International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

Comparison Between The Efficacy Of Capsule Ferriboost Versus Ferrous Fumarate In Treatment Of Iron Deficiency Anemia In Females

Sudarshan S. Joshi
Department of Pharmaceutics,
Allana college of pharmacy, University of Pune. Maharashtra

Date of Submission: 10-08-2021 Date of Acceptance: 29-08-2021

ABSTRACT
Iron deficiency anemia was found to be the primary cause of anemia occurring to pregnant women after the dilutional anemia. Pregnant females are more liable to iron deficiency due to the increasing demand of the growing uterus and growing fetus as compared to non-pregnant females. Definition of anemia differs according to the gestational age but widely speaking, females with Hb levels less than 11 gm/dl with microcyric hypochromic anemia, with low serum ferritin , low serum iron and high TIBC can be diagnosed with IDA.
Anemia has major consequences on both the mother and the fetus. As regard the maternal complications; there was found to be higher rates or preterm labor, infections and postpartum hemorrhage. Low iron stores in the growing fetus can suffer from low birth weight and major developmental delays in first few years of their lives.
The standard of care in iron deficiency treatment is oral iron supplementation during pregnancy according to the WHO. The capsule Ferriboost is the combination of lactoferrine , chelated iron and vitamins. Current guidelines recommend the dose of 60 to 120 mg of elemental iron of ferrous fumarates per day for a minimum duration of 3 months in pregnant women.
The main prevailing problem in the treatment of patients with iron deficiency is the frequent development of side effects. For example , the most frequently reported side impacts are gastrointestinal negative events such as nausea, heartburn, pain, constipation and diarrhea regardless of the iron preparation type.
The overall rise in hemoglobin with FERRIBOOST after 4 weeks was greater relative to ferrous fumarate in this research. On the other side, gastrointestinal adverse events with ferrous fumarate happened more frequently than FERRIBOOST. FERRIBOOST improves the delivery of intestinal iron and can enable iron absorption even in an acidic medium, which is better than ferrousfumarates. Along with the absence of side effects, lactoferrin plus chelated iron administration resulted in very high compliance among treated women so is considered a much safer and more effective substitutes for IDA treatment for pregnant females than ferrous fumarate.
KEYWORDS Iron deficiency anemia, Ferriboost, Ferrous sulphate, Serum ferritin, TIBC, Haemoglobin.

I. INTRODUCTION

Iron is an essential nutrient for living cells and it is pivotal during pregnancy, in particular for the developing fetus through maternal iron transfer as well as in the neonate through breast-feeding and in the childhood through diet. Iron deficiency (ID) is considered the most important nutritional disorder in the world, being more prevalent in pregnant women where represents a high risk factor for maternal and infant health associated with preterm delivery, fetal growth retardation, low birth weight, and inferior neonatal health [(1).] ID is also frequent in children where is related to decreased brain functions [(2, 3).] Moreover, women of reproductive age can be affected by ID due to iron loss during the menses. An early diagnosis and a prompt management of ID and ID anemia (IDA) are highly recommended. ID is characterized by the low levels of total serum iron (TSI) and serum ferritin (sFtn). Conversely, IDA is characterized by low concentrations of hemoglobin (Hb) and low number of red blood cells (RBCs) in addition to TSI and sFtn low levels.

The human body contains 3–4 g of iron localized in hemoglobin of erythrocytes (about 2.0–2.5 g), in ferritin (Ftn) within hepatocytes and macrophages (about 0.5–1 g), in myoglobin, and in

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

iron-containing enzymes (about 0.5 g). A minor iron source, deriving from an equilibrated diet, provides about 15 mg of iron per day of which only about 10%, corresponding to 1–2 mg, is absorbed due to its exceptionally poor bio-availability. A major iron source involves the recycling of iron from the lysis of senescent erythrocytes by macrophages (about 20 mg/day) [4, 5].

Ferriboost is unique combination of chelated iron , Bovin Lactoferrine and vitamins, it may assist in the management of dietary iron deficiency. Iron requirements may be increased in vegetarians, early adolescents, pregnant women and during the female reproductive period Iron deficiency is the most common nutrient deficiency in the world, and is one of the few nutrient deficiencies to affect both developing and industrialised countries. The World Health Organisation states that 'iron deficiency affects more people than any other condition, constituting a public health condition of epidemic proportions'.1 Dietary iron deficiency most commonly affects individuals at risk of low iron intake, or those with increased requirements. This includes those with protein calorie malnutrition such as the elderly and vegetarians; also those at life stages where there is a rapid increase in blood volume including infancy, adolescence and pregnancy. Secondary causes of iron deficiency not related to dietary intake, or which may exacerbate dietary iron deficiency include; blood loss, menorrhagia, inefficient absorption and increased destruction of red blood cells. Iron deficiency symptoms include fatigue, rapid heart rate and rapid breathing on exertion. Iron deficiency severely effects work capacity, impairs physical and cognitive development and can be a significant burden on productivity and quality of life. Iron functions as part of several proteins and enzymes, however haem represents the largest group. Iron exists in the centre of haem, which enables oxygen transport to tissues by haemoglobin. Haemoglobin collects oxygen as it passes through the lungs and carries about 98.5% of the total oxygen found in blood. Myoglobin, another haem protein, transports oxygen into muscles.[2-4] In iron deficient states total haemoglobin content is reduced, and symptoms of deficiency are a reflection of reduced oxygen availability. Iron supplementation improves haemoglobin status in children, pregnant women, athletes and non-anaemic individuals. ferriboost contains iron which assists in maintaining normal, healthy blood contains iron to support normal healthy blood, as well as cofactors to assist the absorption of iron from dietary sources. Iron supplementation improves markers of iron deficiency including serum iron, ferritin, haemoglobin and mean cell volume (MCV). The prevalence of fatigue reported in clinical practice is estimated between 14%-27%, and is 3 times more likely to occur in women. Unexplained fatigue can be caused by iron deficiency[6,7].

