RESEARCH
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PROSPECTIVE STUDY OF SAFETY AND EFFICACY OF INTRAVENOUS FERRIC CARBOXY MALTOSE IN IRON DEFICIENCY ANAEMIA IN WOMEN ATTENDING GYNAECOLOGICAL CLINIC.

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Abstract
BACKGROUND: Iron deficiency anaemia is the common nutritional deficiency amongst women of child bearing, perimenopausal and postmenopausal age in both the developed and developing countries and is a leading cause of Anaemia. There are various intravenous iron preparations available for the treatment of IDA. Ferric carboxymaltose (FCM), a nondextran intravenous iron, is an effective and a safe option which can be administered in high single doses directly over 7-8 minutes or diluted in saline for infusion without serious adverse effects.
METHODS: Total dose of ferric carboxy maltose (FCM) was calculated on the basis of Haemoglobin deficit and body weight using GANZONI FORMULA. FCM is administered as an infusion diluted in sterile 0.9% NaCL solution. The drug was administered under direct supervision and infusion was immediately stopped in case of any side effects. The patient should be followed up after 3 weeks of total dose infusion to assess the status of iron stores and increase in haemoglobin.
RESULTS: Mean age of the participants was 25.34 ± 5.09 years in which 42% of the subjects were primiparous and 58% were multiparous. Among them 96% were having pallor. 2% of the subjects had a pre iron Hb of <7, 98% had Hb between 7.1-9 and the mean pre iron Hb was 7.76 ± 0.48. Post Iron Hb, 12% had Hb between 7.1-9, 88% had Hb of 9.1-11 and the mean post iron HB was 9.40 ± 0.66. In the present study a statistically significant difference was observed between the mean Pre-Iron and Post Iron Hb levels
CONCLUSION: Due to properties like ultra-short duration of treatment i.e. ability to administer 1000 mg doses in a single sitting, fewer adverse reactions and better compliance makes FCM the first-line drug in the management of iron deficiency anemia in postpartum, perimenopausal and postmenopausal women causing a faster and higher replenishment of iron stores and correction of Hb levels. Also use of high doses reduces the number of infusions, enabling the possibility of cost reductions compared to multiple administrations

INTRODUCTION

Iron deficiency is recognized as a common nutritional deficiency amongst women of child bearing, perimenopausal and post menopausal age in both the developed and developing world and is a leading cause of Anaemia. Iron deficiency leads to fatigue, cardio-respiratory problems, reduced immunity, increased chances of infection etc.,

There are various possible forms of iron preparations used in the treatment of iron deficiency anaemia. Oral iron supplementation is the preferred initial treatment. However, oral iron often leads to adverse effects, such as nausea, vomiting, constipation and abdominal pain leading to poor compliance and a poor response to therapy. In addition, chronic inflammatory conditions may cause poor absorption of iron. Oral iron preparations are also not appropriate for the treatment of severe iron deficiency anaemia where rapid replenishment of iron stores is required. In these cases, intravenous iron preparations are preferred.

There are various intravenous iron preparations available for the treatment of IDA. Some of these preparations require multiple small infusions to prevent labile iron reactions wile iron dextran is associated with a risk of potentially serious anaphylactic reactions.

Ferric carboxymaltose (FCM), a nondextran intravenous iron, is an effective and a safe option which can be administered in high single doses without serious adverse effects. FCM can be administered directly over 7-8 minutes or diluted in saline for infusion

METHODOLOGY:

Total dose of ferric carboxy maltose (FCM) was calculated on the basis of Haemoglobin deficit and body weight using GANZONI FORMULA

TOTAL IRON DEFICIT (mg) = [Body weight (kg) x Target Hb – Actual Hb(gm%)] x 0.24 +Depot iron (mg)

Depot iron = 15mg/kg in case of body weight < 35kgs and 500mg in case of weight > 35 kgs

A single dose of FCM should not exceed 1000mg of iron (20ml/day) or 15 mg of iron (0.3ml/kg body weight). Not more than 1000mg of iron (20ml) should be administered in one week.

FCM is administered as an infusion diluted in sterile 0.9% sodium chloride (NaCL) solution. Upto 500mg FCM can be diluted with 100 ml NaCL and administered over 6 minutes.

