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Evaluation of efficacy, safety and cost effectiveness of oral iron and injectable iron sucrose and ferric carboxy maltose in pregnant women in 2nd and 3rd trimester in anaemia

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Abstract

Objective: To compare the efficacy safety and cost effective of oral iron and injectable iron sucrose and FCM in pregnancy in 2nd and 3rd trimester.

Methods: A prospective randomised control trial study in 300 women with HB 7-9gm% done in department of obstetrics on Gynae in Muzaffarnagar Medical College, Muzaffarnagar.

Result: Mean changes in Hb: oral iron 9.14gm%, inj.iron sucrose 10.54gm%, inj FCM 11.66gm%. The value of p is < 0.00001. The result is significant at p ≤0.05. Mean changes in PCV: oral iron 25.1%, inj iron sucrose 36.7%, inj FCM 37.46%. The value of p is <0.00001. The result is significant at p ≤ 0.05.Mean changes in MCV: oral iron 74.5Fl. The value of p is 0.172115. The result is not significant at p ≤ 0.05., inj iron sucrose 72.52.4Fl, inj FCM 80.4Fl. The value of p is < 0.00001. The result is significant at p ≤ 0.05.Mean changes in MCHC: oral iron 32.9%, inj iron sucrose 37.6%, inj FCM39.31%. The value of p is < 0.00001. The result is significant at p ≤ 0.05 Mean changes in serum feritin oral iron 28.95 µg/l, inj iron sucrose 29.25 µg/l, inj FCM 47.3µg/l. The value of p is < 0.00001. The result is significant at p ≤ 0.05.Mean changes in serum iron oral iron 36.27µg/dL, inj iron sucrose 38.1 µg/dL, inj FCM 73.8 µg/dL. The value of p is < 0.00001. The result is significant at p ≤ 0.05. Mean decrease in TIBC: oral iron 369µg/dL, inj iron sucrose 330µg/dL, inj FCM 324 µg/dL. The value of p is < 0.00001. The result is significant at p ≤ 0.05. Regarding efficacy both oral iron and injectable group was statistically significant. The value of p is < 0.00001. The result is significant at p ≤ 0.05.

Conclusion: We can conclude from this study that injection FCM is a promising alternative for IDA as its compliance is better than others, it can be safely used for correction of anaemia without any side effects over the mother and fetus.

Keywords: IDA, FCM, Iron sucrose, Anaemia in pregnancy. Injectable iron

Introduction

Anaemia is the commonest medical complication met within pregnancy. India is among the countries with highest prevalence of anemia in the world. Prevalence of Iron deficiency anemia among pregnant women is 58% and among non-pregnant non-lactating is 50% and among adolescent girls it is 56% according to National Family Health Survey-3. It is estimated that about 20 to 40% of maternal deaths in India are due to anaemia. Anaemia contributes to about 50% of Global Maternal Deaths. In WHO ranking, Iron deficiency anaemia is 3rd leading cause of Disability Adjusted Life year lost for females in age group 15 to 44 years.

WHO defined anemia as hemoglobin less than 11 gm% during pregnancy and post-partum period. WHO estimates that, of the 529000 maternal deaths occurring every year, 136000 or 25.7% take place of India, where two-thirds of maternal deaths occur after delivery, post-partum hemorrhage being the most commonly reported complication and the leading cause of death (29.6%).

Various iron preparations available for the treatment of iron deficiency anemia. Oral iron is the preferred route of administration for mild anemia. However, oral iron supplementation often leads to various adverse effects. Packed cell transfusion is reserved for cases with severe anemia but carries significant risk of transmissible diseases as well as risk of anaphylactic and allergic reactions. Intravenous iron preparations like iron dextran, iron sucrose and ferric carboy maltose (FCM) have been considered as an alternative to oral iron sucrose requires repeated doses infusion.[1,8] Ferric carboxy maltose is a novel molecule composed of a polynuclear iron (III) hydroxide complexes to carboxy maltose.

