COMPARISON OF FERRIC CARBOXYMALTOSE AND IRON SUCROSE COMPLEX FOR TREATMENT OF IRON DEFICIENCY ANEMIA IN PREGNANCY: RANDOMIZED CONTROLLED TRIAL

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Abstract

Introduction: Anaemia is the most common physiologic disorder in women. Industrialized and semi-industrialized nations have a major problem, while resource-poor nations have a bigger problem. Public health issues like anaemia might affect pregnancy. 40% of fertile but non-pregnant women have low iron.

Methods: The Rajkiya Mahila Chikitsalya Department of Obstetrics and Gynecology in Ajmer undertook an open label randomised clinical trial. The institute's ethics committee approved (IEC). All ladies were carefully assessed and recruited after meeting inclusion and exclusion criteria. A computer-generated random number table assigned 200 pregnant women aged 28–34 weeks to one of two groups in a 1:1 ratio.

Results: The P value of 0.0001 shows that ferric carboxylates increase Hb significantly. The FCM group had significantly higher MCV levels than the IS group at 4 weeks (87.10 ± 3.90 vs 91.51 ± 2.25; p0.0001) and 8 weeks (94.55 ± 2.89 vs 98.15 ± 2.08). FCM had a considerably higher MCH value (31.2 pg) than IS (39.7 pg), P = 0.0001. RDW increased to 21.9 percent in the IS group and 22.4 percent in the FCM group at admission. At four weeks, intravenous iron preparation injections reduced RDW to 18.9% in the IS group and 19.78% in the FCM group. FCM rose more than Iron sucrose. 231 and 280 μg/L for IS and FCM groups. It was statistically significant. Both groups had 12 μg/L S. ferritin at admission. However, iv iron preparation elevated S. ferritin in both groups. FCM rose more than Iron sucrose at 4 and 8 weeks. 231 and 280 μg/L for IS and FCM groups. It was statistically significant.

Conclusion: Anemia secretly hinders pregnancy, growth, and future generations. Anemia and its effects in pregnant women are being reduced. In pregnancy, compliance, and gastrointestinal adverse effects limit oral iron therapies. Parenteral iron therapy addresses compliance and tolerance.

Keyword: Anemia, FCM, Iron sucrose

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Introduction

The most prevalent physiologic malfunction that affects women throughout their lives is anaemia. It is a serious issue in industrialized and semi-industrialized nations, and it gets worse in nations with limited resources. Anemia is a significant problem for public health that might have negative effects on pregnancy. Women who are fertile but not pregnant have low iron levels in about 40% of cases.[1]

Throughout a woman's life, anaemia is the most prevalent physiologic derailment. In industrialized and semi-industrialized nations, it is a serious issue, and in nations with limited resources, it becomes even more problematic. Anemia is a significant public health problem that can have negative pregnancy outcomes. The percentage of fertile, non-pregnant women with low iron is about 40%.[2]

Because of changes in social norms, way of life, and health-seeking behaviors, there are significant regional differences in the prevalence of anaemia in pregnancy.

The prevalence of anaemia in pregnancy is estimated to be 41.8 percent worldwide, with rates ranging from 35 to 60 percent in Africa, Asia, and Latin America, and 20 percent in affluent nations. Anemia can affect pregnant women anywhere in the world. Anaemia is thought to be present in 5.7 percent of Americans, 75% of Gambians, and 65–75% of Indians.[3]

The present study was aimed to evaluate the comparison of ferric carboxymaltose and iron sucrose complex for treatment of iron deficiency anemia in pregnancy: Randomized controlled trial.

Methods

The Department of Obstetrics and Gynecology at Rajkiya Mahila Chikitsaly in Ajmer conducted this investigation as an open label randomised clinical trial. The ethical committee of the institute granted permission (IEC). All women were carefully evaluated and enlisted for recruitment after meeting inclusion and exclusion requirements.

