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# Comparative study of iron sucrose versus ferric Carboxymaltose in the management of iron deficiency Anaemia in pregnancy

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**Abstract**
**Objectives:** Iron deficiency anemia is the most common hematological but manageable health problem encountered among the pregnant women globally but more common in developing countries like India.
**Methods:** It is interventional prospective comparative study conducted in Department of Obstetrics and Gynaecology at Dr. Yashwant Singh Parmar Govt. Medical College & Hospital Nahan, Sirmour (H.P) over a period of 2years from April 2017- April 2019. 100 pregnant patients with hemoglobin in the range 7gm/dl - 9 gm/dl between 16 to 34 weeks gestation were selected randomly. Patients were divided into two groups 50 each. Group 1 is Iron Sucrose (IS) group- patients were treated with intravenous iron sucrose in multiple doses on alternate days on 0,2,4,6 and 8, 200mg per day, total of 1000mg. Group 2 is Ferric Carboxymaltose (FCM) group were treated with intravenous FCM 1000mg single dose. In both group Hemoglobin and Serum ferritin were assessed before and after (3 & 6 weeks) parenteral therapy.
**Results:** There is significant rise of hemoglobin >2 gm/dl in Group 2 (FCM) as compared to in Group 1 (Iron sucrose). The single dose regime of FCM group was having very good compliance as compared to Iron sucrose group.
**Conclusion:** Intravenous Ferric carboxymaltose is more effective and safer as compared to Intravenous Iron sucrose in the management of anemia during pregnancy.

**Keywords:** Iron deficiency anemia, iron sucrose, ferric carboxymaltose, hemoglobin, serum ferritin

## Introduction

Iron deficiency anemia is the most common and major hematological, nutritional deficiency but manageable health problem encountered among the pregnant women globally but more common in developing countries especially in tropics like India especially in under privileged population. Iron Deficiency Anemia is the most common anemia with significant effect over health status [1]. According to WHO about 591,000 peri-natal deaths and 115,000 maternal deaths globally are due to iron deficiency anemia directly or indirectly [2]. Prevalence of anemia in South Asian countries is the highest in the world. About half of the global maternal mortality due to anemia occur in South Asian countries and India contributes to 80% of it [3]. WHO, defined anemia in pregnancy as hemoglobin levels < 11gm% and hematocrit < 33%? [4]. ICMR (Indian medical Council and research) has categorized anemia during pregnancy as - Mild anemia - Hb -10 - 10.9gm%, Moderate anemia -Hb - 7 - 9. gm%, Severe anemia - Hb – 4.6 - 6gm%, very severe anemia- Hb- < 4gm% [5]. Anemia affects all age groups starting from puberty and adolescence to peri-menopausal age. High incidence of anemia in India are because of low dietary intake of iron, poor bio-availability of iron, faulty food habits, phytate rich Indian diet, chronic blood loss during menses and high prevalence of infections like malaria and hookworm infestations [6].
So Many women have low or empty iron stores already at the start of pregnancy. A large French study, which included a total of 6648 women, showed depleted iron stores (serum ferritin <15 µg/L) in one out of five women (22.7%) of childbearing age [7]. During pregnancy, the physiological need for absorbed iron increases from 0.8 mg/day in the first trimester to 7.5 mg/day in the third trimester [8]. Dietary iron intake does not compensate for this strongly increased iron demand. Consequently, the risk of iron deficiency and, ultimately, iron deficient anemia increases during pregnancy. The condition gets aggravated in pregnancy due to increase demand of the growing fetus.

General symptoms of anemia are fatigue, dizziness, and impaired immune response predisposing to infections [9]. Anemia during pregnancy is associated with increased morbidity and mortality of pregnant women and their developing fetuses [10]. Iron deficiency anemia has been shown to be associated with an increased risk of premature birth and low birth weight [11], preeclampsia [12], placental abruption, and increased peripartum blood loss [13] as well as cardiac failure and related death [14-16].

In pregnant women, oral iron is often used for prophylaxis of iron deficiency and is recommended as first-line treatment for pregnant women with iron deficiency anemia [17].

