



Comparative Study of Iron Supplements in South Indian Antenatal Women with Iron Deficiency Anemia

R. Geetha^{1*}, S. Rageshwari², S. Parvathavarthini³, K. R. Sowmia⁴, S. Priestly Vivekkumar⁵, Simhadri V. S. D. N. A. Nagesh⁶, A. Umamageswari⁷

^{1,2,3,4} Department of Pharmacology, Tagore Medical College and Hospital, Chennai, Tamil Nadu-600127, India.

*Corresponding author's E-mail: pharmacology@tagoremch.com

Article History	Abstract
Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 25 Nov 2023	<p>BACKGROUND: Iron deficiency anemia is the most common nutritional disorder in the world. It is a major public health problem particularly among pregnant women with adverse effects on the mother and the new born. Iron supplementation is universally recommended to correct or prevent iron deficiency. AIMS & OBJECTIVE: The present study was conducted to compare the efficacy and tolerability of three oral iron preparations in anemic pregnant women of more than 14 weeks of gestation. MATERIALS AND METHODS: Randomized Control trial, done at Tagore Medical College and Hospital, Chennai. 60 antenatal women were selected; they were divided into three groups, 20 in each group. They were treated with Carbonyl iron, ferrous sulphate and ferrous fumarate. Hemoglobin estimation was done at 0 day, 30th and 60th day. Adverse effects were monitored. RESULTS: Data analysis showed an increase in haemoglobin levels in all three groups after the 30th day ($p < 0.05$). Carbonyl iron showed highly significant increase ($p < 0.05$) in the haemoglobin level as compared to the other two drugs at the end of the 60th day. CONCLUSION: Carbonyl iron is superior in efficacy when compared to ferrous sulphate and ferrous fumarate and is better tolerated. So carbonyl iron is safe in pregnancy and can be given as a supplement to treat iron deficiency anemia during pregnancy.</p>
CC License CC-BY-NC-SA 4.0	Keywords: Antenatal women, carbonyl iron, iron deficiency anemia.

1. Introduction

Anemia is a global public health problem. In pregnant women anemia is due to iron deficiency, which is the most common nutrient deficiency in the world. According to WHO data, prevalence of anemia in pregnant women is 14% in developed countries and 51% in developing countries.[1] In India the prevalence of anemia is 65-75% in pregnant women, this high prevalence is due to poor socioeconomic status, dietary habits, poor health status, multi parity and less birth spacing. 20% of all maternal deaths are contributed to anemia.[2,3]

Anemia is defined as a qualitative or quantitative deficiency of circulating haemoglobin, leading to decreased oxygen carrying capacity of the red blood cells to the tissues.[4] It is divided into three degrees, mild (10.9-9.0 gm %), moderate (8.9-7.0 gm %) and severe (<7.0 gm %).[5]

During pregnancy, women go through a variety of physiological changes especially in the blood circulatory system. Average iron requirement is 4 mg/ day throughout pregnancy; this varies from 2.5 mg/day in early pregnancy to 6-8 mg/day from 32 weeks onwards. Iron deficiency anemia occurs because of the increased iron requirements that are needed to supply the expanding blood volume of the mother and the rapidly growing fetus and placenta.

Iron absorption in food is less than 10%, this requires at least 40-60 mg of iron in the diet to achieve 4-6 mg of absorption and if the pre pregnancy iron stores are low then the amount of iron needed during the last half of the pregnancy cannot be met with diet alone.[6,7]

Iron deficiency anemia during pregnancy has been associated with preterm delivery, perinatal mortality, maternal postpartum depression and impaired mental development and cognitive ability of the offspring.[8] So iron supplementation is considered as mandatory to improve the iron status of the mother during pregnancy.[9] Ministry of Health, Government of India recommends 200 mg of elemental iron with 1mg folic acid in the second half of pregnancy for a period of 100 days.

