Efficacy and tolerability of ferrous sulphate vs iron peptone + ferrous ascorbate in pregnancy:An observational study

Neha Mistry[1], Harsh Joshi[2], Shikha Sood[3,*], Sushma Shah[4], Supriya Malhotra[5]

[1]MBBS Student, [2]Junior Lecturer, [3]Professor, [4,5]Professor & HOD, [2,3,5]Dept. of Pharmacology, [4]Dept. of Obstetrics and Gynecology, Smt NHL Municipal Medical College and Seth VS General Hospital, Ahmedabad, Gujarat, India

***Corresponding Author:**Dr. Shikha Sood
Email: shikhavsood@gmail.com

Abstract

Introduction: Iron stores in pregnancy are essential in preventing negative outcomes for both infant and mother. The association of iron deficiency anemia (IDA) in pregnancy is high in spite of iron supplementation being in regular practice. The main signs and symptoms of IDA are fatigue, breathlessness, weakness, pallor and rapid heartbeat and the treatment to this is giving iron supplements. Intolerability of oral iron preparations results in decreased compliance. Tolerability is influenced by several factors – age, body mass, socioeconomic status (genetic variants).

Aims/Objectives : To compare the efficacy and tolerability of two iron preparations (oral); Iron Peptone + Ferrous Ascorbate (IP+FA) Vs Ferrous Sulphate in the treatment of IDA during pregnancy

Material and Methods: A prospective, observational, cross sectional study was conducted at the Department of Obstetrics and Gynecology, V.S. Hospital Ahmedabad, a tertiary care teaching hospital. Second and third trimester pregnant females diagnosed with anemia (Hb< 11gm/dl) were included in the study. Patients who were not willing to give informed consent were excluded from the study.

Results: We collected data of 59 Patients diagnosed with anemia (Hb between 7-10.9 gm/dl) , 35 women received ferrous sulfate and 23 were given IP+FA and both groups were followed up after 30 days. There was significant increase in hemoglobin in both the groups. The change in hemoglobin (Hb) of women receiving ferrous sulfate was 9.129±1.098 gm/dl with p value of 0.701 and those receiving IP+FA was 9.490±1.909 gm/dl with p value of 0.102. There was no significant difference in efficacy between the two treatment groups. Most common adverse drug reaction (ADR) during therapy were nausea (31.9%) , followed by constipation (27.6%) and heart burn (25.5%) patients. Other ADRs like metallic taste, vomiting, headache and epigastric pain were less common. IP+FA had more adverse drug reactions than patients receiving ferrous sulfate.

Conclusion: The efficacy of both iron preparations was found to be similar with patients receiving IP+FA having greater number of ADRs

Keywords: Iron deficiency anemia, Efficacy, Iron supplements, Tolerability

Introduction

Iron deficiency in the periconceptional period of pregnancy affects fetal development and mother's health.[1,2] According to WHO, more than 30% of the world's population is anemic, majority suffering from IDA.[3] The incidence of IDA in pregnancy is high even thoughiron supplementation is in regular practice. Intolerability of oral iron preparations results in decreased compliance. Tolerability is influenced by several factors e.g. age, body mass, socioeconomic status (genetic variants).[4] The main causes of iron deficiency are inadequate iron absorption or increased iron requirements and inadequate iron intake.[5]

Management of IDA involves two components; identifying and eradicating the cause of iron deficiency and correction of anemia. Correction mainly includes dietary improvement, oral iron supplementation and parenteral iron therapy.[6] The oral route is preferred to replace iron stores and treat mild to moderate IDA and for prophylaxis.[7] Whereas parenteral route is used to treat severe IDA, intolerance to oral iron preparations and malabsorption.[8]

Conventional oral iron preparations include ferrous sulphate, fumarate and succinate while newer preparations include ferrous ascorbate.[9] Newer preparations like iron sucrose and ferrous ascorbate are available and frequently prescribed with the consideration that they are better. Noncompliance is largely related to side effects. 10-40% patients suffer Gastrointestinal adverse effects e.g. constipation, diarrhea, epigastric discomfort, nausea, severe abdominal pain and vomiting. Gastrointestinal adverse effects can be as high as 70% in pregnancy.[10,11] They can be decreased by food but food decreases absorption by 10-40%.[12]

