Original Research Article

Effectiveness of intravenous ferric carboxy maltose(FCM) in improving hemoglobin level amongst postpartum women with moderate to severe anemia in a tertiary care hospital

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Abstract

Background: Postpartum Anemia (PPA)has been defined as hemoglobin(Hb)of <10 gm% during the postpartum period. The most common cause of anaemia in the world is iron deficiency. Each ml of blood loss results in loss of 0.5 mg iron. Because FCM has a neutral pH and physiological similarity, it can be given in high doses over a short period of time with minimal danger of hypersensitive reactions, and no test dosage is necessary. The safety and efficacy of IV FCM in the treatment of postpartum iron deficient anaemia are assessed in this study. **Aims & objectives**: Present study was done to estimate the changes in Hb level 6 weeks after IV FCM administration in postpartum women with Hb level of 5–9 g/dl who delivered at our tertiary care institute. **Materials & methods:** This was a prospective observational study conducted at MGMMC & MY Hospital Indore's Department of Obstetrics and Gynecology (MP).Study was conducted after taking ethical clearance. Total 100 patients were included in present study. Patients received single dose of 1 gm IV FCM. Hb, PCV, RBC indices, Serum ferritin and reticulocyte count were reassessed on day 42 of the treatment. The data was analysed statistically. A p value of< 0.05 was considered significant for all statistical purposes. **Results:** In this study most common age group was 21-25 years(47%),patients with parity 2 were most common (39%).(53%)study patients had vaginal delivery,(42%)had Caesarean delivery & (5%) had instrumental delivery. Statistically significant difference was noted between baseline & day 42 values of Hb, Serum ferritin, & RBC indices. **Conclusion:** Administration of single dose of IV FCM offers a promising treatment for pregnant women with moderate to severe iron defeciency anemia.

Keywords: FCM, Serum ferritin, postpartum anemia.

Introduction

The postpartum period encompasses the six weeks following childbirth. The World Health Organization (WHO) defines postpartum anaemia (PPA) as haemoglobin (Hb) levels of less than 10 gm% in the postpartum period.The most common cause of anaemia in pregnancy is iron deficiency in both the developed and developing world[1]. In a survey from a north Indian village in the postpartum period, around 70% of women were found to be anaemic[2]. Antepartum iron deficit, iron needs from the developing foetus, and peripartum blood loss deplete maternal iron reserves, resulting in postpartum anaemia. Each ml of blood lost resulted in a loss of 0.5 mg of iron. Anemia (occurring in pregnancy or postpartum) has been implicated as a significant direct and indirect maternal and perinatal morbidity and mortality. The consequences of anemia are cardiac failure, anaesthetic hazards, shock, postpartum haemorrhage, sepsis, venous thrombosis and pulmonary embolism[3]. In India, postpartum haemorrhage or anaemia is responsible for roughly 36% of all maternal deaths[4]. Therefore treating puerperal anemia also improves maternal and new-born health during breastfeeding and restores maternal iron and hemoglobin status before subsequent conception.

Oral iron preparations in mild to moderate & red blood cell (RBC) transfusions in severe IDA were considered as mainstay treatment. But, oral iron supplementation can lead to significant gastro-intestinal (GI) side effects resulting in non-compliance in many patients . Blood transfusions are likely to be appropriate in individuals with haemoglobin 7 g/dL, although not always if alternative medication is available or if the individual is clinically adequately compensated, as blood transfusions have their own set of drawbacks, such as the transmission of HIV and HbSAG. Because the absorption issues of oral iron are eased and IV iron generates a faster increase in haemoglobin concentration and iron reserves, IV iron may be chosen. High medicine prices and the requirement for supervised treatment in a hospital or outpatient facility are both disadvantages of IV iron. FCM is an intravenous iron preparation, which can be used in postpartum females. FCM has a neutral pH (5.0-7.0) and physiological osmolarity, which makes it possible to administer its higher single doses over shorter time periods (single dose up to 1000 mg over 15 min) than other parenteral preparations[5]. 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. In this study, we evaluate the effectiveness of IV FCM in the treatment of postpartum iron deficiency anemia

Material and methods

The study was carried out at MGMMC & MY Hospital Indore in Department of Obstetrics and Gynaecology (MP). The study lasted six months (august 2021 to january 2022). The institutional ethical committee gave its approval for the study.

Inclusion criteria

Postpartum women (post-delivery and post caesarean) with moderate to severe iron defeciency 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,

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- Anemia due to chronic disease and worm infestation.
- Hemoglobinopathies, sickle cell disease,
- Not willing to participate & follow up

Total 100 patients were included in the study after proper counselling regarding IV FCM administration in local language. Written valid informed consent was taken. Demographic data like age, education, socioeconomic status, height, weight was recorded in Performa. A comprehensive clinical history (menstrual, obstetric), prior treatment history, including iron therapy, oral iron compliance, and chronic medical illness were all obtained. 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 & were reassessed on day 42 of the treatment.

