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Original Research Article

Comparative Analysis of Intravenous Ferric Carboxymaltose vs Intravenous Iron Sucrose for the Treatment of Iron Deficient Anaemia in Pregnancy

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Abstract

Background and Aim: The most typical anaemia with a substantial impact on health is iron deficiency anaemia. Pregnant women experience a serious haematological and nutritional shortage, yet it is a controllable health issue. Oral iron is frequently used as a preventative measure and is advised as the first-line treatment for iron deficiency anaemia in pregnancy. In the current study, the effectiveness and safety of intravenous Ferric Carboxymaltose (FCM) against intravenous Iron Sucrose Complex (ISC) for treating iron deficiency anaemia in pregnancy are being compared.

Material and Methods: At a tertiary care teaching hospital in India, this prospective, comparative interventional study was conducted among the obstetrics and gynaecology departments. There were 200 instances in the study, which were divided into two groups of 100 cases each at random. 100 cases in Group A are treated with intravenous iron sucrose treatment. Group B: 100 cases are treated with intravenous iron carboxymaltose in this group. Following the start of treatment and four weeks and ninety days later, all patients were monitored. After 90 days, investigations on serum iron, haemoglobin, and RBC indices were conducted.

Results: In the study, there was a statistically significant variation in the haemoglobin distribution between the two groups. ($P<0.005$) Patients in the ferric carboxymaltose group had an average blood ferritin level of 98.10 21.14 (mg/L). Patients on the iron sucrose group had a mean blood ferritin level of 22.90 4.09 (mg/L). In the study, there was a statistically significant variation in the serum ferritin distribution between the two groups.

Conclusion: The results of our investigation revealed a considerable rise in Hb and ferritin levels in both groups following treatment, however the increase was greater in the group that received injection FCM than in the group that received injection iron sucrose. Moreover, this study proved that FCM is less dangerous than iron sucrose.

Keywords: Ferric Carboxymaltose, Iron Sucrose Complex, Iron Deficiency Anaemia, Serum Ferritin.

Introduction

One of the main health problems in the globe is anaemia. The most prevalent type of nutritional insufficiency affecting both industrialised and developing nations is iron deficiency anaemia. In the general population, iron deficiency (ID) and iron deficiency anaemia (IDA) are common, especially in children, women with abnormal uterine bleeding (AUB), during pregnancy, and in the postpartum period [1,2]. Since iron is necessary for all major metabolic pathways and is a functional component of haemoglobin, low iron levels have an impact on how much energy can be produced. Underperformance, tiredness, sensitivity to stress, and fatigue are some common symptoms of ID [3-6].

India accounts for 80% of the global maternal mortality from anaemia, of which South Asian nations account for almost half [7]. Anemia in pregnancy is described by the WHO as having a haemoglobin level of 11 gm% and a hematocrit of 33%. FOGSI (The Federation of Obstetric and Gynecological Societies of India) has suggested a cut off haemoglobin of 10 gm/dl for India because using 11 gm/dl as a cut off for the definition of anaemia is likely too high for India. Anemia during pregnancy is classified by the Indian Medical Council and Research (ICMR) as mild anaemia (Hb 10–10.9 gm%), moderate anaemia (Hb 7-9 gm%), severe anaemia (Hb 4-6.9 gm%), and very severe anaemia (Hb 4 gm%). The National Academy of Science Panel on Nutrition and Pregnancy has established a definition for iron deficiency in pregnancy as a ferritin level less than 12 ng/ml.

The physiological requirement for absorbed iron rises during pregnancy, from 0.8 mg per day in the first trimester to 7.5 mg per day in the third. This significantly increased iron need is not offset by dietary iron intake. A substantially higher expansion of plasma volume than that of red cell volume during pregnancy is what accounts for the small decline in haemoglobin levels and hematocrit values. The second trimester is when the difference in the rates at which erythrocytes and plasma are added to the maternal circulation is largest. The condition gets aggravated in pregnancy due to increase demand of the growing fetus [8].

Anemia generally causes fatigue, lightheadedness, and a weakened immune system that makes a person more susceptible to infections. Increased morbidity and mortality of pregnant women and their growing foetuses are linked to anaemia during pregnancy. Premature birth, low birth weight babies, preeclampsia, placental abruption, increased peripartum blood loss, heart failure, and deaths resulting from the condition have all been linked to iron deficiency anaemia [9,10].

Oral iron is frequently used during pregnancy to prevent iron deficiency and is advised as the first line of treatment for expectant mothers who have iron deficiency anaemia [11]. Oral iron replacement, on the other hand, has proven to be ineffective for treating moderate to severe iron deficiency anaemia in the second and third trimesters and is frequently accompanied by noncompliance due to gastrointestinal side effects like nausea, diarrhoea, heartburn, bloating, constipation, and dark stools.

Thus, guidelines advise doctors to think about intravenous (i.v.) iron administration in pregnant women if iron deficiency anaemia is intolerable to oral iron, there is not enough of an increase in haemoglobin following oral iron treatment, or if quick haemoglobin reconstitution is required [12,13].

