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Comparative study of safety and efficacy of intravenous iron sucrose complex and oral ferrous sulphate in treatment of iron deficiency anaemia during puerperium

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Abstract---Background: Consequences of postpartum iron deficiency anaemia have been associated with fatigue, depression, cognitive dysfunction, stress, and anxiety. It can also interrupt mother-child bonding. Present study was aimed to compare safety and efficacy of intravenous iron sucrose complex and oral ferrous sulphate in treatment of iron deficiency anaemia during puerperium. Material and Methods: Present study was single randomized control trial, conducted in postpartum female, >18 years, diagnosis of postpartum anemia within the first 48 hours postpartum with a hemoglobin level 8 – 10 gm/dl. Results: Oral iron group had a mean baseline Hb of 8.86 ±0.54 and post treatment mean Hb after 2 weeks was 9.39 ± 0.48 and after 4 weeks was 10.35 ± 0.46. Statistically significant difference was noted in baseline and post treatment Hb levels at 2 and 4 weeks score ($p<0.05$). For the I.V iron group Hb score shows that the baseline mean was 8.70 ± 0.50 and post treatment mean Hb after 2 weeks and 4 weeks was 9.94 ± 0.48 and 11.19 ± 0.57 respectively. Statistically significant difference was noted in baseline and post treatment Hb levels at 2 and 4 weeks score ($p<0.05$). Rise in mean Hb for oral iron group was 1.49 ± 0.60 and for I.V iron group was 2.50 ±

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0.64, difference was statistically significant. Conclusion: Parameters in the iv iron sucrose group showed highly significant increase and a faster rate of improvement. For management of postpartum anaemia iv iron administration is as efficacious as oral iron and an option to correct postpartum anaemia at the earliest.

***Keywords*---**iv iron sucrose, postpartum anaemia, iv iron, oral iron

Introduction

WHO has defined anaemia during pregnancy as haemoglobin concentration of less than 11 gram% and a haematocrit of less than 33%.[1] Anaemia during pregnancy can be physiological, nutritional (iron deficiency, folic and or vitamin B_{12} deficiency), anaemia of chronic diseases (chronic malaria, tuberculosis), hereditary (thalassemia's, sickle cell haemoglobinopathies, hereditary haemolytic anaemia), chronic blood loss (hookworm infestation, bleeding piles). Amongst above mentioned causes nutritional anaemia is a most common worldwide problem with the highest prevalence in developing countries, and iron deficiency anaemia being the most common cause of nutritional anaemia in the world and in developing countries.[2]

The physiological effects of pregnancy and blood loss at birth can exacerbate anaemia.[3] Blood loss from delivery is one of the most common causes of anaemia.[4] Postpartum haemoglobin levels of <10gm/dl are observed in up to 30% of women, with more severe anaemia Hb <8gm/dl is seen in 10% of women.[5]

According to the National Pregnancy Nutrition Surveillance System, 29.8% of women who were not previously anaemic during pregnancy become anaemic after delivery[5].Consequences of postpartum iron deficiency anaemia have been associated with fatigue, depression, cognitive dysfunction, stress, and anxiety. It can also interrupt mother-child bonding[6]. Present study was aimed to compare safety and efficacy of intravenous iron sucrose complex and oral ferrous sulphate in treatment of iron deficiency anaemia during puerperium.

Material and Methods

Present study was single randomized control trial. study was conducted at tertiary health care centre in the department of obstetrics and gynaecology. Study duration was of 18 months. Study was approved by institutional ethical committee.

Inclusion criteria

- Postpartum female, >18 years, diagnosis of postpartum anemia within the first 48 hours postpartum with a hemoglobin level 8 – 10 gm/dl.

Exclusion criteria

- Injectable iron therapy during present pregnancy.

- Peripartum blood transfusion.
- Intolerance to iron derivatives.
- Women with signs of infections.
- Women with hepatic or renal dysfunction.

Study was explained to patients & written consent was obtained for participation. Patients who satisfied the selection criteria were evaluated for hemoglobin and other color indices within 48 hours post-delivery. For study purpose patients were randomly divided into 2 groups comprising of 100 patients each.