However, oral iron substitution has shown to be insufficient for the treatment of moderate to severe iron deficiency anemia in second and third trimester, and is often associated with noncompliance due to gastrointestinal side effects like nausea, diarrhea, heartburn, bloating, constipation and dark stools [18]. Therefore, guidelines recommend that physicians consider intravenous (i.v.) iron administration in pregnant women with severe iron deficiency anemia (Hb < 9.0 g/dL), and in case of intolerability to oral iron as well, insufficient Hb increase after oral iron treatment or if there is a need for rapid Hb reconstitution [17-19]. Intravenous (i.v.) iron preparations provide greater and more rapid repletion of iron stores than oral iron therapy without the gastrointestinal side effects associated with oral substitution [18]. Parenteral therapy promises a better response in anemic patients and can obviate the need for blood transfusions in the antenatal and postpartum period [20].

The most commonly used intra venous iron preparation is Iron Sucrose. It does not require test dose and safe. The only disadvantage is limited dose can be given at one time. The maximum permissible dose is 200mg per day or 600 mg per week and requires multiple hospital visits and puts a heavy burden on hospital resources.

Ferric carboxymaltose (FCM) is the latest i.v. iron formulation which can be used at high doses and allows rapid administration (up to 1000 mg in a single dose infused in 15 min). Because it is free of dextran and its derivatives, FCM does not cross-react with dextran antibodies [21, 22] and never needed the administration of a test dose. More recently, the European Medicines Agency (EMA) concluded that no test dose should apply to i.v. iron products authorized in the European Union; yet staff and facilities to evaluate and manage anaphylactic or anaphylactoid reactions should be immediately available [23]. FCM molecule is novel iron complex which consist ferric hydroxide core chelated in a carbohydrate shell and this complex taken up by macrophages as a whole avoiding iron toxicity and oxidative stress [22].

## Materials and Methods

The present study was conducted in the Department of Obstetrics and Gynecology, Dr. Yashwant Singh Parmar, GMCH, Nahan, Sirmour, (HP). This was an intervention Prospective Comparative Study done over a period of two year (April 2017-2019) after approval from hospital ethical committee. The antenatal women attending Department of OBG were the source of our sample. 100 antenatal women were studied, 50 of whom were given Iron Sucrose infusion and the remaining 50 were given Ferric Carboxymaltose infusion.

### Inclusion Criteria

Antenatal women attending between 16-34 weeks of gestational age, with hemoglobin between 7gm% to 9 gm%, Serum ferritin level < 30 mcg/L, microcytic hypochromic anemia, with iron intolerance to oral therapy, likely to come for follow up, willing for enrolment in study.

### Exclusion Criteria

Anemia due to other cause, presence of chronic infections like hepatitis, HIV, known case of hypersensitivity to iron preparations, serum transaminase > 1.5 times, serum creatinine level >2mg/dl and Thalassemia,

A detailed clinical history (menstrual, obstetric), previous treatment history, including iron therapy, compliance with oral iron and chronic medical illness. Demographic data like age, education, socioeconomic status, height, weight was recorded in Performa. Complete general physical examination and obstetric examination was done. Routine antenatal investigations were done according to standard departmental protocol. Investigation related to anemia like hemogram, peripheral blood smear, red cell indices (MCHC, MCV, MCH), Hb electrophoresis, serum ferritin levels, serum iron were done.

### Total Iron Requirement was calculated

Total iron dose required (mg) = 2.4 x Body weight(kg) x (Target Hb - Actual Hb) + 500mg (storage iron).

Target Hb level has been taken as 11 gm/dl or %

Routine deworming of all antenatal women done by oral albendazole tablet 400mg.

### Group 1: Iron Sucrose (IS)

Iron sucrose was given in a dose of 200 mg intravenously 100 ml 0.9% Normal saline over a period of 30mins. on alternate days until the total dose was administered, not to exceed 600 mg per week. The first few ml was infused intravenously over a period of 15 mins, if there was no adverse reaction remaining amount was infused over 30 mins period.

### Group 11: Ferric Carboxymaltose (FCM)

Ferric carboxymaltose was given in 0.9% Normal Saline as follows

100 - 500 mg in 100ml NS - 15 mins duration
500 - 1000mg in 200ml NS - 30 mins duration,

Maximum dose per sitting was 1000mg. Subsequent doses if needed were planned on 7$^{th}$ and 14$^{th}$ day.

