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Examination and Contrast the Adverse Effect Profiles of Various Iron Preparations

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ABSTRACT:

Background: Iron deficiency is the most widespread single dietary deficit in the world,1 affecting more than a third (more than 2 billion) of the worldwide population. 2 As a result of their increased iron needs, pregnant women are especially prone to iron deficiency and iron-deficiency anaemia. In underdeveloped nations, the prevalence of iron-deficiency anaemia in pregnant women ranges from 35 to 75% (mean: 56%), whereas it averages 18% in prosperous nations. 3, 4 India reports an incidence rate of 87% in Central Asia, where the incidence rate is quite high. An estimated ninety percent of cases of anaemia in India are attributable to iron deficiency. **Aim's & Objectives**: To study and compare adverse effect profile of various iron preparations prescribed. **Materials & Methods:** The study protocol was submitted to the Institutional Ethics Committee (IEC) for review and approval. After receiving approval from the appropriate authorities, the study was conducted on 120 pregnant women between the ages of 18 and 35 who attended the antenatal clinic at Santosh Medical College and Hospital in Ghaziabad. The research was done over the course of one year, from 11 August 2011 to 12 July 2012. **Results:** Compliance with Ferrous ascorbate was much greater at 73% compared to compliance with Ferrous fumarate (61.7%) and Carbonyl iron (55.4%). The incidence of adverse effects associated with oral iron preparations was 54.4% overall. These differences were statistically significant. The group with the highest occurrence was Carbonyl iron (61.5%), followed by Ferrous fumarate (57.6%) and Ferrous ascorbate (45.6%). **Conclusion:** This study was conducted to evaluate the efficacy, safety, and tolerability of three iron preparations: ferrous fumarate, ferrous ascorbate, and carbonyl iron. The traditional and economical iron preparation is ferrous fumarate. Ferrous ascorbate and Carbonyl iron are two novel iron preparations that are purportedly more effective and have a better tolerability profile than classic iron preparations, Ferrous sulphate and Ferrous fumarate.

Keywords*:* Pregnancy, Physiologic, Adaptation, Hematopoietic

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INTRODUCTION:

Iron insufficiency is the most prevalent single dietary deficiency in the world, impacting over one-third (nearly 2 billion) of the global population. [2] Pregnant women are particularly susceptible to iron shortage and iron-deficiency anaemia due to their increased iron requirements. In impoverished countries, the prevalence of iron-deficiency anaemia in pregnant women is reported to range from 35 to 75% (mean: 56%), but in affluent nations, the prevalence averages 18%. 3, 4 The frequency is extremely high in Central Asia, with India reporting a rate of 87%. An estimated 90 percent of anaemia occurrences in India are attributed to iron deficiency. [5,6]

During their reproductive years, women in India and other underdeveloped nations are always in a state of iron deficiency. Their iron stores are underdeveloped as a result of poor diet, dietary habits, frequent illnesses, menstrual blood loss, and several pregnancies. Thus, the ordinary Indian woman approaches her reproductive years, and especially pregnancy, deficient in iron and folate. [7-11] The risk of developing iron deficiency anaemia is greatest during pregnancy because iron requirements are significantly higher than the average absorbable iron intake. Frequent occurrence of iron deficiency anaemia during pregnancy indicates that physiologic adaptations are frequently insufficient to meet the increased demands, and iron stores are inadequate to meet the increased iron requirements for red blood cell mass expansion in the mother, as well as for the development of the foetus and placenta. [12-14]

The greatest concern with anaemia during pregnancy is the potential for severe effects on both mother and foetus. With rising anaemia severity, maternal morbidity and death increase progressively. In India, 20% of all maternal deaths are related to anaemia during pregnancy, and anaemia contributes to another 20% of maternal mortality. [17-19] It is believed that anaemia contributes to a ninefold increased risk of perinatal death. [16] During pregnancy, iron deficiency anaemia has been related with an increased risk of low birth weight, premature delivery, and perinatal mortality. [15]

In regions where the prevalence of anaemia in pregnancy is 40%, the World Health Organization suggests supplementing the diet with 60 mg of elemental iron and 400 g of folic acid daily for six months throughout pregnancy. In regions where the prevalence of anaemia in pregnancy is 40%, the same dosages are recommended for 6 months during pregnancy and 3 months after delivery. 9 In certain impoverished nations, however, oral iron doses as high as 240 mg per day have been utilised, but in many affluent nations 30 mg of elemental iron is suggested per day.