Women's iron requirements are increased during pregnancy; Ferriboost supports a healthy pregnancy and the wellbeing of pregnant women. During pregnancy, women's iron requirements increase dramatically from the second trimester. In the first trimester, the cessation of menses reduces the need for iron, however as pregnancy progresses iron requirements for foetal growth rise steadily in proportion to foetal weight. In the second trimester, an increase in oxygen consumption by both mother and foetus is associated with major haematological changes. These changes include an increase in total blood volume, plasma volume and red blood cell mass, consequently leading to a 30% increase in haemoglobin mass. In pregnancy, adequate iron is important to reduce the risk of complications associated with iron deficiency including preterm delivery, prematurity, and small gestational age birth weight.6,9 Iron is also essential for normal development of the foetus, especially the brain. Iron deficiency in foetal life and infancy may have deleterious effects on cognitive and behavioural development. The RDI of iron in pregnancy is 27mg; a substantial increase from 18mg in non-pregnant women. Studies in pregnant women have shown dietary intake does not change dramatically during pregnancy. For this reason, ferrokinetic, as well as dose response studies suggest a supplemental dose of between 30-40mg of elemental iron per day is required to prevent iron deficiency in pregnant women. Supplementation should begin as early as possible.[2,6,9] Iron plays an integral role in the production of energy.. Haem dependent cytochromes transport oxygen and electrons through the respiratory transport chain, for the synthesis of adenosine triphosphate (ATP). The transfer of electrons through the chain occurs via the change in the oxidation state of iron. A number of non-haem iron containing enzymes are also essential for energy production and include; NADH dehydrogenase, succinate dehydrogenase and ubiquinone-cytochrome C reductase.

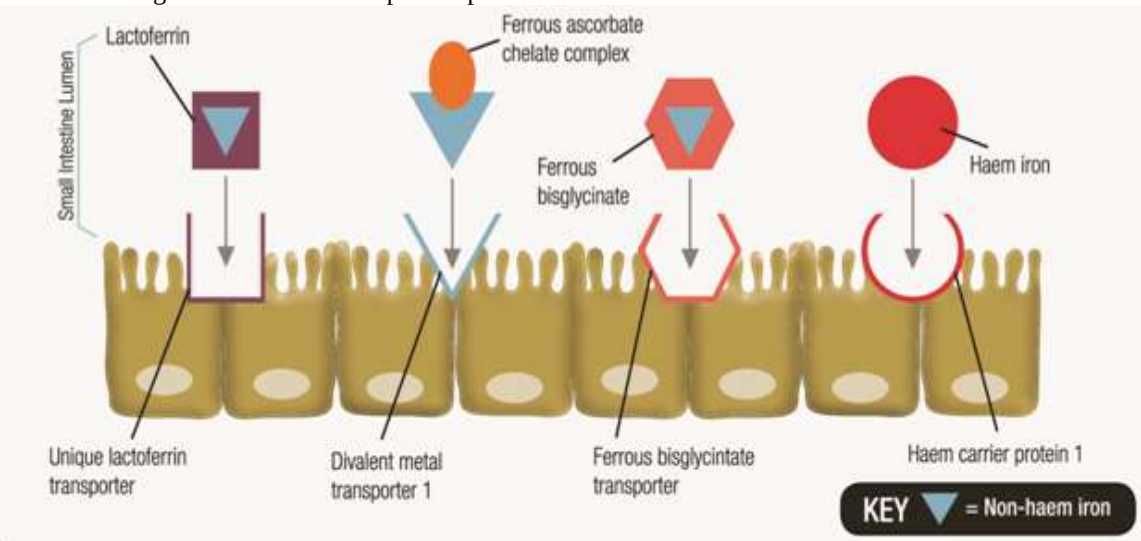
Vitamin C assists the absorption of dietary iron. Dietary iron is absorbed in two forms; haem and non-haem. Haem iron is soluble and readily absorbed through the small intestine. Non-haem

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

iron is less readily absorbed. It is found in plant foods, and must first be cleaved from food components. Chelates and ligands are compounds that bind to metal ions and may either inhibit or enhance absorption. Enhancers of iron absorption include acids. At a low pH, ascorbic acid enhances the absorption of non-haem iron by acting as a reducing agent. By reducing dietary ferric iron to ferrous iron, this complex, termed ferrous ascorbate chelate remains soluble and enhances the uptake of non-haem iron.[10,11]

