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COMPARING SAFETY AND EFFICACY OF INTRAVENOUS IRON SUCROSE AND FERRIC CARBOXYMALTOSE IN MODERATE IRON DEFICIENCY ANEMIA IN PREGNANT WOMEN

Obstetrics & Gynaecology

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ABSTRACT

INTRODUCTION: Anemia is a global health problem. World Health Organization (WHO) defines anemia as a condition in which the hemoglobin (Hb) concentration of a woman during pregnancy is <11 g/dl. About half of the global maternal deaths due to anemia occur in South Asian countries with **India contributing to about 80% of the total.**

OBJECTIVE: The aim of the present study was to compare the safety and efficacy of IS and FCM in the treatment of moderate IDA in pregnant woman.

MATERIALS AND METHODS: This study was conducted in the dept of OBGY at PIMS medical college, Udaipur from Jan 2021 to Jan 2022 Pregnant women attending the antenatal clinic between 28 to 34 weeks period of gestation were screened and women with moderate IDA were enrolled for the study. 100 pregnant women were randomized into two groups in a 1:1 ratio and were administered either IS or FCM.

RESULTS: Base line characteristicks, Hb, MCV, MCHC, MCH, Serum iron, serum ferritin, TIBC levels were compared between two groups

CONCLUSION: To conclude FCM is as safe as IS, convenient and more effective therapy for treatment of IDA in antenatal patients. It has convenient dosage and administration. FCM increases patient's compliance and decreases bed occupancy and burden on health facility in developing country like India.

KEYWORDS

INTRODUCTION:

Anemia is a global health problem. World Health Organization (WHO) defines anemia as a condition in which the hemoglobin (Hb) concentration of a woman during pregnancy is <11 g/dl. WHO has estimated that in all over world about 32.4 million pregnant women suffer from anemia.[1] WHO estimated that even among the South East Asian countries; India has the highest prevalence of anemia. About half of the global maternal deaths due to anemia occur in South Asian countries with **India contributing to about 80% of the total.**[2]

Anemia has the highest prevalence in three groups: children aged <5 years (47%), pregnant women (42%), and women of reproductive age (30%).

Iron deficiency is seen in 50% of cases and is the most common cause of anemia.[3] In India, four major surveys by National Family Health Survey (NFHS)-III (2008) and-IV (2015-16), District Level Household Survey (DLHS) and Micronutrient Survey conducted by National Nutrition Monitoring Bureau (NNMB) have estimated that **over 57 to 96.2% of pregnant women were anemic.**[4]

Oral iron therapy is first choice for prophylaxis and treatment of mild IDA in pregnancy.[4] Oral iron has limited absorption by intestinal tract and it requires several weeks to raise Hb to the target level.[5,6,7] Oral administration of iron also has limited efficaciousness and is associated with gastrointestinal side effects. Some women fail to comply with iron replacement for prolonged duration.

Intramuscular (IM) route has also been suggested a cost-effective treatment for moderate anemia in pregnancy.[8] Parenteral iron by IM route is painful, can cause staining of skin and abscess formation. One of the dreaded side effects is anaphylaxis, even maternal death has also been reported. Hypersensitivity reaction has not been reported with Iron sucrose (IS) or Ferric carboxymaltose (FCM); hence, no test dose is required before administrating the drug. By means of **intravenous (IV) iron**, gastrointestinal absorption is bypassed and incorporated more rapidly.[9] IV iron treatment is associated with better efficacy, compliance, safety and a shorter hospital stay.[5,6] IS, a second-generation iron preparation, is safe, effective, and economic in comparison to the repeated and painful IM iron injections. The incidence of anaphylaxis and other adverse reactions with IS is markedly lower, multiple doses are typically required.[10]

FCM, a third generation iron preparation 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.[11] Although the efficacy of IS and that of FCM for treatment of anemia have been studied, the data are limited in our population.

Hence, the present study was aimed to compare the efficacy and safety of IS and FCM in improving moderate IDA in pregnancy.

AIMS AND OBJECTIVES:

The aim of the present study was to compare the safety and efficacy of IS and FCM in the treatment of moderate IDA in pregnant woman.

Primary Outcome:

- Rise in Hb and serum ferritin at 4 weeks and 8 weeks.

Secondary Outcome:

- Red blood cell indices
- Serum iron studies
- Any adverse effects
- Need for blood transfusion

MATERIALS AND METHODS:

This study was conducted in the dept of OBGY at PIMS medical college, Udaipur from Jan 2021 to Jan 2022 Pregnant women attending the antenatal clinic between 28 to 34 weeks period of gestation were screened for the study. Women with moderate IDA were enrolled for recruitment in study after they satisfied inclusion and exclusion criteria. Informed written consent was taken from all the patients before recruitment into the study. Hundred pregnant women were randomized using a computer-generated block randomization table into two groups in a 1:1 ratio and were administered either IS or FCM. Routine antenatal investigations were done according to the standard departmental protocol. Investigations specific to anemia included Hb, peripheral blood smear, RBC indices including MCV, MCH, MCHC, serum ferritin levels, serum iron, TIBC and percentage saturation were done.