The general condition of antenatal period, blood pressure, pulse rate was noted before infusion and every 5 mins during infusion. Fetal heart rate was monitored before and after infusion. Any minor and major adverse effects were noted. Hemoglobin level and serum ferritin was done after 3 and 6 weeks.

### Statistical analysis

The statistical data was done by statistical package for social science (SPSS)

## Results

Results were encouraging with good patient satisfaction, satisfactory rise in Hb and serum ferritin, easy administration of dose and minimal side effects. Epidemiology, both the groups were compared with age, socioeconomic class, parity and residence. Both the group were comparable on base line characteristics. Patients were taken from all age group of 19-41 year of age and most of the patients were below 30 years of age. Most of the patients were multipara in both groups and most of the patients were illiterate

**Table 1:** Baseline comparison of epidemiological data between both group

| Variable | Group I(IS) | Group II(FCM) |
|---|---|---|
| Mean age (years) | 25.01+_ 3.48 | 23.7+_ 3.56 |
| Mean gestational age(weeks) | 32.43+_1.8 | 30.23+_ 2.36 |
| Primigravida | 32% | 41% |
| Multigravida | 68% | 59% |
| Rural | 44% | 42% |
| Urban | 56% | 58% |
| Literate | 26% | 30% |
| Illiterate | 74% | 70% |
| Unemployed | 77% | 79% |

**Table 2:** Comparison of two groups according to the results obtained

| Variable | Group I(IS) | Group II(FCM) |
|---|---|---|
| Baseline hemoglobin(g/dl) | 8.28 g/dl | 8.27 g/dl |
| Haemoglobin (g/dl) at 3 weeks | 8.92 g/dl | 9.83 g/dl |
| Haemoglobin (g/dl) rise at 3 weeks | 0.64 g/dl | 1.56 g/dl |
| Haemoglobin (g/dl) at 6 weeks | 10.1 g/dl | 10.9 g/dl |
| Haemoglobin (g/dl) rise at 6 weeks | 1.82 g/dl | 2.6 g/dl |
| Baseline serum ferritin(mcg/L) | 14.2 | 12.6 |
| Serum ferritin(mcg/L) at 3 weeks | 104.6 | 146.4 |
| Serum ferritin (mcg/L) rise at 3 weeks | 90.4 | 133.8 |
| Serum ferritin (mcg/L) at 6 weeks | 93.4 | 124.3 |
| Serum ferritin (mcg/L) rise at 6weeks | 79.2 | 111.7 |

Mean Hb in patients of Group I (IS) was 8.28 g/dl and that of Group II(FCM) was 8.27 g/dl both groups being statistically comparable ($p< 0.0001$).

At three weeks post treatment, mean total Hb level was significantly higher in Group II as compared to that of Group I (9.83 g/dl verses 8.92 g/dl $p< 0.0001$). Mean rise in Hb was 0.64g/dl in Group I and 1.56 g/dl in Group II (Table 2).

At six weeks after treatment mean total hemoglobin level was significantly higher in Group II as compared to Group I (10.9g/dl verses 10.1g/dl $p< 0.0001$). At six weeks mean rise in Hb level in Group I was 1.82 g/dl as compared to 2.6 g/dl in group II (Table 2), the rise is highly significant statistically ($p< 0.0001$). At six weeks after treatment in Group I patients rise in Hb was from 0.64 to 1.82 only, while in Group II was significantly more from 1.56 g/dl to 2.6 g/dl (Table 2).

**Table 3:** Post treatment rise in hemoglobin (g/dl) at 6 weeks

| Rise in Hb g/dl | Group I(IS) No. % | Group II (FCM) No. % |
|---|---|---|
| 0.5 – 0.99 | 02 | 00 |
| 1.0 – 1.49 | 43 | 13 |
| 1.5 – 1.99 | 05 | 18 |
| 2.00 – 2.49 | 00 | 12 |
| >2.5 | 00 | 07 |
| Total | 50 (100) | 50 (100) |

Mean baseline serum ferritin in Group I was 14.2mcg/L and in Group II was 12.6mcg/L, the difference being statistically insignificant (p=0.21). At 3 weeks post-treatment mean total serum ferritin level was significantly higher in Group II as compared to Group I(146.4mcg/L verses 104.6mcg/L, $P< 0.0001$). Total rise in mean serum ferritin level at three weeks was more in Group II as compared to Group I (133.8 vs 90.4mcg/L). Statistically the rise was higher ($p< 0.0001$) Table 2.