Patients do not always respond satisfactorily to oral iron therapy, however, because to noncompliance caused by side effects. Approximately 6–12% of people using iron preparations experience gastrointestinal problems characterised by colicky abdominal discomfort, nausea, vomiting, diarrhoea, and gastric distress. [24] Comparing the efficacy, tolerability, and compliance of novel iron preparations (ferrous ascorbate and carbonyl iron)

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with a classic iron preparation (ferrous sulphate or fumarate) in pregnant women was the purpose of the present study. Due to the unavailability of ferrous sulphate tablets containing 50 mg or 100 mg of elemental iron in India, the tablet containing 60 mg of elemental iron had to be administered twice daily in order to compare its efficacy with that of other iron preparations. However, because twice-daily dosing would be a factor in poor compliance, ferrous sulphate was excluded from the study. Therefore, Ferrous fumarate, which is nearly identical to ferrous sulphate in terms of efficacy and side effect profile, was included in the trial to compare with some newer oral iron treatments.

METHODS & MATERIALS:

The study protocol was submitted to the Institutional Ethics Committee (IEC) for review and approval. After receiving approval from the appropriate authorities, the study was conducted on 120 pregnant women between the ages of 18 and 35 who attended the antenatal clinic at Santosh Medical College and Hospital in Ghaziabad. The study was done for one year, from August 11 to July 12. It was a prospective, randomised, parallel group, single-center, 12-week study with an open label. The individuals were randomly separated into subgroups based on the prescription iron supplements. The trial lasted for a total of 12 weeks.

Prior to enrollment and screening, all patients involved in the trial provided written informed consent. A thorough history was gathered and a physical examination was performed in accordance with a format that had been tested and prepared for the purpose.

All eligible women who granted informed consent were sequentially enrolled and assigned randomly to one of three groups (A, B, or C) using a randomization table. Ferrous fumarate, 300 mg tablet, comprising 100 mg elemental iron (Tab. Steadifer, Steadfast Pharma; 1 tablet orally once daily) was administered to Group A, while Group B received [24]. Ferrous ascorbate, 100mg elemental iron (Tab. Ferricip-XT, Cipla Pharma; 1 tablet orally once daily), and Carbonyl Iron, 100mg elemental iron (Tab. Carbonyl Iron, Cipla Pharma; 1 tablet orally once daily) (Cap. Carbol-FZ, Gopal Pharma; 1 capsule orally once daily).

One-way ANOVA with post-hoc Student-Newman-Keuls was used to examine quantitative data. Multiple comparison for within-group analysis and two-tailed student's test Paired t-test for comparisons between groups. p-values 0.05 were regarded as significant. Mean, standard deviation, and standard error were determined when relevant. The parameters were described using Mean Standard Deviation and/or percentages.

The Plain vial samples were centrifuged for 10 minutes and the serum separated and stored at –20ºC till the assay was performed. The assay was performed as per the manufacturer's instructions. 101

PRINCIPLE: Serum ferritin was estimated by micro ELISA technique using human ferritin enzyme immunoassay test kit, which uses a solid phase enzyme linked immuno-sorbent assay technique. The assay is based upon microplate, coated with highly specific anti-human ferritin antibodies.

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During this procedure the binding of the analyte as well as formation of the sandwich complex and enzymatic color reaction takes place during three different reaction phases.

Quantitative data was analyzed using one-way ANOVA with post-hoc Student-Newman-Keuls Multiple comparison for within the group analysis and student's two-tailed Paired t-test for between the group comparisons. p-value < 0.05 was considered significant. Mean, SD and SE were calculated wherever applicable. The parameters were described in terms of Mean ± SD and/or percentages.

RESULTS:

Table 1: Effect of oral iron formulations on hemoglobin levels (mean ± sd in g/dl)

Group	Study Period			p - value		
	0 weeks	6 weeks	12 weeks	0-6	6-12	0-12
A	10.07 ± 1.53	10.53 ± 1.39	11.12 ± 1.26	NS	NS	p<0.05
B	10.00 ± 1.26	10.79 ± 1.11	11.78 ± 0.82	p<0.05	p<0.01	p<0.001
C	10.48 ± 1.33	10.90 ± 1.25	11.28 ± 1.27	NS	NS	NS

Table 2: Effect of Different Oral Iron Formulations On Pcv (Mean ± Sd In %)

Group	Study-Period			p - value		
	0 weeks	6 weeks	12 weeks	0-6	6-12	0-12
A	33.71 ± 4.38	35.54 ± 3.65	37.59 ± 3.46	NS	NS	p <0.001
B	32.33 ± 4.13	35.42 ± 3.33	38.17 ± 3.41	p<0.01	p<0.05	p<0.001
C	33.34 ± 3.85	36.06 ± 3.03	37.65 ± 2.93	NS	NS	p<0.01

Table 3: Comparison Of Smear Conversion Rate, Tolerability & Compliance

	FERROUS FUMARATE	CARBONYL IRON	p-value
Conversion rate	21.43%	26.32%	p < 0.01
ADR	57.58%	61.5%	p < 0.01
Compliance	61.82 ± 11.37%	54.94 ± 10.11%	p<0.05

DISCUSSION:

Iron deficiency is one of the world's most prevalent nutrient deficits. Pregnant women are particularly susceptible to iron shortage and iron-deficiency anaemia due to their increased iron requirements. With rising anaemia severity, maternal morbidity and death increase progressively. During pregnancy, iron deficiency anaemia has been linked to an increased risk of low birth weight, premature delivery, and perinatal mortality. 15 Frequently, interventions are undertaken to avoid the reduction in haemoglobin concentration and iron

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reserves that occur during pregnancy. To prevent and cure iron insufficiency, oral iron supplements are necessary since food absorption cannot keep up with growing iron demands.

