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AN INTERVENTIONAL STUDY OF INTRAVENOUS FERRIC CARBOXYMALTOSE (FCM) AMONG POSTPARTUM WOMEN WITH MODERATE ANEMIA AT A TERTIARY CARE HOSPITAL

Obstetrics & Gynaecology

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ABSTRACT

Objective: Present study was conducted to estimate the changes in hemoglobin level 6 weeks after intravenous administration of ferric carboxymaltose postpartum women with hemoglobin level of 7–9 g/dl who delivered at our tertiary care health institute. **Material and Methods:** The present study was an interventional, prospective study conducted in the Department of Obstetrics and Gynaecology at Government Medical College & Hospital, Aurangabad, Maharashtra. Total 60 patients were included in present study. Patients received single dose of 1 gm intravenous FCM. Haemoglobin (g/dl), Haematocrit (%), RBC indices (MCV, MCH, MCHC), serum ferritin and reticulocyte count were reassessed on day 42 of the treatment. Statistical analysis was done by applying ANOVA and t-Test to test each pair of means. For all statistical purposes, p value < 0.05 was considered significant. **Results:** In present study most common age group was 21-25 years (52 %), patients with parity 2 were most common (42 %). 65% study patients had vaginal delivery, 28 % had Caesarean delivery & 7 % had instrumental delivery. Statistically significant difference was noted between baseline & day 42 values of haemoglobin (g/dl), serum ferritin, PCV (%) & RBC indices (MCV, MCH, MCHC) in study patients. **Conclusion:** Intravenous administration of single dose of ferric carboxymaltose offers a promising treatment modality for pregnant women with moderate iron deficiency anaemia.

KEYWORDS

ferric carboxymaltose, serum ferritin, postpartum anemia, parenteral iron

INTRODUCTION

Anemia during pregnancy was defined by the World Health Organization and Centre for Disease Control and Prevention (CDC) as a hemoglobin concentration of less than 11 g/dL.[1] Anaemia in pregnancy is one of the most common clinical conditions in Obstetrics practice. The most common cause of anaemia in pregnancy is iron deficiency in both the developed and developing world.[2]

Most women with postpartum anemia have antepartum iron deficiency, with iron demands from the developing fetus and with peripartum blood loss further depleting maternal iron reserves. Anemia in pregnancy is an important indirect cause of maternal death in developing countries. The common consequences are cardiac failure, anaesthetic hazards, shock, postpartum haemorrhage, sepsis, venous thrombosis and pulmonary embolism.[3,4] Anemia (occurring in pregnancy or postpartum) has been implicated as a significant cause of direct and indirect maternal and perinatal morbidity and mortality.[5]

Therefore treatment of puerperal anemia is important for improving maternal and new-born health during breastfeeding and for the restoration of the maternal iron and hemoglobin status before subsequent conception. Oral iron preparations & red blood cell (RBC) transfusions were considered as mainstay treatment of IDA. But, 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 possible.[6]

Institutional guidelines and trial data suggested that blood transfusions are likely to be appropriate in patients with hemoglobin < 7 g/dL but not necessarily if alternative therapy is available or if the individual is clinically well compensated.[7,8] Intravenous (IV) iron may be preferred because the absorption challenges of oral iron are mitigated and because IV iron produces a more rapid increase in hemoglobin concentration and iron stores. Disadvantages of IV iron include increased drug costs and the need for supervised treatment in a hospital or outpatient facility.[9]

Ferric carboxymaltose is an intravenous iron preparation, which can be used in postpartum females. The ferric carboxymaltose (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 very low levels of non-transferrin bound iron, avoiding iron toxicity and oxidative stress.[10]

Many postpartum females have moderate iron deficiency anemia, required correction. Postpartum women are usually discharged 48 hours after delivery from health facility. This window can be used as an opportunity to treat postpartum anemia by administration of a single dose of FCM. Present study was conducted to estimate the changes in hemoglobin level 6 weeks after intravenous administration of ferric carboxymaltose postpartum women with hemoglobin level of 7–9 g/dl who delivered at our tertiary care health institute.

MATERIAL AND METHODS

The present study was an interventional, prospective study conducted in the Department of Obstetrics and Gynaecology at Government Medical College & Hospital, Aurangabad, Maharashtra. Study duration was of 6 months (July 2019 to January 2020). Approval for present study was obtained from institutional ethical committee.

