



# Single Dose of Intravenous Ferric Carboxymaltose Prevents Anemia for 6 Months among Moderately or Severely Anemic Postpartum Women: A Case Study from India

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## ABSTRACT

The effectiveness of intravenous ferric carboxymaltose (FCM) in quickly increasing normal hemoglobin concentration and replenishing body iron reserves up to 6–12 wk is known; however, its long-term effectiveness is unknown. In this study conducted in northern India during August 2018 to February 2019, 100 postpartum women within 48 h of delivery with a hemoglobin concentration between 5.0 and 9.9 g/dL were included. A single dose of intravenous FCM was administered. The hemoglobin and serum ferritin concentrations were measured at baseline and at 6 mo. Out of 100 women recruited, 57 (57%) returned for the follow-up visit at 6 mo. The mean ( $\pm$  SD) hemoglobin and serum ferritin concentrations at baseline were  $8.6 \pm 1.1$  g/dL and  $15.8 \pm 17.2$  ng/mL, respectively, and at 6 months were  $12.5 \pm 1.2$  g/dL and  $72.0 \pm 52.0$  ng/mL, respectively. The mean increase in hemoglobin concentration was  $3.9$  (95% CI: 3.5, 4.3) g/dL ( $P < 0.001$ ) and for serum ferritin was  $53.8$  (95% CI: 41.8, 65.8) ng/mL ( $P < 0.001$ ). The study was registered prospectively in the Clinical Trials Registry–India (CTRI) as CTRI/2018/06/014332. *Curr Dev Nutr* 2021;5:nzab078.

**Keywords:** anemia, ferric carboxymaltose, ferritin, hemoglobin, long-term, postpartum, parenteral

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## Introduction

The effectiveness of intravenous ferric carboxymaltose (FCM) in increasing hemoglobin and serum ferritin concentrations has been demonstrated in many studies. However, most of these studies have reported the findings up to 6 to 12 wk after administration of FCM (1–6). To the best of our knowledge, only 2 studies measured hemoglobin and serum ferritin concentrations among postpartum women, 6 mo after administration of intravenous FCM (7, 8). Therefore, the question of whether, or when, to repeat FCM administration among women who had already received FCM remains largely unanswered. To bridge this gap in knowledge, this study was conducted among postpartum women with a hemoglobin concentration of 5.0–9.9 g/dL. The objective of the study was to measure the change in mean hemoglobin and serum ferritin concentrations between baseline and 6 mo after the administration of a single dose of intravenous FCM.

## Methods

### Study design and setting

A single-arm prospective study was conducted at a subdistrict hospital (SDH) in district Faridabad, Haryana, India. The SDH was a

50-bed secondary-care health facility. Annually, >4000 deliveries are conducted at this hospital. Adhering to the national guidelines, women with normal vaginal delivery were discharged 48 h after delivery. The study was conducted during August 2018 to February 2019.

### Study participants

Moderately and severely anemic (hemoglobin concentration between 5.0 and 9.9 g/dL) postpartum women were eligible for recruitment in the study. The eligible women were offered a single dose of intravenous FCM. Women who were known to be suffering from renal or hepatic impairment, had a hemoglobin concentration <5 g/dL, were allergic to iron formulations, received any form of parenteral iron or blood transfusion during the current pregnancy, or had any chronic/systemic illness or blood disorders were excluded.

### Sample size

The study planned for 2 follow-up measurements of hemoglobin and serum ferritin at 6 wk and 6 mo, respectively. The sample size calculation for the first follow-up was based on the following formula:  $n = [(Z \alpha/2 + Z \beta) 2/d^2] \times \text{variance}$ , assuming an SD of mean change in hemoglobin of 1.2 g/dL, to detect a 0.5 g/dL difference in hemoglobin (5), with a power of 95% and nonresponse rate of 20%. The minimum required sample was 90 participants. Taking into account further loss

**TABLE 1** Distribution of participants by sociodemographic and other baseline characteristics

Characteristics	Participants who completed the 6-mo follow-up (n = 57), n (%)	Participants who did not complete the 6-mo follow-up (n = 39), n (%)	P
Age			
18–25 y	38 (66.7)	28 (71.8)	0.894
26–30 y	18 (31.6)	11 (28.2)	
31–35 y	1 (1.7)	0 (0.0)	
Preterm delivery			
Period of Gestation (POG) <259 d	8 (14.0)	7 (18.0)	0.777
Period of Gestation (POG) ≥260 d	49 (86.0)	33 (82.0)	
Parity			
1	21 (36.8)	15 (38.5)	0.975
2	18 (31.6)	11 (28.2)	
3	15 (26.3)	11 (28.2)	
4	3 (5.3)	2 (5.1)	
BMI (kg/m <sup>2</sup> )			
Underweight (BMI <18.5)	11 (19.3)	4 (10.3)	0.555
Normal weight (BMI 18.5–24.9)	33 (57.9)	28 (71.8)	
Overweight (BMI 25–29.9)	11 (19.3)	6 (15.4)	
Class I obesity (BMI 30–34.9)	2 (3.5)	1 (2.6)	
Birth weight of the newborn			
<2500 g	17 (29.8)	10 (25.6)	0.818
≥2500 g	40 (70.2)	29 (75.4)	
Hemoglobin, mean ± SD, g/dL	8.6 ± 1.1	8.2 ± 1.1	0.102

to follow-up at the second measurement point at 6 mo, the sample size was increased to 100.

