Iron Sucrose vs Ferric Carboxymaltose: In Search of Better Treatment Option in Cases of Post Partum Iron Deficiency Anemia

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ABSTRACT

Introduction: Anemia is the most common hematological abnormality diagnosed during pregnancy. As per WHO, anaemia during pregnancy is defined as haemoglobin concentration of less than 11 gm%. The objective of this study was to compare the safety and efficacy of intravenous iron sucrose and I.V. ferric carboxymaltose in treating postpartum iron deficiency anemia.

Material and Methods: A comparative, interventional, prospective study was carried out in 100 postpartum patients with Anemia (Hb level between 7 to 11 gm/dl) in the department of obstetrics and gynaecology, Government Medical College, Bhavnagar, Gujarat, India from June 2016 to July 2017. The subjects were randomized in two groups. First group receiving 1000 mg of intravenous iron sucrose divided in five doses on alternate days (200 mg each) and Second group receiving 1000 mg of intravenous ferric carboxymaltose.

Results: Maximum number of patients in our study were belonged to low socioeconomic group, significantly higher number of women achieved rise of Hb >2gm/dl in FCM group.26 women in FCM group achieve Hb rise of >2gm/dl as compared to only 11 in iron sucrose group, which was highly significant (*p*value <0.001). Mean rise of Hb was 1.9 gm/dl for FCM group and 1.66gm/dl for iron sucrose group, which was also significant. Serum ferritin level in ferric carboxymaltose group was rises more (83.9 ng/ml) as compared to (76.06 ng/ml) iron sucrose group. Unpaired't' test was used to test the significance of rise and compare the rise between two groups.

Conclusions: Ferric carboxymaltose is an efficient and better alternative to Iron Sucrose in treating postpartum anemia. It has an added advantage of single dose regime with lower side effects.

Keywords: Iron Sucrose, Ferric Carboxymaltose, Postpartum Iron Deficiency Anemia.

INTRODUCTION

Childbirth should be a joyous event. However, unforeseen medical problems such as postpartum hemorrhage or postpartum anemia can develop and make this time very difficult.

Iron deficiency anemia is very much prevalent in the India, amongst women of child bearing age, especially in under privileged population.[1] Anemia is estimated to about 20 percent of all maternal deaths and nine times higher risk of perinatal mortality. Postpartum anemia is observed in up to 27% of women. [2] It is a major contributing factor and indirect cause of maternal death.

Postpartum anemia is associated with longer hospital stays, depression, anxiety, persistent ill health, and lactation failure in mother and delayed development in infants.[3]

In view of fetal and maternal risk associated with iron deficiency anemia, treatment of anemia would lead to considerable reduction in risk which affects pregnancy, fetal outcome and postpartum period. Adequate and early treatment of anemia in post-partum period will have improved life quality in women in child bearing age group.[4]

The treatment of choice for postpartum anemia depends on the severity and/or additional maternal risk factors or co-morbidities. Puerperal patients who have iron deficiency anemia are likely to have high iron requirement.[5]

In addition, an inflammatory reaction can occur, particularly following surgically assisted deliveries and caesarean section, leading to iron sequestration in macrophage. So, Iron demand increses.[6]

In most of these cases oral iron is not enough since the endogenous iron stores are already depleted and less iron is provided for sufficient erythropoesis. As compliance to oral iron therapy is very poor and also the results are unpredictable, parenteral iron therapy is better option to treat such patients.[7]

Over the past years various routine methods like oral iron, intramuscular and intravascular iron and blood transfusions were used to treat anemia during postpartum period,

But, orally given iron has side effects like intolerance, nausea, vomiting, epigastric pain, diarrohea, constipation, unpredictable absorption rate and poor compliance.[8]

Various compounds like iron dextran (IM/IV), iron sorbitol (IM), iron sucrose (IV), ferric carboxymaltose etc. are available for parenteral therapy, Iron dextran was given intramuscularly cause considerable pain, skin staining, bleeding, tissues necrosis, arthralgia, myalgia, sterile abscess, and atrophy, However, threat of unpredictable anaphylactic reactions by these conventional parenteral iron preparations prevented their wider use. So to avoid these conditions we require a new mode of iron therapy with better efficacy, less side effects and better compliance for which iron sucrose and ferric carboxymaltose gives better results in various study.