Ferrous bisglycinate is a superior form of iron when compared to ferrous sulphate Ferrous bisglycinate is a patented form of non-haem iron possessing unique attributes, namely a low molecular size and neutral ionic charge, that enhance its bioavailability and tolerability. The low molecular weight allows the mineral to be absorbed directly through the intestinal wall without first needing to be cleaved. Furthermore, the neutral electric charge ensures the mineral is less likely to deleteriously interact with other nutrients in the digestive system. This is particularly important as iron can inhibit the absorption of minerals including zinc and calcium, and it can also oxidise antioxidants including vitamin C and E. Due to these attributes, it is believed that ferrous bisglycinate may be absorbed similarly to haem iron.10 A number of clinical trials have investigated the superior absorption of ferrous bisglycinate. It has also been demonstrated that there are only marginal differences in absorption when comparing intake with and without a high phytate meal. This further exemplifies how the bisglycinate form does not interact with foods known to inhibit iron absorption.[5,8,11,14]

Figure 1 : Ferriboost Improve uptake and utilization of Haem and Non-Haem Iron



II. MATERIALS AND METHODS

Female patients within 18-21 years of age with clinically proven IDA satisfying the inclusion criteria were screened and recruited. This was followed by randomization and grouping and baseline investigations. A 4 week treatment regimen and analysis of post-therapy investigations was done, which evaluated the efficacy of the treatment given. The Institute Ethical Committee clearance was obtained before the study initiation. Results from a previous study conducted on Italian pregnant women was used to calculate sample size. A two-sided t-test helped detect superiority of FERRIBOOST over oral ferrous sulphate. A minimum sample size of 12 per group was required to have a 90% chance (alpha error of 0.05) of detecting an increase in Hb level to 11.5 g/dL (SD of 0.6 g/dL) in the Oral ferrous sulphate group and 12.7 g/dL (SD of 0.9 g/dL) in the experimental group.14 On adjustment for non-compliance in the Oral ferrous sulphate arm to 40%, a sample size of 68 was arrived at. Written informed consent was obtained from those fulfilling the inclusion criteria and willing to participate in the study. A detailed history and clinical examination was performed on the participants. Venous blood was drawn for baseline assessment of iron parameters and other routine tests. The participants were randomized into 3 arms, using a computerized randomization chart. Numbered containers were used as a method

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

of allocation concealment. The study drug was sealed in sequentially numbered identical containers according to the allocation sequence and being distributed as per the protocol into their respective groups. The control arm received Oral ferrous sulphate 333 mg (100 mg elemental iron) once-daily empty stomach. The study arm received Bovin Lactoferrine 2 g once-daily empty stomach and the third arm received Cap Ferriboost (Table 1). These supplements were administered orally for a period of 30 days. Bovin Lactoferine was given as a powder and had to be reconstituted in 200 mL of potable water before consumption.

Patients with IDA and Hb levels between 8 and 11 mg/dL were included.

A clinical assessment was performed after obtaining a detailed history. Eight milliliter (8.5ml) of venous blood was collected from the subject under strict aseptic precautions for routine investigations including complete blood count (total count (TC), differential count (DC), ESR, Hb), peripheral smear, serum urea, serum creatinine, serum bilirubin, serum glutamic oxaloacetic transaminase/serum pyruvic transaminase (SGOT/ SGPT). Subjects' iron status was assessed by monitoring serum iron, serum ferritin, total iron-binding capacity (TIBC), serum transferrin saturation and unsaturated iron-binding capacity (UIBC). Statistical analysis was performed using SPSS version 17 software. Continuous variables were described as means along with their SDs, while discrete variables were expressed as frequencies and percentages. Within each group, the mean change in hemoglobin and iron parameters from baseline to post-therapy was assessed using student's paired t-test. A one way analysis of variance (ANOVA) helped assess the significance of change in parameters between the three groups. A nonparametric Wilcoxon signed rank test was used to analyze serum ferritin.

III. RESULTS

A total of 202 students were screened for the clinical presence of conjunctival pallor. A complete blood count and peripheral smear was undertaken on 102 students who were found to exhibit clinical pallor. 20 of them did not fit the inclusion criteria and were excluded from the study. The 82 students recruited into the study were randomly allotted into three groups. As per the inclusion criteria, all the participants of the study belonged to the female gender. The mean age of the study participants was found to be 20.15 ± 0.650 years ranging from 18 to 21 years. There was no significant variation in age within group or between the three groups. The baseline and post-treatment values of TC, DC, ESR, SGOT, SGPT, Sr. Urea, Sr. Creatinine and Sr.Bilirubin were found to be normal in all the subjects.

Participants in Group I (Ferrous Sulphate Arm) showed a mean increase in haemoglobin of 0.020 g/dl which was not found to be statistically significant ($p = 0.717$). Participants in Group II (Bovine Lactoferrine Arm) showed a significant increase in their haemoglobin levels post-therapy with a mean increase in haemoglobin of 0.8688 g/dl .). Participants in Group II1 (Ferriboost Arm) showed a significant increase in their haemoglobin levels post-therapy with a mean increase in haemoglobin of 1.3688 g/dl There was no significant difference in baseline values between the three groups. However, a significant difference in the rise in haemoglobin values in Group II and III ($p=0.877$).