Iron sucrose is the kind of intravenous iron that is most frequently utilised. It is safe and does not call for a test dose. The only drawback is that just a small dose can be administered at once. The maximum tolerated dose, which necessitates many hospital visits and places a significant strain on hospital resources, is 200 mg per day or 600 mg per week. The newest intravenous iron formulation, ferric carboxymaltose (FCM), enables for quick delivery and substantial quantities of iron (up to 1000 mg administered in a single dosage in 15 minutes). FCM does not cross-react with dextran antibodies since it is free of dextran and its derivatives, hence a test dose was never necessary. Its exceptional safety profile and convenience for both patients and medical professionals are the result of its very low immunogenicity potential. The cost-effectiveness of iron replacement therapy will also be improved by the capacity to administer high dosages in a single session.

In the current study, the effectiveness and safety of intravenous Ferric Carboxymaltose (FCM) against intravenous Iron Sucrose Complex (ISC) for treating iron deficiency anaemia in pregnancy are being compared.

Material and Methods

A prospective comparative interventional analytical investigation was conducted. The research was conducted over a 12-month period in India's tertiary care teaching hospital's department of obstetrics and gynaecology.

Pregnant women with iron deficiency anaemia, gestational ages between 16 and 34 weeks, and a single viable foetus without abnormalities met the qualifying requirements. This study excluded pregnant women who had anaemia caused by factors other than iron deficiency, had a history of blood transfusions and erythropoietin treatment during the current pregnancy, other medical conditions that complicated pregnancies, had a history of haematological diseases, or had a specific allergy to iron derivatives.

There were 200 cases in the study, which were divided into two groups of 100 cases each at random. 100 cases in Group A are treated with intravenous iron sucrose treatment. Group B: 100 cases are treated with intravenous iron carboxymaltose in this group.

A thorough clinical history (menstrual and obstetric), a history of prior treatments, including iron therapy, compliance with oral iron, and a list of chronic medical conditions were obtained at enrollment. A thorough examination was conducted, which included anthropometry, a general physical examination, and an obstetric examination. According to the established departmental protocol, routine prenatal examinations were performed. Red cell indices such as mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width (RDW), haemoglobin electrophoresis, serum ferritin levels, serum iron, total iron binding capacity (TIBC), and transferrin saturation were performed as part of anemia-specific investigations. The patients in the FCM group received i.v. FCM following the calculation of the overall iron shortage. A lengthier infusion protocol (30 min) than the manufacturer's (15 min) was employed due to the lack of safety data for its usage in pregnancy. The maximum dose per sitting was 1000 mg, which was diluted in 200 ml of 0.9% normal saline and given as an IV infusion over 30 min. Patients in the ISC group received 200 mg of ISC in 200 ml of NS over 15-20 min twice weekly until the dosage was finished, with a weekly maximum of 600 mg. Before and after the infusion, the patient's overall health, blood pressure, and pulse rate were recorded. Fetal heart rate was also monitored before and after the infusion. Every woman received a daily dose of 5 mg of folic acid. Any negative effects—small or significant—were highlighted. Following the start of treatment and four weeks and ninety days later, all patients were monitored. After 90 days, investigations on serum iron, haemoglobin,

and RBC indices were conducted. At follow-up visits, patients reported minor or serious adverse effects. Hemoglobin level change from baseline after 90 days was the main outcome. Changes in ferritin levels, improvements in serum iron studies and RBC indices, treatment safety and adverse effects, and perinatal outcome were considered secondary outcomes.

Statistical Analysis

Microsoft Excel 2007 was utilized to compile and input the collected data, which was then exported to the data editor page of SPSS version 15 for analysis (SPSS Inc., Chicago, Illinois, USA). The level of significance and confidence level for each test were set at 5% and 95%, respectively.

Results

The patients in the ferric carboxymaltose group had a mean haemoglobin of 10.80 1.20 gm%. The patients in the iron sucrose group had a mean haemoglobin of 9.54 0.09 g%. In the study, there was a statistically significant variation in the haemoglobin distribution between the two groups. (P<0.005)

Patients in the ferric carboxymaltose group had an mean blood ferritin level of 98.10 ± 21.14 (mg/L). Patients on the iron sucrose group had a mean blood ferritin level of 22.90 ± 4.09 (mg/L). In the study, there was a statistically significant variation in the serum ferritin distribution between the two groups. (P<0.05) (Table 3)

Table 1: Distribution of anemia among study participants

Hemoglobin (gm/dl)	Degree of Anemia	IV Iron Sucrose	IV Ferric Car boxy Maltose (FCM)	Total	P value
<6	Severe	0	10 (10%)	10	0.14
6-7	Moderate	62 (62%)	32 (%)	94	
8-9.5	mild	38 (38%)	58 (58%)	96	
Total		100	100	100	

Table 2: mean values comparison of hemoglobin between IV ferric carboxy maltose (FCM) vs IV iron sucrose