Group A - These patients were given 120mg of elemental iron daily orally.The drug being available with the hospital pharmacy in the form of ferrous sulphate salt with each tablet of 120 mg with elemental iron of 60 mg in each tablet. Hence, 2 tablets were given to the patient daily, along with iron tablet, folic acid (5mg) vitamin C (600 mg) and B complex were given common to both groups.
Patients of Group B: were continuing with their tablets of folic acid, vitamin C, & B complex till day 30. They were given IV iron sucrose 200mg on day 2 and 300mg on day 4.

Blood investigations were done thrice in both group patients. Firstly within first 48 hours postpartum repeated after 2 weeks and after 4 weeks. In each examination the following were evaluated: Hemoglobin (Hb) Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC) and Reticulocyte count (RC), and iron studies which included Serum Iron, Total Iron Binding capacity (TIBC), Transferrin Saturation.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Results

Oral iron group had a mean baseline Hb of 8.86 ±0.54 and post treatment mean Hb after 2 weeks was 9.39 ± 0.48 and after 4 weeks was 10.35 ± 0.46. Statistically significant difference was noted in baseline and post treatment Hb levels at 2 and 4 weeks score ($p<0.05$). For the I.V iron group Hb score shows that the baseline mean was 8.70 ± 0.50 and post treatment mean Hb after 2 weeks and 4 weeks was 9.94 ± 0.48 and 11.19 ± 0.57 respectively. Statistically significant difference was noted in baseline and post treatment Hb levels at 2 and 4 weeks score ($p<0.05$). Rise in mean Hb for oral iron group was 1.49 ± 0.60 and for I.V iron group was 2.50 ± 0.64, difference was statistically significant.

Table No 1
Comparison among study groups for Hb (gms/dl)

Hb (gms/dl)	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std. Dev.	Mean	Std. Dev.		
Hb (gms/dl) (24-48 hrs)	8.86	0.54	8.70	0.50	2.257	0.025
Hb (gms/dl) (2 Wks)	9.39	0.48	9.94	0.48	8.104	< 0.001
Hb (gms/dl) (4 Wks)	10.35	0.46	11.19	0.57	11.393	< 0.001
Increase in Hb(gms/dl)	1.49	0.60	2.50	0.64	11.389	<0.001

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment MCV (Fl) score at 2 and 4 weeks score ($p<0.05$). Rise in mean MCV (Fl) for oral iron group was 7.44 ± 4.75 and for I.V iron group was 11.25 ± 5.21, difference was statistically significant.

Table No 2
Comparison among study groups for MCV (FI)

MCV (FI)	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std. Dev.	Mean	Std. Dev.		
MCV (FI) (24-48 hrs)	71.56	6.81	71.13	6.17	0.465	0.643
MCV (FI) (2 Wks)	74.42	6.01	76.83	3.70	3.419	0.001
MCV (FI) (4 Wks)	79.00	4.91	82.38	2.01	6.358	<0.001
Increase in MCV (FI)	7.44	4.75	11.25	5.21	5.395	<0.001

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment MCH (pg) score at 2 and 4 weeks score ($p<0.05$). Rise in mean MCH (pg) for oral iron group was 4.50 (±2.17) and for I.V iron group was 5.90 (±1.97), difference was statistically significant.

Table No 3
Comparison among study groups for MCH (pg)

MCH (pg)	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std. Dev.	Mean	Std. Dev.		
MCH (pg) (24-48 hrs)	24.60	3.34	24.25	2.27	0.847	0.398
MCH (pg) (2 Wks)	26.44	3.00	26.88	1.87	1.257	0.210
MCH (pg) (4 Wks)	29.09	2.43	30.15	1.39	3.780	0.0002
Increase in MCH (pg)	4.50	2.17	5.90	1.97	4.778	<0.001

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment MCHC (%) score at 2 and 4 weeks score ($p<0.05$). Rise in mean MCHC (%) for oral iron group was 3.85 ± 2.23 and for I.V iron group was 7.61 ± 2.91, difference was statistically significant.

Table No 4
Comparison among study groups for MCHC % ,

MCHC %	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std.Dev.	Mean	Std.Dev.		
MCHC % (24-48 hrs)	27.72	3.26	27.91	2.68	0.454	0.650
MCHC % (2 Wks)	29.15	1.86	30.32	1.96	4.369	0.00002
MCHC % (4 Wks)	31.57	1.81	35.52	30.08	1.310	0.192
Increase in MCHC (%)	3.85	2.23	7.61	29.91	1.252	0.212

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment Reticulocyte Count % score at 2 and 4 weeks score ($p<0.05$). Rise in in Reticulocyte Count%. Rise in mean Reticulocyte Count %, for oral iron group was 0.70 ± 0.28 and for I.V iron group was 0.98 ± 0.28, difference was statistically significant.