Oral iron is a less than ideal treatment, however, with gastrointestinal toxicity occurring in >35% to 59% of patients, and a long course needed to resolve anaemia and replenish stores. Time factor is important for correction of anaemia particularly when patient presents with anaemia during end of 2nd or 3rd trimester. Fastest way to correct anaemia is blood transfusion but not recommended in all cases.[5]

Hence present study is conducted to find out best iron preparation and route considering efficacy, safety and cost for treatment of iron deficiency anaemia in pregnancy.

Materials and Methods

It was an prospective randomized control trail study, 300 antenatal women in Department of Obst. & Gynae, in patients of IInd & IIIrd Trimester pregnancy with moderate iron deficiency anemia. Total 300 antenatal patients having hemoglobin concentration

between 7 – 9.9 gm% (ICMR) due to IDA considered for this study.

Blood Investigations: Hemoglobin, PCV, MCHC, MCV, Peripheral blood smear, Serum Ferritin, Serum Iron, Serum Total Iron Binding capacity, Stool-ova and cyst and occult blood, Urine for albumin RBCs and pus cells, Ultrasonography for fetal well-being (colour Doppler & CTG if required).

Total number of patients 300

Patients was taken in two groups A & B (100 patients each Group)

Group A: Oral Iron (100 cases)

Group B: Injectable Iron Sucrose (100 cases).

Method: 200 mg iron sucrose diluted in 100 ml. of normal saline and injected slowly intravenously over the period of 20-30 minutes. Can be repeated 48 hours or alternate day according to the requirement.

Injectable Ferric Carboxy Maltose (FCM) (100 cases).

Method: 500 mg FCM diluted in 250 ml. of normal saline intravenously over period of 45 minutes can be repeated once a week. (Injectable iron two weeks given till the calculated total iron dose is achieved)

Follow up after weeks

Inclusion Criteria: Gestational age of 14-34 weeks, Hemoglobin concentration between 7- 9.9 gm%, Age 20-35 years, Singleton Pregnancy.

Exclusion Criteria: History of fever or any chronic illness like malaria, dengue, diarrhea, dysentery & piles, gastrointestinal disorder like hyperacidity, peptic ulcer or patients with any kind of sepsis, Medical disorder like tuberculosis, diabetes, renal and hepatic disorder, Obstetrical complicating factors like PIH, APH, Patients with hemoglobin between 7 gm% or more than 9 gm%, Pregnancy with any congenital Anomaly.

Table 1: Oral Therapy

	Mean	P value
Base line Hb	8.13	$p \leq 0.05$
Hb after 4 weeks	9.14	
PCV	22.6	$p \leq 0.05$
PCV after 4 weeks	25.1	
MCV	73.2	p 0.172115
MCV after 4 weeks	72.52	not significant
MCHC	30.3	$p \leq 0.05$
MCHC after 4 weeks	32.9	
Serum Ferrtin	12.9	$p \leq 0.05$
Serum Ferrtin after 4 weeks	28.95	
Serum Iron	36.3	$p \leq 0.05$
Serum Iron after 4 weeks	36.27	
TIBC	28.2	$p \leq 0.05$
TIBC after 4 weeks	369	

Table 2: Injection sucrose

	Mean	P value
Base line Hb	8.06	$p \leq 0.05$
Hb after 4 weeks	10.4	
PCV	29.2	$p \leq 0.05$
PCV after 4 weeks	36.7	
MCV	67.2	p 0.172115
MCV after 4 weeks	74.5	not significant
MCHC	31.3	$p \leq 0.05$
MCHC after 4 weeks	37.6	
Serum Ferrtin	24.2	$p \leq 0.05$
Serum Ferrtin after 4 weeks	29.25	
Serum Iron	35.5	$p \leq 0.05$
Serum Iron after 4 weeks	38.1	
TIBC	494	$p \leq 0.05$
TIBC after 4 weeks	330	