Different types or combinations of iron supplements are available, and the majority are inexpensive. Commonly utilised salts are ferrous sulphate (32% elemental iron) and ferrous fumarate (33% elemental iron). An iron salt that is already in the reduced state, such as ferrous fumarate, is not dependent on gastric acidity for absorption. Ferrous ascorbate is a synthetic molecule composed of ascorbic acid and iron; hence, it is believed to be more absorbable than conventional oral iron supplements. Carbonyl iron is a more recent iron preparation that comprises microparticles of uncharged elemental iron and is said to be very effective, with tolerable side effects and safe even at very large dosages. In order to evaluate the efficacy, tolerability, and compliance of three iron preparations, Ferrous fumarate, Ferrous ascorbate, and Carbonyl iron, the current study was conducted.

In the present investigation, the baseline levels of Hemoglobin and other haematological parameters did not differ substantially between groups, indicating the absence of bias that could have skewed the results in favour of one group. Statistically, the difference between Carbonyl iron (26.3%) and Ferrous fumarate (21.4%), in terms of peripheral smear conversion rate, was highly significant.ADRs were reported by 61.5% of pregnant women in the Carbonyl iron group and by 57.6% of pregnant women in the Ferrous fumarate group; this difference was statistically highly significant.

Therefore, the tolerability of Ferrous fumarate was much higher than that of Carbonyl iron. Compliance with Ferrous fumarate was around 61.8%, while compliance with Carbonyl iron was approximately 55%; this difference was statistically significant.Overall, it may be expected that there is little difference in efficacy between Ferrous fumarate and Carbonyl iron, although Ferrous fumarate is much superior to Carbonyl iron in terms of compliance and tolerability.

According to Bala Suman et al, ferrous fumarate and carbonyl iron are similarly effective in correcting haematological parameters, but ferrous fumarate is better tolerated and has less adverse drug reactions (ADRs) than carbonyl iron. [24]

CONCLUSIONS:

Iron deficiency is one of the world's most prevalent nutrient deficits. Pregnant women are particularly susceptible to iron shortage and iron-deficiency anaemia due to their increased iron requirements. With rising anaemia severity, maternal morbidity and death increase progressively. During pregnancy, iron deficiency anaemia has been linked to an increased risk of low birth weight, premature delivery, and perinatal mortality. [14-18] Frequently, interventions are undertaken to avoid the reduction in haemoglobin concentration and iron reserves that occur during pregnancy. Routine oral iron supplementation is a key component of prenatal care worldwide.

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Different types or combinations of iron supplements are available, and the majority are inexpensive. However, new iron complexes and fixed dose combinations with vitamins and other micronutrients are being offered with claims of greater compliance and haematological response. This study was conducted to evaluate the efficacy, safety, and tolerability of three iron preparations: ferrous fumarate, ferrous ascorbate, and carbonyl iron. The traditional and economical iron preparation is ferrous fumarate. Ferrous ascorbate and Carbonyl iron are two novel iron preparations that are purportedly more effective and have a better tolerability profile than classic iron preparations, Ferrous sulphate and Ferrous fumarate.

Therefore, it is evident from the preceding explanation that Ferrous ascorbate is more beneficial in preventing and treating iron deficiency anaemia in pregnant women. In terms of effectiveness, tolerability, and compliance, ferrous ascorbate outperforms ferrous fumarate and carbonyl iron. The improved compliance can be due to the decreased occurrence of adverse effects, indicating that Ferrous ascorbate is more tolerable. The higher efficacy and superior haematological response with ferrous ascorbate may be related to a higher absorption of iron due to the presence of ascorbic acid, and these data are consistent with what Kanshansky[26] and Kipps[21] have stated. In addition to reporting improved haematological response and enhanced absorption when iron is combined with ascorbic acid, they also documented a substantial rise in the incidence of deleterious effects with increased uptake. Our results contradict the concluding section of the report. Further investigations with a bigger patient group are required to enhance the results of the present study and demonstrate the increased usefulness of ferrous ascorbate for normal prenatal treatment.

REFERENCE:

1. Hentze, M.W.; Muckenthaler, M.U.; Galy, B.; Camaschella, C. Two to tango: regulation of Mammalian iron metabolism. Cell 2010, 142, 24-38.