Dose calculation / total drug infusion for FCM

The cumulative dose required for Hb restoration and repletion of iron stores is calculated by the following Ganzoni formula:

Cumulative iron deficit (mg) = body weight in kg x (Target Hb - Actual Hb g/dL) × 2.4 + iron storage depot (mg). For patients ≤ 66 kg: The calculated cumulative dose is to be rounded down to the nearest 100 mg. For patients > 66 kg: The calculated cumulative dose is to be rounded up to the nearest 100 mg.

FCM was exclusively given as an IV drip infusion in this trial. IV drip infusion - maximum single dose of 1000 mg (20 mL) diluted in 250 mL sterile 0.9 percent sodium chloride solution over 15 minutes not more than once a week and not more than 0.3 mL FCM injection (15 mg iron)/kg body weight or calculated cumulative dose.

Over the course of 15 minutes, patients were given a single shot of 1000 mg ferric carboxymaltose (FCM) in 250 ml normal saline intravenously. 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 paired 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 this study the most common age group was 21-25yrs.

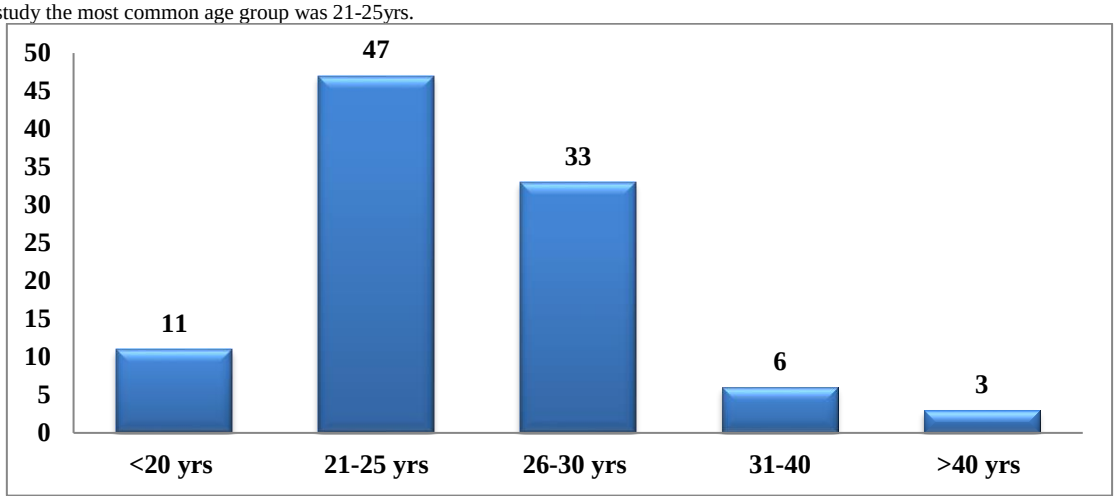

Fig 1: Distribution According To Age

General characteristics of study patients are shown in table 1

Table 1: General Characteristics

Variables	No. of patients (%) / Mean +/-SD
Body weight (kg)	63.04+/-7.1
Hemoglobin level before infusion (gm/dl)	7.4+/-0.8
History of oral iron intolerance	31(31%)
Gestational age at delivery (weeks)	38.3+/-1.3
Serum ferritin (ng/dl)	32.0+/-12.4
History of blood transfusion in present pregnancy	47%
History of oral intolerance in present pregnancy	57%

IDA is most common in patients with parity 2 (39 %) followed by parity 3 patients (33%) & then patients with parity 1 (19 %)

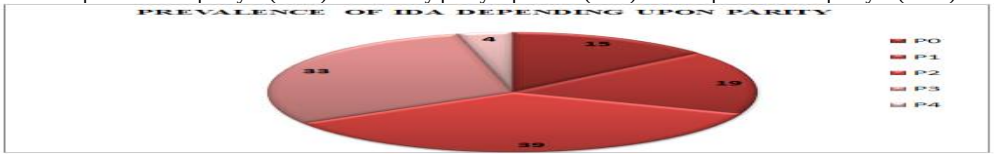

Figure 2

Out of all, 53% patients had vaginal delivery, 42 % had Caesarean delivery & 5% had instrumental delivery