Oral iron is effective, safe, low cost but there may be failure in effectiveness due to noncompliance, achlorhydria, inflammatory bowel disease or unrecognized bleeding. The most widely used are ferrous salts; the use of these is limited by low and variable absorption, chelation by food products and free radical mediated mucosal luminal damage.[13] Ferric compounds do not have these disadvantages however they are generally less soluble at physiologic pH and precipitate intraluminally as hydroxide or phosphate and therefore have poor bioavailability. The Generic names of drugs used for treatment of iron deficiency are Cabonyl iron, Ferrous ammonium citrate, Ferrous fumarate, Ferrous gluconate, Ferumoxytol in patients of Chronic Kidney Disease, Lectoferrin, Ferric carboxy maltose, Ferrous sulphate, Ferrous ascorbate, Ferrous bisglycinate.

Patients who receive intravenous iron show significantly higher improvement in Hb and ferritin levels. Oral administration of Bovine lectoferrin (BLF) caused Hb and total serum iron values to increase to a greater extent than oral administration of ferrous sulphate in 30 days independent of the trimester of pregnancy.[14]

Pregnant anemic women should receive daily elemental iron about 120mg until their Hb rises to 11gm/dl. There after she can resume standard daily antenatal iron to prevent recurrence of anemia.[15] Ferrous bisglycinate in a dose of 25mg/day appears to be adequate to prevent IDA in more than 95% women during pregnancy.[16]

It is impossible in routine clinical practice to ensure compliance with oral iron tablets on a day to day basis, whereas intravenous iron therapy surmounts this problem of compliance completely. Efficacy and safety of intravenous Iron sucrose with daily oral ferrous Sulfate showed that Intravenous Iron sucrose corrects IDA during pregnancy more quickly than oral iron.[17]

Objective of the present study was to compare the efficacy and tolerability of two oral iron preparations; Iron peptone + Ferrous Ascorbate Vs Ferrous sulphate in the treatment of IDA in pregnancy.

Material and Methods

This prospective, observational, cross sectional study was conducted at the Department of Obstetrics and Gynecology at a tertiary care teaching hospital. The study began after the approval of Institutional Ethics Committee (IEC). Informed consent was obtained from all patients enrolled in the study. Patients attending Out Patient Department (OPD) and/or admitted in the ward of Obstetrics and gynecology department and who were diagnosed to suffer from anemia (Hb- < 11gm/dl) were included in the study. Patients who were not willing to give informed consent were excluded from the study. Patients with anemia underwent clinical and laboratory investigation (hemoglobin, red blood cell indices and/or Vitamin B12). The hematological reports were assessed by treating physician to decide treatment with oral iron preparations. Patients with hemoglobin between 7-10.9 (g/dL) were treated with oral iron preparations. Some patient (severe anemic) also went for Vit B12 assessment and their results were recorded. During follow up patients hematological status were assessed again and the difference in Hb was noted. Other adverse drug reactions were also noted.

The baseline data of the patients was recorded in a pretest case record form. Each patient was followed up after one month and assessed for clinical and hematological parameters and adverse drug reactions (ADRs). The data was recorded in Microsoft Excel Worksheet and analyzed by Fisher's exact test and paired't' test and unpaired 't' test with the help of GraphPad Prism 5.0 software. ANOVA and Pearson Chi square test were applied with the aid of statistical package for social science (SPSS software, version 24.0). $P < 0.05$ considered as statistically significant.

Treatment Groups

Active supplements were ferrous sulfate – 200mg, given orally twice daily. Second drug was Iron peptone – 10 mg + ferrous ascorbate – 90 mg, given orally once daily. 35 women received ferrous sulfate – 200mg,taken twice daily for 30 days and 23 were given IP + FA tablets, taking once daily for 30 days. All were requested for follow up after 30 days.

Results

Out of the total 59 patients majority of patients were in the age group of 21-25 years and were severely anemic. About 22% patients were of 15-20 years age group, 2.3% patient belonged to 31-35 years age group and 2.3% were above 35 years of age. The weight distribution of the patients is shown in Table 1.