2. Latunde-Dada, G.O.; Takeuchi, K.; Simpson, R.J.; McKie, A.T. Haem carrier protein 1 (HCP1): Expression and functional studies in cultured cells. FEBS Lett. 2006, 580, 6865-6870.

3. Hahn PF, Carothers EL, Darby WJ. Iron metabolism in human pregnancy as studied with the radioactive isotope Fe59. Am J Obstet Gynecol 1951; 61: 477-486.

4. Sharma JB: Nutritional anaemia during pregnancy in non-industrialized countries: Progress in obstetric and gynaecology: John Stud (Editor). 15th ed. Spain: Churchill Livingstone; 2003; P.103-111.

5. Bothwell Thomas H: Iron requirements in pregnancy and strategies to meet them; Am J Clin Nutrition; 2000 ;72(suppl) : 257S–64S

6. Hallberg L. Iron balance in pregnancy. In: Berger H (Editor). Vitamins and minerals in pregnancy and lactation. Nestle Nutrition workshop Series. New York : raven Press 1988.

7. K. Kalaivani: Prevalence & consequences of anemia in pregnancy; Indian J Med Res; 130, Nov 2009, 627-633

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4 ,2022**

8. Scholl TO, Hediger,ML, Fischer RL, ShearerJW Anemia vs. iron deficiency: increased risk of preterm delivery in a prospective study. Am J[23]Clin Nutr,1992; 55: 985-988

9. Brabin BJ, Premji Z, Verhoeff F. An analysis of anemia and child mortality. J Nutr. 2001;131:636S-645S. [Abstract]

10. Prema K, Neela Kumari S, Ramalakshmi BA. Anaemia and adverse obstetric outcome. Nutr Rep Int 1981; 23 : 637-43.

11. Lister VG, Rossiter CE, Chong M. Perinatal mortality. Br J Obstet Gyn 1985; 92 (Suppl 5) : 88-99.

12. VR Sreeraman; March,2011; Iron Deficiency During Pregnancy Affects Baby's Brain: Study [MedIndia]. Available at: http://www.medindia.net/news/Iron-Deficiency-During-Pregnancy-Affects-Babys-Brain-Study-82637-1.htm#ixzz1UppjUf00

13. Fenton V, Cavill I, Fisher. Iron stores in pregnanc. Br J Heamatol 1977; 37: 145.

14. Puolakka J, Janne O, Pakarinen A, Vinko. Serum ferritin in the diagnosis of anemia during pregnancy. Acta Obstet Gynecol Scand Suppl 1980; 95: 57-63.

15. Breymann C. Iron deficiency and anemia in pregnancy: modern aspects of diagnosis and therapy. Blood Cells Mol.Dis. 2002; 29: 506-516.

16.P. F. Hahn, W. F. Bale, J. F. Ross, W. M. Balfour, and G. H. Whipple; Radioactive iron absorption by gastro-intestinal tract; Jounal Exp Med. 1943 September 1; 78(3): 169–188.

17. Huff RL, Hennessy TG, Austin RE. Gorcica: Plasma and Red cell iron turnover in normal subjects and in patients having various hematopoitic disorders; J Clin Invest 1950; 29: 1041-1052.

18. Stoltzfus RJ, Dreyfuss ML. Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia. International Life Sciences Institute/I L S I Press, 1998.

19. RG Viveki, A.B. Halappanavar, P.R. Viveki, S.B. Halki, V.S. Maled, P.S. Deshpande: Prevalence of Anemia and Its Epidemiological Determinants in Pregnant Women; Al Ameen Med Sci; 2012; 5; (3): 216-223

20. Nielsen P, Gabbe EE, Fischer R, Heinrich HC. Bioavailability of iron from oral ferric polymaltose in humans. Arzneimittelforschung. 1990;40:754–760. [PubMed]

21. Agarwal, M.B., Rathi, S.A. (2006). An open label, Randomized, comparative clinical study to assess the efficacy and tolerability of ferrous ascorbate versus carbonyl iron in the treatment of iron deficiency anemia. International Journal of Gynaecology and Obstetrics, India, 9, 13-20.

22. Ganguly S. et al : Comparison between Ferrous Ascorbate and Colloidal Iron in the Treatment of Iron Deficiency Anemia in Children from Kolkata, India; British Journal of Medicine & Medical Research, 2(2): 195-205, 2012.

ISSN PRINT 2319 1775 Online 2320 7876

 UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4 ,2022

23. Huebers HA, et al: Absorption of carbonyl iron. J Lab Clin Med, Nov 1986, 108(5):473-8.

24. Bilimale A., Anjum, J., Sangolli H. N., Mallapur M.: Improving Adherence to Oral Iron Supplementation during pregnancy. AMJ, 2010, 3, 5, 281-290. Doi 10.4066/ AMJ.2010.291