College Lahore*
[2]*Assistant Professor, Medicine Deptt Rashid Latif Medical College Lahore*
[3]*Associate Professor, Department of Biochemistry. Rai Medical College Sargodha.*
[4,5]*Assistant Professor, Gynaecology Sialkot Medical College Sialkot*
[6]*Associate professor, Anatomy M.Islam Medical & Dental College Gujranwala*
Correspondence to: Asma Kazi

ABSTRACT

Background & objectives: Many pregnant women in Pakistan have iron deficiency anemia (IDA), a dietary deficit. It affects both the mother's and the foetal' health. Oral iron supplementation usually relieves IDA symptoms. Oral iron supplements are hazardous to the GI mucosa, and sensitivity is common. Poor therapeutic compliance leads to treatment failure. Ferrous ascorbate (FeA) and iron hydroxide polymaltose complex (IPC) reportedly improve gastrointestinal discomfort and increase patient compliance compared to ferrous sulphate (FS). These preparations reportedly improve hemoglobin levels and iron stores more quickly than FS. This analysis compared FS's efficacy and safety to IPC and FeA.

Place of Study: Rashid Latif Medical College Lahore

Duration of Study: February 2019 and October 2021

Methods: It was a randomized, parallel, open label, investigation among pregnant women of gestational age from 10 to 28 weeks with moderate anemia. Patients were randomly selected to receive either FS, IPC or FeA. They were then followed up for 3 months to look for improvement in the hemoglobin levels and other hematological indicators or any adverse drug response.

Results: With the exception of 3 months, when the FeA group had a significantly higher hemoglobin level in comparison to the FS group ($P < 0.05$), the hemoglobin levels were comparable across the three groups. The overall risk profiles for side effects were likewise equal across the research groups, with the exception of epigastric discomfort, which was more frequently reported in the FS group.

Conclusions: The findings of the study indicated that FS, IPC, and FeA all have an efficacy and safety profile in the treatment of IDA associated with pregnancy that is comparable to one another.

Keywords Anemia, ferrous ascorbate , ferrous sulphate ,iron hydroxide polymaltose ,pregnancy

INTRODUCTION

Iron-deficiency anaemia is the most common nutritional deficiency. Clinically, it presents as hypochromic microcytic anaemia with low blood indices and serum ferritin. IDA is the most common anaemia in reproductive-age women. In underdeveloped nations, it affects 30 to 70% of pregnant women. 60-70% of pregnant women in Pakistan have anaemia. Anemia affects both the mother and the unborn child. It causes early delivery, uterine development retardation, low birth weight, postpartum haemorrhage, heart failure, and infections.

In most situations, iron supplementation can treat IDA. Iron salts including ferrous sulphate, fumarate, and gluconate are widely used to treat and prevent IDA. Oral iron supplements, which are usually ferrous (Fe2+) s are hazardous to the GI mucosa, and sensitivity to them is common. Poor patient compliance causes ineffective treatment. This causes stomach difficulties (nausea, vomiting, abdominal pain, constipation and diarrhoea). Iron hydroxide polymaltose complex (IPC) and ferrous ascorbate (FeA) claim to have fewer gastrointestinal side effects, resulting in improved patient compliance. These preparations may raise hemoglobin and iron stores more quickly than FS.

The current study compared the efficacy and safety of FS to other iron preparations, such as IPC and FeA, for treating IDA in pregnant women.

MATERIAL AND METHODS

The research was carried out between February 2019 and October 2021 at a single center, and it comprised of a randomized, parallel-group, open-labeled study. After the patients were provided all of the information that was necessary regarding the study, a formal informed consent was also gathered from each patient.

Inclusion criteria: Participants in this trial were pregnant women who were attending the hospital between the ages of 10 and 28 weeks and had blood hemoglobin levels between 6.8 and 9.8 g/dl (considered to be moderate anemia). They also had to have been microscopically diagnosed with microcytic hypochromic anemia.

Exclusion criteria: We did not include pregnant ladies who satisfied the following criteria: low hemoglobin levels (less than 6.8 g/dl); severe concurrent illness (cardiovascular, renal, hepatic, or any other systemic disease); history of chronic inflammation (rheumatoid arthritis, gout, or any other systemic disease); patients with active internal bleeding (such as bleeding piles, peptic ulcer, or oesophageal varices); family history of thalassemia, sick

Outcome variables: In this particular experiment, the levels of serum ferritin and blood hemoglobin served as the outcome variables that were examined.

Sample size: In order to detect a difference of five percentage points in the percentage of patients getting normal hemoglobin level (>10 g/dl) by the 60th day of treatment using an alpha value of 0.05 and a power value of 75 percent , each group needs to have a minimum of twenty-five patients.

