

**Original article:**

## **Comparative study of iron supplements: Its efficacy and tolerability**

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### **Abstract**

**Introduction:** Increased iron requirements to supply the expanding blood volume of the mother and the rapidly growing fetus and placenta can cause iron deficiency anemia. Plenty of oral iron formulations are available. A comparative study was planned to find out the best oral iron supplement for improving iron deficiency anemia in pregnant females as well as to compare their tolerability, as this ultimately influences the patient compliance and the therapeutic outcome. In present study, 2 conventional marketed formulation (ferrous sulphate, ferrous fumarate) are compared with a newer iron supplement (carbonyl iron) in the antenatal women for correction of anemia of pregnancy.

**Materials and methods:** 90 Pregnant women between 20 to 40 years of gestational age 14-20 weeks (judged by ultrasonographic and clinical inspection) and serum hemoglobin (Hb) levels between 9 - 11gm/dl were included to participate in study. 3 groups of 30 participants each were formed. Group A participants received Carbonyl Iron formulation 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 2 months.

**Results:** Increase in Hb levels at the end of 2 months therapy was significant ( $p < 0.05$ ) for all the 3 groups. Differences in the mean hemoglobin levels between the 3 groups at the end of therapy of 2 months showed statistically significant difference ( $p < 0.05$ ). However, no significant difference was found between the mean Hb values of patients receiving ferrous sulphate and ferrous fumarate ( $p > 0.05$ ) as compared to carbonyl iron receiving patients who had significant difference with other two groups.

**Conclusion:** Carbonyl iron is effective in the treatment of iron deficiency anemia in pregnant women as compared to the conventional iron formulations because of its superior efficacy in elevating haemoglobin levels as well as it is better tolerated than other iron formulations.

**Key Words:** Antenatal women, carbonyl iron, hemoglobin concentration, iron deficiency anemia

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### **Introduction**

Incidence of iron deficiency anemia (IDA) is being particularly high in many underdeveloped tropical countries like India where it remains a major contributing factor to maternal morbidity and mortality and also high perinatal mortality.<sup>1</sup> Iron deficiency is commonest cause of anaemia in pregnant women. According to WHO datasheet, prevalence of anemia in pregnant women is 51% in developing countries.<sup>2</sup> In India the prevalence is more towards higher levels around 65-

75% in pregnant women, this can be attributed to poor socioeconomic status, poor health status, dietary habits, less birth spacing and multi parity.<sup>3</sup>

The requirements of iron increase during pregnancy, as in the third trimester, a pregnant woman needs six times more iron than a nonpregnant woman. Increased iron requirements to supply the expanding blood volume of the mother and the rapidly growing fetus and placenta can cause IDA.<sup>4</sup> WHO recommends a hemoglobin concentration value of a minimum 11.0 gm% during pregnancy.<sup>5</sup> Maternal iron

deficiency anemia early in pregnancy can result in low birth weight subsequent to preterm delivery as well as association exists between maternal anemia and lower infant apgar score. Therefore, iron supplementation is mandatory to improve or maintain the iron status of the mother during pregnancy.<sup>6-8</sup> 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.

Plenty of oral iron preparations are available. Iron salts like ferrous sulphate, ferrous fumarate and ferrous gluconate are extensively prescribed for the prevention and treatment of iron deficiency. Carbonyl Iron is a pure form of elemental iron which was mainly used for the fortification of foods.<sup>9</sup> Bioavailability of iron supplements increases with the increasing dose, with ferrous fumarate having high bioavailability.<sup>10</sup> However, gastrointestinal disturbances like nausea, epigastric pain and constipation are commonly associated with ingestion of iron salts. Food and chelating drugs in the gastrointestinal tract may interfere with rate of absorption and decrease the bioavailability of iron.<sup>11</sup> This leads to variability in the Hb correction during anemia in pregnancy.

Therefore, a comparative study was planned to find out the best oral iron supplement for improving iron deficiency anemia in pregnant females as well as to compare their tolerability, as this ultimately influences the patient compliance and the therapeutic outcome. In present study, 2 conventional marketed formulations (ferrous sulphate, ferrous fumarate) are compared with a newer iron supplement (carbonyl iron) in the antenatal women for correction of anemia of pregnancy.

#### **Materials and methods**

A Randomized Control trial was conducted in the

Outpatient Department - Antenatal Clinic of MediCiti institute of medical sciences, Telangana, India. Ethical approval was obtained from institutional ethics committee prior to initiate study.

Pregnant women between 20 to 40 years of gestational age 14-20 weeks (judged by ultrasonographic and clinical inspection) and serum hemoglobin (Hb) levels between 9 - 11gm/dl were included to participate in study. Exclusion criteria was pregnant women of less than 14 weeks of gestation, Hb < 9gm/dl, Patients with complications like excessive emesis, peptic ulcer, diabetes, hypertension, eclampsia, Thyroid disorders, patients not willing to participate, history of oral iron intolerance and multigravida.

90 antenatal women were enrolled to participate in study. Written informed consent was taken prior to initiate trial from participants. 3 groups of 30 participants each were formed. Group A participants received Carbonyl Iron formulation 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 2 months.

