



**FERRIC CARBOXY MALTOSE A SAFE AND EFFECTIVE ALTERNATIVE IN
CORRECTING IRON DEFICIENCY ANEMIA PRIOR TO MAJOR ELECTIVE
GYNECOLOGICAL SURGERIES**

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ABSTRACT

Background: Preoperative anemia is a common and potentially serious hematological problem in elective surgery and increases the risk for peri operative red blood cell transfusion. Transfusion is associated with postoperative morbidity and mortality. Ferric carboxy maltose is a novel intravenous iron formulation promising intervention to reduce peri operative transfusion. **Objective:** To evaluate the efficacy and safety of Ferric carboxy maltose in subjects with iron deficiency anemia preoperatively in major gynecological surgeries. **Materials and Methods:** It is a single group interventional study. 100 women requiring major gynecological surgeries with iron deficiency anemia were administered with single dose of 1000mg FCM after clinical and biochemical assessment. The subjects were reassessed between 7th days to 21st day of infusion. Side effects, compliance were noted. **Results:** There was statistically significant rise of both Hb and S. Ferritin (2.28gm% & 729.82 ng/ml). All the blood indices showed statistically significant improvement after the intervention. There was clinical improvement in the symptoms and signs after the intervention. No serious adverse events were noted. **Conclusion:** Ferric carboxy maltose is safe and effective alternative to blood transfusion for correcting iron deficiency anemia in a shorter duration prior to elective gynecological surgeries.

KEY WORDS: Ferric carboxymaltose, Preoperative anaemia, Gynecological surgery, Blood transfusion.

INTRODUCTION

Women are at higher risk of iron deficiency anemia due to blood loss at regular intervals in the form of menstrual loss, pregnancy, and under nutrition¹. The prevalence of preoperative anemia ranges from 5% to 75%, depending on patient susceptibilities and the proposed surgical procedure.²

Blood transfusion is like liquid organ transplant. It is a lifesaving procedure but only as volume replacement in conditions of acute blood loss. There are many adverse events associated with the blood transfusion which overweigh its advantages. Adverse reactions to transfused blood components occur despite multiple tests, inspections, and checks.

Oral iron therapy is currently the treatment of choice for the majority of patients with iron deficiency anemia but it has disadvantages like poor absorption, poor compliance and gastro-intestinal (GI) side effects, longer time for action. Intravenous iron started 3-4 weeks prior to scheduled procedure helps in restoring iron stores

faster and more effectively than oral iron and may result in reduced blood transfusion requirements.³⁻¹⁰

Ferric carboxymaltose complex is a non-dextran containing IV iron agent designed to be administered in large doses by rapid IV injection. The ability to safely inject a single dose as large as 1000 mg in as little as 15 minutes renders this novel agent a potentially ideal choice for the treatment of preoperative IDA.

MATERIALS AND METHODS

This study was conducted in department of OBG VIMS Bellary over a period of 10 months. Research and academic committee approved the study protocol prior the initiation of the study.

The women planned major gynecological surgeries for various indications, and whose Hb between 6gm% and 10gm% were subjected for complete clinical and laboratory evaluation which included -Complete blood count, peripheral smear, S Ferritin was done along with liver and renal function test. The subjects with proven

IDA along with care taker were counseled regarding the options available for correcting anemia in their own language. The subjected giving informed consent for FCM were enrolled in the study Total 100 women were enrolled.

The subjects were infused with single dose of 1000mg of Ferric carboxy maltose in 200 ml of 0.9% normal saline over 20 to 30 minutes. Subjects were monitored carefully during the infusion and observed for 4hrs after infusion for any adverse events. No adverse event lead to discontinuation of drug before completion of infusion. The subjects were reassessed over 3 weeks for clinical and hematological improvement.

Data analysis: The collected data was entered into an excel sheet. After appropriate data cleaning, the data sheet was transferred and analyzed using SPSS software

version – 20. Descriptive statistics were used to describe the study variables of the subjects. To compare the continuous variable data before and after the intervention was tested using Paired 't' test.

RESULTS

The most common diagnosis for which the patient posted for surgery was AUB (36%), followed by genital prolapse (20%), fibroid (19%) and pelvic inflammatory disease (19%) (Table1) A significant number of subjects were relieved of symptoms of anemia after the intervention.(Table2) Majority of the women showed improvement in terms of peripheral smear.(Table 3)Statistically significant improvement was found in both Hb & S Ferritin levels - 2.28gm% & 729.82ng/ml respectively(Table 4,5). All the blood indices show Improvement after the intervention (Table6) 10% of the the subjects experienced minor side effects. (Table7)

Table 1: Indications for surgery

Indications	Number
AUB	36
Genital prolapse	20
PID	19
Adenomyosis	10
Ovarian cyst	10
Others	5
Total	100

Table- 2: Symptomology among the patients

Symptoms	Before treatment		After treatment	
	Frequency	Per cent	Frequency	Per cent
Easy fatigability	88	88	0	00
Weakness	61	61	03	03
Loss of appetite	13	13	01	01
Palpitation	06	06	00	00
No symptoms	08	08	96	96

Table-3: Peripheral smear finding among the patients

Peripheral smear	Before treatment	After treatment
Dimorphic anemia /Microcytic hypochromic	41	08
Normocytic hypochromic	45	06
Normocytic normochromic	14	82
Total	100	100

Table-4: Changes in Haemoglobin concentration among the patients

Haemoglobin (Gm %)	Mean	SD	N
Pre HB %	8.41	1.18	100
Post HB %	10.69	0.92	100
Mean difference	2.28	0.91	
Paired t statistic	-25.07	P value	0.00