Total iron requirement was calculated by using Ganzoni's formula [total iron requirement (in mg) = body weight (in kg) × (target hemoglobin – actual hemoglobin, g/dL) × 2.4 + allowance for iron stores]. We set the target hemoglobin at 12.0 g/dL, and allowance for iron stores as 500 mg. The calculated dose was rounded to the nearest 100 mg, and the maximum single dose was capped at 1000 mg.

A trained nurse administered the FCM injection (Orofer®; Emcure Pharmaceuticals Limited) as an intravenous infusion with 100 mL of 0.9% normal saline over 15 min, under the supervision of a physician, within 48 h of delivery.

A trained nurse measured the hemoglobin concentrations using a digital hemoglobinometer (HemoCue 201+; HemoCue AB-hemoglobin photometer) from capillary blood, following the standard methodology (9).

For estimation of serum ferritin, 3 mL of venous blood from the cubital fossa was collected with aseptic precautions. Serum was separated and stored at –20°C. Serum ferritin concentration was measured by enhanced chemiluminescence assay on a VitrosECiQ machine (Ortho Clinical Diagnostics™ 8356636).

### Quality assurance

After estimating hemoglobin for every 30 samples, a quality control was run for the HemoCue 201+. Serum ferritin was estimated in the laboratory of the Department of Biochemistry at the All India Institute of Medical Sciences (AIIMS), New Delhi. Periodic calibration of the test equipment was done. The laboratory had an internal and external quality-assurance program in place.

### Ethical considerations

The study was approved by the Institutional Ethics Committee, AIIMS, New Delhi (no. IEC-138/06.04.2018, RP-26/2018). Informed written consent was provided by the participants. The study was registered prospectively in the Clinical Trials Registry–India (CTRI), reference CTRI/2018/06/014332.

### Statistical analysis

Data were analyzed using STATA version 12 (Stata Corp LLC). Continuous data are expressed as mean (± SDs) and categorical data are expressed as frequencies and percentages. Paired *t* test was applied for hemoglobin and serum ferritin concentrations. A *P* value <0.05 was considered statistically significant.

### Results

Initially, 100 postpartum women with moderate to severe anemia were enrolled in the study (10). Fifty-seven (57%) women returned for a follow-up visit at 6 mo after the administration of FCM. None of the women reported any major illness or underwent any surgery or received blood transfusions during the follow-up period of 6 mo. **Table 1** shows demographic and other characteristics of women who were available at 6-mo follow-up and those who were lost to follow-up. There was no significant difference between the 2 groups.

Changes in concentrations of hemoglobin and serum ferritin at 6 wk and 6 mo are shown in **Table 2**. The mean (± SD) requirement of FCM was 909.3 ± 97.6 mg. Mean (± SD) hemoglobin concentrations at baseline and 6 wk after administration of FCM were 8.5 ± 1.1 g/dL

**TABLE 2** Change in mean hemoglobin and serum ferritin concentrations after administration of intravenous ferric carboxymaltose

Variable	Group 1: Women who completed the 6-mo follow-up (n = 57)				Group 2: Women who did not complete the 6-mo follow-up (n = 39)			
	Baseline mean $\pm$ SD (95% CI) (A)	After 6 wk, mean $\pm$ SD (95% CI) (B)	After 6 mo, mean $\pm$ SD (95% CI) (C)	Mean change 6 wk to 6 mo (B - C) <i>P</i> = 0.813	Baseline mean $\pm$ SD (95% CI) (a)	After 6 wk, mean $\pm$ SD (95% CI) (b)	Mean change (a - b) <i>P</i> < 0.001	<i>P</i> (group 1 vs. group 2)
Hemoglobin, g/dL	8.6 $\pm$ 1.1 (8.3-8.9)	12.5 $\pm$ 1.3 (12.2-12.8)	12.5 $\pm$ 1.2 (12.2-12.8)	0.0 $\pm$ 0 (-0.5-0.4), <i>P</i> = 0.813	8.3 $\pm$ 1.1 (8.0-8.6)	12.9 $\pm$ 1.2 (12.5-13.3)	4.6 $\pm$ 1.6 (4.1-5.1), <i>P</i> < 0.001	0.170
Serum ferritin, ng/mL	18.7 $\pm$ 21.0 (13.2-24.2)	157.7 $\pm$ 145.0 (120.1-195.3)	72.0 $\pm$ 52.1 (58.5-85.5)	85.7 $\pm$ 19.9 (45.9-125.4), <i>P</i> < 0.001	11.4 $\pm$ 7.4 (9.1-13.7)	146.5 $\pm$ 78.4 (122.0-171.1)	135.1 $\pm$ 74.1 (111.8-158.3), <i>P</i> < 0.001	0.708

and  $12.6 \pm 1.3$  g/dL respectively, and 68.4% of the anemic postpartum women became nonanemic.