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Both these compounds are safe in post-partum period and have less chances of hypersensitivity reactions (no test dose required).[9]

Iron sucrose used since many years, but, its use is limited to low dose due to local and systemic side effects in higher doses. Intravenous iron carboxymaltose therapy seems to be a safe, convenient and more effective method for treating anemia during postpartum period than intravenous iron sucrose therapy.[10]

we have prospectively monitored the response to IV iron sucrose multiple dose and ferric carboxymaltose single dose in a cohort of 100 postpartum patients with mild and moderate anemia over 15 days period.

We have not included patients with severe anemia (Hb<7) as most of this patient are hemodynamically unstable and required blood transfusion.

METHOD AND MATERIALS

The study was a prospective comparative interventional analytical study. Study period was 1 year and carried out in the department of obstetrics and Gynaecology at Sir T Hospital, Bhavnagar from June 2016 to June 2017.

Study Population

The study population included all women who delivered at Sir T. Hospital during the study period.

Sample Size

The study comprised of 100 cases which are to be randomly distributed into two groups consisting of 50 cases each.

Group - A: 50 cases in this group receive intravenous iron sucrose therapy.

Group - B: 50 cases in this group receive intravenous iron carboxymaltose therapy

Eligibility criteria

Inclusion criteria

- 18-45 years old.
- Postpartum
- Normal Vaginal Delivery
- No infection.
- Hb 7 to 10g/dl

Exclusion Criteria

- History of parenteral iron intolerance
- Having thalassemia or sickle cell disease
- History of Chronic bleeding or renal failure
- Vitamin B12 or folate deficiency
- postpartum hemorrhage and caeserian section
- Previous blood transfusions
- Calculation of total iron requirement Iron deficit was calculated by the formula:
- Total iron dose required (mg) = 2.4 × Body weight (kg) × (Target Hb - Actual Hb in g/dl) + 500 mg.
- Group A: Intravenous injections (iron sucrose complex) Iron sucrose complex was given as 200 mg elemental Iron (2 ampules of 5 ml) in 100 ml of 0.9% normal saline and infused over 30 min. every alternate days up to 5dose.
- Group B: Intravenous injections (Iron carboxymaltose complex)

  They are available as ampules of 10 ml containing 500 mg of elemental iron. Total 1000 mg/20 ml in 250 ml of 0.9% normal saline infused over 15-20 min

The participants consent were sought and obtained after adequate information about all aspects covered by the study. Voluntary participation including the right to decline, being in the study or to withdraw their participation at any time they wish to do so was emphasized. They were ensured of receiving the same care whether they agree to participate or not. A signed consent form was mandatory since there is a chance of severe drug reaction.

All the women informed that obtained data is confidential and only for research purpose. Ethical clearance was obtained from the Human Ethics Committee of the Government Medical College Bhavnagar, IRB (HEC) no.578//2016.

STATISTCAL ANALYSIS

Data of the questionnaire and results of blood tests were entered and analysed in Microsoft excel 2007. Statistics were calculated using enSTAT software. baseline characteristics, data between comparison group like hemoglobin level, ferritin level values and adverse effects were reported in percentages. UNPAIRED T Test is used compare data between two Groups, *p*value < 0.05 was taken as statistically significant.

RESULTS

Results were encouraging with satisfactory rise in Hb and serum ferritin, good patient satisfaction, minimal side effects and easy administration of dose. Epidemiologically, both the groups were compared with age, socio economic class, parity, and residence.

Both the group were comparable on base line characteristics. Patients studied were from all the age groups and most of the patients (56) were belonged to age group of 20-24 years and

Epidemiological data	Group A	Group B	*P* Value
Age			
20-24 yrs	27	29	
25-29 yrs	12	18	
30-35 yrs	11	03	
Mean±SD	24.74±4.1	24.06±2.75	NS
Economic class			
Class 4	05	07	
Class 5	45	43	NS
Parity			
1	19	14	
2	16	16	
3	08	10	
>3	07	10	NS
Residence			
Rural	22	21	
Urban	28	29	NS
Literacy			
Literate	13	16	
Illiterate	37	34	NS

Table-1: Baseline comparison of epidemiological data between both group.

Hb level (gm/dl)	Group A	Group B	*P* Value
Hb level before starting therapy			
7-8	06	17	
8.1-9	42	29	
9.1-10	02	04	
Hb level before therapy (Mean±SD)	8.536±0.45	8.385±0.56	NS
Hb level after therapy (Mean±SD) Mean rise of Hb level	10.19±0.42 *P* Value< 0.0001 1.66	10.28±0.70 *P* Value< 0.0001 1.9	NS >0.05significant

Table-2: Hemoglobin level before and after 2 weeks of therapy in both groups.