Table -5: Change in Serum Ferritin levels among the patient

Serum Ferritin(ng/ml)	Mean	SD	N
Pre Ferritin levels	23.83	35.86	100
Post Ferritin levels	753.65	310.30	100
Mean difference	729.82	300.35	
Paired t statistics	-24.29	P value	0.00

Table-6 change in the hematocrit indices

Hematocrit indices	Mean	SD	N
Packed cell volume (%)			
Pre PCV	30.00	4.59	100
Post PCV	35.33	2.85	100
Mean difference	5.33	3.65	
Paired t statistic	-14.60	P value	0.00
Mean Corpuscular Volume (Fl)			
Pre MCV	74.22	6.44	100
Post MCV	79.15	4.25	100
Mean difference	4.93	4.46	
Paired t statistic	-11.05	P value	0.00
Mean Corpuscular Haemoglobin (Pg)			
Pre MCH	22.88	3.93	100
Post MCH	26.06	2.76	100
Mean difference	3.19	3.19	
Paired t statistic	-9.98	P value	0.00
Mean Corpuscular Haemoglobin concentration (%)			
Pre MCHC	29.77	2.23	100
Post MCHC	30.85	2.25	100
Mean difference	1.08	2.17	
Paired t statistic	-4.97	P value	0.00

Table -7: Side effects

Side effect	Frequency
Pain	5
Fever	1
Skin rash	3
Urticarial	1
Total	10

DISCUSSION

The main purpose of the study was to test Ferric carboxymaltose as an effective and safe alternative to blood transfusion in correcting pre-operative anaemia. Reducing blood transfusions in perioperative medicine is a clinical priority.

Females are prone to undergo surgeries in their life time due to pregnancy related issues or menstrual problems. Among the women of reproductive age group the incidence of AUB ranges between 10% and 30%¹¹ %. Hence in a poor resource country like ours where prevalence of anaemia is more this study has more relevance.

In a multicenter comparative study on the efficacy of intravenous ferric carboxymaltose and iron sucrose¹² for correcting preoperative anaemia in patients undergoing major elective surgery. Clinical and laboratory data of 76 anaemic surgical patients receiving preoperative FCM (500– 1000 mg per

session) to replenish total iron deficiency (Ganzoni's formula) were prospectively collected. A previous series of 84 anaemic surgical patients receiving preoperative IS (100 – 200 mg per session) served as the comparator group.

Compared with patients receiving IS, those with FCM attained iron replenishment more frequently (82% vs 62%, respectively=0.007) with fewer treatment sessions [2 (1) vs. 5 (2), respectively; P, 0.001], showed a higher final Hb level with a trend towards a higher rate of anaemia correction, and received intra operative, postoperative, or both ABT less frequently. There were no i.v. iron-related life-threatening adverse events, and the frequency of mild adverse events was similar with both i.v. product.

In a randomized controlled trial by van Wyck et.al¹³, in 2009 A total of 477 subjects with anaemia, iron deficiency anaemia and heavy uterine bleeding were randomly assigned to receive IV ferric

carboxymaltose (< 1000 mg over 15 min, repeated weekly to achieve a total calculated replacement dose) or oral ferrous sulfate 325 mg (65 mg of elemental iron) prescribed orally thrice daily for 6 weeks. In patients assigned to the IV ferric carboxymaltose group, an increase in Hb level of 2.0 g/dL or more, within 42 days after baseline (82.0% vs. 61.8%; 95% CI of treatment difference, 12.2%-28.3%; $p < 0.001$), more achieved a 3 g/dl or more increase (53% vs 36% , $p < 0.001$). Patients treated with Ferric carboxymaltose compared to those prescribed ferrous sulfated reported greater gain in vitality and physical function and experienced greater improvement in symptoms of fatigue ($p < 0.05$). There were no serious side effects.

Thus the author concluded that in patients with iron deficiency anaemia due to heavy uterine bleeding, rapid IV administration of large doses of a new iron agent, Ferric carboxymaltose, is more effective than oral iron therapy in correcting anaemia, replenishing iron stores, and improving quality of life. A cost analysis was performed from a Spanish National Health Service perspective and taking into account both drug acquisition costs (20.07euro per 100 mg for FCM, E11.57 per 100 mg for IS) and i.v. administration costs (time in day hospital, nursing, saline, giving sets, dressing, etc). For these patient populations, the treatment cost analysis showed that FCM could provide 63 euro savings per treatment compared with IS (95% CI 23.8 – 101.1; $P = 0.002$).

In our study there was statistically significant improvement in the Hb % with mean of 2.28gm% (1.38gm% to 3.19gm %) The improvement in serum ferritin levels was also statistically significant with a mean difference of 729.82 ng/ml. A significant number of subjects were relieved of symptoms of anemia after the intervention. All the blood indices and the peripheral smear showed significant improvement. The total incidence of adverse effects was 10% and all of them were minor reactions. Hence the study gives similar results as with the studies discussed above and proves that FCM is a potent and safe alternative to blood transfusion.

Since in the form of FCM we can transfuse 1000mg of iron in single setting safely, it is a more cost effective and patient compliant form of parenteral iron preparation compared to existing preparations.

CONCLUSION

Ferric carboxy maltose is safe and effective alternative to blood transfusion for correcting iron deficiency anemia in a shorter duration prior to elective gynecological surgeries. It hastens recovery from postoperative anaemia. It may facilitate iron replacement and offer additional benefits for both the patient and the health system.

Declaration

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Conflict of interest: None declared

Ethical approval: Taken from institutional ethical committee prior to initiation of the study.

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