Hemoglobin mean values (gm/dl)	IV Ferric Car boxy Maltose	IV Iron Sucrose	P value
Before treatment	7.80	7.54	
Four weeks after treatment	9.52	9.18	0.54
90 days after treatment	10.80	9.54	0.002*

* indicates statistically significance at p≤0.05

Table 3: Comparison of mean values of serum ferritin between the two groups

Ferritin (mg/l) mean values	Patient of IV Ferric Car boxy Maltose (FCM) (n=100)	Patient of IV Iron Sucrose(n=100)	P value
Before treatment	21.05	20.04	0.45
90 days after treatment	98.10	22.90	0.003*

* indicates statistically significance at p≤0.05

Discussion

Parenteral iron therapy has traditionally been administered using iron sucrose to treat anaemia in pregnant women. While FCM can be provided in a higher quantity at a time, the main drawback of iron sucrose is its limited maximum permitted dose per week,

necessitating numerous visits to supply the essential iron dose.

The current study shown that ferric carboxymaltose and iron sucrose complex can be employed in pregnant women with iron deficiency anaemia not only to restore iron reserves but also to address haemoglobin deficits. After 4 weeks and after 90 days, the haemoglobin level increased in both modalities, which is consistent with earlier studies [14-18].

However, the increase in haemoglobin was slightly greater in the FCM-treated individuals compared to the iron sucrose-treated patients. All treatment modalities resulted in an increase in serum ferritin levels, whereas patients receiving FCM had a greater increase. All of the adverse reactions that were reported were minor, readily curable, and primarily limited to local reactions at the infusion site. There were no significant adverse effects linked to the treatment. There was no sign of an allergic reaction. There was no venous thrombosis reported. None of the negative events necessitated additional medical treatment.

When compared to Iron sucrose, FCM had a considerably lower burden of treatment, resulting in comparable gains in haemoglobin levels with a 12-fold lower total dose and 12-fold shorter exposure time. For some patients, a single dose of FCM may correct IDA without the need for recurrent administration, making it a more practical alternative to iron sucrose. The first study on the use of FCM for treatment IDA in pregnancy was published by Christoph P *et al* [19] the study concluded comparable safety and tolerability of FCM to ISC and that FCM offers the advantage of much higher iron dosage at a time reducing the need for repeated application and increasing patient's comfort. In contrast, the current study revealed that after 90 days, the haemoglobin levels in the FCM group were considerably greater than those in the ISC. FCM and oral iron therapy were examined by Breymann C *et al* to treat IDA in pregnant women. In people who are taking FCM, VanWyck *et al*. found an increase in haemoglobin of 2 gm/dl in the first week and 4 gm/dl after 2-4 weeks of therapy [20]. Jose *et al*. demonstrated that the FCM group had a considerably larger mean growth in haemoglobin at 12 weeks than the iron sucrose group [21]. Khan *et al* study's revealed a statistically significant increase in Hb in the FCM group compared to the iron sucrose group [22]. After 2 and 4 weeks of treatment, Sumathy *et al*. found an increase in haemoglobin levels among the iron sucrose group of 1.65 gm/dl and 2.35 gm/dl, respectively [23].

Serum ferritin levels are a major determinant of body iron reserves. Patients with anaemia and women with iron deficiency but no anaemia had significantly higher ferritin levels after receiving FCM infusions, according to research by Froessler *et al* [16] Serum ferritin levels in the two groups in the current study were comparable at baseline and 12 weeks later. Although FCM generates a quick increase in iron stores, it can be deduced that over the long run, ISC is just as capable of providing similar supplements for restocking iron reserves.

According to Kumari *et al* patients in the iron sucrose group had serum ferritin levels increase from 77.91 ng/dl to 182.86 ng/dl and those in the FCM group had levels increase from 78.05 ng/dl to 195.39 ng/dl [24]. Serum ferritin levels significantly increased in the FCM group compared to the Iron sucrose group, according to a study by Lunagariya *et al* [25]. According to a study by Khan *et al*, the FCM group saw a considerable rise in serum ferritin compared to the iron sucrose group. 22 Kharde *et al*. explained the mean rise in ferritin level, which occurred during the second and sixth weeks of therapy with iron sucrose, from 11.47 ng/ml to 47.69 ng/ml and 53.47 ng/ml, respectively [26].

Our study's limited sample size and shorter study period were one of its drawbacks. To assess the security and effectiveness of

intravenous ferric carboxymaltose therapy versus iron sucrose therapy in an Indian setting, large sample trials are needed.

Conclusion

The results of our investigation revealed a considerable rise in Hb and ferritin levels in both groups following treatment, however the increase was greater in the group that received injection FCM than in the group that received injection iron sucrose. Moreover, this study proved that FCM is less dangerous than iron sucrose. There were no reported severe negative effects. In cases of iron deficiency anaemia during pregnancy, ferric carboxymaltose is a well-tolerated, secure, and efficient substitute for iron sucrose. FCM offers the benefit of administering a big dose in a single sitting, causing an early rise in haemoglobin levels, requiring fewer doses overall, resulting in fewer hospital trips, and costing less overall for transportation, infusion equipment, and patient discomfort from repeated needle pokes.

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