Inclusion criteria

Postpartum women (post-delivery and post caesarean) with moderate iron deficiency anaemia (hemoglobin 7-9 gm %), hemodynamic stable and willing to participate in the study.

Exclusion criteria

- Women with secondary postpartum hemorrhage,
- Women with anaphylaxis to iron substitutes,
- Any cardiac, renal, hepatic or endocrine disease,
- Anemia due to chronic disease and worm infestation.
- Hemoglobinopathies, sickle cell disease,
- Not willing to participate & follow up

Patients were properly counselled regarding intravenous FCM administration in local language & if willing then included in study. Written valid informed consent was taken. After applying inclusion & exclusion criteria, total 60 patients were included in present study.

Demographic data like age, education, socioeconomic status, height, weight was recorded in Performa. A detailed clinical history (menstrual, obstetric), previous treatment history, including iron therapy, compliance with oral iron and chronic medical illness was taken. Baseline investigations i.e. complete blood count, peripheral smear for type of anemia, RBC indices (MCV, MCH, MCHC), serum ferritin and reticulocyte count were done on day 2 or 3 of postpartum in study patients & were reassessed on day 42 of the treatment.

Patients received intravenous Ferric carboxymaltose (FCM) as single

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shot of 1000mg in 250 ml normal saline over 15 minutes. No test dose was given. They were monitored for vitals, any sensitivity reactions like rashes, chills, anaphylactic reaction or hypotension etc. during the period of infusion. Any adverse effects observed during this period in both the groups were recorded. Statistical analysis was done by applying ANOVA and t-Test to test each pair of means. For all statistical purposes, p value < 0.05 was considered significant. Results were analysed statistically using SPSS version 24 software.

RESULTS

In present study most common age group was 21-25 years.

Table 1: Distribution according to age.

Age (years)	No. of patients	Percentage
<20	5	8%
21-25	31	52%
26-30	14	23%
31-35	7	12%
36-40	2	3%
>40	1	2%

Study patients general characteristics are shown in table 2.

Table 2 – General characteristics

Variables	No. of patients (%) / Mean ± SD
Age (years)	23.13 ± 4.42
Hemoglobin (gm/dl) Level before infusion	7.58 ± 0.75
BMI (kg/m2)	22.7 ± 6.2
Received Oral Iron Supplements for > 100 days in present pregnancy	25 (42 %)
History of Oral Iron intolerance	16 (27 %)
Gestational Age At delivery (weeks)	37.3 ± 3.6
S. Ferritin (ng/ml)	32.7 ± 13.6

Patients with parity 2 were most common (42 %) followed by primipara patients (27 %) & patients with parity 3 (25 %).

Table 3: Prevalence of IDA depending on parity.

Parity	No. of patients	Percentage
Primipara	16	27%
P2	25	42%
P3	15	25%
P4 or more	4	7%

65% study patients had vaginal delivery, 28 % had Caesarean delivery & 7 % had instrumental delivery.

Table 4- Mode of delivery

Mode Of Delivery	No. of patients	Percentage
Vaginal	39	65%
Elective Caesarean	3	5%
Emergency Caesarean	14	23%
Instrumental	4	7%

All patients received complete dose of FCM. Only 2 patients had adverse events noted after completion of intravenous FCM administration. Patients had slight burning sensation at injection site, headache, nausea/vomiting & pruritus. Symptoms were mild & no additional treatment required. No patients had systemic adverse events such as hypotension, angioedema or anaphylactic shock.

Table 5 Drug related adverse events

Adverse event*	No. of patients	Percentage
Any adverse event	2	3%
Local (injection site irritation) - Slight burning sensation	2	3%
Headache	2	3%
Nausea/Vomiting	2	3%
Pruritus	2	3%

(*- one or more adverse events can be noted in one patient)

Statistically significant difference was noted between baseline & day 42 values of haemoglobin (g/dl), serum ferritin, PCV (%) & RBC indices (MCV, MCH, MCHC) in study patients.