Table No 5
Comparison among study groups for Reticulocyte count, RC (%)

RC (%)	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std.Dev.	Mean	Std.Dev.		
RC (%) (24-48 hrs)	0.58	0.18	0.56	0.17	0.782	0.435
RC (%) (2 Wks)	1.09	0.31	1.07	0.24	0.556	0.579
RC (%) (4 Wks)	1.28	0.35	1.52	0.33	5.048	<0.001
Increase in RC (%)	0.70	0.28	0.96	0.28	6.541	<0.001

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment Reticulocyte Count % score at 2 and 4 weeks score ($p<0.05$). Rise in Serum iron (mg/dl). Rise in mean Serum iron (mg/dl) for oral iron group was 61.06 ± 18.68 and for I.V iron group was 87.91 ± 14.30, difference was statistically significant.

Table No 6
Comparison among study groups for Serum iron mg/dl

Serum iron mg/dl	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std. Dev.	Mean	Std.Dev.		
Sr Iron (24-48 hrs)	42.48	13.80	37.17	11.67	2.940	0.004
Sr Iron (2 Wks)	79.91	11.39	87.98	11.13	5.068	0.001
Sr Iron (4 Wks)	103.54	17.70	125.08	9.25	10.782	<0.001
Increase in Serum Iron (mg/dl)	61.06	18.68	87.91	14.30	11.413	<0.001

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment TIBC (ug/dl) at 2 and 4 weeks score ($p<0.05$). Reduction in mean TIBC (ug/dl) for oral iron group was 117.62 ± 35.21 and for I.V iron group was 165.85 ± 30.38 , difference was statistically significant.

Table No 7
Comparison among study groups for TIBC (ug/dl)

TIBC (ug/dl)	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std.Dev.	Mean	Std.Dev.		
TIBC (ug/dl) (24-48 hrs)	501.44	30.38	509.28	31.31	1.797	0.074
TIBC (ug/dl) (2 Wks)	435.85	25.03	418.32	25.73	4.883	0.001
TIBC (ug/dl) (4 Wks)	383.82	26.66	343.43	29.71	10.119	<0.001
Reduction in TIBC(ug/dl	117.62	35.21	165.85	30.38	10.371	<0.001

In Oral iron group & I.V iron group statistically significant difference was noted in baseline and post treatment Transferrin saturation% at 2 and 4 weeks score ($p<0.05$). Increase in Transferrin saturation% for oral iron group was 10.42 ± 2.88 and for I.V iron group was 13.23 ± 3.23, difference was statistically significant.

Table No 8
Comparison among study group for Transferrin saturation%

Transferrin saturation%	Oral Iron		IV Iron		Unpaired T test	P value
	Mean	Std.Dev.	Mean	Std.Dev.		
Trans Sat (%) (24-48 hrs)	10.31	2.32	9.89	1.90	1.403	0.162
Trans Sat (%) (2 Wks)	15.46	2.82	16.71	2.51	3.319	0.001
Trans Sat (%) (4 Wks)	20.73	2.89	23.12	3.04	5.703	<0.001

Increase in Trans Sat	10.42	2.88	13.23	3.23	6.493	<0.001

Discussion

Currently, the standard treatment for anaemia is oral iron supplementation. However, this is limited by patient noncompliance and gastrointestinal symptoms such as nausea, vomiting, and constipation.[7] Absorption of oral iron is influenced by the dosage, the patient's iron storage, and the proximity of taking the medication relative to mealtime. This method of treatment is slow to take effect, often requiring several weeks for results to transpire.[8]

Alternative treatment methods for treatment of anaemia include intravenous (IV) iron therapy or blood transfusion. Blood transfusions are very costly and come with great risk, contributing to the increased popularity of IV iron therapy treatment.[9] Hematologic changes, like Hb and ferritin, are fairly rapid with IV iron therapy and have a positive effect on the body's iron storage which is measured by the ferritin level. Intravenous iron administration with iron sucrose has been available for several years. Iron sucrose has an excellent safety record.[10]

