

EFFECTS OF ORAL VERSUS PARENTRAL IRON ON WOUND HEALING AND ANEMIA IN POSTPARTUM PERIOD -COMPARATIVE OBSERVATIONAL STUDY

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Received : 21/05/2023
Received in revised form : 29/06/2023
Accepted : 11/07/2023

Keywords:

Anemia, postpartum period, parenteral iron wound healing.

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DOI: 10.47009/jamp.2023.5.4.314

Source of Support: Nil,

Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (4); 1578-1582



Abstract

Background: Postpartum anemia is associated with longer hospital stay, recurrent infections, poor wound healing depression, anxiety, and delayed infant development. Adequate and early treatment of anemia in post-partum period will have improved quality of life in women of child bearing age group. Objectives of the study were to assess the clinical effects of treatments for postpartum anaemia by oral and parenteral iron, to evaluate the effects of iron therapy on wound healing and hospital stay and to improve maternal health and reduce the hospital stay of patients. **Material & Methods:** The present prospective study was conducted in the department of Obstetrics and Gynaecology at Maternity hospital SKIMS Soura, in the northern region of India from September 2019 to September 2020. It was a prospective comparative observational study. A total of 200 patients with postpartum iron deficiency anemia were taken up in the study. Baseline hemoglobin was between 7 and 10 g/dL. These were divided into two random groups of oral iron (Group A) and IV iron (Group B). Hemoglobin level was measured at admission and on day 14. Adverse effect profile for each group was tabulated. Mean and standard deviation were calculated for each group and compared. Hospital stay and wound healing was compared in both the groups. **Results:** Our study indicates that postpartum anemia and the complications related to it can be treated effectively by iron therapy and the parenteral iron therapy was more advantageous. **Conclusion:** Iron therapy improves haemoglobin level which in return enhances the delivery of nutrients and oxygen to the tissues, hence better wound healing and lesser hospital stay.

INTRODUCTION

Postpartum anemia is observed in up to 27% of women.^[1] Postpartum anemia is associated with longer hospital stay, depression, anxiety, and delayed infant development.^[2] Women often complain of tiredness, shortness of breath, easy fatigability, recurrent infections, poor wound healing. Iron therapy is important in proper wound repair. It has been seen that in patients with delayed wound healing there is impaired sequestration of iron by macrophages involved in wound healing. Adequate and early treatment of anemia in post-partum period will have improved quality of life and adequate wound healing but the treatment of choice for postpartum anemia depends on the severity and/or additional maternal risk factors or comorbidities Worldwide, anaemia contributed to approximately 20% of the 515,000 maternal deaths in 1995.^[3] Puerperal patients who have iron deficiency anemia are likely to have high iron requirement.^[4] There is an increased inflammatory response after surgically

assisted deliveries and caesarean section, due to which there is iron sequestration in macrophages. So Iron demand increases.^[5] The standard approach to treatment is oral supplementation. Transfusions are used in case of acute blood and in severe or symptomatic cases.⁶ However there are a number of adverse reactions of blood transfusion including mismatched transfusion, anaphylaxis and risk of transmission of infections. Therefore, parenteral iron treatment is expected to be advantageous in cases in which treatment with oral iron is not possible due to gastrointestinal (GI) side effects, in patients with poor compliance, or in patients with severe anemia.^[7] It has been seen anemia in postpartum period not only causes delayed wound healing, but also makes the patients stay in the hospital critical and prolonged. Their stay is usually never uneventful, thus affecting the wellbeing of the patients and their return to work. Prolonged hospital stay in patients increases their burden both psychological and financial. Anemia when treated effectively results in better perfusion of

tissues which in return helps in better wound healing and early discharge from hospital.

Iron Preparations

Oral iron

Oral iron therapy has been used conventionally to correct anaemia and replenish iron stores. Therapeutic Guidelines suggests ferrous sulfate at a dose of 325–650 mg daily (equivalent to 105–210 mg elemental iron), however other guidelines recommend higher doses. However its tolerability varies from person to person. Ferrous fumarate and gluconate salts are equally effective in practice. Carbonyl iron and polysaccharide-iron complex are also used orally in the prevention and treatment of anemia. The advantages to oral iron supplements include cost, safety and ease of access. However there are several adverse effects such as constipation, dysgeusia and nausea which reduce adherence and hence effectiveness, particularly when the recommended duration of therapy is 3–6 months.

