THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (July–August 2017) 67(4):253–257
DOI 10.1007/s13224-017-0971-x

ORIGINAL ARTICLE

Comparative Study of Efficacy and Safety of Ferric Carboxymaltose Versus Iron Sucrose in Post-partum Anaemia

Nalini Sharma[1] · J. Lalnunnem Thiek[1] · Tanie Natung[2] · Santa Singh Ahanthem[1]

Received: 14 September 2016 / Accepted: 25 January 2017 / Published online: 22 February 2017

About the Author

Nalini Sharma is working as assistant professor of Obstetrics and Gynaecology in North-eastern Indira Gandhi Regional Institute of health and medical Sciences (NEIGRIHMS), Shillong, Meghalaya. She is having 15 years of post-PG experience. She has many national and international publications. She is having keen interest in laparoscopic surgeries, high-risk pregnancy and social obstetrics.

Nalini Sharma is an Assistant Professor at Department of Obstetrics and Gynaecology, North-eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India; Lalnunnem Thiek is a Senior resident at Department of Obstetrics and Gynaecology, North-eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India; Tanie Natung is an Assistant Professor at Department of Ophthalmology, North-eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India; Santa Singh Ahanthem is a DNB Professor and head at Department of Obstetrics and Gynaecology, North-eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.

✉ Nalini Sharma
nalinisharma100@rediffmail.com

J. Lalnunnem Thiek
drjionthiek@gmail.com

Tanie Natung
natungtanie@gmail.com

Santa Singh Ahanthem
drsanta@rediffmail.com

Abstract

Background The incidence of post-partum anaemia (PPA) is 14–24%. Treatment of PPA with injectable iron replenishes the iron store. Ferric carboxymaltose complex (FCM) is a non-dextran containing intravenous iron agent, having a very low immunogenic potential, designed to be administered in large doses in a short period of time.

[1] Department of Obstetrics and Gynaecology, B 1 D, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya 793018, India

[2] Department of Ophthalmology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India

Objective To compare the efficacy and safety of intravenous FCM and iron sucrose (IS) in post-partum iron-deficiency anaemia.

Material and Method In this prospective, comparative study, 120 post-partum women with iron-deficiency anaemia (Hb < 10 g%) were divided into two groups. A fixed dose of 1000 mg of FCM or IS was given within 10 days of delivery. Hb and serum ferritin were repeated 14 days post-transfusion.

Result There is a mean increase in Hb (*P* value 0.000, 0.000) and ferritin (*P* value 0.000, 0.000) in both the groups. For intergroup comparison, independent Student's *t* test was performed which showed FCM was superior to IS (*P* value 0.000 and 0.000).

Conclusion In our study, FCM was very effective in improving Hb concentration as well as in early replenishment of iron stores in patients with PPA. Large doses given in a short period of time not only save hospital resources but also improve patient satisfaction. It has significant benefit for use in the outpatient department. From this study, we can recommend its use in post-partum women with iron-deficiency anaemia.

Keywords Ferric carboxymaltose · Iron sucrose · Post-partum anaemia · Efficacy

Introduction

Anaemia is the most common nutritional deficiency in the world. Globally, anaemia affects 1.62 billion people which constitute to 24.8% of the total population and the group with the greatest number of individuals affected being pregnant women (41.8%) [1]. Menstrual blood loss, pregnancy and delivery are the main causes of anaemia in reproductive-age women. Anaemia is an important cause of maternal mortality. Complaints like lethargy, easy fatigability, dizziness, lactation failure, post-partum depression are not unusual findings in patients with post-partum anaemia (PPA). It is estimated that 20–40% of maternal deaths in India are due to anaemia [1]. Post-partum anaemia has been defined by WHO as an Hb level of <10 g% during post-partum period [2]. The prevalence of PPA is high ranging from 4 to 27% [3]. The need for treatment of PPA could not be over-emphasized considering its consequences. Different preparations of iron supplements have been in use for treatment of iron-deficiency anaemia, whereas blood transfusion is an option for more severe cases of anaemia. Oral iron supplementation gives satisfactory results in raising haemoglobin level but side effects like nausea, constipation, gastritis tend to affect the compliance. Intravenous iron preparations have been used for treating iron-deficiency anaemia with a promising result and making it possible to avoid blood transfusion and side effects of oral iron preparation [4]. Iron sucrose (IS) has been widely used for treating anaemia with promising result. The efficacy and safety of IS have been established. Multiple dosing is required for IS which decreases the compliance. Ferric carboxymaltose (FCM) is non-dextran containing intravenous iron agent, having a very low immunogenic potential and therefore not predisposed to high risk of anaphylactic reactions, designed to be administered in large doses in a short period of time, with very less side effects overcoming the limitations of the existing intravenous iron agents [5]. The safety and efficacy of FCM in patients with iron-deficiency post-partum anaemia with significant improvement of Hb level have been reported previously [6]. FCM is cost effective and requires less frequent hospital visits which improve patient compliance. This study was designed to test the efficacy of FCM over IS in treating PPA.

