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"INTRAVENOUS FERRIC CARBOXYMALTOSE (FCM): A BOON TO FUTURE"

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Abstract-

Background: Postpartum anemia imposes a disproportionately substantial disease burden during a critical period of maternal-infant interaction. Postpartum anemia requires prevention and treatment not only for that particular period but also to ensure good health with enough iron stores at the start of the next pregnancy. Among various parenteral iron preparations, single-dose intravenous (FCM) ferric carboxymaltose is more effective to cure anemia.

Material & Methods:

This was an observational prospective interventional study in 120 anemic postnatal women in Government Medical College, Akola- Maharashtra. Patients with Hb <10 grams were assigned to this study and were given intravenous FCM. Data were collected and statistical analysis was performed. Treatment potency was assessed through repeat hemoglobin (Hb) and ferritin titers which indicate the iron (Fe) stores. Drug safety was assessed by the evaluation of drug reactions.

Results :

A significant rise in Hb, MCV, and ferritin levels was observed after 1 week and 1 month after receiving Inj.FCM. The mean change in the hemoglobin levels were 0.845 and 2.405 on day 7 and at day 28 respectively. Mean changes in the MCV levels were 3.06 and 6.42 on day 7 and on day 28 respectively. The mean change in the Sr. Ferritin levels was 102.56 ng / ml on day 28. This means the change in the Sr. Ferritin level was statistically significant with a 'P' value < 0.0001.

Conclusion:

Intravenous ferric carboxymaltose is an efficacious and safe drug to treat postpartum anemia in women of reproductive age.

Keyword- Postpartum anemia, IV FCM, Hemoglobin

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INTRODUCTION-

The burden of Iron Deficiency Anemia (IDA) during pregnancy and postpartum continues to remain high in India. More than 2/3rd of pregnant women suffer from anemia of which 95% are due to IDA. About 84% of women are iron deficient in the first postpartum week. According to National Family Health Survey 4 (NFHS 4, 2015-16) 45.7 % (Urban) and 52.1 % (Rural) of antenatal women in India are anemic (1).

Coverage of antenatal care has improved in India, especially after the implementation of the National Rural Health Mission, which was launched in 2005 to provide accessible, affordable, and quality health care to rural populations, but care during the postpartum period remains poor. (2) Oral iron preparations are being used for centuries as an easy, cost-effective, and preferred method to treat anemia, but in certain circumstances, the efficacy of oral irons may be questioned due to its faulty intake, faulty absorption, related side effects, and different bioavailability of different iron preparations and unpredictable attitude of the patient. Parenteral iron preparation offers a benefit over oral iron in being more reliable, better bioavailable, no gastrointestinal side effects, and thus better response, though, sometimes they may cause allergic and anaphylaxis reactions. (3) With the challenge of optimizing iron delivery, new intravenous complexes have been developed in the last few years. A very good example of this is Ferric carboxymaltose (FCM).

MATERIAL AND METHOD-

One Hundred twenty (n=120) postpartum women with a diagnosis of iron deficiency anemia after the delivery and admitted in the department (IPD) of obstetrics and gynecology of tertiary health center were enrolled in the study after fulfilling the inclusion criteria.

INCLUSION CRITERIA:

Postpartum women with iron deficiency anemia and hemoglobin range from 7 to 10 gm. Typing of anemia was done by investigations such as:

HAEMOGRAM

PERIPHERAL SMEAR

SERUM FERRITIN

Women who were willing to take part in the study and given informed written consent.

EXCLUSION CRITERIA:

Women with anemia other than iron deficiency anemia.

Vitamin B12 Deficiency

Folate Deficiency

Patients with infection

Patients suffering from chronic bleeding

Renal Failure

Patients with a history of previous blood transfusions

Patients with a history of Iron Intolerance

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Patients with a history of hematological disorder (thalassemia /sickle cell disease)
Patients with a history of acute blood loss

DOSE CALCULATION AND ADMINISTRATION:

The amount of iron needed by the patient is calculated by the following formula.
Cumulative Iron Deficiency = BW in Kg X (Target Hb – Actual Hb) X 2.4 + Iron Storage depot (500)
But Inj. Ferric carboxymaltose is administered in a single dose once a week by intravenous route. Ferric carboxymaltose 1000 mg [single dose] infused over for at least 15 minutes. It is administered as a maximum single dose of 1000 mg (20 ml) diluted in 250 ml sterile 0.9% sodium chloride solution infused over 15 minutes not more than once in a week.