Parenteral iron: Treatment with IV presents several advantages such as faster and higher increase in hemoglobin levels and replenishment of body iron stores. Various parenteral iron preparations available in market include Iron dextran, Ferric gluconate, Iron sucrose, Ferric carboxymaltose. However, there is an increased incidence of serious Adverse events reported with iron dextran and ferric gluconate due to which these are.

MATERIALS AND METHODS

The present prospective study was conducted in the department of Obstetrics and Gynaecology at Maternity hospital SKIMS Soura, in the northern region of India from September 2017 to March 2019. It is a prospective comparative observational study. Study population included all women who delivered at Maternity Hospital SKIMS Soura during the study period. recommended only when extreme clinical conditions are present and other options unavailable. The use of iron sucrose is limited to low dose due to local and systemic side effects (metallic taste, nausea, dizziness and local irritation), in higher doses. Recently, ferric carboxymaltose has been introduced. This preparation can be used intravenously in high doses with up to 1000 mg infused in 15 min with low risk of side effects.⁸ The risk of anaphylaxis or serious hypersensitivity reactions is very low, and a test dose is also not required.

A total of 200 patients with postpartum iron deficiency anemia were taken up in the study. They were randomly distributed into two groups consisting of 100 cases each. Group A: 100 cases in this group received oral iron. Group B: 100 cases in this group received intravenous ferric carboxymaltose therapy. Inclusion criteria was Postpartum patients with haemoglobin between 7gm/dl and 10gm/dl 8gm/dl after 24 hours of delivery and willing to give both verbal and written consent. World Health Organization (WHO) has defined postpartum anemia

(PPA) as hemoglobin (Hb) of <10 gm% in postpartum period.⁹ However patients with anaemia other than iron-deficiency anemia, known history of allergy to injection iron, who received blood transfusion in postpartum period and patients with renal diseases, hepatic dysfunction, thromboembolism, seizures and drug abuse were excluded from the study.

Investigations

Include complete hemogram, peripheral blood smear for cell morphology. These were done before starting iron therapy. However the parameters of assessment were:

Peripheral blood smear (before treatment).

Hemoglobin estimation was done by Sahli's method (before and after treatment).

Calculation of total iron requirement Iron deficit was calculated by the formula: • Total iron dose required (mg) = $2.4 \times \text{Body weight (kg)} \times (\text{Target Hb} - \text{Actual Hb in g/dl}) + 500 \text{ mg}$. In group A: women were advised to take 200 mg ferrous sulphate twice daily for 1 month and in group B they received intravenous injections of Ferric carboxymaltose complex, which 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 was infused over 15–20 min.

Ferric carboxymaltose and iron sucrose was provided free of cost under Janani Shishu Surakhsha Karyakaram (JSSK) scheme.

Macroscopic status of wound of patients was assessed on day 14 and day 28.

Patient were followed on day 7, day 14 and day 28 for estimation of hemoglobin and to assess the impact of postpartum treatment, on rise in haemoglobin, wound healing and hospital stay.

Statistical Methods

Statistical package for social sciences ver.22 was used for data analysis. The result was expressed in percentages or mean SD as specified. Pearson's Chi-square test was used to analyse categorical data. P value less than .05 was taken statistically significant.

RESULTS

There was a satisfactory rise in haemoglobin, good patient satisfaction, minimal side effects, better wound healing lesser hospital stay in patients who received intravenous ferric carboxymaltose.

Both the group were comparable on base line characteristics. Patients studied were from all the reproductive age groups and most of the patients (113) belonged to age group of 25–29. Total 76% and 70% patients in either groups respectively were from lower socio economic class according to Modified Kuppaswamy Classification. Most of the patient were primipara in both groups and most of the patients were residing in rural areas (140 patients) and on the ground of literacy majority of the patients (132) were illiterate.