TABLE- 6 Mean Haematological parameters before & after intravenous FCM administration

	Hemoglobin (gm/dl)	S. Ferritin (μ/dl)	PCV (%)	MCV(fl)	MCH(pg)
Baseline	7.58 ± 0.75	32.7 ± 13.6	23.8 ± 3.6	72.5 ± 7.6	22.3 ± 5.9
Day 42	9.15 ± 1.23	62.2 ± 31.7	27.5 ± 4.7	79.3 ± 8.7	27.6 ±7.1
P Value	0.01*	0.001*	0.004*	0.02*	0.02*

(*-p value < 0.05 was considered significant.)

DISCUSSION

Clinical manifestations of anaemia includes skin or mucosal pallor, lack of energy and shortness of breath, fatigue, lack of concentration which may present in different grades depending on the severity of anaemia. Common etiology for anemia in reproductive age group females are nutritional deficiency due to low dietary intake of iron, phytate-rich Indian diet, faulty food habits, strict vegetarian diet, repeated pregnancies or pregnancy losses at very short intervals, pregnant females not taking supplementary medications, chronic blood loss like in malaria, hookworm infestation, haemorrhoids, etc.[11]

Complications due to anemia in postpartum women are increased incidence of puerperal infection, sub involution of uterus, lactation failure, poor wound healing, etc. Postpartum women with iron deficiency anemia are also at risk of adverse effects requiring medical interventions such as red blood transfusion, cardiovascular problems, reduced physical and cognitive performance, reduced immune function, tiredness and increased depressive episodes.[6]

Parenteral iron therapy promises a better response in these patients and can obviate the need for blood transfusions in the antenatal and postpartum period & also helpful in patients with intolerance of or non-adherence to oral iron and malabsorption states.[12] Parenteral iron therapy is more compliant, efficacious, have better tolerance & causes rapid replenishment of iron stores.[13] In a systematic review to compare different injectable iron preparations in pregnancy, the authors failed to document the safety of any of the injectable iron therapies over others. The choice of injectable iron therapy is mainly determined by cost and convenience of administration.[14]

FCM is a safe intravenous agent in pregnancy with multiple advantages, such as large dose administration per sitting, early rise in hemoglobin level, lesser total number of required doses (convenient dosing), hence lesser number of hospital visits and total cost involved in transportation, equipment required for infusion and the discomfort caused to the patient due to multiple needle pricks.[15]

The rapid delivery option of a large single dose of ferric carboxymaltose is a promising treatment modality for peripartum women who needs correction of iron deficiency and anaemia. Other IV iron formulations that have low dosage limits, such as iron sucrose (200 mg). The disadvantage with ferric carboxymaltose is its high cost in comparison to other parenteral iron preparations, which is well compensated with lesser number of hospital visits and shorter duration of hospital stay.[16]

Body iron stores are largely determined by serum ferritin levels. Froessler et al.[17] have documented significantly increased ferritin levels after FCM infusion in patients with anemia and in women with iron deficiency and no anemia. Similar findings were noted in present study. Sultan P et al.[18] in their systematic review and meta-analysis for oral versus intravenous iron therapy for postpartum anemia noted that, absolute hemoglobin concentrations at 6 weeks postpartum were almost 1 g/dL higher (equivalent to 1 unit red blood cell transfusion) in women receiving IV compared to oral iron. Compared with oral iron, women receiving intravenous iron had higher hemoglobin concentrations at week 6 postpartum and a lower risk of gastrointestinal side effects. In present study similar findings were noted.

Other studies in postpartum women compared the safety and efficacy of FCM versus oral iron. Faster and greater hemoglobin responses were achieved in FCM treated patients compared to those receiving oral iron and FCM replenished iron stores efficiently.[19] IV iron formulations like FCM that rapidly restore body iron stores with fewer infusions are likely to be associated with decreased hospital resource use and lower costs compared to IV iron regimens requiring multiple infusions.[20]

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Administration of a single dose of FCM will be of immense value to the health systems as it will reduce visits of the patients & will be convenient both to the patients and health-care professionals.

CONCLUSION

Correction of postpartum moderate IDA by single large dose of ferric carboxymaltose is an effective method. No serious adverse were noted in present study. Intravenous administration of single dose of ferric carboxymaltose offers a promising treatment modality for pregnant women with moderate iron deficiency anaemia. Anemia correction with ferric carboxymaltose in peripartum period can reduce the perinatal patients' complications and improves overall maternal health.

Conflict of Interest: None to declare

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