A wide variety of oral iron preparations are available. As ferrous iron is most efficiently absorbed, ferrous salts like ferrous sulphate, ferrous fumarate and ferrous gluconate are commonly used. Carbonyl Iron is a pure form of elemental iron which was mainly used for the fortification of foods. Carbonyl does not refer to the composition of iron particles but rather to the manufacturing process in which the controlled heating of vaporized iron pentacarbonyl leads to the deposition of uncharged elemental iron as microscopic spheres of $< 5 \mu$ in diameter.[10]

A comparative study on iron supplements is a must to find out the best drug for improving anemia and also necessary to compare their tolerability, as this influences the patient compliance and the therapeutic outcome. Our study is the only study where 2 conventional iron supplements (ferrous sulphate, ferrous fumarate) are compared with a newer iron supplement (carbonyl iron) in the antenatal women of South Indian population..

2. Materials and Methods

This study was an Experimental study - Randomized Control trial, done in the Outpatient Department - Antenatal Clinic of Tagore Medical College and Hospital, Chennai. The study was started after obtaining approval from the Institution Ethics Committee of Tagore Medical College and Hospital, Chennai.

Pregnant women between 20 to 40 years of age with more than 14 weeks of gestation and serum hemoglobin levels between 9 - 11gm/dl were included in the study. Pregnant women of less than 14 weeks of gestation, hemoglobin levels less than 9gm/dl, Patients with complications like bleeding piles, excessive emesis, active peptic ulcer, diabetes, hypertension, eclampsia, hypothyroidism and hyperthyroidism, patients not willing to sign written informed consent, those with history of oral iron intolerance and Multiple pregnancy were excluded from the study.

65 antenatal women were screened, 5 patients were excluded as they were not willing to sign the written informed consent forms. 60 antenatal women were enrolled as per selection criteria. The purpose, procedure and benefits of the study were explained in detail to the participants and then written informed consent was obtained in their own language.

They were randomly allocated into 3 groups with 20 antenatal women in each group. Group A received Carbonyl Iron 100 mg once daily, Group B received ferrous sulphate 200 mg thrice daily and Group C received Ferrous fumarate 200 mg twice daily for a period of 60 days.

A preformed open ended questionnaire was given to evaluate their nutritional status and tolerability to the given iron supplements. The following details were obtained, regarding - age, occupation, educational status, anthropometric measurements, diet history, gestational age, method of contraception used, previous obstetric history i.e., Type of delivery (normal or caesarean), number of abortions, duration between this pregnancy and the last one. Also baseline haemoglobin status and side effects to the iron supplements given were noted.

Before start of the study random blood sugar, urine routine and stool for ova, cyst and occult blood were done for all the participants.

Haemoglobin estimation was done on day 0, 30th and 60th day after enrolment. The patients were advised to take iron rich foods like jaggery, liver, egg yolk, dry fruits, green leafy vegetables, cereals and sprouted pulses.

At each follow up visit, the patients were subjected to general and obstetric examination, compliance was checked by verbal inquiry. Verification was done by checking the empty packets of the drugs brought by the participants of the study. The patients were noted for their improvement and enquired about any drug induced side effects.

Efficacy evaluation was done by estimating hemoglobin at baseline, 30th day and 60th day of the treatment. Primary efficacy variable was rise in hemoglobin levels at the end of the therapy, analyzed on Coulter Cell Counter. Clinical safety was evaluated based upon the nature and severity of adverse effects if any, recorded at baseline, 30th day and 60th day of the treatment.

Statistical Analysis:

The data obtained at the end of the study was analyzed using SPSS vs 20 software. The hemoglobin values are given in mean and standard deviation. One way ANOVA was done to compare the baseline hemoglobin percentage values of all 3 groups. Repeat measures ANOVA was performed separately for each group.

Mixed repeated measure ANOVA was done for the comparison among the 3 groups for three different time intervals. Chi-square test was used to analyze adverse drug reactions of patients in all three groups. p value of <0.05 was considered as the level of significance.

3. Results and Discussion

This study was an experimental study - Randomized Control trial, done in the Outpatient department - Antenatal clinic of Tagore Medical College and Hospital, Chennai. 60 antenatal women were enrolled as per the selection criteria; these women were randomly divided into 3 groups.