Hemoglobin Response

Mean hemoglobin before starting of therapy in group A was (8.04± 0gm/dl) and in group B was (8.02± 0.05gm/dl). A significant improvement was observed with IV Ferric carboxymaltose, the mean Hb was increased from 8.02 ±0.05 gm/dl to 9.8 ± 0.76 gm/dl on day 7 (p < 0.05) in group B. The respective values of mean hemoglobin in this group on day 14 and 28 was (10.9±1.02gm/dl) and (11.8±0.7). There was no significant rise of hemoglobin in group A at the end of 7 days. However the mean hemoglobin in group A (oral group) was (9.50±0.68gm/dl) on day 14 and (10.02±.4gm/dl) on day 28. This was statistically significant (p value 0.05).

In group A 56 patients and in group B 68 patients had Microcytic Hypochromic Anemia. Both the group

were comparable on baseline hematological parameters.

In group A superficial wound gaping was seen in 40% and 13% patients on day 14 and 28 respectively. However in group B no impairment in wound healing was seen at the end of 14 and 28 days.

The mean duration of hospital stay in group A was 8.8 days, which was far great as compared to group B 3.75 days. Adverse reactions were milder in both the groups and mostly affected to local reactions, rate of adverse effect is 37% in oral iron group and 1% in ferric carboxymaltose group. While group A complained of gastrointestinal side effect, like nausea, dyspepsia and constipation, in group B only one patient had local rash.

Table 1: Age wise Distribution of Cases

Age in years		Group A	Group B	Total
20-24	Count	2	22	24
	% of Group	2%	22%	12%
25-29	Count	65	48	113
	% of Group	65%	45%	56.50%
30-34	Count	33	30	63
	% of Group	33%	33%	31.50%
Total	Count	100	100	200
	% of Group	100.00%	100.00%	100.00%

Mean age group in Group A is 29.11 years & in Group B is 29.350 which is statistically insignificant. No patients from either Group discontinued the study.

Table 2: Distribution of Patients According to Residence

Residence		Group A	Group B	Total
Urban	Count	33	27	60
	% of Group	33%	27%	30%
Rural	Count	64	76	140
	% of Group	64%	76%	70%
Total	Count	100	100	200
	% of Group	100%	100%	100%

Table 2: shows that the majority of patients in both the groups belonged to rural areas (64% in group A and 76% in group B).

Table 3: Comparison of Pre-Treatment and Post-Treatment Hb

Group	Mean	Day7	Day14	Day28
A(Oral)	8.04	8.5	9.05	10.02
B(IV)	8.02	9.8	10.9	11.8

Table 3: shows mean hemoglobin 8.04 g% pretreatment and 10.02g% post-treatment in group A and therefore, a rise by 1.98 g% in 4 weeks. The mean hemoglobin 8.02 g% pre-treatment and 11.8 g% post-treatment in group B and therefore, a rise by 3.78g% post-treatment. This is statistically significant study (P value <0.05).

Table 4: Comparison of Pretreatment Peripheral Blood Film

PBF at D0		Group		Total
		A	B	
MHA	Count	56	68	124
	% of Group	56.00%	68.00%	62%
NHA	Count	44	32	76
	% of Group	44.00%	32.00%	38%
Total	Count	100	100	200
	% of Group	100.00%	100.00%	100.00%

MHA - Microcytic hypochromic anemia; NHA-Normocytic hypochromic anemia

Table 5: Comparison of Mean Duration of Hospital Stay and Mode of Delivery

	Group A	Group B
Mean Duration of Hospital stay in days	8.8	3.75
Mode of Delivery By LSCS In %	70	74

Table 6: Comparison of wound healing

Superficial wound gaping	Group A(Oral iron)	Group B(Iv)
Day14	40%	Nil
Day28	13%	Nil

Table 6 shows that patients treated with parenteral iron ferric carboxymaltose had no wound impairment while the group treated with oral iron had superficial wound gapping in 40% patients on day 14 and 13% on day 28 respectively.