A computer-generated random number table was used to assign 200 pregnant women between the ages of 28 and 34 weeks to one of two groups in a 1:1 ratio. Pregnant women with proven moderate IDA (Hb 7 g/dl to 9.9 g/dl), who are between the ages of 18 and 45, are carrying a singleton, and have a gestational age between 28 and 34 weeks meet the inclusion criteria. Multiple pregnancies, hypertension, diabetes mellitus, chronic liver disease (serum transaminases more than 1.5 times the upper limit of normal), renal disorders (serum creatinine > 2 mg/dl), cardiovascular disease, thyroid disorders, intestinal resection, bypass, hemosiderosis, and hemochromatosis were among the exclusion criteria.

Data Analysis

For statistical analysis, data were entered into a Microsoft® Excel workbook and exported into SPSS v21.0 (IBM, USA). The Chi square test was used to compare frequency and percentage expressions of categorical data. The student t-test was used to compare quantitative data that was presented as mean and standard deviation. Statistics were considered significant if P 0.05.

Results

Baseline Characteristics

The average age of women in the iron sucrose group was found to be 27.56±6.88, whereas the average age of women in the FCM group was 28.92±6.96 (see Table 1). Age was found to be comparable between the two groups with a p value of 0.167, or non-significant. Patients in the IS group had a mean weight of 57.51 kg, while those in the FCM group had a mean weight of 58.24 kg. No discernible variation in weight between these two groups was discovered when considering the p value of 0.522. In the FCM and IS groups, the mean BMI was determined to be 22.77 vs. 23.67, respectively.

No discernible difference between the BMI of patients recruited to two different groups is shown by the P value of 0.057. In this study, 81% of the women in the FCM group and an almost identical 87% of the women in the IS group followed a vegetarian diet. While the proportion of patients eating a non-vegetarian diet was 19% in the FCM group and 13% in the IS group, respectively. Most of the female participants were nonsmokers.

In the FCM group, there were 4% smokers, compared to only 3% in the iron sucrose group. In the FCM group, 52% of patients and in the iron sucrose group, 50% of patients, were from lower socioeconomic groups (including both upper lower and lower). The medium socioeconomic category comprised 42% of the IS group and 37% of the FCM group (including both upper middle and lower middle). While just 8 members of the IS group and 11 of the FCM group participants fell into the upper socioeconomic bracket.

Comparing levels in study population
Hemoglobin level
According to Table 2, both groups' admission hemoglobin was 8.1 gm/dl at baseline. Hb levels were discovered to be elevated at follow-up, reaching 8.7 gm/dl in the IS group and 8.8 gm/dl in the FCM group. Hb levels considerably increased at the 8-week mark, reaching 10.4 gm% against 9.5 gm% in the IS group. The substantial difference in Hb increase caused by injection of ferric carboxylates is indicated by the P value of 0.0001.

MCV level
We found that the baseline MCV levels in group IS where equivalent to the baseline MCV levels in group FCM (71.78±1.89 vs. 71.51±2.25; p=0.371). MCV levels in the FCM group were substantially higher than those in the IS group at 4 weeks (87.10±3.90 vs 91.51±2.25; p0.0001) and 8 weeks (94.55±2.89 vs 98.15±2.08) (Table 2).

MCH level
Participants in the two groups had similar mean MCH picogram values. MCH levels were comparable at baseline (21.6 in Iron sucrose group and 21.5 in FCM group). Following up after 4 weeks, the iron sucrose and FCM groups' respective mean MCH levels were 27 pg and 26.7 pg. While after 8 weeks, the MCH value in the FCM group increased significantly (31.2 pg) compared to the IS group (39.7 pg), P value 0.0001. (Table 2).

MCHC level
At baseline, the MCHC levels in group IS where equivalent to those in group FCM (28.8±1.2 vs. 28.9±1.1; p=0.539), however at 4 weeks (29.0±1.0 vs 30.6±1.5; p=0.001) and at 8 weeks (30.4±1.1 vs. 31.0±1.2; p0.0001), the MCHC levels in group FCM were significantly greater than those (table 2).