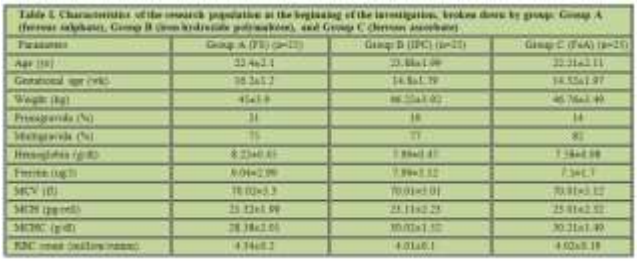
Randomization: The patients were randomly assigned to one of three groups—Group A, Group B, or Group C—using the numbers that were created. Tablets were given out to Group A. (containing 60 mg elemental iron should be taken twice daily). Folic acid tablets were also administered to the subjects during this trial (5 mg). The IPC tablets were administered to Group B. (Containing 100 mg elemental iron once daily and 0.50 mg folic acid must be taken once daily). Group C was given FeA 100 mg elemental iron and 1.5 mg folic acid per day. The same brand of iron and folic acid was given to all groups during the entirety of the course of the study. FS was obtained from a pharmacy that was located in a public hospital. These medications were provided at no cost to the patients. They were not being given any other medications or substances. The obstetrician made all of the decisions regarding the therapeutic regimen, without the investigator making any kind of contribution.

Lab Investigation: Hemoglobin and other parameters (MCV, MCH, MCHC) were measured at baseline (day 0) and periodically (days 30, 60 and 90). Blood reticulocyte count was assessed after one week of iron therapy (day 7) and serum ferritin levels were measured at the beginning and end of the trial (day 90).

RESULTS

167 patients were evaluated. Inclusion criteria were pregnant women with microcytic hypochromic anemia and hemoglobin levels between 6.8mg and 9.9 mg/dl (moderate anemia). Thirty-seven patients were eliminated because they declined (n=7) or did not match the inclusion criteria (n=24). The remaining 136 patients were randomly assigned to three groups after providing informed permission. Ferrous sulphate (FS), iron hydroxide polymaltose complex (IPC), and ferrous ascorbate (FS) were the three categories (FeA). 75 patients (25 from each group) completed the study and were assessed for findings .

Age, weight, gestational age, and baseline haematological parameters such hemoglobin concentration, serum ferritin, MCV, MCH, MCHC, and RBC count were equivalent between the three groups (Table I).On day 7, all study patients' reticulocyte counts were above 1.5%, indicating a favorable response to iron therapy. All three groups receiving FS, IPC, and FeA had higher hemoglobin levels on days 30, 60, and 90 than at baseline . At day 90, FS and FeA had different hemoglobin levels (P<0.05). The difference between FS and IPC and FeA and IPC at day 90 was not statistically significant .



Parameter	Group A (FS) (n=25)	Group B (IPC) (n=25)	Group C (FeA) (n=25)
Age (y)	22.4±2.1	23.88±3.09	22.21±2.11
Gestational age (wk)	38.2±3.2	34.8±3.79	34.52±3.97
Weight (kg)	45±1.9	46.22±3.02	46.76±3.49
Primigravida (%)	21	18	14
Multigravida (%)	75	77	82
Hemoglobin (g/dl)	8.23±0.85	7.89±0.87	7.58±0.98
Ferritin (ug/l)	8.04±2.99	7.89±3.32	7.3±3.7
MCV (fl)	78.02±3.3	79.01±3.01	79.01±3.32
MCH (pg/cell)	25.12±1.99	25.11±2.25	25.01±2.32
MCHC (g/dl)	28.38±2.05	30.02±1.32	30.21±1.89
RBC count (million/mm3)	4.34±0.2	4.01±0.1	4.02±0.18

Study groups	Day 0 (n=25)	Day 30 (n=25)	Day 60 (n=25)	Day 90 (n=25)
Group A - FS	7.42±0.01	8.28±0.51	9.11±0.59	10.01±0.58
Group B - IPC	7.19±0.84	8.38±0.68	9.21±0.01	10.44±0.32
Group C - FeA	7.59±0.08	8.45±0.81	9.34±0.08	10.2±0.11
F^*<0.05 hemoglobin levels				

DISCUSSION

In underdeveloped countries, IDA causes morbidity and mortality. It's the most frequent kind of anemia in pregnant Indian women and affects mother and baby. The Indian government and WHO suggest FS for the treatment of IDA, hence it's the most common iron preparation supplied to anemic pregnant women. FS is cheap and effective, but it often causes gastrointestinal side effects, reducing patient compliance. Several iron preparations claim to be more effective and tolerable than FS.