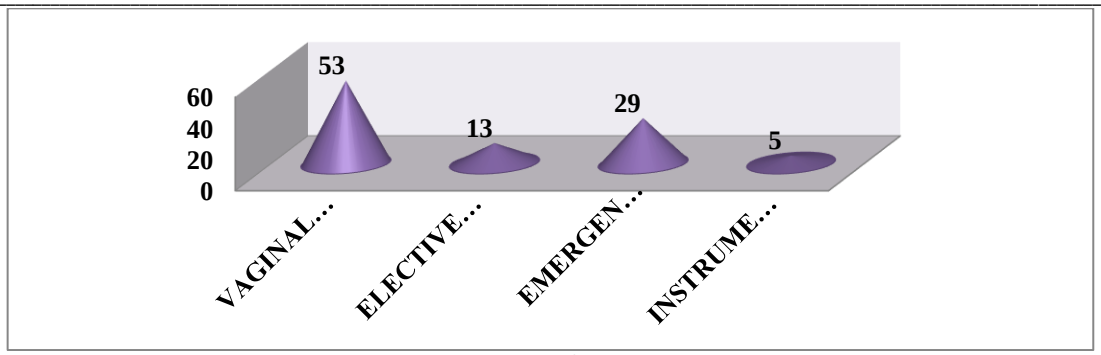

Fig 3: Mode of Delivery

All of the patients received the full dose of FCM. After intravenous FCM treatment, only two patients had adverse effects. A minor burning sensation at the injection site, headache, nausea/vomiting, and pruritus may occur in some patients. Symptoms were mild & no additional treatment required. There were no systemic side effects such as hypotension, angioedema, or anaphylactic shock in any of the patients.

Table 2: drug related adverse events

Adverse events *	No. of patients (%)
Local (injection site irritation)-slight burning sensation	07
Headache	03
Nausea/ vomiting	04
Pruritus	05
Systemic adverse events (hypotension, angioedema , anaphyactic shock	00

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

The mean (SD) Hb at baseline and 6 weeks after administration of FCM was 7.5(0.9) g/dl and9.03 (1.3) g/dl, respectively. The mean (95% confidence interval [CI]) increase in the Hb level 6 weeks after administration of FCM was 1.53 (1.49 to 1.57) g/dl. This rise in Hb concentration was statistically significant (P 0.001).The mean (SD) ferritin at baseline and 6 weeks after administration of FCM was32.01 (12.42)mcg/dl and 64.55 (5.88)mcg/dl.

Table 3: Mean hematological parameters before & after IV FCM administration

	Hb(g/dl)	S.Ferritin (mcg/dl)	PCV(%)	MCV(fl)	MCH (pg)
BASELINE	7.48 +/-0.81	32.01 +/- 12.42	29.76 +/- 4.98	73. 85 +/- 6.98	24.45 +/- 2.82
DAY 42 (6 WEEKS)	9.03 0.64	64.55 5.881618	35.78 4.38	77.10 4.40	26.43 3.50
P VALUE	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

(*-p value < 0.05 was considered significant)

Discussion

To summarize, the most common age group suffered PPA in this study was 21-25 yrs with parity 2. The increase in Hb level was 1.53 (1.49 to 1.57) g/dl on average (95 percent CI). 6 weeks following FCM administration among postpartum women who had moderate-to-severe anemia(Hb: 5–9.9 g/dl). During the same period, the mean(95% CI) increase in serum ferritin level was32.01 (31.9 to 31.14) ng/ml. Both the changes were statistically significant (P < 0.01).

Our findings are consistent with those of a number of other studies that have demonstrated the safe and effective use of FCM in the postpartum period. Other published research from throughout the world found that 4–6 weeks following FCM therapy, Hb levels increased by 2.4 to 4.4 g/dl[7,8]. In patients taking FCM, Van Wyck et al. reported a 3 g/dL increase in Hb in 2–4 weeks[9].

In the study by Seid *et al*. FCM achieved a Hb rise of 3 g/dL or more. Seid *et al*. reported that the ferritin levels were replenished at day 42 in the patients receiving FCM[6].

None of the individuals in our study needed to stay in the hospital for an extended period of time. They recovered without incident. This further supports our position that when oral iron therapy is ineffective, entire dosage infusion therapy should be considered. Adverse reactions do occur with various iron therapies. The most prevalent side effect of oral iron treatment is gastrointestinal problems.

FCM treatment has a reported incidence of side effects ranging from 6.3 percent to 10.6 percent[5,6,9]. In this study adverse events in the form of local (injection site) reaction, nausea, vomiting, pruritus occur in around 15% cases. One or more adverse event can be noted in one patient.

Conclusion

In patients with Post partum anemia, parenteral iron therapy offers a better response and can eliminate the need for blood transfusions in the postpartum period. It is also beneficial in individuals with sensitivity to or non-adherence to oral iron and malabsorption disorders.[10] Single large dose of FCM is an effective method for correction of moderate to severe postpartum IDA. This can reduce the perinatal complications like puerperal infection, sub involution of uterus, lactation failure, poor wound healing, etc and improves overall maternal health. FCM increases serum ferritin and haemoglobin levels, as well as restores iron stores more quickly. It has a low risk of side effects. Patients expressed higher overall satisfaction since they received the medicine in a single dosage (within 15 minutes of arriving at the hospital).National health authorities should develop guidelines to address iron deficiency throughout pregnancy and postpartum, lowering maternal mortality, morbidity, and newborn morbidity and ensuring a prosperous future for both mothers and children in an increasingly globalised world.

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