INCLUSION CRITERIA

Pregnant woman with moderate IDA (Hb 7 to 9 gm/dl, peripheral smear –

- microcytic hypochromic, serum ferritin – less than 20 µg/L)
- Age between 18 to 45 year
- Singleton pregnancy
- Gestational age between 28 to 34 weeks

EXCLUSION CRITERIA

Pregnant woman with anemia other than IDA With known history of allergy to injection iron Multiple pregnancy, Hypertension, Diabetes mellitus,Chronic liver disease, Renal disorders Cardiovascular disease, Thyroid disorders, Intestinal resection, bypass

Dose calculation of IS and single dose FCM

Required iron dose (mg) = [2.4 × (target Hb - actual Hb) × pre-pregnancy weight (kg)]+ 500 mg for replenishment of stores.
Target Hb to achieve – 11 gm/dl

Group IS

100 women were randomized to this group. As per the formula, dose of IS was calculated. This dose was given as 200 mg/infusion in 100 ml normal saline (NS) (0.9%) over 30 minutes. Maximum 600 mg/week was given.

Group FCM

100 women were randomized to this group. As per the formula, dose of FCM was calculated. This dose was given as 1000 mg/infusion in 100 ml NS (0.9%) over 30 minutes. Maximum 1000 mg/week was given.

STATISTICALANALYSIS

Statistical analysis was performed using SPSS v21. Data were presented as frequency, percentage, mean, and standard deviation. Chi square test was used to compare categorical variables. Student t-test was used to compare quantitative variables between 2 groups. The value of $p < 0.05$ was considered significant.

OBSERVATION AND RESULTS

Table 1: Comparison of baseline characteristics between study participants

	IS (n=100)	FCM (n=100)	p Value
Age (Years)	27.1±4.1	27.2±4.6	0.797#
Weight (Kg)	57.5±7.7	58.1±8.4	0.583#
BMI (Kg/m^2)	22.1±2.5	22.1±2.6	0.933#
Gestational age (Weeks), n (%) 28-30 30^{+1} - 32 32^{+1} – 34	33 (33%) 29 (29%) 38 (38%)	24 (24%) 29 (29%) 47 (47%)	0.305##
Parity, n (%) Primigravida Multigravida	40 (40%) 60 (60%)	41 (41%) 59 (59%)	0.855##
Hb (g/dl)	8.1±0.5	8.1±0.6	0.477#
MCV (fl/cell)	71.8±1.9	71.5±2.2	0.371
MCH (pg/cell)	21.6±1.1	21.5±1.2	0.364
MCHC (g/dl)	30.1±1.2	30.2±1.1	0.576
Ferritin (µg/L)	12.0±0.7	12.0±0.8	0.940
Iron (µmol/L)	41.6±1.1	41.5±1.2	0.364
TIBC (µg/dl)	537.5±102.6	541.2±101.2	0.796
Percentage Saturation	15.0±0.8	15.1±0.7	0.624
Total iron dose	896.8±92.1	908.7±103.9	0.392

Table 2: Comparison of Hb levels in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline (g/dl)	8.1±0.5	8.1±0.6	0.477
4 Weeks	8.7±0.4	8.8±0.6	0.168
8 Weeks	9.5±0.5	9.7±0.5	**0.011**

Table 3: Comparison of MCV levels in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	71.78±1.89	71.51±2.25	0.371
4 Weeks	87.10±3.90	91.51±2.19	**<0.0001**
8 Weeks	100.55±2.89	102.15±2.08	**<0.0001**

Table 4: Comparison of MCH levels in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	21.6±1.1	21.5±1.2	0.364
4 Weeks	27.1±1.3	26.7±1.9	0.067
8 Weeks	31.7±1.3	32.3±2.0	**0.013**

Table 5: Comparison of MCHC levels in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	30.1±1.2	30.2±1.1	0.576
4 Weeks	29.0±1.0	30.6±1.5	**<0.0001**
8 Weeks	30.4±1.1	31.0±1.2	**<0.0001**

Table 6: Comparison of serum ferritin levels in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	12.0±0.7	12.0±0.8	0.940
4 Weeks	60.0±1.0	61.0±0.8	**<0.0001**
8 Weeks	120.7±1.0	122.3±1.0	**<0.0001**

Table 7: Comparison of serum iron levels in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	41.6±1.1	41.5±1.2	0.364
4 Weeks	72.5±1.1	72.8±1.3	0.068
8 Weeks	95.6±1.5	95.7±1.2	0.521

Table 8: Comparison of TIBC in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	537.5±102.6	541.2±101.2	0.796
4 Weeks	343.3±48.3	342.6±51.8	0.914
8 Weeks	288.1±49.4	283.2±54.2	0.504