Each group was administered with three different iron supplements carbonyl iron, ferrous sulphate and ferrous fumarate for a period of 60 days. Hemoglobin estimation was done at baseline, 30th day and 60th day. The baseline hemoglobin values did not differ significantly at the beginning of the study in all the 3 groups (p > 0.05).

TABLE 1: Hemoglobin (gm %) of the patients at baseline and during the study period in the treatment groups

Group	Drugs	Haemoglobin (gm%)						p value
		Baseline 0 day		30 th day		60 th day		
		MEAN	SD	MEAN	SD	MEAN	SD	
A (n=20)	Carbonyl Iron	8.62	0.74	10.52	0.68	11.8	0.60	<0.05
B (n=20)	Ferrous Sulphate	9.12	0.66	10.00	0.77	10.53	0.76	<0.05
C (n=20)	Ferrous Fumarate	8.63	0.94	9.60	0.96	10.44	0.98	<0.05

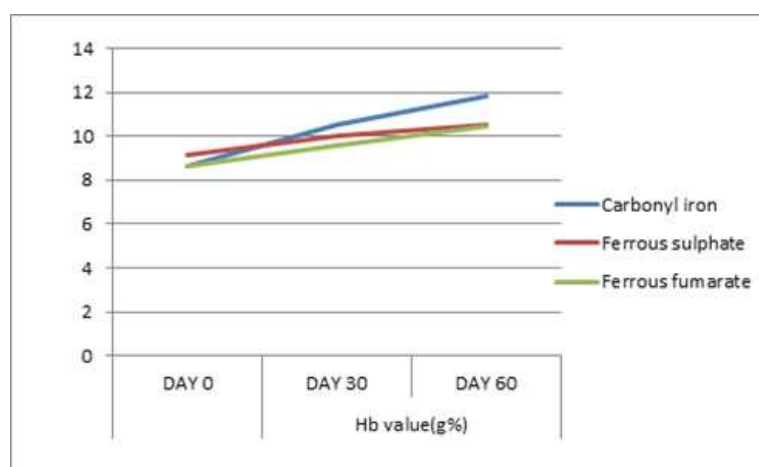


Figure 1: Shows the diagrammatic representation of the Hemoglobin (gm %) of the patients at baseline and during the study period in the treatment groups.

The table 1 shows hemoglobin percentage (gm %) of the patients at baseline and during the study period in the treatment groups. The improvement in the haemoglobin levels at the end of 2 months was significant (p < 0.05) for all the three treatment groups. One way ANOVA was done to find the differences in the mean hemoglobin levels between the three groups at the end of the 60th day and was found to be highly significant (p<0.001).

However, the Post Hoc Tukey HSD test showed that there was no significant difference between the mean hemoglobin values of patients receiving ferrous sulphate and ferrous fumarate (p>0.05) as compared to the patients receiving carbonyl iron who had significant difference with other two groups.

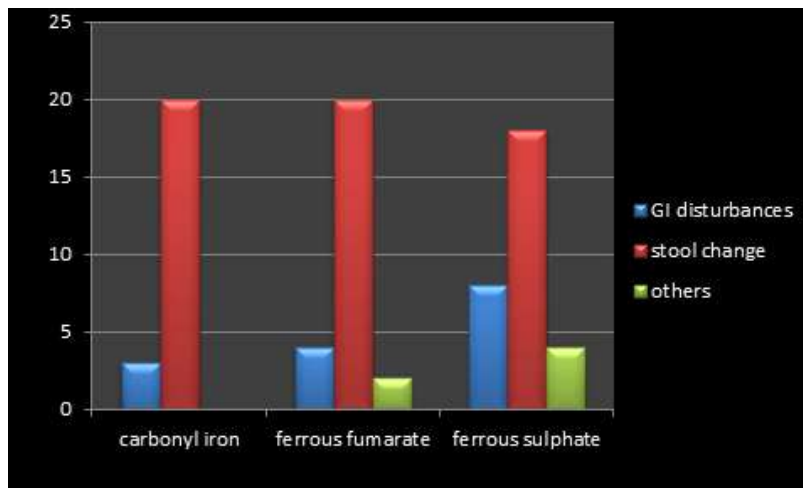


Figure 2: Shows the side effects that occurred in the antenatal women during the study period.

