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Original Research Article

Intravenous ferric carboxymaltose for anaemia in pregnancy

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ABSTRACT

Background: Anaemia in pregnancy is associated with unfavourable consequences both for the mother and the fetus and is a major cause of maternal and perinatal mortality and morbidity.
Methods: The study was conducted over a period of one year in which 100 pregnant females who met the inclusion criteria were administered ferric carboxymaltose (FCM) preparation.
Results: There was significant rise in mean haemoglobin and serum ferritin after transfusion of ferric maltose in the patients with very less adverse effects.
Conclusions: FCM, because of its high efficacy and safety can revolutionize the management of iron deficiency anaemia (IDA) in pregnancy.

Keywords: Iron deficiency anaemia, Ferric carboxymaltose, Haemoglobin

INTRODUCTION

Anaemia during pregnancy is one of the most common issue encountered both in developing and developed countries.[1] Peri –partum iron deficiency anaemia (IDA) is associated with significant maternal, fetal and infant morbidity. Poor outcomes for the fetus and infant include: preterm birth, fetal growth restriction, intra uterine death, low Apgar scores and infection.[2] Progression from iron deficiency to iron deficiency anaemia (IDA) in pregnancy is common due to the increased demand for iron during pregnancy required to support maternal hemoglobin mass expansion as well as the growing fetus and placenta.[3] This is further aggravated by blood loss associated with delivery. Deliveries by both caesarean section and vaginal deliveries that require instrumentation/intervention represent an even greater risk of increasing a woman's vulnerability for peri-partum blood transfusion, chronic IDA and iron store depletion, all compromising maternal well-being. However, this recognition has not resulted in a universal approach of iron supplementation .[4,5,6]

According to world health organization (WHO), anaemia in pregnancy has been defined as hemoglobin <11 gm and hematocrit<33%. As per center of disease control and prevention (CDC) defined as Hb<10.5 gm% during 1st and 3rd trimesters and Hb<11 gm% during 2nd trimester.[7] Indian council of medical research (ICMR) had categorized anaemia as mild Hb 10-10.9 gm%, moderate 7-9.9 gm%, severe Hb 4-6.9 gm%, very severe Hb<4 gm%.[8] Anaemia during pregnancy in India contributes as cause to 20% maternal death directly and 50% for associated causation.[9]

Iron deficiency is potentially both preventable and treatable. Effective management strategies that allow women to replenish iron stores, both antenatal or during labor, restore hemoglobin values and are likely to enhance the health of the mother and infant .[10] For many decades the mainstay treatment of IDA has been oral iron and red blood cell (RBC) transfusions. However, oral iron supplementation can lead to significant side effects resulting in non-compliance in many patients and the risks for RBC transfusion are well described and should be avoided whenever.[11,12] Intravenous iron formulations

offer an alternative approach in the presence of moderate or severe anaemia, intolerance of or non-adherence to oral iron and malabsorption states.[13] Intravenous iron is less commonly used as fear of anaphylaxis with iron dextran formulations, and long infusion time with iron polymaltose, have led to reluctance amongst clinicians.[14] The development of dextran free parenteral iron formulations with an improved safety profile, and a more rapid delivery time suggests that intravenous iron should be considered as a mainstay treatment for moderate to severe IDA.[15]

Iron Sucrose and Ferric carboxymaltose (FCM) are dextran free intravenous iron alternatives. Ferric carboxymaltose (FCM) is a newer dextran-free iron formulation with a near neutral pH, physiological osmolarity and increased bio availability which allows for single dose, short 15 minute infusion time and higher dosing (up to 1000 mg).[16] FCM is novel non-dextran with type I complex administered rapidly 500mg in 100ml NS over 6 mins and 1000-1500 mg in 250 ml NS over 15 minutes as intravenous infusion.[17] These properties make FCM an attractive alternative to iron sucrose in terms of risk profile, efficacy, patient comfort and convenience, staff and institutional resource utilization.

The primary aim of this study was to assess the use of intravenous FCM in the correction of IDA in pregnant women. The secondary aims were to determine the extent and severity of adverse effects of FCM.

METHODS

This study was conducted in the Post Graduate Department of Obstetrics and Gynecology, Sri Maharaja Gulab Singh Hospital, Jammu and Kashmir, over a period of one year from June 2019 to July 2020 in which 100 pregnant females who met the inclusion criteria were considered for this study.

Inclusion criteria

In the study inclusion criteria for the selection of the pregnant female was Singleton pregnancy and gestational age 28-36 weeks

Exclusion criteria

In the study inclusion criteria for the selection of the pregnant female was pregnancy<28 weeks period of gestation, Known history of hypersensitivity to any iron preparations, Prior history of blood transfusion or anticipated need for blood transfusion during the study, history of any disease associated with iron overload e.g. thalassemia, haemochromatosis, or any other iron storage disorder, Known case of hypothyroidism, multiple pregnancy, serious medical condition or any uncontrolled systemic disease e.g. chronic renal disease, severe cardiovascular disease, chronic or acute hepatic disorder, tuberculosis etc, known case of hepatitis B/C infection or of acquired immune deficiency syndrome (HIV/AIDS), evidence of any significant congenital anomaly on ultrasound.