	Group A	Group B	p value
Hb rise >2gm/dl after 2 weeks	22%	52%	<0.001 Significant
Hb>11gm/dl after 2 weeks	6%	14%	<0.001 Significant

Table-3: Percentage of patients achieving outcome after 2 weeks of therapy.

Parameters	Group A pre therapy Mean ± sd	Group B pre therapy Mean ± sd	p value
Serum ferritin (ng/ml)	14.16 ± 3.55	13.34 ± 3.37	0.2369(not significant)
MCV (fL)	65.24 ± 3.87	66.52 ± 6.045	0.2115 (not significant)
MCH (pg/cell)	27.43± 1.52	28.23 ± 1.502	0.0065(significant)
MCHC (gm/dl)	26.5± 1.82	26.83 ± 2.257	0.4651 (not significant)
Parameters	**Group A after 2 week of therapy Mean ± sd**	**Group B after 2 week of therapy Mean ± sd**	**p value**
Serum ferritin (ng/ml)	76.066 ±16.56	83.95 ± 14.37	0.0125 (significant)
MCV (fL)	68.16 ± 3.791	70.11± 5.34	0.0361 (significant)
MCH(pg/cell)	28.39± 1.83	28.36 ± 1.349	0.89(not significant)
MCHC (gm/dl)	28.69± 1.59	28.89 ± 2.082	0.5753 (not significant)

Table-4: Mean serum ferritin level and haematological parameters before and after therapy in both groups.

Adverse effect	Group A	Group B
Pain at injection site	6	5
Itching and rash	3	2
Abdominal pain, palpitation	2	0
Headache	3	3
Nausea, vomiting	2	2
Anaphylactic reaction with hypotension	0	0
Total	16	12
Hospital stay in days (mean ± sd)	10.16 ± 1.095	3.12 ± 0.39

Table-5: Comparison of adverse effect and mean days of hospital stays between both groups.

most of the patients (86) were below 30 year of age. Total 88 patients were from lower socio economic class According To Modified B.J. Prasad Classification. Most of the patient were multipara In Both Groups and most of the patients were residing at rural areas (57 patients) and on the ground of literacy majority of the patients (71) were illiterate.

Mean Hb before starting of therapy in group A was 8.536± 0.45 and in group B was 8.386± 0.5. While comparing mean rise of Hb level between groups A (1.66gm/dl) and B (1.9 gm/dl), Group B had significant rise of Hb level after 2 weeks (table 1-3).

In Group B (FCM Group) 52% of patient had rise of Hb >2gm/dl as compared to 22% in iron sucrose group.

Similarly, haemoglobin level of >11gm/dl was achieved in 14% patient in FCM group as compared to 6% in iron sucrose group which was significant.

Both the group were comparable on baseline haematological parameters like mean serum ferritin level, MCV, and MCHC except MCH.

Rise in serum ferritin level after 2 weeks of therapy was higher in group B (83.95 ± 14.37) as compared to group-A (76.066 ±16.56) which was significant (p value 0.0125).so ferric carboxymaltose replenish the store faster (table-4).

In TABLE NO-5 mean duration of hospital stay in group A was 10.16 DAYS, and it was very less in group B 3.12 days.

Adverse reactions were milder in both the groups and mostly affected to local reactions, rate of adverse effect is 32% in case of iron sucrose group and 24% in iron carboxymaltose group (table-5).

DISCUSSION

Nutritional anemia in pregnancy and postpartum period is a major public health problem especially in India and most common is iron deficiency anemia.

Our study indicates that postpartum anemia can be treated effectively by ferric carboxymaltose as compared to iron sucrose with additional advantage of single infusion and less side effects and better patient compliance. In our study,

majority of cases were of lower socioeconomic status (87%), illiterate (71%), younger than 30 years of age (86%).

In India, early age of marriage and childbearing is more prevalent in rural economically backward areas, low socioeconomic status causes poor maternal health because of illiteracy, customs and beliefs, refusal for taking nutritional and health services provided by government, place of women in society which have more value of male children, poor nutrition, look of personal hygiene etc. compromise quality of female life.

