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ROLE OF FERRIC CARBOXYMALTOSE FOR ANEMIA IN PREGNANCY.

KEYWORDS

Pregnancy, Iron deficiency anaemia, peripartum anaemia, intravenous Ferric carboxymaltose, Red blood cell transfusion.

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ABSTRACT

AIMS AND OBJECTIVES –The aim of the study was to assess the safety and efficacy of intravenous Ferric carboxymaltose in pregnant women for correction of mild, moderate and severe anaemia in the second and third trimester.

Current options for treatment are limited, these include oral iron supplementation, which can be ineffective and poorly tolerated and red blood cells transfusion, which carry an inherent risk and should be avoided. Ferric carboxymaltose is a new treatment option that may be better tolerated.

METHODS: It was a prospective observational study; 50 anaemic pregnant women received Ferric Carboxymaltose (FCM) upto 15mg /kg between 24 - 40 weeks of pregnancy (median 35 weeks G. age). Efficacy of treatment was assessed by rise in Hb% level after 3 & 6 weeks post infusion.

RESULTS: - Intravenous ferric Carboxymaltose infusion, significantly increased the Hb% above baseline levels in all women. Increased Hb values were observed after 3 weeks – 6 weeks.Ferritin values increased significantly after the infusion. Foetal heart rate monitoring did not indicate a drug related negative impact on the foetus. > 80% of women reported an improvement in their well being. No serious side effects were found and minor side effect was seen in 5 patients.

CONCLUSIONS: Ferric Carboxymaltose is a safe and effective treatment of iron deficiency anaemia in pregnancy.

Iron deficiency is recognised as a common nutritional deficiency amongst women of child bearing age in both the developed and developing world. Peripartum iron deficiency anaemia is associated with significant maternal, foetal & infant morbidity. Poor outcome for the foetus and infant include – preterm birth, foetal growth restriction, intrauterine foetal death, low APGAR score & infections. Peripartum maternal iron deficiency has also been associated with childhood development problems and negative mother-infant interactions. There is increased incidence of iron deficiency anaemia during pregnancy because of increased requirement to support maternal haemoglobin mass expansion as well as growing foetus and placenta.

Iron deficiency is potentially both preventable and treatable. Effective management strategies that allow woman to replenish iron stores, both antenatal or during labour restore haemoglobin values and likely to enhance the health of mother and infant.

For many decades the main stay of treatment for iron deficiency anaemia has been oral iron and RBC transfusions. However, oral iron supplementation can lead to significant effects resulting in non compliance in many patients and the risk of RBC transfusion are well described and should be avoided whenever possible.

Intravenous iron formulations offer an alternative approach in the presence of moderate or severe anaemia. Intravenous iron less-commonly causes anaphylactic reactions. 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 iron deficiency anaemia.

Iron source and Ferric Carboxymaltose are dextran free intravenous iron alternatives. Iron sucrose and Ferric carboxymaltose are dextran free intravenous iron alternatives. When compared to oral iron, Ferric carboxymaltose is superior with respect to the rate of both haemoglobin increase and iron store replenishment, combined with good safety profile.

Ferric Carboxymaltose is a newer dextran free iron formulation with a near neutral PH, Physiological osmolarity and increased bioavailability which allows for single dose, short 15 min infusion time and higher dosing (up to 1000 mg).

The primary aim of this study was to assess the use of intravenous ferric carboxymaltose in the correction of iron deficiency anaemia in pregnant women.

MATERIAL & METHODS:-

Informed consent was taken from the patient. The study was performed in Medical college based hospital.

Pregnant women with documented Iron deficiency anaemia, defined as Hb < 11.0 g/dl who presented as outpatient were infused with Ferric Carboxymaltose 1000 mg in 200 ml of Normal saline within 15-20 minutes. A total of 50 women were included. Maternal blood pressure was taken on every five minutes during infusion and foetal heart rate was assessed before and after infusion. Blood samples were taken to measure haemoglobin and in some cases ferritin levels prior to infusion and then again at 3 wks & 6 wks post infusion. Women were observed for one hour post infusion before being discharged home.

The date were analysed using Graph pad Prisms using p values of ≤ 0.05 to indicate significance. Available preinfusion, post infusion and post partum haemoglobin, ferritin and transferritin saturations levels were compared using ANOVA test.