RDW
RDW was raised in patients at the time of admission up to 21.9 percent in the IS group and 22.4 percent in the FCM group, levels that were comparable. RDW decreased after receiving intravenous iron preparation injections, reaching 18.9 percent in the IS group and 19.78 percent in the FCM group at four weeks. RDW levels fell more in the FCM group (13.2%) than in the IS group at the 8-week follow-up (14.56 percent). Statistics reveal statistical significance at P = 0.014. (Table 2).

Serum ferritin
S. ferritin levels (12 micrograms/L) at admission were equivalent in both groups. S. ferritin levels in both groups were discovered to be raised following iv iron preparation, nevertheless. At both subsequent visits, at 4 and 8 weeks, the rise in the FCM group was greater than in the Iron sucrose group. 231 and 280 micrograms per liter, respectively, for the IS and FCM groups. There was a statistically significant difference here (table 2).

Side effect profile
In the current study, we found that group FCM experienced considerably fewer adverse events than group IS (p=0.041). None of the patients in our study had arthralgia, hypotension, congestive heart failure, or allergic responses. 7 participants in the IS group and 3 participants in the FCM group both experienced injection site thrombophlebitis. Four and two women in the IS and FCM groups, respectively, complained of headaches (table 3).

Number of visits
For parenteral iron therapy, patients in the IS group had to go to the hospital 4-5 times. The average number of visits was 4.6, and most individuals only had one FCM treatment. Consequently, this study revealed a significantly lower number of visits in the FCM group (Table 4).

Discussion
The mean age of women in iron sucrose group was found to be 27.56±6.88 while mean age of women in FCM group was 28.92±6.96. It was observed that age was comparable in both groups with p value 0.167 i.e., non-significant. The mean weight of patients enrolled in IS group was 57.51±8.0 kg and that of FCM group was 58.24±8.10 kg.

Considering the p value of 0.522, no significant difference was found in weight between these two groups. The mean BMI was found to be 22.77 vs 23.67 in FCM and IS group respectively. P value 0.057 shows no significant difference between BMI of patients recruited to two different groups.

In a study by **Jose et al**,[4] The FCM and ISC groups had comparable mean ages (27.5±3.9 vs 26.2±3.6 years; p = 0.10). In a study by **Mahey et al**,[5] the mean age was 35.7 ± 8.2 years, and the mean weight was 56.41±2.0 vs 55.6±9.3, with no

statistically significant difference (P=0.76) between groups.

Most of the patients had normal BMI in both groups comparing to study done by **Froessler et al**,[6] The mean BMI was in the overweight range, and women with iron deficiency and severe anemia were significantly younger (p = 0.01) and had a significantly lower BMI than women with ID but no anaemia (p 0.01).

Our study also found that MCV levels in groups IS and FCM increased significantly at 4 and 8 weeks when compared to baseline MCV levels (p<0.0001), MCH levels in groups IS and FCM increased significantly at 4 and 8 weeks when compared to baseline MCH levels (p<0.0001), and MCHC levels in groups IS and FCM differed significantly at 4 and 8 weeks when compared to baseline MCHC levels (p0.0001). In a study, by **Ram et al**,[7] It was discovered that after 12 weeks of treatment in both groups, all other hematological parameters changed significantly from the baseline.

The FCM group had slightly higher mean changes in mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), and red cell than the iron sucrose group, but the difference was not statistically significant.

S. ferritin levels (in micrograms /l) were comparable in both groups at admission (12 micrograms/L). However, after iv iron preparation, S. ferritin levels were found elevated in both groups. On both follow up visits, at 4 weeks and 8 weeks, rise was more in FCM group as compared to Iron sucrose group. 231 micrograms / L in IS group and 280 micrograms / L in FCM group. This difference was statistically significant.