Participants in Group I (Ferrous Sulphate Arm) showed a mean increase in serum iron concentration of 1.526 mcg/dl which was not found to be statistically significant ($p=0.752$). Participants in Group II (Bovine Lactoferrine Arm) showed a significant increase in their serum iron concentration values post-therapy with a mean increase in serum iron concentration of 17.933 mcg/dl ($p= 0.012$). Participants in Group III (Combination Therapy Arm) also showed a significant increase in their serum iron concentration values post-therapy with a mean increase in serum iron concentration of 18.3575 mcg/dl ($p=0.011$). There was no significant difference in baseline values of serum iron concentration between the three groups. There was no significant difference in the rise in serum iron concentration levels between the three groups ($p = 0.095, 0.198, 0.991$).

Participants in Group I (Ferrous Sulphate Arm) showed a mean decrease in TIBC of 16.371 mcg/dl which was not found to be statistically significant ($p= 0.287$). Participants in Group II (Bovine Lactoferrine Arm) showed a significant decrease in TIBC values post-therapy with a mean decrease in TIBC of 113.49 mcg/dl ($p < 0.001$). Participants in Group III (Combination Therapy Arm) also showed a significant decrease in their TIBC values post-therapy with a mean decrease in TIBC of 115.902 mcg/dl ($p = 0.01$). There was no significant difference in baseline values of TIBC between the three groups. Post-therapy TIBC values of Group II and III were significantly different from that of Group I ($p=0.616$).

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

Participants in Group I (Ferrous Sulphate Arm) showed a mean decrease in UIBC of 18.891 mcg/dl which was not found to be statistically significant ($p = 0.307$). Participants in Group II (Bovine Lactoferrine Arm) showed a significant decrease in UIBC values post-therapy with a mean decrease in UIBC of 138.2819 mcg/dl ($p < 0.001$) Participants in Group III (Combination Therapy Arm) also showed a significant decrease in their UIBC values post-therapy with a mean decrease in UIBC of 118.28mcg/dl ($p = 0.004$). There was no significant difference in baseline values of UIBC between the three groups. Post-therapy the UIBC values of Group II and III were significantly different from that of Group I ($p < 0.01$, $p = 0.01$ respectively). There was no significant difference in the post-therapy UIBC values between Group II and III ($p = 0.844$) When a difference in difference analysis was carried out, the fall in UIBC values of Group II and III were significantly more than that observed in Group I ($p = 0.001$,0.039 respectively) There was no significant difference in change in UIBC values observed between Group II and III ($p= 0.668$).

Participants in Group I (Ferrous Sulphate Arm) showed a mean increase TSAT of 0.84764% which was not found to be statistically significant ($p = 0.477$). Participants in Group II (Bovine Lactoferrine Arm) showed a significant increase in TSAT values post-therapy with a mean increase in TSAT of 7.7428% ($p = 0.001$). Participants in Group III (Combination Therapy Arm) also showed a significant increase in their TSAT values post-therapy with a mean increase in TSAT of 8.0432% ($p = 0.001$).

There was no significant difference in baseline values of TSAT between the three groups. Post-therapy TSAT values of Group II was significantly different from that of Group I ($p = 0.017$). There was no significant difference in the post-therapy TSAT values between Group II and III or between Group I and III ($p = 0.951$, 0.078 respectively). When a difference in difference analysis was carried out, the rise in TSAT values of Group II and III were significantly more than that observed in Group I ($p = 0.008$, 0.03 respectively). There was no significant difference in change in TSAT values observed between Group II and III ($p = 0.983$). Eleven participants reported adverse effects to their medication. Most of the adverse effects were reported on questioning the participants at the end of the study period. The only exception was a single case of gastritis who was treated with H2-blocker during the study period. Figure 5 demonstrates the group-wise split up. Gastritis, constipation, nausea, vomiting and loose stools were the side effects noted in the participants during the study duration. Eighty of the 82 recruited participants completed the study. The two drop outs belonged to Group III. One was diagnosed with infective hepatitis and was not available for follow-up. The other drop out resorted to intravenous iron instead of taking her oral medications and voluntarily dropped out of the study. The compliance in Group I was found to be 44%. The compliance in Group II and III was 94% each.

IV. DISCUSSION

Oral ferrous sulphate is the most commonly prescribed drug for treating iron deficiency anaemia. The poor compliance, GI adverse drug reactions and the variable bioavailability of oral ferrous sulphate emphasize a need for a better oral formulation. Lactoferrin, a glycoprotein structurally resembling transferrin, is believed to play a role in iron absorption. Previous studies conducted in Italian pregnant women and Japanese athletes have shown beneficial effects of bovine lactoferrin in treating iron deficiency anaemia. Hence, a randomized, active controlled, open-labelled, 3 armed parallel study was designed to compare the efficacy of oral bovine Lactoferrine (as single agent and in combination with ferrous sulphate) with oral ferrous Sulphate in treating iron deficiency anaemia. The prevalence of anaemia amongst nursing students in our study was found to be 35%. This is comparable to previous studies conducted in India, that have stated that at least 40% of asymptomatic nurses in their study had biochemical evidence of iron deficiency anaemia.[23]Our results show significant improvement in haemoglobin and most iron parameters in participants of Group III (Combination Therapy Arm) compared to Group I (Ferrous Sulphate Arm). 106 The significant increase in haemoglobin and serum iron concentration values following therapy in both Group II and III ($p < 0.05$) The participants in the ferrous sulphate arm failed to register improved haemoglobin levels and iron parameters. This is in accordance with a study conducted in Italian pregnant women in 2010 who were prescribed 156 mg of elemental iron for 30 days. This study documented a parallel fall in serum IL-6 levels which may lead to a hepcidin mediated down regulation of ferroportin resulting in decreased enteral iron absorption. The rise in haemoglobin

