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Ferric carboxymaltose: Boon for anaemic pregnant patients

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Abstract
Background: Iron deficiency is a major cause for anaemia. IDA is associated with significant maternal, fetal and infant morbidity. Iron deficiency is potentially both preventable and treatable. Current treatment options are limited and include oral iron supplementation, which can be ineffective and poorly tolerated and red blood transfusions which carry an inherent risk and should be avoided. Ferric caboxymaltose is a new treatment option that is better tolerated and has rapid improvement in hemoglobin levels. This study was designed to assess safety and efficacy of ferric caboxymaltose in pregnant anaemic patients.
Methods: It was a prospective observational study included 50 anaemic pregnant patients who received ferric carboxymaltose in second and third trimester of pregnancy. Effectiveness was assessed by repeat haemoglobin estimation after 4 weeks. Safety was assessed by analysis of adverse reactions and foetal heart rate monitoring during infusion.
Results: Most of the women were in age group 20-25 yrs and had mild anaemia as per WHO guidelines. Intravenous ferric carboxymaltose significantly improved hemoglobin levels in all women which was statistically significant p value (0.00). No serious adverse events were noted.
Conclusion: Intravenous ferric carboxymaltose is a safe and effective treatment option for anaemia in pregnant patientsn.

Keywords: Iron deficiency Anaemia, ferric-carboxymaltose, pregnant patients, safety, efficacy

Introduction

Iron deficiency is recognized as a common nutritional deficiency amongst women of child bearing age [1]. Physiological need for absorbed iron increases from 0.8 mgld in first trimester to 7.5 mgld in 3rd trimester [2]. WHO has classified anaemia into mild (9-11 gm%) moderate (7-9 gm%) and severe (<7 gm%)categories [3].

Iron deficiency is a major cause for anaemia. IDA is associated with significant maternal, fetal and infant morbidity. Women with iron deficiency are at increased risk of medical interventions such as red blood transfusion [4]. They are also at increased risk of cardiovascular problems, reduced physical and cognitive performance, reduced immune function weakness and increased depressive episodes [5]. In fetus and neonate it can cause preterm birth, fetal growth restriction, intrauterine fetal demise, low Apgar scores and increased risk for infections [6]. It has also been associated with childhood development problems [7] and negative mother infant interactions such as increase in negative statements and decreased responsiveness [1].

During pregnancy there is increased demand of iron for maternal hemoglobin mass expansion as well as growing fetus and placenta. Deliveries both by caesarean and vaginal delieveries that require instrumentation / intervention are at even greater risk [5] for blood loss and consequent complications of anaemia and hence compromise maternal well being [8].

Iron deficiency is potentially both preventable and treatable. During pregnancy, oral iron is often used for prophylaxis of iron deficiency and is recommended as first line treatment for iron deficiency anaemia [9]. However, it is often associated with significant gastro intestinal side effects and is insufficient for the treatment of severe iron deficiency anaemia [8]. Hence it has been recommended that intra venous iron should be considered in patients with severe iron deficiency anaemia, in case of intolerability to oral iron as well as insufficient hemoglobin rise after oral iron supplementation or if there is a need for rapid hemoglobin rise as in patients near term [10, 9, 8]. Intravenous (i.v.) iron preparations provide greater and more rapid repletion of iron stores than oral iron therapy without the gastro intestinal side effects associated with oral iron [8].

In case of severe anaemia RBC transfusions are often used but should be avoided where ever possible due to well known complications [11].

Risk of anaphylactic reaction with iron dextran formulations has led to reduction in use of intra venous iron therapy also iron polymaltose has long, infusion time that has led to reluctance among physician for using this formulation [12].

The development of dextran free parenteral iron formulation with an improved safety profile and rapid delivery time has revolutionized use of this modality for treatment of iron deficiency anaemia and it should be considered main stay treatment for moderate to severe IDA [13].

Iron sucrose and ferric carboxy maltose are dextran free intravenous iron afternatives. Serious side effects are rare with iron sucrose, however minor side effects can occur in 18% of patients which in part may be attributed to its non physiological physical properties like high PH and high osmolarity.

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 [2]. As it is free of dextran it does not cross react with dextran antibodies [14, 15] and do not need administration of a test dose. The FCM molecules consist of an iron hydroxide core chelated in a carbohydrate shell and this complex is taken up as a whole by macrophages, leading to a very low levels of nontransferrin bound iron, avoiding iron toxicity and oxidative stress [15]. These properties make ferric carboxymattose an attractive alternative to iron sucrose in terms of risk profile, efficacy, patient comfort and convenience, staff and institutional resource utilization.