In study by **Khan and Gupta et al**,[8] Patients with serum ferritin levels less than 30 mcg/dl were chosen, and the majority of patients in both groups had pretreatment serum ferritin levels ranging from 10 to 19.9 mcg/l. At 2 weeks post treatment, the rise in mean serum ferritin was 84.78±10.53 in Group A (iron sucrose), and 123.80±16.03 in Group B (FCM), which is statistically significant. Study done by Jose et al, Patients were followed for up to 12 weeks and serum ferritin levels were found to be lower at 12 weeks compared to 8 weeks.

In our study, we found that RDW levels in group IS where comparable to RDW levels in group FCM at baseline (21.9±5.76 vs 22.43±5.32; p=0.499), but at 4 weeks (18.43±4.67 vs 19.78±3.98; p=0.029), and at 8 weeks (15.56±5.43 vs 16.76±6.34; p=0. 152), RDW levels in group FCM fell significantly. In a study by **Jose et al**,[4] at baseline RDW level was (21.9 ± 6.0 vs 20.5 ± 5.5; P=0.24)

Conclusion

Anemia is a secret disease that interferes with conception, stunts growth, and harms future generations. To reduce anaemia and related consequences during pregnancy in reproductive-age women, efforts are ongoing. Oral iron treatments are often used for this, although compliance and gastrointestinal side effects limit their use in pregnancy. Parenteral iron therapy addresses tolerance and compliance. Iron sucrose, which raised haemoglobin levels but required repeated visits due to its modest amount, replaced iron sorbitol and iron dextran intramuscular injections, which had negative effects.

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Table 1: Baseline Characteristics

	Inj FCM (n=100)	Inj Iron Sucrose (n=100)	P value
Age (Years)	27.56±6.88	28.92±6.96	0.167
Weight (Kg)	58.24±8.10	57.51±8.0	0.522
BMI			
Underweight (less than 18.5)	20	14	0.006
Normal (18.5-24.9)	40	60	
Overweight (25-29.9)	26	10	
Obese (more than 30)	14	14	
Mean BMI	22.77±2.94	23.67±4.07	0.057
Diet			
Veg	81	87	0.247
Non-Veg	19	13	
Smoking	3	4	0.700
Socio Economic Status			
Lower	52	50	0.660
Middle	37	42	
Upper	11	8	

Table 2: Comparing levels in study population.

	IS (n=100)	FCM (n=100)	P value
Hemoglobin (g/dl)			
Baseline	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	10.4±0.5	<0.0001
MCV levels			
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	94.55±2.89	98.15±2.08	<0.0001
MCH (in pg)			
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	29.7±1.3	31.2±2.0	<0.0001
MCHC			
Baseline	28.8±1.2	28.9±1.1	0.539
4 Weeks	30.2±1.0	31.1±1.5	<0.0001
8 Weeks	32.4±1.1	34.0±1.2	<0.0001
RDW (in %)			
Baseline	21.9±5.76	22.43±5.32	0.499
4 Weeks	18.93±2.67	19.78±2.98	0.049
8 Weeks	14.56±3.43	13.2±4.34	0.014
Serum ferritin			
Baseline	12.0±0.7	12.0±0.8	0.940
4 Weeks	180.0±5.0	220.0±6.0	<0.0001
8 Weeks	231.7±5.7	280.3±7.3	<0.0001

Table 3: Comparison of adverse events in the study population

	IS (n=100)	FCM (n=100)	p Value[#]
Injection site Thrombophlebitis	7	3	0.194
Vomiting	3	0	0.245
Fever	1	1	1.000
Headache	4	2	0.678

Gastritis	4	3	0.407
Overall	19	9	**0.041**

Table 4: Number of visits

	IS (n=100)	FCM (n=100)	p Value[#]
Number of visits	4.6	1	<0.0001