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

(0.030g/dl) in Group I much less than a previous study (1.05 g/dl) conducted among pregnant women in India in the Guntur District by Chandrakala Kambar et al.[80] This disparity may be attributed to better compliance and longer duration of therapy amongst the pregnant women. 107 On the contrary, the mean rise in serum iron concentration in our study (1.544 mcg/dl) is thrice that reported by their study (0.5 g/dl).[2] This may be due to increased utilization of iron resulting in minimal rise in serum iron concentration in pregnant women of that study. The marginal rise in haemoglobin (0.028 g/dl, $p = 0.717$) and serum iron concentration (1.5264 mcg/dl, $p = 0.752$) in Group I was significantly lower compared to Group II and III ($p < 0.05$) which paralleled an increase in serum iron concentration levels in both the groups. This significant improvement is contrary to what was observed amongst cancer patients with anaemia of chronic disease who were given 200 mg of lactoferrin along with erythropoietin. Hence the beneficial effect of lactoferrin that is seen in cases of nutritional iron deficiency does not extrapolate to Anaemia of Chronic Disease. There was no significant difference in the iron parameters and haemoglobin levels from base line to post-therapy between Groups II and III thereby quelling any belief on the possible haematological benefits of combining ferrous sulphate and lactoferrin fortified bovine colostrum. The participants who received lactoferrin fortified bovine colostrum reported fewer adverse effects (4%, 13%) than those on ferrous sulphate (36%). This is in accordance with previous studies that have also noted considerable adverse effects with ferrous sulphate. The most common adverse effect reported in this study was gastritis, followed by altered bowel movements. Further studies are required to 109 determine the role of lactoferrin fortified bovine colostrum in reducing the incidence of adverse drug reactions when given in combination with ferrous sulphate as has been demonstrated by the lower incidence of adverse effects reported in the arm that received both. Significant improvement in haemoglobin and iron parameters was observed in participants who received Capsule Ferriboost. The mechanism by which lactoferrin improves iron parameters and hematologic parameters is yet to be understood. The iron binding capacity of lactoferrin, the iron content of lactoferrin fortified bovine colostrum or the IL-6 mediated hepcidin regulation may contribute to the effect of lactoferrin in iron metabolism. A lower incidence of adverse drug reactions amongst participants on Cap Ferriboost further justifies the utility of lactoferrin fortified bovine colostrum in correcting iron deficiency anaemia. A study of larger scale may be carried out to further ascertain the efficacy of lactoferrin fortified bovine colostrum in treating iron deficiency. Further studies with purified lactoferrin are warranted to avoid difficulties in interpretation of the data. A study duration of at least 3 months or more would be desirable to assess the effect of lactoferrin on iron stores. Zinc protoporphyrin assay and RBC indices and counts would provide a better assessment of iron status of an individual.

REFERENCE:

1. Shersten Killip, John M. Bennett, Mara D. Chambers. Iron Deficiency Anaemia. American Family Physician. March 1, 2007; Vol. 75, No 5: 671 – 678.
2. Ministry of Health and Family Welfare Government of India. Guidelines for Control of Iron Deficiency Anaemia. 2013; Table 2.1:6.
3. Manu Tiwari, Col. Jyoti Kotwal , Anupam Kotwal, Maj Priyanka Mishra, Brig Vibha Dutta, Brig Sanjiv Chopra. Correlation of haemoglobin and red cell indices with serum ferritin in Indian women in second and third trimester of pregnancy. Medical Journal of Armed Forces India. 2013; 69: 31-36.
4. Matthew W. Short, Jason R., Domagalski. Iron Deficiency Anemia: Evaluation and Management. American Family Physician. Jan 2013; 87(2): 98-104.
5. L. Adlerova, A. Bartoskova, M. Faldyna Lactoferrin: A review Veterinarni Medicina. 2008; 53(9): 457–468.
6. Alex D. Sheftel, Anne B. Mason, Prem Ponka. The Long History of Iron in the Universe and in Health and Disease. Biochimica et Biophysica Acta. Mar 2012;1820(3): 161–187.
7. Guerinot M.L., Microbial iron transport. Annual Review of Microbiology. 1994; 48:743–72.
8. De Luca N.G., Wood P.M., Iron uptake by fungi: contrasted mechanisms with internal or external reduction. Advances in Microbial Physiology. 2000;43:39-74.
9. Martin Hynes. Iron Metabolism. Journal of Clinical Pathology.1948;1:57.
10. S.S. Nadadur, K. Srirama and Anuradha Mudipalli. Iron transport & homeostasis mechanisms: Their role in health & disease.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