Objectives

To evaluate the efficacy and safety of FCM injection in improving haemoglobin level in PPA and compare it with IS in treating PPA.

Materials and Methods

It was a prospective, comparative study done over a period of one and half years from January 2015 to July 2016 in the department of Obstetrics and Gynaecology, of a tertiary care health centre in the north-eastern region of India. Post-partum patients with haemoglobin of less than 10 gm/dl were included in the study. Patients with anaemia other than iron-deficiency anaemia, who received blood transfusion and with known history of allergy to injection iron, were excluded from the study. Complete haemogram, serum ferritin and peripheral blood smear for cell morphology were done before administering iron injection. First consecutive 60 patients were given a fixed dose of 1000 mg injection iron sucrose (Group A), and the other 60 patients were given fixed dose of 1000 mg injection ferric carboxymaltose (Group B). Iron sucrose is given by an infusion of 200 mg diluted in 200 ml of normal saline over 20–30 min every alternate day till the required dose is completed. A maximum of 600 mg IS was given per week. Ferric carboxymaltose is given by infusing 1000 mg of FCM in 250 ml of normal saline over 15 min. Patients were observed for any side effects like headache, nausea, diarrhoea, vomiting, pain and burning at injection site, rigour, fever, hypotension and hypertension, tingling sensation, itching or any other side effects for 1 h. Complete

haemogram and serum ferritin were repeated after 2 weeks from the last dose of injection IS and injection FCM.

Statistical Analysis

Firstly, descriptive statistics was used to calculate the mean ± SD. To compare the means of parameters of both the groups, independent Student t test was performed. A 95% limit and 5% level of significance were adopted. Therefore, a *P* value of less than 0.05 was considered significant. Statistical analysis was performed using the SPSS software package (SPSS for Windows, version 22.0; SPSS, Inc, Chicago, IL, USA).

Results and Observations

The study included 120 post-partum patients with iron-deficiency anaemia. First consecutive 60 patients (Group A) were treated with injection IS, whereas the next consecutive 60 patients (Group B) received injection FCM.

The demographic profile and baseline clinical data like age, parity, the presence of antenatal anaemia, mode of delivery, history of post-partum haemorrhage were comparable in the two groups (*P* value >0.05) (Table 1). There was no significant difference in the baseline haemoglobin and serum ferritin level of both the study groups (*P* value >0.05).

Table 1 Demographic and baseline data

Parameters	Group A (IS)*	Group B (FCM)**	*P* value
Age	29.9 ± 5.10	27.38 ± 4.65	0.552
Parity	2.78 ± 2.05	2.58 ± 1.853	0.576
Antenatal anaemia	39(65%)	40(66.66%)	0.849
Mode of delivery (LSCS)	19(31.6%)	18(30%)	0.845
Post-partum haemorrhage	2(3.33%)	2(3.33%)	0.563
Mean Hb (g%)	7.528 ± 0.51	7.528 ± 0.60	0.182
Mean ferritin	67.48 ± 35.26	66.5 ± 33.91	0.819

* Iron sucrose

** Ferric carboxymaltose

The mean Hb after treatment with IS and FCM was 9.2 and 10.46 g/dl, respectively, which is statistically significant (*P* value 0.000 and 0.000) (Table 2). The mean ferritin after treatment with IS and FCM was 181.35 and 292.41 ng/dl, respectively, which is also statistically significant (*P* value 0.000 and 0.000) (Table 2).