Table 3: Injection FCM

	Mean	P value
Base line Hb	8.065	$p \leq 0.05$
Hb after 4 weeks	11.66	
PCV	30.48	$p \leq 0.05$
PCV after 4 weeks	37.46	
MCV	70.79	p 0.172115
MCV after 4 weeks	80.4	not significant
MCHC	31.44	$p \leq 0.05$
MCHC after 4 weeks	39.31	
Serum Ferrtin	24.76	$p \leq 0.05$
Serum Ferrtin after 4 weeks	47.3	
Serum Iron	33.84	$p \leq 0.05$
Serum Iron after 4 weeks	73.8	
TIBC	491.7	$p \leq 0.05$
TIBC after 4 weeks	324	

Table 4: Side effects

	Nausea		Vomiting		Heart Burn		Stomach Pain/ Stomach Upset		Headache		Hypotension		Metalic taste		Dyspepsia		Hot flashes		Black Stools		Teeth discoloration	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Oral Iron Group	24	31.58	20	26.32	38	50.00	48	63.16	0	0.00	0	0.00	66	86.84	68	89.47	10	13.16	2	2.63	56	73.68
Inj. Sucrose Group	1	1.32	1	1.32	4	5.26	2	2.63	5	6.58	0	0.00	0	0.00	4	5.26	3	3.95	4	5.26	0	0.00
Inj. FCM Group	10	13.16	2	2.63	3	3.95	1	1.32	1	1.32	0	0.00	0	0.00	0	0.00	2	2.63	3	3.95	0	0.00

Table 5: Comparison of Costs (according to the target Hb 11 gm/dL of oral iron group injection sucrose group & injection FCM group)

	Base Line Charges	No. of Visits	No. of Doses	Average Travelling Charges/visit RS	Additional Charges/ Dose in RS (dripset, veinflon, NS)	Charges after attaining target	Target
Oral Iron Group	20	9	100 tabs	50	0	2450	NA in all
Inj. Sucrose Group	210	10	8 doses (16 inj)	50	200	5460	A
Inj. FCM Group	2000	3	2	50	200	4150	A

Table 6: Comparison of efficacy between oral iron group, inj. Sucrose groupe & inj. FCM group

Blood indices (Avg.)	Increase in Hb		Increase in PCV		Increase in MCV		Increase in MCHC		Increase in Serum Ferritin		Increase in Serum Iron		Decrease in TIBC		P Value
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	
Oral Iron Group	9.14	0.39	25.1	0.6	74.5	8.09	32.9	0.96	28.95	44	36.27	9.2	369	11.2	The value of *p* is < 0.00001. The result is significant at p ≤ 0.05
Inj. Sucrose Group	10.4	0.58	36.7	2.99	80.4	6.76	37.6	6.88	29.25	3.09	38.1	3.1	324	15.6	
Inj. FCM Group	11.66	0.44	37.46	2.718	72.52	18.24	39.31	8.47	47.3	3.20	73.8	2.115	324	83.83	

Discussion

Iron is perhaps the most import heavy metal in man and its absorption and metabolism have been intensively researched for a century, many questions remain unanswered. In particular, the worldwide problem of iron deficiency has not yet been solved.

In pregnancy condition worsens and effects of anemia on pregnancy are well documented like low birth weight baby, increase preterm births and perinatal mortality. Iron deficiency in fetus can lead to sometimes irreversible damage to the central nervous system, with impairment of psychomotor development. Increased iron requirement in pregnancy and the puerperium carries with it an increased susceptibility to iron deficiency and iron deficiency anaemia. The total requirement of iron during pregnancy is approximately 1000 mg[2]. Usually, this iron is mobilized from iron stores. However, women with poor iron stores become iron deficient during pregnancy. Haemoglobin less than 5g% is associated with cardiac decompensation and pulmonary oedema. Bloodloss of even 200 ml in third stage of labour can cause sudden shock and death in these women.