The Indian Journal of Medical Research. October 2008;128:533-544.
11. Karen H. C. Lim, Lynn J. Riddell, Caryl A. Nowson, Alison O. Booth, and Ewa A. Szymlek-Gay. Iron and Zinc Nutrition in the Economically- Developed World: A Review. Nutrients. Aug 2013; 5(8): 3184–3211.
12. Namik Ozbek. Concise Review: Absorption And Transport of Iron. Medical Journal of Islamic World Academy of Sciences. 2010;18(4):133-138,
13. Adriana Donovan, Cindy N.Roy, and Nancy C. Andrews. The Ins and Outs of Iron Homeostasis. Physiology. 2006; 21:115–123.
14. F. Dupic, S. Fruchon, M. Bensaid, O. Loreal, P. Brissot, N. Borot, M. P. Roth and H. Coppin. Duodenal mRNA expression of iron related genes in response to iron loading and iron deficiency in four strains of mice. Gut. Nov 2002; 51(5): 648–653.
15 Paesano, R. et al. (2009). The influence of lactoferrin, orally administered, on systemic iron homeostasis in pregnant women suffering of iron deficiency and iron deficiency anaemia. Biochimie 91:44-51.
16. Abu Hashim H, Foda O, Ghayaty E. Lactoferrin or ferrous salts for iron deficiency anemia in pregnancy: A meta-analysis of randomized trials. Eur J Obstet Gynecol Reprod Biol. 2017;219:45-52.
17. Rosa L, Cutone A, Lepanto MS, Paesano R, Valenti P. Lactoferrin: A Natural Glycoprotein Involved in Iron and Inflammatory Homeostasis. Int J Mol Sci. 2017;18(9):1985.
18. Paesano R, Pacifici E, Benedetti S, Berlutti F, Frioni A, Polimeni A, et al. Safety and efficacy of lactoferrin versus ferrous sulphate in curing iron deficiency and iron deficiency anaemia in hereditary thrombophilia pregnant women: An interventional study. Biometals. 2014;27(5):999-06.
19. Natik H. Duaa A. Hussein. The concentration of lactoferrin and its relationship with minerals and amino acids in cow's milk. Scientific Papers. Series D. Animal Science. Vol. LIX. 2016;59.
20. Mohamed R, Mohamed K, Ragab D, Abd-Elhamid S, Adel A. Oral lactoferrin versus ferrous sulphate and ferrous fumerate for the treatment of iron deficiency anemia during pregnancy. Journal of Advanced Nutrition and Human Metabolism. 2015;2:e740.
21. Abu HH, Foda O, Ghayaty E. Lactoferrin or ferrous salts for iron deficiency anemia in pregnancy: A meta-analysis of randomized trials. Eur J Obstet Gynecol Reprod Biol. 2017;219:45-52.
22. Chandrakala K, Zahedabano, Meenakumari A. Comparative study of efficacy and safety of iron polymaltose complex with ferrous sulphate in antenatal women with moderate anemia. IOSR-JDMS. 2013;9:9-13.
23. Adamson JW. Iron deficiency and other hypoproliferative anemias. In: Braunwald E, Fauci AS, Kasper DL (Eds.). Harrison's Principles of Internal Medicine 17th Edition. New York: McGraw Hill. 2008:628-33.
24. Koikawa N, Nagaoka I, Yamaguchi M, Hamano H, Yamauchi K, Sawaki K. Preventive effect of lactoferrin intake on anemia in female long distance runners. Biosci Biotechnol Biochem. 2008;72(4):931-5.
25. Chow JK, Werner BG, Ruthazer R, Snydman DR. Increased serum iron levels and infectious complications after liver transplantation. Clin Infect Dis. 2010; 51(3):e16-23.
26. Maccio A, Madeddu C, Gramignano G, Mulas C, Sanna E, Mantovani G. Efficacy and safety of oral lactoferrin supplementation in combination with rHuEPO-beta for the treatment of anemia in advanced cancer patients undergoing chemotherapy: Open-label, randomized controlled study. Oncologist. 2010;15(8):894-902.
27. 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;10(2):e0117383.

Table 1: Group I (Ferrous Sulphate Arm) Descriptive Statistics

Parameters	Sample	Minimum	Maximum	Mean	S.D
Haemoglobin (g/dl)	Baseline	7.5	10.5	9.00	0.76271
Haemoglobin (g/dl)	Post-therapy	7.5	11	9.25	0.90895

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

Sr. Ferritin (mcg/dl)	Baseline	0.399	139.1	69.74	25.5678
Sr.Ferritin (mcg/dl)	Post-therapy	2.153	181.7	91.92	27.8976
Sr.Iron (mcg/dl)	Baseline	9.02	116.7	62.88	22.4356
Sr.Iron (mcg/dl)	Post-therapy	12.99	161.74	87.36	23.3245
Sr.TIBC (mcg/dl) Baseline	Baseline	301.78	689.67	495.72	75.8978
Sr.TIBC (mcg/dl) Post-therapy	Post-therapy	270.06	688.63	479.34	72.1783
Sr. UIBC (mcg/dl) Baseline	Baseline	239.12	659.43	449.27	81.2314
Sr.UIBC (mcg/dl) Post-therapy	Post-therapy	158.46	609.12	383.79	74.3457
Sr.TSAT (%) Baseline	Baseline	1.75	18.93	10.34	4.35671
Sr. TSAT (%)	Post-therapy	2.17	24.78	13.475	5.43829