ADMINISTRATION OF INJ.FCM

During the period of infusion, the vitals of patients were observed. Patients were also looked for any hypersensitivity reactions like rashes, chills, anaphylactic reactions or hypotension, etc.
All the patients were made to undergo baseline investigations after enrollment.
The investigations were repeated on day 7 and on day 28 after the drug intervention. The following investigations were done 'Before' and 'After' intervention. Mean change in haemoglobin and serum ferritin was analyzed. The efficacies were assessed on day 7 and day 28.Safety parameters are assessed immediately after giving a drug.

EFFICACY MEASURES:

Primary outcome:
The primary endpoint of the study is an improvement in hemoglobin level at the end of the study.
Secondary outcome:
The secondary endpoint of the study is improvement in serum ferritin levels at the end of the study.

ADVERSE EVENT MONITORING:

Any adverse event that occurred was recorded in the case proforma.

STATISTICAL ANALYSIS-

Statistical analysis was carried out using the Students paired' test and repeated measures ANOVA test for comparing quantitative data within the study groups before and after the study.
Statistical significance is indicated by conventional symbols:
*P <0.05: Statistically significant
**P <0.001: Statistically highly significant

RESULTS:

In our study, the greatest numbers of patients were in the third decade of their life. Patients aged between 22-25 years accounted for 40% of the total patients and 30% of the patients had ages between 26- 29 years. In our study, most of the patients had parity 1 or 2 with a large number of multiparas. Patients with parity 1 and parity 2 accounted for 40.83% and 36.66% respectively. Large numbers of the deliveries were LSCS and it accounted for 55% of total deliveries followed by vaginal delivery which occurred in 45% of patients. In our study maximum 81.66% of the patients were belonged to

rural areas and 18.33% of patients belonged to urban areas. 41.66% of the patients belong to class 4 and 39.16% of the patients were from class 5 of Kuppuswamy socioeconomic class scale. (Table-1)

In our study mean hemoglobin levels at baseline were 8.185 ± 0.5079 gm% which increased to 9.030 ± 0.4419 gm% on day 7. At the end of the study, the mean hemoglobin levels reached to 10.59 ± 0.3653 gm%. The mean change in the hemoglobin levels were 0.845 and 2.405 on day 7 and on day 28 respectively. This mean change in the hemoglobin level was statistically significant with 'P' value < 0.0001*. (Table-2)

In our study mean Sr. ferritin levels at baseline were 33.24 ± 10.17 which increased to 135.8 ± 18.00 at the end of the study. The mean change in the Sr. ferritin levels was 102.56 ng/ ml on day 28. This mean change in the Sr. ferritin level was statistically significant with 'P' value < 0.0001*. (Table-3 & 4)

In our study, very few patients developed ADR amounting to 5.8 % out of all studied patients. Out of them, 2.5% of patients had sweating, 1.66% had nausea and 1.66% had dizziness after administration of the drug. No serious adverse drug reaction notes in any patients. No patients required stoppage of treatment. (Table-5)

DISCUSSION:

In our study, the mean change in Hb after 1 month was 2.41 g/dl and the mean change in serum Ferritin was 102.56 ng /ml. These Findings are corresponding to the study done by Borse et al (4) (Table-6)

In a study done by Borse D S et al, the mean increase in Hb after 2 weeks was 3.1±0.50 g/dl and 4.0±70 g/dl at 6 weeks. The mean increase in serum ferritin levels after 2 weeks was 210.40±38.50 and 270.25±14.60 ng/ml after 6 weeks.

Lunagariya M et al (6) carried out a study in which they found that a significantly higher number of women achieved a rise of Hb >2gm/dl in FCM group which was highly significant (p value <0.001). The mean rise of Hb was 1.9 gm/dl for the FCM group.

Serum ferritin level in the ferric carboxymaltose group raised more (83.9 ng/ml). Our study findings were similar to these findings. The mean rise of Hb and Sr.ferritin in our study is slightly more than in this study.

The mean rise in Hb was 2.41 g/dl after 4 weeks in our study which is slightly less than the study by Rathod s et al (8) but with a significant difference (p value <0.0001) and the mean rise in Sr.ferritin was 102.56 ng/ml which is in accordance with the study by Rathod S et al. Adverse drug reactions were significantly less in our study which was similar to the study done by Rathod S. et al.

The mean change in Hb after 4 weeks is 2.41 gm/dl which is in accordance with the study done by Damineni SC et al(5) which has a mean change in Hb after 6 weeks is 3.2 g/dl.

Breyman C et al (7) study has a mean change in Hb after 4 weeks as 4.4 gm which is higher than our study and the mean change in Sr ferritin after 12 weeks is 93.5 ng/ml. In our study, the mean change in Sr. ferritin is in accordance with this study.