Contraindication include a history of anaphylaxis or reaction to parenteral iron therapy, first trimester of pregnancy, active acute or chronic infection and chronic liver disease [16]. Each 10 ml vial contains 500 mg of iron as ferric carboxy maltose. Patients on FCM should be carefully monitored during and at least 30 min following each infusion. A careful risk / benefit evaluation is required before use in pregnant women and FCM should not be used during pregnancy unless clearly necessary. Treatment with FCM should be confined to second and third trimester if the benefit is judged to outweigh the potential risk for both mother and fetus [17].

Most commonly reported adverse reactions is nausea followed by headache, dizziness and hypertension most serious ADR is anaphylactoid reaction which is rare [17].

To date there are no adequate and well controlled trials of FCM use in pregnant women. The primary aim of this study was to assess the use of intravenous ferric carboxy maltose in the correction of iron deficiency anaemia in pregnant women. The secondary aim was to evaluate extent and severity of adverse effects on mother and fetus.

Methods

This prospective study was carried out between July-18 to July-19 at Mahaveer Hospital Indore. Women with documented IDA defined as Hb less than 10 were included in this study. 50 patients with IDA who were in 2nd and 3rd trimester were included in this study. 500 mg of ferric carboxymaltose was given over a period of 20-25 min. Maternal blood pressure was taken every 5 min during infusion and FHR was assessed before and after infusion. According to routine antenatal care blood samples were collected to measures hemoglobin prior to infusion and 4 weeks later. Women were observed for one hour post infusion, before being discharged home. Demographic characteristics and baseline data included maternal age, gestational age, educational level and gravida para status. Outcome data was collected in terms of hemoglobin rise and adverse events.

Results

Table 1: Distribution of patient's according to age group

20-25	**23**
26-30	16
31-35	4
36-40	7
Total	50

Most of patients were in age group 20-25 yrs i.e.23(46%).

Table 2: Distribution of patient's according Weeks of pregnancy

24-28	**11**
28-32	24
32-36	15
Total	50

Most patients were in 28 to 32 weeks of gestation i.e. 24(48%).

Table 3: Distribution of patient's according severity of anaemia

Mild 9-10	**27**
Moderate 7-9	15
Severe <7	08
TOTAL	50

Most of patients were mildly anaemic i.e.27(54%).

Table 4: Distribution of patient's according to Educational status

Illiterate	**2**
5th	8
10th	17
12th	10
Graduate	13
Total	50

Most patients were educated upto 10thi.e. 17(34%)

Table 5: Mean rise of hemoglobin after ferric carboxy maltose administration

Mean preinfusion hemoglobin	8.72
Mean postinfusion hemoglobin	10.86
P value in paired t test	0.00

There was a significant rise in haemoglobin levels after ferric carboxymaltose injection.

Table 6: Number of women experiencing drug related adverse effect following infusion of ferric carboxy maltose.

Local injection site irritation	**1**
Hypotension	1
Headache	1
Nausea /vomiting	2
Pruritus	1
Total	6

No serious adverse events were reported in any of 50 women receiving an infusion. Only 6(12%) experienced mild adverse effects.

Discussion

We found that in women with IDA ferric carboxymaltose significantly increased hemoglobin levels in all patients. Further, we demonstrate that ferric carboxymaltose appears to be safe and effective treatment modality for correction of IDA as no serious adverse events and only few minor adverse events have been reported.

Many women develop iron deficiency during pregnancy, a

condition that can have serious maternal and fetal implications [18].

IDA is also an important indirect cause of maternal mortality. In the majority of cases anaemia can be treated effectively with oral iron preparations. However, many women develop moderate to severe IDA despite oral iron supplementation as demonstrated in current study where 80% of women were on oral iron, or due to drug intolerance (15% in the current study), non adherence or predisposing pathology such as malabsorption or inflammatory bowel disorders for these women intravenous iron administration may be a more effective treatment modality. A recent Cochrane review concluded that large, good quality trials, assessing clinical outcomes (including adverse effects) as well as the effects of treatment by severity of anaemia are required [19].

In the absence of these studies observational safety and efficacy data may help identify potential benefits and risks. Safety has been demonstrated in two such studies [20, 21].

Froessler *et al.* [25] performed a study on 65 anaemic pregnant women who received FCM. In this study also it was found that hemoglobin levels improved significantly 66% reported improvement in their well being after treatment. only 13% had minor side effects. These are consistent with our study.

The rapid delivery option of a large single dose of ferric carboxy maltose offers a promising treatment modality for pregnant women over other I/V iron formulation like iron sucrose which have low dosage limits. The other treatment modality for severe anaemia is RBC transfusions which is associated with well described adverse events and risks, and should ideally be avoided. Also it is both costly and ever increasingly short supply [20-22], Thus it shows clearly that ferric carboxymaltose not only spares resources but also optimizes the health of women throughout and beyond her pregnancy into the challenging post partum period [5, 24].

Conclusion

This study approved that intravenous injection of FCM significantly improved hemoglobin level in anaemic pregnant patients. No serious adverse events were recorded. A prospective randomised controlled trial is warranted for a more detailed analysis of pregnancy outcomes.