As compared to western women whose iron stores are sufficient and they need 30-40 mg elemental iron per day for anaemia prophylaxis in pregnancy, the stores in Indian women are deficient and they need 100 mg elemental iron per day for prophylaxis. For treatment of anaemia, dose recommended is 200 mg elemental iron per day. In the present study, 6-10g% Haemoglobin was taken as cut-off. Intravenous iron is superior to oral iron with respect to increase in Haemoglobin and faster replenishment of body iron stores. Also, it reduces the need of blood transfusions, and it can be given an outpatient basis.

In the present study 7-9 (moderate anemia according to ICMR classification) Haemoglobin was taken as cut off and target 11% as target Hb. Intravenous injectable (iron sucrose, FCM) is superior to oral because of better compliance and no interference with absorption as it causes faster increase in haemoglobin and fastest replenishment of body iron stores. Also it reduces the need of blood transfusions.

Hookworm is one of the well-established causes of anaemia in developing countries. Routine antihelminthic therapy in pregnancy is required.

Iron FCM has revolutionized anemia management in pregnancy. Our study has shown that it is a highly and rapidly effective therapy without major side effects. There are also other modalities for the treatment of iron deficiency. Anaemia like oral iron and iron shows both of them have some or other drawbacks. Oral iron has poor absorption, frequent gastrointestinal side effects, metallic taste and poor compliance. Iron sucrose can cause reaction & require severe repeated dose at every alternate day. However, iron FCM is safe and can be repeated after a week.[3] It is convenient and cost effective (as compared to blood transfusion and Inj. Sucrose) in pregnant iron-deficient women who are unable to obtain an adequate amount of iron rapidly by oral route. By treatment with iron FCM it is possible to eradicate the commonest medical disorder of pregnancy, thereby dramatically reducing maternal mortality and morbidity. Although iron sucrose is safe as it is a dextran-free complex. The risk of allergic reactions is extremely low, it is also cost effective as it is an alternative to blood transfusion but hospitalization time is longer as compared to FCM. There is faster clinical recovery by both injection sucrose & Injection FCM than with oral iron therapy in iron deficiency anemia. Recent evidence suggest that iron, FCM & iron sucrose can be safely given with no adverse effect on liver.

Thus transfusion is a reliable method with excellent results in the treatment of anaemia but is associated but is associated with high risk for transmission of viral infections (HIV, Hepatitis C Virus, Hepatitis B and Cytomegalo virus) and serious transfusion cross reactions.[4] Therapy with iron FCM gives a good opportunity to avoid the risk of hemotransfusional infections, incompatible hemotransfusions. Through this prospective study, it has been proved that parentrally administered iron sucrose iron FCM elevates haemoglobin with no serious event were recorded. Intravenous iron sucrose FCM administration is highly safe and effective. But FCM is more cost effective than iron sucrose as less amount of dosage given in FCM for correction of anemia and reaching to the target Hb.

Therefore this study consolidate that Ferric Carboxy Maltose is well tolerated in women with pregnancy in II and III trimester is highly safe, effective than compare to inj. Sucrose and oral iron.

Conclusion

Injectable iron efficacy seen to be statistically significant($p < 0.00001$). Regarding safety no major side effects were noted with oral iron therapy, except some minor side effects. In Injectable iron efficacy was seen to be statistically significant($p < 0.00001$). Regarding cost effectiveness though cost of one Inj. FCM was higher than Inj. Iron Sucrose and Oral therapy, average cost to attain target Hb (Hb from 7-9.9gm% to 11gm%) of FCM was less as compare to Inj. Iron Surcose & Oral Iron while 25% of oral iron patients lost to follow up. Though all iron preparations are mainstay of treatment of anaemia in pregnancy, but in current scenario Inj. FCM seems superior followed by Inj. Sucrose & Oral Iron Therapy for definite treatment of anaemia in pregnancy in second & early third trimester of pregnancy. Although, both injectables iron achieved the target Hb.[6,7]

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