In this study, FS was compared to FeA and IPC. The increase in hemoglobin three groups were between 0.74 and 0.77 g/dl after one month and 1.56-1.74 after two months. Beutler E et al reported a 1.63-1.84 g/dl rise in hemoglobin after 75 days of iron treatment. This study employed ferrous fumarate and feredetate. Over the trial period, hemoglobin improved in all three groups. Hemoglobin rose most with FeA, then IPC, and least with FS.

By days 30 and 60, hemoglobin levels were equivalent across the three groups, however at day 90, FeA had a considerably greater level than FS (P<0.05). Rahman MM et al found a larger rise in hemoglobin with FeA than FS. In this investigation, there was no significant difference in mean hemoglobin levels between IPC and FS groups even at day

IPC produces a considerable boost in hemoglobin and related anemia indices in pregnant women with anemia, according to Tolkien Z et al. The dose and duration of iron therapy in the present study were similar to Haddad L et al. This study also measured serum ferritin levels as an indicator of body iron reserves. Serum ferritin levels were 8.62-8.84 ug/l, indicating low iron reserves. At day 90, serum ferritin was greatest in the FeA group, followed by IPC and FS, but the difference was not significant. Tolkien Z et al. found similar results. MCV, MCH, MCHC, and RBC count showed equivalent improvement across all groups, indicating improved iron status in anemic patients. All three iron salts improved anemia parameters and restored iron reserves relative to baseline.

Tolerability and compliance are equally crucial in treating IDA as bioavailability and efficacy of the iron salt. Epigastric pain, nausea, vomiting, constipation, diarrhoea, and stomach pain were prevalent. All three study groups experienced similar side effects, except for epigastric pain in the FS group. Previous investigations have demonstrated that FS is associated with a higher incidence of gastrointestinal side effects, although efforts to increase gastrointestinal tolerance with IPC and FeA have shown only minimal improvement . IPC, which contains iron in ferric form, causes less gastrointestinal side effects since it doesn't generate ROS20. In a trial of anemic pregnant women by Tolkien Z et al, IPC had fewer side effects and better compliance than FS. FeA has fewer side effects and better compliance than FS.

This modest experiment with 75 individuals needs a bigger sample size to further assess the efficacy and safety of iron preparations. A single- or double-blind research would have offered more useful information on drug safety than the open-label approach. Overall, FS, IPC, and FeA have equivalent efficacy in treating IDA of pregnancy, but IPC and FeA have fewer gastrointestinal side effects.

REFERENCES

1 Stevens GA, Finucane MM, De-Regil LM, et al. Global, regional, and national trends in hemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. Lancet Glob Health. 2013;1(1):e16–e25.

2 Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood. 2006;107(5):1747–1750.

3 CDC (1989) CDC criteria for anemia in children and childbearing-aged women. MMWR Morbidity and mortality weekly report.

4 WHO (2001) Iron deficiency anemia: assessment, prevention and control. WHO/NHD/01.3, Geneva. World Health Organization, Switzerland

5 WHO (2011) VMNIS. Hemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System, WHO, Geneva, World Health Organisation, Switerzerland

6 Daru J, Cooper NA, Khan KS. Systematic review of randomized trials of the effect of iron supplementation on iron stores and oxygen carrying capacity in pregnancy. Acta Obstet Gynecol Scand. 2016;95(3):270–279.

7 Malhotra P, Kumari S, Kumar R, et al. Prevalence of anemia in adult rural population of North India. J Assoc Phys India. 2004;52:18–20.

8 Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: A systematic review and meta-analysis. PLoS One 2015;

9 Haddad L, Hawkes C, Udomkesmalee E, et al. Global Nutrition Report 2016: From Promise to Impact: Ending Malnutrition by 2030. Washington: International Food Policy Research Institute; 2016.

10 Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. Am J Clin Nutr. 2016;103(2):495–504.

11 Murray-Kolb L (2012) Maternal mortality, child mortality, perinatal mortality, child cognition, and estimates of prevalence of anemia due to iron deficiency. CHERG

12 Breymann C. Iron deficiency anemia in pregnancy. Semin Hematol. 2015;52(4):339–347.

13 Milman N. Anemia–still a major health problem in many parts of the world! Ann Hematol. 2011;90(4):369–377.

14 Geng F, Mai X, Zhan J, et al. Impact of fetal-neonatal iron deficiency on recognition memory at 2 months of age. J Pediatr. 2015;167(6):1226–1232.

15 Congdon EL, Westerlund A, Algarin CR, et al. Iron deficiency in infancy is associated with altered neural correlates of recognition memory at 10 years. J Pediatr. 2012