The mean increase in hemoglobin 6 mo after the administration of FCM was 3.9 (95% CI: 3.5-4.3) g/dL ( $P < 0.001$ ), whereas the mean increase in serum ferritin was 72.0 (95% CI: 58.5-85.5) ng/mL ( $P < 0.001$ ).

At 6 wk, 63.2% ( $n = 36$ ) of study participants were nonanemic and 36.8% ( $n = 21$ ) were anemic. Of these nonanemic participants ( $n = 36$ ), 69.4% ( $n = 25$ ) remained nonanemic at 6 mo.

Of 36.8% ( $n = 21$ ) of study participants who were anemic at 6 wk, 52.4% ( $n = 11$ ) became nonanemic at 6 mo, whereas 47.6% ( $n = 9$ ) remained anemic. Among 39 participants who could not be followed up at 6 mo, 78.4% ( $n = 29$ ) were nonanemic and 21.6% ( $n = 10$ ) were anemic at 6 wk. The difference between these 2 groups in terms of anemia at 6 wk was not statistically significant ( $P = 0.275$ ).

After 6 mo, 20 women (35%) were anemic, of whom 5 had hemoglobin concentrations  $< 11.0$  g/dL. Only 3 of the 57 women had serum ferritin concentrations  $< 20$  ng/mL.

Mean hemoglobin concentrations remained high from 6 wk to 6 mo (12.5; 95% CI: 12.2-12.8 g/dL). Although there was a significant decline in serum ferritin concentrations (85.7; 95% CI: 45.9-125.4 ng/mL;  $P < 0.001$ ) from 6 wk to 6 mo, the concentrations were significantly higher than baseline (53.8; 95% CI: 41.8-65.8 ng/mL;  $P < 0.001$ ).

## Discussion

The majority (64.9%) of the moderately or severely anemic postpartum women who received a single dose of FCM remained nonanemic (hemoglobin  $> 12.0$  g/dL) 6 mo later. Among the anemic women ( $n = 20$ ), 75% had mild anemia. Many studies have attested to a quick (within 6 wk) and significant increase in hemoglobin concentration following the administration of FCM to anemic antenatal and postpartum women. This study is one of the first few that documented a sustained effect of FCM in treating anemia and replenishing body iron reserves among moderately or severely anemic postpartum women. These findings have significant clinical implications, particularly in those countries where anemia is a public health problem.

Despite extensive review of the literature, only 2 studies were found that reported the long-term effect of FCM on hemoglobin and serum ferritin concentrations among postpartum women (7, 8). Becuzzi et al. (7) constructed a retrospective cohort of moderately anemic postpartum women (hemoglobin: 9.6-10.5 g/dL). Six months postintervention, mean hemoglobin was  $13.3 \pm 0.8$  g/dL and serum ferritin concentration was  $57.7 \pm 49.3$  ng/mL (7). These findings are similar to those in our study. A study conducted in Tanzania reported a substantial increase in hemoglobin and serum ferritin concentrations (358 ng/mL) after intravenous FCM, and reported a sustained increase in hemoglobin and a significant decline in serum ferritin concentrations from 6 to 52 wk, which is in line with the findings of our study (8). Long-term beneficial effects of FCM have also been reported among patients with pulmonary arterial hypertension (11).

The finding that 9 women who were anemic at the end of 6 mo were anemic at 6 wk also indicates that they may be nonresponders

to intravenous FCM. They might be suffering from anemia due to causes other than iron deficiency. The following factors could potentially affect hemoglobin at 6 mo after FCM administration: oral iron intake, other nutritional supplements, dietary preferences, duration of breastfeeding, onset of menstruation and amount of menstrual blood loss, use of contraception, parasitic infestation, and malaria. Efficacy of FCM has already been demonstrated in controlled research settings. This study measured the effectiveness of FCM in a field setting. C-reactive protein, an indicator of chronic inflammation, was not measured in this study, which could inflate the serum ferritin concentration.

Mean hemoglobin at baseline and anemia prevalence at 6 wk were not significantly different between women who were lost to follow-up and those women included in the study. Therefore, the validity of the findings is unlikely to have been affected.

In conclusion, the administration of a single dose of FCM to moderately and severely anemic postpartum women not only treats anemia but also replenishes body iron reserves up to 6 mo.

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### Data Availability

Data described in the manuscript, code book, and analytic code will be made available on request to the corresponding author.

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