Total dose was calculated by formula:

2.4 × Body weight in kg × (Target Hb - Actual Hb in g/dl) + iron storage depot (mg).

Target Hb has been taken as 11 g/dl as per WHO. For FCM maximum single dose of 1000 mg (20 ml) diluted in 250 ml sterile 0.9% normal saline was given over a period of 15 minutes. Each patient was kept under observation in the hospital for at least 4 hours for signs of any intolerance. All minor and major local and systemic side effects were documented. Delayed side effects of both the drugs were addressed and a protocol was followed to monitor them. Result was assessed by measuring the rise in Hb (g/dl) and serum ferritin (mcg/L) at 2 weeks treatment and adverse effects were tabulated.

Data was entered using Statistical Package for Social Sciences and in Microsoft excel software. Continuous variables were summarized in the form of mean and standard deviation. Categorical variables were summarized as percentage.

RESULTS

In our study, there was higher incidence of anaemia among pregnant females of reproductive age group that constituted about 60% of total patients (Table 1).

Table 1: Distribution of pregnant females according to age (n=100).

Age (years)	Percentage (%)
<20	10
21-25	60
26-30	19
31-35	09
36-40	01
>40	01

Table 2: Distribution of pregnant females according booking status and residence (n=100).

	Percentage (%)
Booking status	
Booked	16
Unbooked	84
Residence	
Urban	46
Rural	54

In our study 84% of females in our study were unbooked cases of the hospital and 46% belonged to urban areas

depicting lack of self-care and non-compliance even inn educated class of people (Table 2).

Multigravida females are more vulnerable to develop anaemia during pregnancy compared to primigravida females in our study constituting about 59% of total patients. Less inter pregnancy intervals, low socio economic background, nutritional deficiency is more in multigravida females (Table 3).

Table 3: Prevalence of IDA depending on parity.

Parity	Percentage (%)
Primigravida	41%
Multigravida	59%

The dose requirement for treatment of IDAs less with FCM. Maximum patients required 1-2 doses. 1 patient of severe anaemia was treated with 5 doses of FCM (Table 4).

Table 4: Number of doses administered.

No of doses (vials)	Number
1-3	99
4-6	1
>6	0

Mean Hb was high with FCM and average Hb post treatment was 2.91gm/dl which was statistically significant. The mean rise of serum ferritin was also high (64.88 ng/ml) which was also statistically significant (Table 5).

Table 5: Laboratory parameters.

Variables	Pre value (average)	Post value (average)	P value
Hb	8.02 gm/dl	10.93gm/dl	<0.05
Ferritin	29.92 ng/ml	94.8 ng/ml	<0.05

Table 6: Adverse effects of FCM (n=20).

Side effects	N
Local reaction (pain at site)	3
Diarrhoea	5
Nausea	4
Constipation	2
Abdominal pain	2
Headache	1
Skin discolouration	1
Vomiting	2
Hyper/hypotention	0
Hot flushing	0

In the study 20 patients had mild side effects with the administration of FCM, most common being diarrhea (5) followed by nausea (4) and local pain at injection site depicting the safety of FCM (Table 6).

DISCUSSION

FCM is a novel iron complex which consists of a ferric hydroxide core stabilized by a carbohydrate shell. It has a very low immunogenic potential and therefore not predisposed to anaphylactic reactions. It is a macromolecule complex with a molecular weight of 150 Kilo Daltons with a very high stability and half-life (16 hours) On administering, it allows for controlled delivery of iron within the cells of the reticuloendothelial system and subsequent delivery to the iron-binding proteins ferritin and transferrin, with minimal risk of release of large amounts of ionic iron in the serum thus allows rapid administration of high doses of iron in a single sitting without much safety concerns.[18]

Our study showed significant hemoglobin and serum ferritin rise after administration of FCM which were similar to results seen in study conducted by Agarwal D et al with Hb rise of 2.92 gm/dl and ferritin rise of 64.97 ng/ml.[18] Adverse effects seen with carboxymaltose were also very mild and less which were similar to studies conducted by Joshi SD et al and Agarwal D et al.[17,18]

FCM thus seems superior to Iron sucrose for definitive treatment of anaemia 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 are taken into account. Also reduced frequency of venous access reduces the risk of infection.

The key finding of our study is that in women presenting with IDA relatively late in pregnancy, a FCM infusion prior to delivery significantly increased hemoglobin levels and improved iron stores. Further, we demonstrate that FCM appears to be a safe and effective treatment modality for the correction of IDA, as no serious adverse events and only few minor adverse events reported. Reassuringly, patient satisfaction rating and improvement in perceived wellbeing assessed in the postnatal period was high.

CONCLUSION

FCM, because of its high efficacy and safety can revolutionize the management of IDA in pregnancy. Therefore, it must be used as a first line drug for its management to decrease the high incidence and the burden of the disease on our health set up. The rapid delivery option of a large single dose of FCM offers a promising treatment modality for pregnant women who need correction of iron deficiency and anaemia, over other IV iron formulations that have low dosage limits, such as iron sucrose (200 mg). The properties of FCM may also reduce the burden on the patient and the health

care system. Limitation of study: Short and long term maternal and neonatal outcomes after the injection were not noted.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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