RESULTS:- The characteristics of the women receiving ferric carboxy maltose for iron deficiency anaemia are outlined in Table 1. A total of 50 women received Ferric carboxy maltose for antenatal iron deficiency anaemia. Following infusion haemoglobin values were repeated by the obstetric team at 3 weeks and 6 wks post partum. All women responded to the treatment with increased haemoglobin levels.

Of the 50 women entered into the study 31 women had severe anaemia (Hb < 8.0 gm/dl) while 16 women had moderate anaemia (Hb 8.0 – 9.5 g) dl and the remaining 3 women had mild anaemia (Hb – 9.5- 11.0 gm / dl).

Changes in haemoglobin concentration over post infusion period are

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presented in Table 1. The pre infusion haemoglobin level was significantly lower than haemoglobin values measured at all subsequent visits (P< 0.05 in each case).

By 8 weeks post infusion, these values returned back to levels comparable with those observed at 3 weeks post infusion which was still significantly higher than pre-infusion levels. For all three severity groups haemoglobin levels increased post infusion at 3 wks and 6 wks to be significantly higher than base line levels (P<0.01 in all cases). Ferritin values increased significantly after the infusion.

Table – 1. Demographic information of women in the study.

Age	24.3 ± 5.2
BMI	24 ± 6.2
Gravida	4 ± 3
Mode of delivery	
Vaginal	28
Elective C.S	13
Emergency C.S	04
Instrumental	05
Oral iron supplements	33
G. Age at intervention (wks)	33 ± 3.6
Haemoglobin at booking (12 wks)	9.1 ± 1.1
Ferritin at booking (12 wks)	16 mcg/dl ± 1.6

Table. 2. Haemoglobin levels (g/dl) across the testing period for women in the study.

	No. of patients, pre infusion	No. of pts, 3wks post infusion	No. of pts, 6 wks post infusion
Mild 9.5-11.0 g/dl	03	04	13
Mod 8.0–9.5 gm/dl	16	29	34
Severe <8.0 gm/dl	31	17	64

All adverse reactions are presented in table 3.No serious adverse effects were recorded in any of the 50 women receiving an infusion. Minor side effects occurred in 10 pts (20%). One patient required medication with metoclopramide for nausea and vomiting. All other adverse effects were self limiting. Foetal heart rate monitoring did not indicate a drug related adverse effect on the foetal heart rate pattern. Red blood cell transfusion was required in only 1 pt. (2%) for post partum haemorrhage.

Table 3. No of women experiencing drug related adverse events following infusion of Ferric carboxy maltose.

Adverse effect	n%
Local (injection site irritation / burning)	4(8%)
Systemic	
• Hypotension	1 (2%)
• Headache	2 (4%)
• Nausea / vomiting	1 (2%)
• Pruritus	2 (4%)

DISCUSSION

This was a prospective study and the key finding of the study was that women presenting with Iron deficiency anaemia in 3rd trimester can be corrected with Ferric carboxymaltose infusion. Furthermore Ferric carboxymaltose appears to be safe and effective treatment modality for the correction iron deficiency anaemia. In our study, first trimester booking bloods showed only discrete anaemia with mean Hb level of 10.3 g/l, but later on by 3rd trimester the developed moderate to severe iron deficiency anaemia. For some women oral iron supplementation appears to be sufficient to maintain adequate iron stores. However many women develop moderate to severe iron deficiency anaemia despite oral iron supplementation.

The rapid delivery option of a large single dose of Ferric carboxymaltose offers women who need correction of deficiency and anaemia over their I.V iron formulations that have some dosage limits, such as iron sucrose (200 mg). The use of Ferric Carboxymaltose may also reduce the burden on the patients and the health care system.

In our study only one patient required RBC transfusion following a significant PPH.

CONCLUSION – The data from our study is consistent with existing retrospective data that Ferric carboxymaltose in 2nd and 3rd trimester of pregnancy is likely to be safe and effective. Despite moderate to severe anaemia at presentation, labour associated blood loss was tolerated well resulting in low peri partum RBC transfusion rates. No serious adverse events were recorded. Well being also improved for the majority of women after the infusion.

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