Dose between 500mg to 1000mg require dilution with 250 ml NaCL and administration time of 15 minutes. The drug was administered under direct supervision and infusion was immediately stopped in case of any side effects. The patient was followed up after 3 weeks of total dose infusion to assess the status of iron stores and increase in haemoglobin with the help of blood investigations.

RESULTS

Table 1: Age distribution

	Frequency	Percentage
18 – 24	24	48%
25 – 30	18	36%
31 – 35	6	12%
36 – 40	2	4%
Total	50	100%
Mean ± SD	25.34 ± 5.09	

In the present study, 48% of the subjects belonged to the age group of 18-24 years, 36% were aged 25-30 years, 12% belonged to 31-35 years, 4% were aged 36-40 years. Mean age of the participants was 25.34 ± 5.09 years.

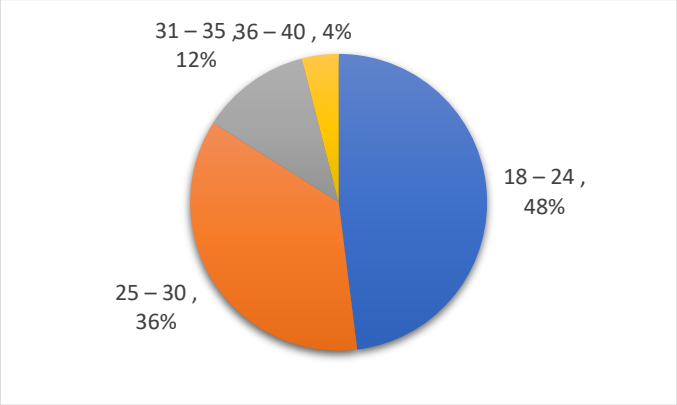

Figure 1: Age distribution

Table 2: Parity

	Frequency	Percentage
Primi	21	42%
Multi	29	58%
Total	50	100%

42% of the subjects were primiparous and 58% were multiparous.

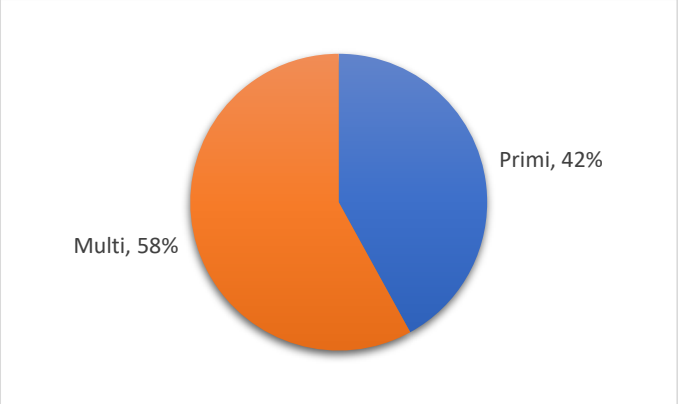

Figure 2: Parity

Table 3: Pallor

	Frequency	Percentage
Yes	48	96%
No	2	4%
Total	50	100%

Among the study subjects 96% were having pallor.

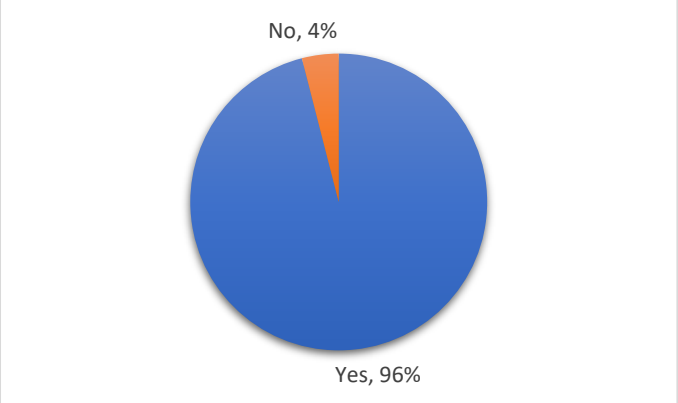

Figure 3: Pallor

Table 4: Peripheral smear

	Frequency	Percentage
Hypochromic microcytic	50	100%
Normocytic normochromic	0	0%
Total	50	100%