Treatment with intravenous FCM improves the hemoglobin level, increases the serum ferritin level, and replenishes the iron store. Furthermore, adverse effects with FCM are lesser as compared to the

other parenteral preparation of iron. As in the majority of the patients, FCM single dose of 1000 mg is sufficient to raise the Hb level and serum ferritin, compliance is much better than other formulations.

CONCLUSION:

Intravenous ferric carboxymaltose is an efficacious and safe drug to treat postpartum anemia in women of reproductive age. Prophylaxis with oral iron in the postpartum period for 90 days sometimes cannot be followed by most of women. Most of the women are noncompliant with oral iron prophylaxis. Therefore, a single dose of Intravenous ferric carboxymaltose prophylaxis as a single dose (1000 mg) is a better alternative to oral iron prophylaxis postpartum barring its cost-effectiveness.

Intravenous FCM is a boon to treat and prevent iron deficiency anemia in patients, especially those belonging to rural health setups.

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DECLARATIONS:

Funding: Jiv Daya Foundation provided Inj.FCM vials free of cost to this institute.

Conflict of interest: None

Ethical approval: Yes. (Reference No.-215/2018)

Abbreviations-

Hb-hemoglobin
FCM-ferric Carboxymaltose
Ng/ml-nanogram per mililitre
g/dl- grams per decilitre
ADR-adverse drug reaction
fL-femtolitre
Sr- Serum

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TABLES

Table 1.Epidemiological Factors

Epidemiological factors	
Age	22-25 yrs
Parity	Multipara
Mode of delivery	LSCS
Residence	Rural
Socioeconomic class	Class 4 and class5

Table 2. Haemoglobin during study period

Parameter	On Day 0	On Day 7	On Day 28	'P' value intra-group †
Hemoglobin levels in Grams (Mean ± SD)	8.185 ±0.5079	9.030 ±0.4419	10.59 ±0.3653	< 0.0001*
Std. Error	0.046	0.040	0.033	
Lower 95% CI	8.094	8.950	10.52	
Upper 95% CI	8.276	9.110	10.65	

Values: Mean ± Standard Deviation, SD: Standard Deviation, *:Statistically significant, †: Using Repeated measure ANOVA.

Table 3. Sr. Ferritin levels during study period

Parameter	On Day 0	On Day 28	'P' value Intragroup †
Sr.Ferritin level ng/ml (Mean ± SD)	33.24 ±10.17	135.8 ± 18.00	< 0.0001*
Std.Error	0.9242	1.636	
Lower 95% CI	31.41	132.5	
Upper 95% CI	35.07	139.0	

Values: Mean ± Standard Deviation, SD: Standard Deviation, *:Statistically significant, ‡: Using paired t test)

Table 4. Comparison Pre-study and Post-study

Parameter	On Day 0	On Day 7	At Day 28	'P' value *intra group*‡
Hemoglobin level in gms (Mean ± SD)	8.185± 0.5079	9.030±0.4419	10.59 ± 0.3653	< 0.0001 *
Sr.Ferritin level ng/ml (Mean ± SD)	33.24 ± 10.17	-	135.8 ± 18.00	< 0.0001 *

Table 5. Incidence of Adverse Drug Reaction (ADR)

Sr.No.	Type of ADR	Number of patients[n]	Percentage %
1.	Nausea	2	1.66
2.	Sweating	3	2.5
3.	Dizziness	2	1.66

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Table 6. Comparison with Different studies

Study	Before FCM administration			After FCM administration					p value
				On Day 7		On Day 28			
	Hb (gms / dl)	MCV (fL)	Sr.Ferritin(mcg/ltr)	Hb(gms / dl)	MCV(fL)	Hb (gms / dl)	MCV(fL)	Sr.Ferritin(mcg/ltr)	
Present study (n=120)	8.18	78.24	33.24	09.03	81.3	10.59	84.6	135.8	<0.0001
Borse DS et al(4) (n=214)	7.87	-	35.52	2wks 10.97	-	6wks 11.8	-	6wks 270	<0.001
Damineni S C et al(5) (n=90)	8.70	-	-	10.66	-	6wks 11.9	-	-	<0.001
Lunagariya M et al(6) (n=100)	8.38	66.52	13.34	2wks 10.28	2wks 70.11	-	-	2wks 83.95	<0.001
Breymann C et al (7) (n=227)	9.66	-	45.5	4wks 14	-	12wks 15.2	-	12wks 139	<0.001
Rathod S et al(8) (n=366)	7.71	-	35.52	2wks 10.87	-	6wks 12.11	-	6wks 142.2	<0.001