Table 7: Distribution of Cases According to Adverse Drug Reaction

Side Effects		Group		Total
		A	B	
None	Count	63	99	162
	% of group	63.00%	99.00%	81%
Gastrointestinal	Count	37	0	37
	% of group	37%	0.00%	18.50%
RASH	Count	0	1	1
	% of group	0.00%	1%	0.50%
Anaphylaxis	Count	0	0	0
	% of group	0.00%	0.00%	0.00%
Total	Count	100	100	200
	% of group	100.00%	100.00%	100.00%

Table 7 shows that the patients who were treated with oral iron had gastrointestinal side effects. However none of the patients treated with iron(oral and parenteral) had anaphylaxis.

DISCUSSION

This study was done to see the effect of oral iron versus parenteral iron ferric carboxymaltose in increasing hemoglobin level in iron deficiency anemia in postpartum period. Also in this study the effects of iron therapy on wound healing and hospital stay of patients was compared. As seen with our study, the majority of anemic population was from the rural area 70% and only 5% from urban area. Lack of awareness, illiteracy and poverty are seen to be the main reasons for high prevalence of anemia in rural areas. Majority of the patients 56.5% belonged to the age group of 25 -29 years. In our study, two groups of patients were randomly made, each having 100 female patients with hemoglobin ≥ 7 gm/dl and < 10 gm/dl after 24 hours of delivery. Group A was given oral iron (200 mg ferrous sulphate twice daily for 1 month) and group B was treated with ferric carboxymaltose (total 1000 mg/20 ml in 250 ml of 0.9% normal saline was infused over 15-20 min). Treatment was started after 24 hours of delivery.

In both the groups, serum hemoglobin and peripheral blood film was done at day 0. Follow up was done day7, day14, day28 and hemoglobin levels were repeated. Also status of wound was compared between the two groups and total days of hospital stay were noted.

There was rapid increase of hemoglobin in patient treated with intravenous ferric carboxymaltose than oral iron therapy. Within 7 days patient responded with ferric carboxymaltose but there was

insignificant response at 7th day in oral iron group. In group The mean haemoglobin (pretreatment) was 8.04 g% and 10.02g%(post-treatment) and therefore, a rise by 1.98 g% in 4 weeks. However in group B the mean haemoglobin was 8.02 g% pre-treatment and 11.8 g% post-treatment and therefore, a rise by 3.78g% post-treatment. Hence ferric carboxymaltose effectively corrects anemia when compared with oral iron and also has lesser side effects and better patient compliance. The overall satisfaction reported by the patients was better as the drug involves minimum hospital stay with time of infusion only 15 minutes. Among the patients in group B only one patient complained of side effects in the form of itching which was localized to upper limbs only and resolved on its own. The incidence of side effect, like gastrointestinal adverse effect, was high in oral iron only.

Majority of patients (62%) in both the groups had microcytic hypochromic anemia. Mean duration of hospital stay was seen longer in patients treated with oral iron due to delayed return of wellbeing and slow rise of haemoglobin as compared to ferric carboxymaltose. An interesting observation was made that patients who were treated with parenteral iron ferric carboxymaltose had no wound impairment while the group treated with oral iron had superficial wound gapping in 40% patients on day 14 and 13% on day 28 respectively. This could be related with prompt and effective treatment of anemia by ferric carboxymaltose. Interestingly iron plays an important role in wound healing. wound macrophages (M2 phenotype) extensively sequester iron throughout

healing, associated with a prohealing.^[10] Iron modulates the macrophage behavior to promote healing. These macrophages produce high levels of chemokine, promoting wound reepithelialization and extracellular matrix deposition. Hence iron mediated modulation of macrophages play a crucial role in wound healing response.^[11]

Limitations

Compliance to oral iron has been a limitation in the studies conducted so far and same was the case with us. Cost of parenteral iron is yet another limitation, however in our study it was supplied free from the department under JSSK scheme.

CONCLUSION

Overall parenteral iron (ferric carboxymaltose) appears to be an effective mode of treatment in postpartum patients with faster recovery and lesser hospital stay in comparison to oral iron. Also the patients who received iron therapy showed better wound healing and the response was much better with ferric carboxymaltose when compared to oral iron. This further supports the role of iron in promotion of wound repair through its modulation of macrophage behavior.

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