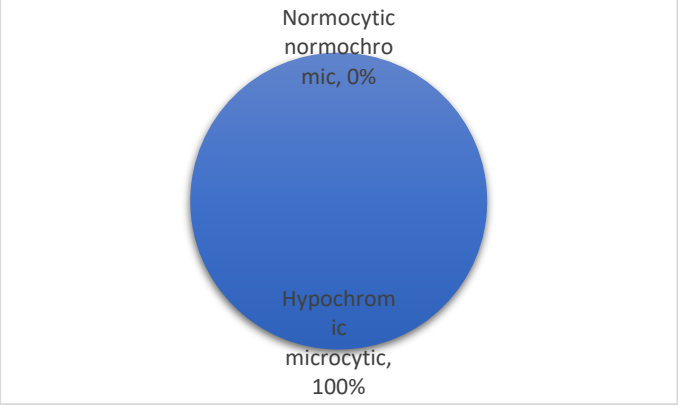

Figure 4: Peripheral smear

Table 5: PCV

	Frequency	Percentage
21 – 25	22	44%
26 – 30	25	50%
31 - 35	3	6%
Total	50	100%
Mean ± SD	26.30 ± 3.22	

PCV was 21-25 among 44% of the subjects, 50% were having a PCV of 26-30, 6% were having a PCV of 31-35. Mean PCV was 26.30 ± 3.22

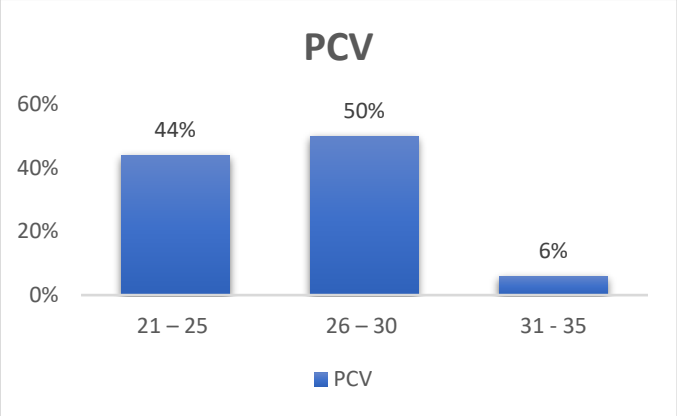

Figure 5: PCV

Table 6: Pre Ferric Carboxy Maltose administration – Hb Level

	Frequency	Percentage
<7 g/dl	1	2%
7.1 – 9 g/dl	49	98%
Total	50	100%
Mean ± SD	7.76 ± 0.48	

2% of the subjects had a pre iron Hb of <7, 98% had Hb between 7.1-9 and the mean pre iron Hb was 7.76 ± 0.48.

Figure 6: Pre Ferric Carboxy Maltose administration – Hb Level

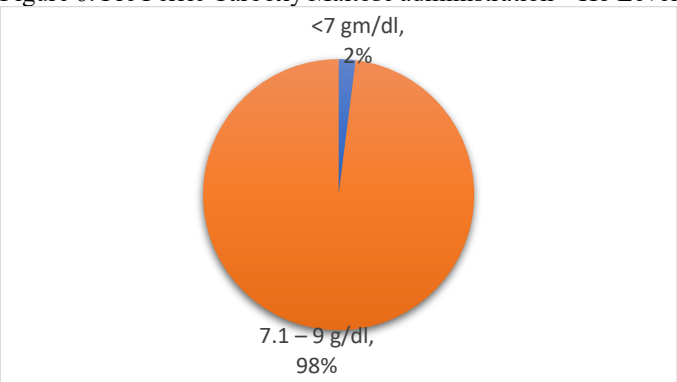

Table 7: Post Ferric Carboxy Maltose administration - Hb level

	Frequency	Percentage
<7 g/dl	0	0%
7.1 – 9 g/dl	6	12%
9.1 – 11 g/dl	44	88%
Total	50	100%
Mean ± SD	9.40 ± 0.66	