In our study total 100 post-partum women with iron deficiency anemia were divided equally and randomly in two group, iron sucrose(Group A) and ferric carboxymaltose (Group B). Both groups were given deworming therapy, baseline investigations done; follow up was done at 14 days and Hb and CBC, Serum Ferritin level repeated.

Most of the studies regarding use of FCM and iron sucrose in PPIDA carried out in western population.

Breymann et al their trial, reported mean age 27.7 years and most of study population belonged to middle and high socioeconomic status in study, both groups were matching in all haematological parameters at the time of recruitment.[11]In our study mean age was 24.4 years and belonged to lower and middle lower socioeconomic class. It is because of early age of marriage practiced in India.

Singh et al in their study on 200 postpartum patients with Anemia and observed that there was significantly higher number of women achieved Hb >11gm/dl in FCM group.88 women in FCM group achieve Hb rise of 2 gm as compared to only 24 in iron sucrose group on 21st day after therapy, which was highly significant (P value <0.001) and mean rise of Hb was 2.086 gm for FCM group and 1.766 gm for iron sucrose group, which was also significant[12].

In our study mean rise of Hb in iron sucrose group was 1.66 gm% and in FCM group mean rise of Hb was 1.98m% which was significant. (p value <0.05) in our study 26 patient in FCM group achieve 2 gm/dl as compared to only 11patient in iron sucrose group, which was highly significant. (p value <0.001).

Verma u. et al in their study followed up patient on 2, 4, 6 and 12 week and reported that In group A of 50 patient (iron sucrose) mean rise of hemoglobin level was 3.95 g/dl and in group B of 50 patient (ferric carboxymaltose) it was 3.32 g/dl at 4 weeks of initial therapy. In group A 100% cases achieved target hemoglobin at 12 weeks after therapy while in group B 98% cases achieved target hemoglobin at 12 weeks after therapy[13].

In our study at 2 week of therapy 14% case in FCM group achieve target haemoglobin as compared 6% case in iron sucrose group.

Patel j et al in their study on day 8 and day 15 of therapy and reported changes in hemoglobin and serum ferritin levels on day 8 and day 15. The mean rise of hemoglobin value was 5.2g/dl for ferric carboxymaltose and 4.1 g/dl for iron sucrose in pregnant women. For postpartum women mean rise of hemoglobin was 4.9g/dl on the 15th day of treatment. Serum ferritin also shows increment in both modalities in 8th and 15th day. But it was not statistically significant in pregnant or post partum women Side effects were reported in 40% among patients treated with iron sucrose as compared to 16.67% in case of ferric carboxymaltose[14].In our study 32% of patient in iron sucrose group and 24% in ferric carboxymaltose reported side effect.

In our study serum ferritin which indicate iron store of body, increased significantly in FCM group than IS group, 83.95±14.37 versus 76.066± 16.56(p value 0.0125). Rise of serum ferritin in iron sucrose group from 14.16±3.55 to 76.0.66±16.56 mg/dl which was significant. And in FCM group from 13.34±3.37 to 83.95±14.37 which was significant. Thus replenishment of iron stores by FCM will prevent the recurrence of IDA.

Registered adverse events were all mild and quickly reversible and mostly restricted to local reactions at the infusion site. There were no treatment-related serious adverse events. No anaphylactic or reaction was detected. No venous thrombosis was registered.

Seid et al reported lower incidence of adverse effects in parenteral group than oral group, no serious reactions in either group. Most common adverse effect in parenteral group was urticarial and in oral group was constipation[15].

Intravenous iron supplementation is highly effective in treating IDA, including pregnancy and postpartum. Compared to oral iron, IV iron results in a much more rapid resolution of IDA, has minimal side-effects, and because it is administered intravenously, it circumvents the problems of compliance[16].

So we treated postpartum IDA with these two compound, one is newer (FCM) and one is widely accepted in current parenteral iron therapy (IRON SUCROSE). We deliberately gave a uniform dose in all women whose Hb between 7-10 gm/dl in an effort to adopt a single universal dose regime, which might be helpful in future to simplify treatment and widely acceptance in medical system.

CONCLUSION

From our study we concluded that, Ferric carboxymaltose is safe and efficient in treatment of iron deficiency anemia in postpartum women as compared to iron sucrose with lesser adverse effect and better patient compliance. As the hospital stay is less in patients receiving ferric carboxymaltose, it increases patient's compliance and decreases bed occupancy and burden on health facility in developing country like India.

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