**Table 3:** Comparison of adverse effect and mean days of hospital stays between both groups

| Adverse reaction | Group I(IS) | Group II(FCM) |
|---|---|---|
| Thrombophlebitis | 4 | 1 |
| Nausea & Vomiting | 2 | 2 |
| Headache | 2 | 1 |
| Dizziness | 2 | 2 |
| Fever / Chills | 2 | 2 |
| Rashes & Itching | 1 | 0 |
| Abdominal pain | 1 | 0 |
| Anaphylactic reaction | 0 | 0 |
| Total | 14 | 08 |
| Hospital stay | 10.2 days | 3.2 days |

Mild adverse reactions were observed in 28% patients in Group I and in Group II 16% patients. No major side effect was noted making the both drugs safe in pregnancy. Mean duration of hospital stay in Group I was 10.2 days and it was very less in Group II 3.2 days.

## Discussion

We as a nation have been battling against anemia since many years. Iron is one of the most abundant minerals in nature and most life forms require it. Ironically, it is also the most common nutrient deficiency in the world leading to anemia, which has now become a serious global health concern. It is alarming to know that the prevalence of anemia in India is as high as 62% and it is projected that India has the utmost prevalence among the South Asian countries [24]. World Health Organization recommends Hb concentration value of minimum 11gm% during pregnancy and in peripartum period. The prevalence pertaining to anemia in pregnancy is 33-89% and incidence being 42% (WHO, 2015) [25]. As per ICMR 2010, 87% pregnant women are anemic out of which 10% have severe anemia. As per NFHS-2, 46% of urban women are anemic [26]. Anemia in pregnancy is associated with unfavorable consequences both for mother and perinatal mortality and morbidity. The detection of anemia in pregnancy and its effective management is available, affordable and possible. This study aimed to compare between parenteral iron sucrose and ferric carboxymaltose which is newer drug approved for use in iron deficiency anemia during second and third trimester.

In our study mean age of patients was 23-25 years of age and mean gestational age was 30-32 weeks. In our study anemia is more common in multigravida than in primigravida. We found that anemia is more common in urban area (due to faulty dietary habits) as compared to rural area.

In our study average rise of hemoglobin at six weeks was1.82 g/dl in Iron sucrose group while 2.6 g/dl in ferric carboxymaltose group. Similarly, there is major difference in rising of serum ferritin in both groups. Average rise of serum ferritn in IS Group was 79.2mcg/L while in FCM Group was 111.7mcg/L.

In our study mean duration of hospital stay in Group I was 10.2 days and it was very less in Group II 3.2 days

This study was conducted with the aim to compare the efficacy and safety of intravenous iron sucrose with ferric carboxymaltose in iron deficiency anemia of pregnancy. Iron sucrose was given as 200mg/day an alternate day while ferric carboxymaltose as 1000mg/week uptill desired iron required. In

this study number of required iron sucrose for desired requirement was 4-6 doses as compared to 1-3 doses of Ferric carboxymaltose.

Ferric carboxymaltose thus seems to superior iron sucrose for definitive treatment of anemia in pregnancy. The only limiting factor is its high cost but this is very well compensated when the number of visits/days of admission in hospital is taken into account. Also reduced frequency of venous access reduces the risks of infection.

## Conclusion

Treatment with FCM resulted in rapid replenishment of iron stores in pregnant women with significantly high Hb rise over a 6 weeks period. The convenient dosing with lesser total number of required doses resulted good compliance. Significantly shorter duration of treatment with FCM when considered in a community setting with a patient friendly dosing causes less discomfort and hospital visits. Because of high efficacy and safety of FCM it must be used as a first line drug in the management of Iron deficiency anemia in pregnancy to decrease high incidence and burden of the disease on our society set up.

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