Table 1: Weight Distribution among patients

Weight Range (Kgs)	Number of patients	Percentage %(n=59)
31 – 40	5	8.4
41 – 50	22	37.2
51 – 60	18	30.5
61 – 70	13	22
More than 70kg	1	1.6

The distribution of patients according to the trimester of pregnancy is shown in Table 2.

Table 2: Duration of pregnancy

Duration of Pregnancy (months)	Number of Patients	Percentage %(n=59)
2	1	1.6
3	4	6.7
4	7	11.8
5	20	33.8
6	21	35.5
7	3	5
8	3	5

Majority of patients were primigravida 31(52.5%); 28(47.5%) patients were multigravid.

There was significant increase in hemoglobin in both Ferrous sulphate and IP +FA groups. The change in hemoglobin levels in women receiving ferrous sulfate was 9.129 ±1.098 gm/dl with p value of 0.701 and in those receiving Iron peptone + ferrous ascorbate was 9.490 ± 1.909 gm/dl with p value of 0.102.(Fig. 1) This showed no significant difference in efficacy between the two treatment groups for IDA.

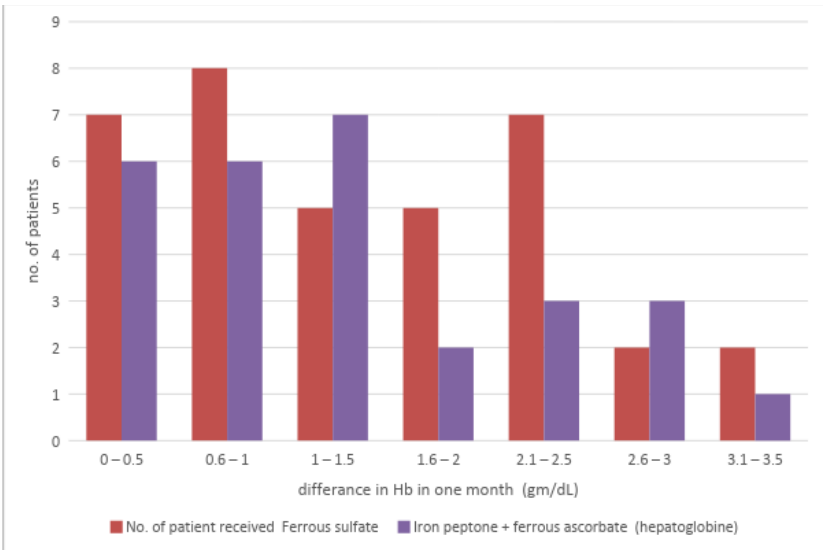

Fig. 1:Comparison of increase in Hb levels afterferrous sulfate and iron peptone + ferrous ascorbate treatment

Most common adverse drug reaction during treatment was nausea in 31.9% patients, followed by constipation (27.6%) and heart burn (25.5%) patients. Other adverse effects like metallic taste, vomiting, headache and epigastric pain were less common. IP + FA had more adverse drug reactions than patients receiving ferrous sulfate. (Table 3)

Table 3: Comparison of adverse effects of both drugs

Adverse Drug Reaction	Number of patients in Ferrous Sulphate Group	Number of patients in IP + FA Group	Total number of patients with ADR	Percentage	P value
Nausea	6	9	15	31.9	0.07
Constipation	5	8	13	27.6	0.12
Heart burn	9	3	12	25.5	0.02
Metallic taste	1	3	4	8.5	0.34
Headache	0	3	3	6.3	0.004
Epigastric pain	2	1	3	6.3	0.56
Vomiting	1	1	2	3.8	0.90

In comparing adverse effects between both groups P-value less than 0.05 was considered significant. So in this data p value of patient having headache with iron peptoneis 0.004 which becomes significant. P value in patients with heart burn with ferrous sulphate is 0.02, is also significant.

Discussion

In our literature search we did not find a head to head comparison of ferrous sulphate with Iron peptone + ferrous ascorbate in pregnancy; this prompted us to take up this study.