Table 2: Group I (Ferrous Sulphate Arm) Paired t-Test

Change in Parameter	Mean	95% Confidence Interval		p-Value
		Lower	Upper	
Haemoglobin	0.03024	-0.12492	0.18541	0.768
Sr. Ferritin	-0.6541	-5.36587	4.05765	0.789
Sr. Iron	1.5264	-8.4068	11.45968	0.723
TIBC	-16.371	-47.8676	15.12456	0.278
UIBC	-18.891	-55.67543	17.89341	0.307
TSAT	0.84764	-1.39567	3.09088	0.439

* $p<0.05$ is considered significant

Table 3 : group 2 Bovin Lactoferrine Arm

Parameters	Sample	Minimum	Maximum	Mean	S.D
Haemoglobin (g/dl)	Baseline	7.5	10.5	9.00	0.82122
Haemoglobin (g/dl)	Post-	7.5	12.5	10.00	1.08934

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

	therapy				
Sr. Ferritin (mcg/dl)	Baseline	0.666	139.1	69.883	28.6754
Sr.Ferritin (mcg/dl)	Post-therapy	2.843	154.67	78.75	30.8924
Sr.Iron (mcg/dl)	Baseline	17.65	81.73	49.69	18.8231
Sr.Iron (mcg/dl)	Post-therapy	17.01	161.14	89.075	39.6724
Sr.TIBC (mcg/dl) Baseline	Baseline	368.78	679.67	524.22	80.9087
Sr.TIBC (mcg/dl) Post-therapy	Post-therapy	299.06	618.63	458.85	77.9876
Sr. UIBC (mcg/dl) Baseline	Baseline	315.12	629.43	472.27	83.0982
Sr.UIBC (mcg/dl) Post-therapy	Post-therapy	158.46	568.12	363.29	92.9872
Sr.TSAT (%) Baseline	Baseline	3.75	16.93	10.34	3.9083
Sr. TSAT (%)	Post-therapy	4.88	50.12	27.50	12.0923

Change in Parameter	Mean	95% Confidence Interval		p-Value
		Lower	Upper	
Haemoglobin	0.8798	0.5743	1.18541	<0.01
Sr. Ferritin	0.8459	-4.36587	6.05765	0.876
Sr. Iron	17.933	4.4068	31.45968	0.012
TIBC	-113.49	-147.8676	-79.12456	<0.01
UIBC	-138.28	-188.67543	-87.89341	<0.01
TSAT	7.7428	3.39567	12.09088	0.01

* p<0.05 is considered significant

Table 5 : Group III (Ferriboost Therapy Arm) Descriptive Statistics

Parameters	Sample	Minimum	Maximum	Mean	S.D
Haemoglobin (g/dl)	Baseline	7.5	10.0	8.75	0.9876
Haemoglobin (g/dl)	Post-therapy	8.0	13.00	10.50	0.8935
Sr. Ferritin (mcg/dl)	Baseline	1.966	90.1	47.016	26.9872
Sr.Ferritin (mcg/dl)	Post-therapy	4.843	200.67	102.75	46.8765
Sr.Iron (mcg/dl)	Baseline	11.65	91.73	51.69	23.6754
Sr.Iron (mcg/dl)	Post-therapy	17.78	131.14	140.03	26.8923
Sr.TIBC (mcg/dl) Baseline	Baseline	356.78	689.67	523.22	98.2767
Sr.TIBC (mcg/dl) Post-therapy	Post-therapy	259.06	648.63	453.84	101.982
Sr. UIBC (mcg/dl) Baseline	Baseline	311.12	619.43	465.27	108.123
Sr.UIBC (mcg/dl) Post-therapy	Post-therapy	159.46	561.12	360.29	110.555

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

Sr.TSAT (%) Baseline	Baseline	2.75	17.93	10.34	5.3219
Sr. TSAT (%)	Post-therapy	3.88	46.12	25.00	8.9932

Table 6: Group III (Ferriboost Therapy Arm) Paired t-Test

Change in Parameter	Mean	95% Confidence Interval		p-Value
		Lower	Upper	
Haemoglobin	1.3698	0.5643	2.17541	0.001
Sr. Ferritin	3.3456	-10.36587	17.05765	0.669
Sr. Iron	17.43	4.4068	30.45968	0.011
TIBC	-93.495	-157.8676	-29.12456	0.01
UIBC	-118.28	-188.67543	-47.89341	0.003
TSAT	8.0432	3.89567	12.19088	0.01

* p<0.05 is considered significant

Figure 2: Mean Hb pre and post intervention.