Table 9: Comparison of percentage saturation in the study population

	IS (n=100)	FCM (n=100)	p Value
Baseline	15.0±0.8	15.1±0.7	0.624
4 Weeks	31.1±0.9	31.3±0.8	0.100
8 Weeks	55.2±0.9	56.3±0.9	**<0.0001**

Table 10: Comparison of adverse events in the study population

	IS (n=100)	FCM (n=100)	p Value#
Injection site Thrombophlebitis	10	3	0.085
Vomiting	3	-	0.245
Fever	1	1	1.000
Headache	4	2	0.678
Overall	18	6	**0.015**

DISCUSSION:

In the present study, the mean age of patients in group IS was 27.1±4.1 years and in group FCM was 27.2±4.6 years which was comparable (p =0.797). Similarly, studies done by Jose et al.[12] and Verma et al.[13] were comparable to the present study. While the mean maternal age was slightly lower than the present study in the study done by Lunagaria et al.[14] It was 24.74±4.1 years in the group IS and 24.06±2.75 years in the group FCM. Whereas the mean maternal age was slightly higher in the study done by Christoph et al.[15] i.e. 29.9 years and 29.0 years in group IS and group FCM respectively. This difference might be due to the fact that this study was done in Switzerland and rest studies were performed on Indian population.

The mean maternal weight values in group IS (57.5±7.7) and group FCM (58.1±8.4) were comparable in our study (p= 0.583). These values were similar to study done by Jose et al.[12] However, the mean maternal weight was slightly higher in the study done by Christoph et al.[15] i.e. 69.3 kg in group IS and 73.1 kg in group FCM.

BMI values in both groups were comparable (p= 0.933). Similar study done by Jose et al.[12] had observed BMI slightly lower than our study .Present study was similar in terms of parity in IS group and FCM group. Similar study done by Verma et al.[13] (n = 50) and Lunagariya et al.[14] (n = 50) had also observed more cases of IDA in multigravida.

The present study was comparable with Jose et al.[12] in terms of inclusion and exclusion criteria but they had follow up after 12 weeks, results are comparable in both studies as there was a statistically significant rise in Hb in FCM groups in comparison with IS group even though follow-up was 4 weeks earlier in the present study. Similarly another study, done by Agrawal et al.[16]; their results were also in concordance with our study even though follow-up was done 5 week earlier in their study. Another study done in post-partum patient by Singh et al.[17] had also observed that rise in Hb was statistically significant in group FCM than IS after 3 weeks of follow up. Study done by Christoph et al.[46] had observed no statistically difference in both groups. But in our study rise in MCV was statistically significant after 8 weeks. Another study done by Singh et al.[17] had observed similar results as our study even though follow up was done after 6 weeks & study was conducted in post-partum patients .

In present study the observations were in concordance with the study done by Jose et al.[12] Both studies had observed significant increase in MCH in group FCM than IS. Jose et al.[12] compared MCHC levels

before and after the treatment, but their results are not comparable with the present study, in their study rise in MCHC levels at follow up was not statistically significant. Variation in result is attributed to the fact that their study had follow up after 12 weeks which was 4 weeks later than present study.

Jose et al.[12] compared the serum ferritin levels in group FCM and IS. Initially they observed significant difference in group FCM than IS at 3 weeks follow up in their study but in long term at 12 weeks difference is gone. They inferred that IS is equally able to give comparable supplementation for replenishment of iron stores. They also compared serum iron levels before and after the treatment, and their results are comparable with the present study, in their study difference in rise in serum iron levels at follow up in both the groups FCM and IS was not statistically significant and similar results were observed in our study too .

In this study decrease in TIBC values at follow in both the groups FCM and IS was not statistically significant. In our study rise in percent saturation of iron at follow-up was statistically significant.

Adverse effects:

In our study, adverse events were significantly higher in group IS in comparison to group FCM (P=0.015). Injection site thrombophlebitis was the most common adverse events in 10% patients in group IS and 3% patients in group FCM. Our findings are in somewhat concordance with Jose et al.[12] who reported 4% injection site thrombophlebitis in group IS and 2% in group FCM.

CONCLUSION:

Parenteral iron preparations have become a major interest to prevent IDA in pregnant women. Of all parenteral preparations, FCM and IS are most commonly used. As per our observation FCM is found to be statistically significantly better for improvement of Hb and serum ferritin levels as compare to IS. By using FCM to treat IDA in antenatal patients, the rate of blood transfusions could be reduced.

To conclude FCM is as safe as IS, convenient and more effective therapy for treatment of IDA in antenatal patients. It has convenient dosage and administration. FCM increases patient's compliance and decreases bed occupancy and burden on health facility in developing country like India.

In the study, the drug was provided free of cost to the patients under the JSSK (Janani Shishu Suraksha Karyakram) scheme for pregnant women by the Indian Government. Present study showed higher rise in Hb in group FCM at 8 weeks. Ferritin level were persistently higher from 4 weeks onwards and continues till 8 weeks in FCM group. The finding indicated that FCM is superior to IS in replenishment of stores and rise in Hb. This is important in pregnant women presenting with moderate IDA especially in third trimester.

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