Side effects were mainly black stools which were seen equally in all the three groups during the treatment period. Gastro Intestinal disturbances were somewhat lesser in group A, who received carbonyl iron, as compared to the group B and group C who received ferrous sulphate and ferrous fumarate respectively. Other complaints like headache was seen in one patient of group B, complaints of metallic taste were observed in one patient belonging to group B and group C respectively.

Iron deficiency anemia in pregnancy is associated with greater risk of perinatal mortality and morbidity [11], low birth weight leading to preterm delivery [12] and lower infant APGAR scores.[13] Since dietary absorption cannot keep up with the increased iron demands during pregnancy, it is mandatory to recommend oral iron supplements in the latter half of the pregnancy.

Various iron salts are available. Ferrous sulphate (32% elemental iron) and ferrous fumarate (33% elemental iron) are the commonly used iron preparations. Carbonyl Iron is a newer oral iron preparation which was mainly used for the fortification of foods.

This study was an experimental study - Randomized Control trial. 60 antenatal women were enrolled as per the selection criteria; they were randomly divided into 3 groups, 20 in each group. Group-A received carbonyl iron, Group-B received ferrous sulphate and Group- C received ferrous fumarate. This study was done for a period of 60 days for each patient.

All 60 patients completed the study. Haemoglobin levels were estimated at baseline, on 30th and 60th day after therapy, in order to assess the efficacy of the iron supplements in improving the degree of anemia.

Mild reticulocytosis usually begins within four to seven days of giving the iron supplements and peaks at 1 ½ weeks. In our study, increase in mean haemoglobin levels was seen after the 30th day in all 3 groups. At the end of the 60th day, the mean haemoglobin increase in the Carbonyl iron group was 3.2 gm% as compared with the ferrous sulphate and ferrous fumarate group which showed a mean increase in hemoglobin by 1.4gm% and 1.8 gm% respectively.

After 60 days when the final values in the treatment group were compared with their respective baseline values, the improvement in the haemoglobin percentage (gm %) was significant ($p < 0.05$) for all the three treatment groups. Similar results were observed in the study conducted by N. Chandrika and KC Vasudha.[14]

In our study about 90% of the patients in the Carbonyl iron group achieved the WHO target of 11 gm% as compared to the ferrous sulphate group where only 20% and the ferrous fumarate group where 35% of the patients were able to achieve the WHO target.

In the study conducted by Sagaonkar Smita et al., the increase in hemoglobin level was more in ferrous fumarate group as compared to the carbonyl iron group, also the percentage of patients reporting constipation and diarrhoea were more in the carbonyl iron.[15]

This finding was contradicted by our study, as carbonyl iron showed highly significant increase in hemoglobin levels and better gastric tolerance as compared to the other two groups. Similar observations were reported by Gordeuk V R et al.[16]

Devasthali et al. compared ferrous sulphate and carbonyl iron in healthy blood donors and found that the overall bioavailability of carbonyl iron was 70% more than that of ferrous sulphate.[17] Study

conducted by Gordeuk et al. showed that patients with mild Iron Deficiency Anemia, can correct anemia and rebuild iron stores with short course of carbonyl iron.[18]

The observations made in the above mentioned studies and the results of the present study suggest that carbonyl iron is effective in the treatment of iron deficiency anemia in pregnant women as compared to the conventional preparations. Limitations to our study were inability to do tests like estimation of serum iron, total iron binding capacity and serum ferritin levels due to cost factor.

These tests would have given us accurate information in assessing the effectiveness of the therapy.

For an anemia free pregnancy, the patient should be advised to attend the antenatal clinic regularly. Nutrition and health education should be encouraged during antenatal care. The patients should be encouraged to take iron supplements along with iron rich foods like jaggery, green leafy vegetables, liver, honey, dates, as the combination increases the Haemoglobin level faster.

4. Conclusion

Carbonyl iron showed highly significant increase in the haemoglobin level. It is superior in efficacy when compared to other two drugs and is better tolerated. So carbonyl iron is safe in pregnancy and can be given as a supplement to treat iron deficiency anemia during pregnancy.

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