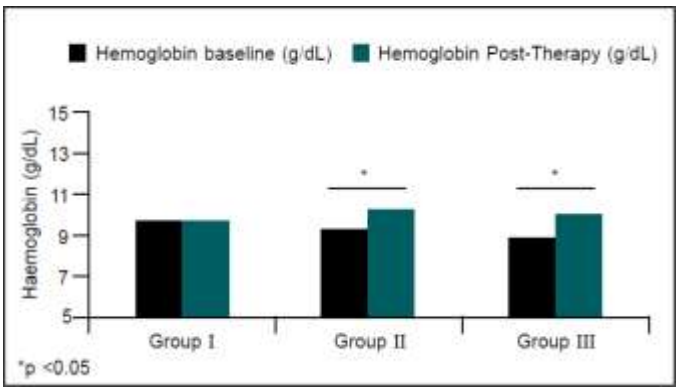
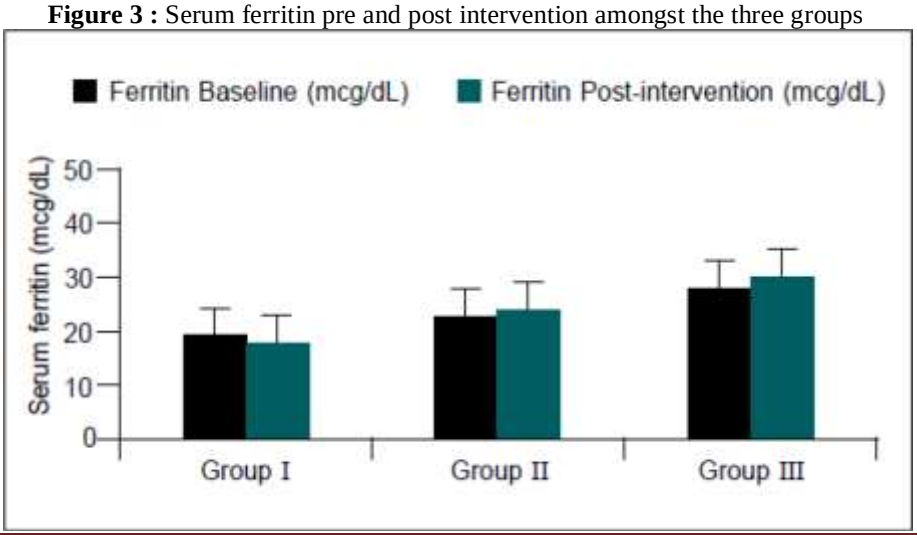
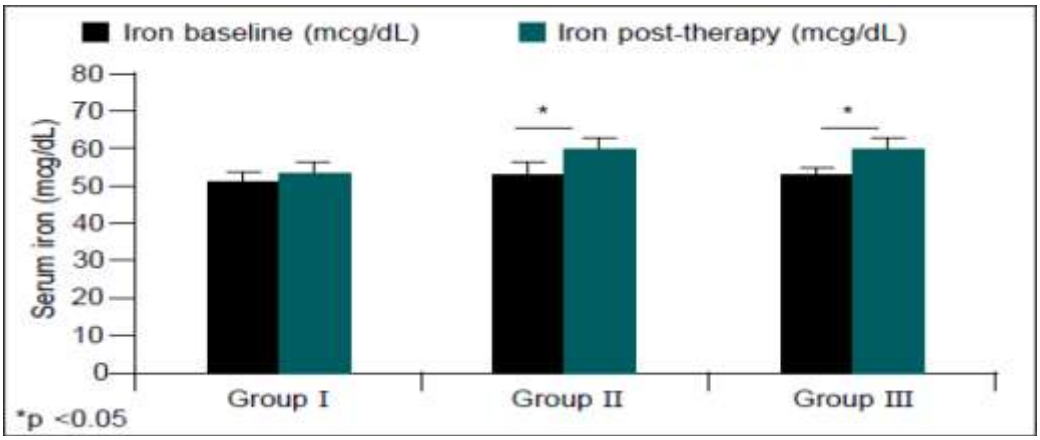


Figure 3 : Serum ferritin pre and post intervention amongst the three groups



International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1649-1659 www.ijprajournal.com ISSN: 2249-7781

Figure 4: Serum Iron pre and post intervention amongst the three groups.



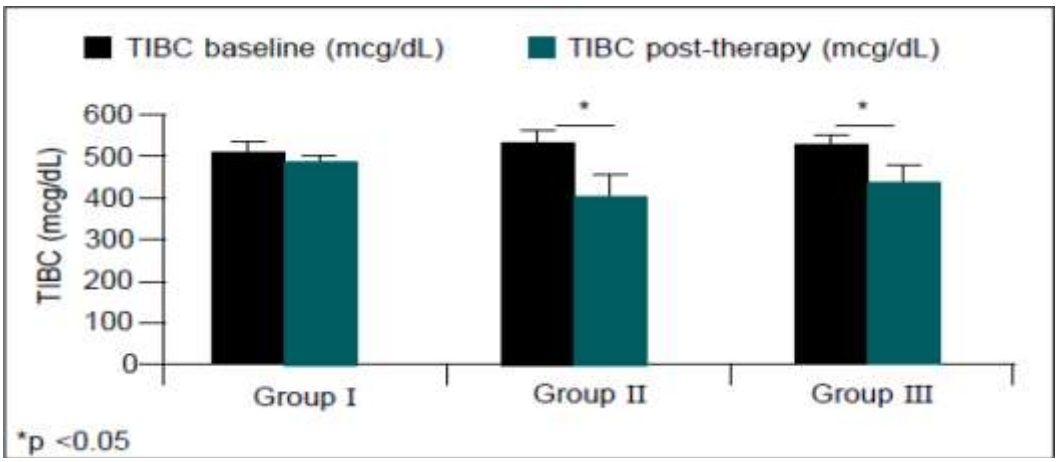


Figure 5: Serum TIBC pre and post intervention amongst the three groups

Figure 6: ADRs noted amongst the three groups.