Post Iron Hb, 12% had Hb between 7.1-9, 88% had Hb of 9.1-11 and the mean post iron HB was 9.40 ± 0.66

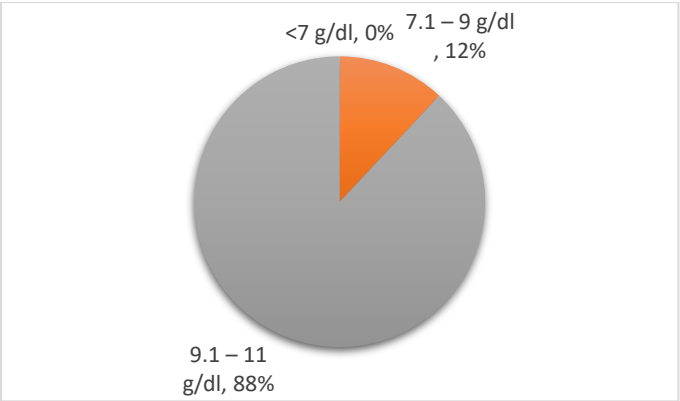

Figure 7: Post Ferric Carboxy Maltose administration - Hb level

Table 8: Pre vs Post iron - Hb levels

	Pre FCM Hb levels	Post FCM Hb levels	Mean change	P value
Mean ± SD	7.76 ± 0.48	9.40 ± 0.66	1.64	<0.0001*

In the present study a statistically significant difference was observed between the mean Pre Iron and Post Iron Hb levels`

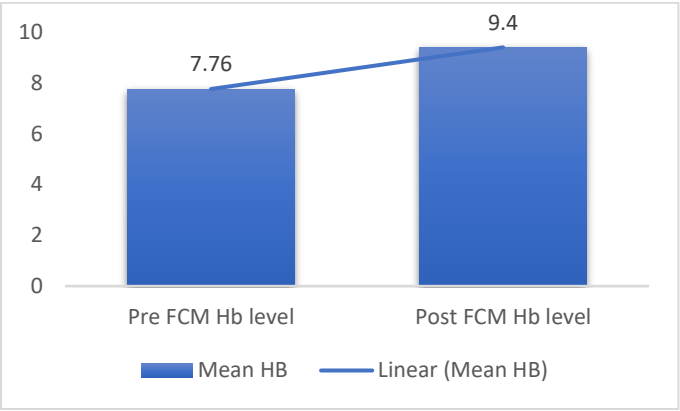

Figure 8: Pre vs Post iron - Hb levels

DISCUSSION

Iron deficiency represents the most widespread nutritional deficiency globally and is the leading cause of anaemia during pregnancy. Anaemia is estimated to affect almost 40% of pregnancies worldwide and is associated with a significantly increased risk of perinatal morbidity and mortality, including risk of low birth weight and preterm birth.[3] Further, the iron status of infants have been demonstrated to mirror that of the mother, with infants born to anaemic women at increased risk of developing iron deficiency anaemia (IDA) in the first year of life. These findings are independent of birth weight or gestational age and occur despite infants born to anaemic women having normal haemoglobin status at birth. Such findings are of particular interest given the previously noted association between IDA in the third trimester and impaired mental development of the offspring.

While haemoglobin status in pregnancy has been demonstrated to be of importance, the role of iron in ameliorating such adverse outcomes in the puerperal period is less clear, although it can be postulated that if the anaemia is due to iron deficiency, replenishing iron stores should restore normal haemoglobin and lead to improved perinatal outcomes.

While oral iron is typically considered first-line treatment, high-dose intravenous (IV) iron therapy has a role in the treatment of varied clinical situations associated with IDA. IV iron is more effective in patients with IBD and in oncology patients receiving erythropoietin-stimulating agents (ESAs) for chemotherapy-induced anemia. IV iron is also preferred when iron requirements are too high to be corrected with oral iron therapy (e.g., gastrointestinal bleeding), when oral iron cannot be properly absorbed (e.g., after gastric bypass or in celiac disease), and when oral iron is not well tolerated because of gastrointestinal side effects. Approximately 10–20% of patients taking oral iron experience nausea, constipation, epigastric discomfort, and vomiting that may lead to noncompliance.