References

1. Beard JL, Hendricks MK, Perez EM, Murray Kolb LE, Berg A, Vernon–Feagans L *et al.* Maternal iron deficiency anaemia affects postpartum emotions and cognition. J Nutr. 2005, 135(2):267-272.
2. Milman N, Bergholt T, Byg KE, Eriksen L, Graudal N. Iron status and iron balance during pregnancy. A critical reappraisal of iron supplementation Acta Obstet Gynecol Scand. 1999; 78(9):749-757.
3. Gautam CS, Saha L, Sekhri K, Saha PK. Iron deficiency in pregnancy and the rationality of iron supplements prescribed during pregnancy, Medscape J med. 2008; 10(12):283. PubMed PubMed central google scholar.
4. Ehrenthal DB, Chichester ML, Cole OS, Jiang X. Maternal risk factors for peripartum transfusions. J women's Health. 2012; 21(7):792-797.
5. Bodnar LM, Cogswell ME, McDonald T. Have we forgotten the significance of post partum iron deficiency? Am J Obstet Gynecol. 2005; 193(1):36-44.
6. Lone FW, Qureshi RN, Emmanuel F. Maternal Anaemia and its impact on perinatal Outome in a tertiary are hospital in Pakistan. East Mediterr Health J. 2004; 10(6):801-807.
7. Beard J. Recent evidence from human and animal studies regarding iron status and infant development. J Nutr. 2007; 137(2):524S-530S. Pub Med Google Scholar.
8. Milman N. Postpartum anaemia: Prevention and treatment Annals of Hematology. 2008; 87(12):949-959.
9. Breymann C, Honegger C, Holzgreve W, Surbek D. Diagnosis and treatment of iron deficiency anaemia during pregnancy and post partum Archives of Gynecology and obstetrics. 2010; 282(5):577-580.
10. Beris P, Maniatis A. Guidelines on intra venous iron supplementation in surgery and obstetrics/gynecology Transfusion Alternatives in Transfusion Medicine. 2007; 9:29-30.
11. Shander A, Javidroozi M, Perelman S, Puzio T, Lobel G. From bloodless surgery to patient blood management Mt Sinai J Med. 2012; 79(1):56-65.
12. Chertow GM, Hsu CY, Johansen KL. The enlarging body of evidence: obesity and chronic kidney disease. J Am Soc Nephrol. 2006; 17(6):1501-1502.
13. Froessler *et al.* Intravenous ferric carboxy maltose for anaemia in pregnancy BMC pregnancy and child birth. 2014; 14:115.
14. Neiser S, Wilhelm M, Schwarz K, Funk F, Geisser P, Burckhardt S. Assessment of dextran antigenicity of intravenous iron products by an immuno diffusion assay Portuguese journal of nephrology and hypertension. 2011; 25(3):219-224.
15. Geisser P. The pharmacology and safety profile of ferric carboxy mattose (ferinject): structure/reactivity relationship of iron, P. Preparations. Portuguese journal of nephrology and hypertension. 2009; 23(1):11-16.
16. Sue R Pavord. UK guide lines on the management of iron deficiency in pregnancy British journal of hematology. 2012; 156:588-600.
17. https://www.medilines.org.uk/eme/product/5910/smpc.
18. Khalafallah AA, Dennis AE, Iron Deficiency anaemia in pregnancy and postpartum: Pathophysiology and effect of oral versus intravenous iron therapy. J Pregnancy, 2012, 10.
19. Reveiz L, Gyte Gillian ML, Cuervo Luis G, Casasbuenas A. Treatments for iron deficiency anaemia in pregnancy. In Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd, 2011.
20. Chirstoph P, Schuller C, Studer H, Irion O, De Jejada BM, Surbek D. Intravenous iron treatment in pregnancy comparison of high dose ferric carboxy maltose VS iron sucrose. J Perinat med. 2012; 40(5):469-474.
21. Myers B. Diagnosis and management of maternal thrombocytopenia in pregnancy Br J Haematol. 2012; 158(1):13-15.
22. Ferraris VA, Davenport DL, Saha SP, Austin PC, Zwischenberger JB. Surgical outcomes and transfusion of minimal amounts of blood in the operating room. Arch Surg. 2012; 147(1):49-55.
23. Greinacher A, Fendrich K, Brzenska R, Kiefel V, Hoffmann W: Implications of Demographics on future blood supply: a population-based cross sectional study. Transfusion. 2011; 51(4):702-709.
24. Bergmann RL, Richter R, Bergmann KE, Dudenhausen JW. Prevalence and risk factors for early post partum anemia. Eur J Obstet Gynecol Reprod Biol. 2010; 150(2):126-131.
25. Froessler B, Collingwood J, Hodyl NA, Dekker G. Intravenous ferric carboxymaltose for anaemia in pregnancy. BMC Pregnancy and Childbirth, article. 2014; 14:115.