Our study was done at the Obstetrics and Gynecology department of a tertiary care teaching hospital. A total of 59 patients were included in the study. It was a prospective follow up observational study to compare the tolerability and efficacy of Ferrous Sulphate and Iron peptone + ferrous ascorbate in pregnancy.The age group of patients ranged from 15 to 35 years, majority was primigravida and in their second and third trimester of pregnancy. Iron preparations are generally not prescribed in the first trimester because iron is notorious for causing gastric irritation, most women already have a sensitive digestive system in first trimester.

Regarding Efficacy no significant difference was observed between the two treatment groups.This finding is similar to a study conducted at the department of Obstetrics and GynecologyatPGI Chandigarh where Ferrous sulphate was compared with Iron polymaltose complex; there was no difference in efficacy between ferrous sulphate and Iron polymaltose complex but adverse effects were more common in the Ferrous sulfate group (78%, P < .001).[18]

In our study greater number of ADRs were observed with IP + FA. Headache was significant with IP + FA and Heart burn was significant with Ferrous sulphate.

In a similar study efficacy and side effects of ferrous sulphate, fumarate, ascorbate, sodium feredetate and ferrous bisglycinate were comparedin the treatment of IDA in pregnancy. There was significant and comparable rise in hemoglobin on day 30 and day 60 in all the five groups. Ferrous ascorbate and ferrous

bisglycinate showed significantly more rise as compared to ferrous sulphate. Maximum side effects were with ferrous fumarate followed by ferrous sulphate, ferrous bisgylycinate, ascorbate and sodium feredetate.[19]

In a similar study oral ferrous aspartoglycinate and ferrous ascorbate were compared in pregnant women with IDA. A double blind, prospective, randomised, multicentre, parallel group comparative clinical study at three different centres in India was done. A total of 73 pregnant women at 12-26 weeks' gestation were divided into two arms. One group received ferrous ascorbate, second group received ferrous aspartoglycinate for a period of 28 days. The mean rise in haemoglobin and ferritin levels on day 14 and 28 was evaluated. At both time points, significantly higher levels of haemoglobin and ferritin were noticed with ferrous aspartoglycinate treatment as compared with ferrous ascorbate.[20]

In another study iron preparations were compared for efficacy and tolerability in normal population. This study had 4 Groups of patients. Group A were given oral liquid ferrous gluconate (75 mg per diem in 2 vials a day); Group B was given solid ferrous gluconate (80 mg per diem in a single effervescent tablet); Group C was given solid ferrous sulphate (105 mg per diem in a single tablet); and Group D was given ferric protein succinylate (80 mg per diem in 2 vials a day). All were given treatment for 30 days. Treatment efficacy was analysed by comparing basal and final parameters using the T-test for paired dependent samples. Analysis of the therapeutic efficacy parameters (red blood cells, hemoglobin, hematocrit and serum iron) showed significant improvements but no statistically significant differences between the groups. Group A with liquid ferrous gluconate was the best tolerated.[21]

In another study carried out at Amrita University, Kochi;Ferric ammonium citrate, ferrous sulphate, ferrous fumarate and ferrous calcium citrate were compared for efficacy and tolerability and no significant differences were observed between them both in efficacy and tolerability.[22]

Strengths of Study

1. This is a prospective study carried out at a tertiary care hospital.
2. Patient acceptability of drug was positive as the treatment was provided from our hospital and patients were of low socio economic status.
3. Estimation of Hemoglobin levels was taken as a primary efficacy end point since it is a rapid, inexpensive and specific test for assessment of IDA.

Limitations of Study

1. The optimal effect of iron intake would have been observed if there were more frequent follow up visits for a prolonged period of time. Unfortunately that could not be accomplished as patients were lost to follow up and authors could get follow up only after one month of initiation of therapy.
2. Serum ferritin could not be measured in all patients as it was not available at our center.

Conclusion

The present study was aimed to measure efficacy and tolerability of iron intake during pregnancy in patients of IDA. Ferrous sulfate and Iron peptone + ferrous ascorbate were most commonly used iron preparations at our center. Our results showed no significant differences in the efficacy in between the treatment groups for treating IDA. Various adverse drug effects were seen like nausea, vomiting and heart burn. Iron peptone + ferrous ascorbate had more adverse drug reactions than patients receiving ferrous sulfate.

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