For many pregnant women, postpartum iron deficiency anaemia (IDA) is inevitable and can be detrimental to the mother and new-born. After childbirth, it is normal for haemoglobin (Hb) levels to drop during the first 24 hours due to the loss of blood during delivery, however the Hb level should rise over the next two to five days and return to normal by the seventh day after delivery.[11] If the Hb level does not rise adequately, postpartum IDA may become a serious problem and may create other problems for the new mother. Postpartum fatigue and a mother's declining health have been linked to IDA. In addition to fatigue, symptoms of anaemia include: inability to concentrate, general apathy, and irritability; all of which can seriously impact a new mother's quality of life.[12] So it is extremely important to determine a treatment that reduces recovery time for women with postpartum anaemia.

Iron-deficiency anaemia is a major health problem worldwide, but responds well to iron supplementation. The responsible constellation factors producing iron deficiency anaemia generally precede the pregnancy, including diet poor in iron content coupled with menstrual losses and a rapid succession of pregnancies in which supplemental iron was not provided. Most women begin their pregnancy with partially or completely depleted iron reserves. Thus, the severity of the anaemia is inversely related to the amount of iron reserves.[13]

Sunayana Verma et al,[14] studied 150 patients, 600 to 800 mg of iron sucrose was given in divided doses, 200 mg on alternate day to half of the patients whereas rest of the patients were given 200mg twice a day dose of ferrous sulphate by oral route for one month. They found that the rise in Hb in oral group was from a baseline of 7.42 gm% to 10.09 gm% and for iv iron sucrose group it was from a baseline of 7.58gm% to 11.5gm% at the end of 4 weeks which was statistically significant.

In the study by Prashant S. Kharde et al.,[15] among 100 postpartum women, Group A received two doses intravenous iron sucrose 200 mg on day 2 and day 4

and the other group Group B received oral ferrous sulphate 200 mg twice daily for 6 weeks. There was significant increase in mean Hb level from 7.76 ± 0.7137 g/dl to 10.78 ± 0.7679 g/dl on day 40 (p value < 0.01) in oral iron group. There was increase in mean Hb level from 7.47 ± 0.7678 g/dl to 11.41 ± 0.7908 g/dl on day 40 in injectable iron group, which was statistically significant. (p value < 0.01).

Ambreen Mumtaz et al.,[16] studied 80 postpartum patients, group 1 received intravenous ferrous sucrose and group 2 patients took oral ferrous sulphate twice daily for 6 weeks. On day 7 in group 1, haemoglobin rose from 8.4 to 11 gm/dl whereas in group 2, Hb rose from 7.8 to 8.3 gm/dl. On day 14 Hb reached to 11.4 gm/dl in group 1 and 9 gm/dl in group 2. This showed that the rise in haemoglobin level was rapid in intravenous group than in the oral group however at the end of 40 days there was no significant difference in haemoglobin levels between the groups.

C Giannoulis et al.,[17] studied 104 anaemic postpartum women.78 women who received a total amount of 300 mg iron sucrose in three days. 26 women, who received orally 800 mg iron protein succinylate daily for four weeks. Results obtained at the end of the study showed in group A, the increase of Hb mean level was 4.6 gm/dl and in group B the increase in haemoglobin mean level was 2.3 gm/dl.

In present study, other colour indices such as MCV (Fl) (In oral group the baseline value was 71.56 and at the end of 4 weeks was 79. In iv iron sucrose group the baseline value was 71.73 and at the end of 4 weeks was 82.38), MCHC (%) (In oral group the baseline value was 27.72 and at the end of 4 weeks was 31.57. In iv iron sucrose group the baseline value was 27.91 and at the end of 4 weeks was 35.52.), and Transferrin Saturation (%) (In oral group the baseline value was 10.31 and at the end of 4 weeks was 20.73. In iv iron sucrose group the baseline value was 9.89 and at the end of 4 weeks was 23.12.) Thus in these colour indices it showed significant increase in iv iron sucrose group on comparison with oral iron group.

Conclusion

Parameters in the iv iron sucrose group showed highly significant increase and a faster rate of improvement. For management of postpartum anaemia iv iron administration is as efficacious as oral iron and an option to correct postpartum anaemia at the earliest.

Conflict of Interest: None to declare

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