Mean increase in Hb and serum ferritin in IS and FCM groups was 1.68, 3.14 g% and 113.87, 125.91 ng/dl, respectively (Table 3).

On comparing both the groups using independent Student t test, we found that increase in Hb concentration and serum ferritin level in FCM was found statistically significant over IS group (*P* value 0.000 and 0.000) (Table 3).

Adverse drug reactions were very less in both the groups (*P* value >0.05) (Table 4). Burning at the injection site and headache occurred one in each group. Tingling sensation was present in one woman in IS group. Fever was present in one woman in FCM group. None of the women had hypotension, hypertension, nausea, vomiting, diarrhoea, and flushing, itching or severe anaphylactic reaction in either of the groups.

Discussion

Ferric carboxymaltose is non-dextran iron complex that consists of a ferric hydroxide core stabilized by a carbohydrate shell. The design of the macromolecular ferric hydroxide carbohydrate complex permits guarded delivery of iron to the cells of the reticuloendothelial system and subsequent delivery to the iron-binding proteins, ferritin and transferrin, with negligible risk of large amounts of ionic iron being released into the serum [7]. Being its non-dextran-molecule and having a very low immunogenic potential, it is not predisposed to high risk of anaphylactic reactions. These properties allow the administration of large doses (15 mg/kg, maximum of 1000 mg/infusion) in a single and rapid session (15 min/infusion) without the requirement of a test dose and thus makes it suitable as first choice for treatment of iron-deficiency anaemia.

In the present study, we compared the efficacy and safety of FCM with IS in post-partum anaemia. Both IS and FCM are effective in improving Hb (mean increase in Hb 1.68 and 3.14 g%, respectively) concentration and replenishment of iron store (mean increase in ferritin 113.8 and

Table 2 Comparison of mean Hb and ferritin pre- and post-transfusion with iron sucrose and ferric carboxymaltose injection

	Pre-transfusion mean Hb (g%)	Post-transfusion mean Hb (g%)	*P* value	Pre-transfusion Mean Ferritin (ng/dl)	Post-transfusion Ferritin (ng/dl)	*P* value
Group A (IS)	7.528 ± 0.51	9.2 ± 0.50	0.000	64.48 ± 35.26	181.35 ± 38.66	0.000
Group B (FCM)	7.528 ± 0.60	10.46 ± 0.69	0.000	66.5 ± 33.91	292.41 ± 29.04	0.000

Table 3 Comparison of mean increase in Hb and ferritin post-transfusion IS and FCM

Parameter	Group A (IS)	Group B (FCM)	*P* value
Mean difference in increase in Hb (g%)	1.68	3.14	0.000
Mean difference in increase in ferritin (ng/dl)	113.80	125.91	0.000

Table 4 Adverse reactions in IS and FCM groups

	IS group	FCM group
Headache	1	1
Nausea, vomiting, diarrhoea	0	0
Rigour	0	0
Fever	0	1
Pain/burning at injection site	1	1
Hypotension/hypertension	0	0
Tingling sensation	1	0
Itching	0	0
Severe anaphylactic reaction	0	0

125.91 ng/dl, respectively). On comparing both the groups using independent Student t test, we found that increase in Hb concentration and serum ferritin level in FCM was found statistically significant over IS group (*P* value 0.000 and 0.000). Our findings are consistent with other study [8]. Rathod et al. found intravenously administered iron elevated serum Hb and restored iron stores better than oral iron. FCM proved to be statistically better than iron sucrose [8]. In present study, mean increase in ferritin at 2 weeks was 125.91 ng/dl in FCM group as compared to 356 ng/dL in another study [8].

In one of the study, FCM was compared with IS for treatment of preoperative anaemia in patients who were undergoing major elective operations and found that in FCM group, patients attained replenishment of iron more frequently (82% vs 62%, respectively; P value 0.007) [9].