IV iron formulations available, vary in dosing regimens and indications and may be limited by the maximum dose that can be given in a single visit due to instability of the iron-carbohydrate moiety (e.g., iron sucrose and iron gluconate formulations) as well as by anaphylactic reactions due to dextran-containing iron formulations.

Ferric carboxymaltose (FCM) is a stable, non-dextran-containing iron formulation that permits the uptake of iron by the reticuloendothelial system with minimal release of free iron. FCM was developed for rapid IV administration in high doses for the treatment of iron deficiency and the rapid infusion of up to 1000 mg of FCM over 15 min has been shown to be well tolerated. The FCM complex has a nearly neutral pH (5.0–7.0) with a physiologic osmolarity and no dextran cross-reactivity. The iron-carbohydrate FCM complex is more stable than ferric gluconate or iron sucrose, permitting slow and controlled delivery of iron into target tissues.

Contrary to this belief, supplementation of anaemic or non-anaemic pregnant women with iron, folic acid or both, is not associated with improvements in birth weight or gestational age. Despite such uncertainty, both oral and intravenous (IV) iron are commonly utilised in clinical practice. Use of oral iron is usually considered first-line due to convenience and low cost; however, its use is limited by significant gastrointestinal side effects affecting adherence, low absorption rate, and delay in replenishing iron stores. IV iron is considered to be a useful option when treatment with oral iron has failed or when rapid replenishment is required, albeit without strong evidence supporting its role in pregnancy. Increasing use of IV iron in clinical practice has raised some concerns regarding potential harms as iron itself can lead to oxidative stress and inflammatory changes and evidence that administration of oral iron is associated with an increased risk of preterm birth in observational studies but not RCTs. Multiple formulations of IV iron are available, differing on aspects such as the maximum single dose that can be administered in one sitting, the total infusion time and associated administration and medication-related costs

The present study titled " A prospective study of safety and efficacy of intravenous ferric carboxy maltose in iron deficiency anaemia in women attending gynaecological clinic" was carried forward with an aim to study the safety and efficacy of ferric carboxymaltose (FCM) in the treatment of iron deficiency anaemia in postpartum, perimenopausal and post menopausal women and the objective is to study the improvement of haemoglobin (Hb%) after treatment with intravenous ferric carboxymaltose in postpartum, perimenopausal and post-menopausal women with iron deficiency anaemia.

CONCLUSION

- Mean age of the participants was 25.34 ± 5.09 years.
- 42% of the subjects were primiparous and 58% were multiparous
- 96% were having pallor
- PCV was 21-25 among 44% of the subjects, 50% were having a PCV of 26-30, 6% were having a PCV of 31-35. Mean PCV was 26.30 ± 3.22
- 2% of the subjects had a pre iron Hb of <7, 98% had Hb between 7.1-9 and the mean pre iron Hb was 7.76 ± 0.48.
- Post Iron Hb, 12% had Hb between 7.1-9, 88% had Hb of 9.1-11 and the mean post iron HB was 9.40 ± 0.66
- In the present study a statistically significant difference was observed between the mean Pre Iron and Post Iron Hb levels

Important contributing factors responsible for high incidence of anaemia in our country include early marriage, teenage pregnancy, multiple pregnancies, less birth spacing, low iron and folic acid intake and high incidence of worm infections in Indian population. As the number of pregnancies increase the risk of anaemia and its severity goes on increasing, if adequate spacing is not maintained. In this study, it was observed that postpartum women responded wonderfully to intravenous FCM. Due to properties like ultra-short duration of treatment i.e. ability to administer 1000 mg doses in a single sitting, fewer adverse reactions and better compliance makes FCM the first-line drug in the management of postpartum iron deficiency anemia causing a faster and higher replenishment of iron stores and correction of Hb levels. Also use of high doses reduces the number of infusions, enabling the possibility of cost reductions compared to multiple administrations

In the recent times IV iron infusions were most sought after for treating cased of moderate to severe anemia. is always advisable to give IV infusions after a test dose to avoid any complications. For IV infusions FCM is a safe and an effective treatment option for IDA of various etiologies. This intervention was instrumental in treating women with significant antenatal anaemia, resulting in haemoglobin values higher than their pre-treatment values.

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