Prior to study, information regarding - age, occupation, Educational status, anthropometric measurements, diet history, gestational age, previous obstetric history were obtained. Also baseline Hb status and side effects to the iron supplements given were noted. Routine blood and urine examination was done. Haemoglobin estimation was done on day 0, 30<sup>th</sup> and 60<sup>th</sup> day after enrolment. 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. The data obtained at the end of the study was analyzed using

SPSS vs 19software. The hemoglobin values are given in mean and standard deviation. ANOVA test was done to compare the baseline hemoglobin percentage values of all 3 groups and for the comparison among the 3 groups for three different

time intervals. Chi-square test was applied to analyze adverse drug reactions of patients in all three groups. p value of <0.05 was considered as the level of significance.

**Results**

Table 1: Hemoglobin percentage (gm %) at baseline and during the study period

Group	Drugs	Baseline 0 day		30 <sup>th</sup> day		60 <sup>th</sup> day		p value
		MEAN	SD	MEAN	SD	MEAN	SD	
A (n=30)	Ferrous Sulphate	8.89	0.63	9.68	0.74	10.21	0.73	<0.05
B (n=30)	Ferrous Fumarate	8.43	0.89	9.12	0.87	10.03	0.91	<0.05
C (n=30)	Carbonyl Iron	8.69	0.77	10.31	0.71	11.67	0.68	<0.05

The baseline hemoglobin values showed no significant difference at baseline in all the 3 groups. Increase in Hb levels at the end of 2 months therapy was significant (p < 0.05) for all the 3 groups. Differences in the mean hemoglobin levels between the 3 groups at the end of therapy of 2 months showed statistically significant difference (p<0.05). However, no significant difference was found between the mean Hb values of patients receiving ferrous sulphate and ferrous fumarate (p>0.05) as compared to carbonyl iron receiving patients who had significant difference with other two groups.

Side effects were mainly gastrointestinal disturbance nausea, black stools which were associated with consumption of all 3 iron supplements. Gastro Intestinal disturbances were somewhat lesser in patients who received carbonyl iron, as compared to the others.

**Discussion**

Dietary absorption of iron cannot keep up with the increased iron demands during pregnancy responsible for iron deficiency during pregnancy. So, it is

mandatory to recommend oral iron formulations in the latter half of the pregnancy. To obtain an adequate iron store of body, the women should make modification in their diet and should take iron rich foods. Although, this practice is unable to achieve considerable iron store in body because duration of gestation is too short and the benefit of modification of diet is too limited to reduce incidence of IDA during pregnancy. Dietary iron is unable to fulfill iron requirements most of the time during pregnancy, so, it is necessary to advocate oral iron formulations to women with iron stores <500 mg or serum ferritin <70µg/L. <sup>12</sup>Ferrous sulphate (32% elemental iron) and ferrous fumarate (33% elemental iron) are the commonly marketed iron supplements. Carbonyl Iron is a newer one, an oral iron preparation which was mainly used for the fortification of foods.

Effect is seen as mild reticulocytosis in patients that usually begins within 4-7 days of giving the iron supplements and peaks at 10 day. In present study, increase in mean Hb levels was seen after the one month in all 3 groups. At the end of the 2 month, the mean Hb increase in the Carbonyl iron group was

2.98 gm% as compared with the ferrous sulphate and ferrous fumarate group which showed a mean increase in hemoglobin by 1.32gm% and 1.6 gm% respectively.

Differences in the mean hemoglobin levels between the 3 groups at the end of therapy of 2 months showed statistically significant difference ( $p < 0.05$ ). This finding was in accordance of study done by few researchers in past.<sup>13-14</sup> However Sagaonkar Smita et al. found more elevation in Hb levels in ferrous fumarate group as compared to the carbonyl iron group, also the percentage of patients reporting gastrointestinal disturbances like constipation and diarrhoea were more in the carbonyl iron.<sup>15</sup> However in present study, it was seen that carbonyl iron exhibit better gastric tolerance as compared to the other iron formulations. Devasthali et al. found that the overall bioavailability of carbonyl iron was 70% more than that of ferrous sulphate.<sup>16</sup> Gorduek et al. stated that patients with mild IDA, can correct anemia and rebuild iron stores with short course of carbonyl iron.<sup>17</sup> Therefore present study concludes that carbonyl iron is effective in the treatment of IDA in pregnant women

as compared to the conventional iron formulations.

Ferrous sulphate is the oldest form of oral iron supplement used to treat IDA. When given on an empty stomach, side effects like epigastric pain, nausea, vomiting and diarrhea may occur, which are relieved to a certain extent when administered after meals.<sup>18</sup> Carbonyl iron is highly purified small metallic iron particle. Carbonyl describes the process of manufacture of the iron particles, not their composition. Heating gaseous iron pentacarbonyl  $[\text{Fe}(\text{CO})_5]$ , deposits metallic iron as sub-microscopic crystals that form spheres of less than 5  $\mu\text{m}$  in diameter. Solubilisation of carbonyl iron particles by acidity of stomach is a pre-requisite for absorption of carbonyl iron supplement. The slow rate of solubilisation leads to more prolonged absorption which is responsible for low toxicity.<sup>19</sup>

### Conclusion

Carbonyl iron is effective in the treatment of iron deficiency anemia in pregnant women as compared to the conventional iron formulations because of its superior efficacy in elevating haemoglobin levels as well as it is better tolerated than other iron formulations.

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