Hussain et al. compared FCM with iron dextran (ID) in iron-deficiency anaemia and showed FCM had greater efficacy with favourable safety profile [6]. In the same study, mean increase in serum ferritin was 543.2 and 319.7 ng/ml in FCM and ID groups, respectively. Froessler et al. reported use of FCM in second and third trimester of pregnancy and found FCM infusion prior to delivery significantly increased Hb levels and improved iron store and documented its safety [10]. In one of the retrospective studies, FCM was compared with IS. In both the groups, there was significant increase in Hb and ferritin but intergroup difference was not statistically significant. In the same study, doses of iron were different in both the groups [11]. Present study documented safety of FCM in post-partum anaemia. Apart from few minor reactions like tingling sensation, burning at injection site and headache in few women, no major adverse reactions were seen which were comparable to other studies [1, 6–9]. This high tolerance of the drug has been partly due to slow release of the iron from the complex and also attributed to low allergenicity of FCM. Injection site reaction can be a cosmetic concern, and fortunately it was absent in our subjects. It is recommended that flushing the infusion catheter with saline before withdrawing the needle to avoid dribbling of FCM in subcutaneous tissue can prevent discoloration of skin [7].

Present study showed FCM is better and more rapid in improving Hb concentration and replenishment of iron store in PPA. Large doses were given in short period of time which not only save hospital resources but also improve patient satisfaction. It has significant benefits for use in the outpatient department. Initial higher cost of FCM may be balanced by less hospital stay, convenience to the patients and less burden on health providers.

Limitations

There were certain limitations in our studies. Firstly, it was not randomized controlled trial. Secondly, sample size was small. Thirdly, we did not follow up our patients till 6 weeks like other studies. Further well-designed, multicentre, randomized study with more subjects and long-term follow-up may be justified.

Conclusion

Our study showed FCM was very effective in improving Hb concentration as well as in early replenishment of iron stores in patients with post-partum anaemia. Large doses given in a short period of time not only save hospital resources but also improve patient satisfaction. It has significant benefit for use in the outpatient department. From this study, we can recommend its use in post-partum women with iron-deficiency anaemia.

Compliance with Ethical standards

Conflict of interest Nalini Sharma, Tanie Natung, J Lalnunnen Thiek, Santa Singh Ahanthem declare that they have no conflict of interest.

Ethical Approval Institutional ethical committee clearance was obtained for study.

Informed Consent Informed consent was obtained from all patients for being included in study.

References

1. Pavord S, Myers B, Robinson S, Allard S, Strong J, Oppenheimer C, et al. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol. 2012;156:588–600.
2. Kouser S, Kouser S, Malik M, Malik A. safety and efficacy of intravenous iron therapy in postnatal patients with iron def anaemia. J South Asian Fed Obstet Gynaecol. 2011;3:25–7.
3. Milman N. Postpartum anemia I: definition, prevalence, causes and consequences. Ann Haematol. 2011;90:1247–53.
4. Covic A, Mircescu G. The safety and efficacy of IV FCM in anaemic patients undergoing haemodialysis: a multicentre, open-label, clinical study. Nephrol Dial Trasplant. 2010;25(8): 2722–30.
5. Klaire E, Nancy T, Andrea A, Atif K, Shahed A. Efficacy and safety profile of single dose IV FCM in the management of renal anaemia-a single centre experience. Nephrol Dial Transplant. 2013;28(1):363–4.
6. Hussain I, Bhoyroo J, Butcher A. Direct comparison of the safety and efficacy of Ferric carboxymaltose versus iron dextran in patients with iron deficiency anemia. Anemia. 2013;2013: 169107.
7. Friedrisch JR, Cancado RD. Intravenous ferric carboxymaltose for the treatment of iron deficiency. Rev Bras Hematol Hemoter. 2015;37(6):400–5.
8. Rathod S, Samal SK, Mahapatra PC. Ferric carboxymaltose: a revolution in the treatment of postpartum anemia in Indian women. Int J Appl Basic Med Res. 2015;5(1):25–30.
9. Bisbe E, Garcia-Erce JA, Diez-Lodo AI, Munoz MA. multicentre comparative study on the efficacy of intravenous ferric carboxymaltose and iron sucrose for correcting preoperative anaemia in patients undergoing major elective surgery. Br J Anaesth. 2011;107(3):477–8.
10. Froessler B, Collingwood J, Hodyl NA, et al. Intravenous ferric carboxymaltose for anaemia in pregnancy. BMC Pregnancy Child Birth. 2014;14:115.
11. Dillon R, Momoh I, Cameron L, et al. Comparative efficacy of three forms of parenteral iron. J Blood Transfus. 2012;2012: 473514.