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POST PARTUM IRON DEFICIENCY ANEMIA;
COMPARATIVE EFFICACY AND SAFETY OF INTRAVENOUS VS ORAL IRON THERAPY

1. Professor, Department of Pharmacology & Therapeutics Hamdard College of Medicine & Dentistry, HU, Kar.
2. Professor, Department of Physiology Hamdard College of Medicine & Dentistry, HU, Kar.
3. Professor, Department of Pharmacology & Therapeutics Hamdard College of Medicine & Dentistry, HU, Kar.
4. Lecturer, Department of Pharmacology & Therapeutics Hamdard College of Medicine & Dentistry, HU, Kar.

Correspondence Address:
Dr. Syed Mohsin Turab
Professor, Department of Pharmacology & Therapeutics
Hamdard College of Medicine & Dentistry, HU, Kar.
House# C-24, New Rizvia Housing Society Scheeme 33, Opp. Kiran Hospital, Karachi.

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Dr. Syed Mohsin Turab[1], Dr. Muhammad Furqan[2], Dr. Shah Nawaz Jamali[3], Dr. Syeda Amber Zaidi[4].

ABSTRACT… Objectives: To Analyze and compare the effect of oral vs parenteral iron therapy on various hematological parameters in women suffering from post-partum iron deficiency anemia. **Study Design:** Comparative, randomized and prospective study. **Setting:** Department of Pharmacology, HCMD, HU in collaboration with the Dept of Obs/Gynae, JPMC Karachi. **Period:** January to December 2015. **Subjects and Methods:** 40 patients divided in two groups A and B of 20 each. Group A received oral iron (Tab Iberet 525 mg once daily) for a period of 3 months while group B was treated with intravenous iron sucrose complex (Inj Venofer 100mg/Amp) the total no of doses were calculated according to Hemoglobin deficit. Hemoglobin, Hematocrit and MCV were observed at day 0, 45 and 90 of the treatment. **Results:** Group A shows a mean increase of 25.85% at day 90th of the treatment in comparison to this group B shows a much better result with a mean increase of 36.71% in Hemoglobin conc. At the end of 12 weeks therapy. **Conclusion:** Parenteral iron therapy was found to be an effective means of treatment in patients with postpartum iron deficiency anemia.

Key words: Post-partum iron deficiency anemia, oral iron, parenteral iron, hemoglobin.

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INTRODUCTION

Anemia is the decrease in hemoglobin concentration in blood along with lower Hematocrit value. In postpartum period, up to 30% women presents with anemia and their hemoglobin level is <10 g/dl. Severe anemia was observed in 10% women with Hb level below 8 g/dl.[1] In pregnancy World Health Organization defines anemia according to the trimester of pregnancy i.e. in first and third trimester women with Hb level below 11 g/dl and in second trimester with values <10.5 g/dl are labeled as anemic.[2]

Worldwide anemia is one of the most serious global health problems and it is the second leading cause of disability. It is cited in the literature that discussion regarding postpartum anemia was very rare, although iron deficiency anemia in pregnancy was very much emphasized.[3]

One of the major causes of anemia is iron deficiency. In pregnancy there is increased maternal red cell mass and increased demand of fetoplacental unit for iron. These two factors lead to the development of iron deficiency and ultimately anemia.[4] Combination of blood loss after delivery[5] and iron deficiency during pregnancy are the leading causes of a very common obstetric problem known as postpartum anemia.[6]

Different regions of world are classified epidemiologically according to the prevalence of anemia. Areas with 1% to 9.9% prevalence of anemia are classified as mild while moderate and severe are the categories for the areas that have 10% to 39% and more than 40% prevalence of anemia respectively.[7] Reported prevalence of postpartum anemia varies between 4% and 27% worldwide. Anemia is credited for 20% of maternal deaths in the world. 0.5 mg of iron is lost with each ml ob blood loss from the body.[8]

According to one national survey in Pakistan the prevalence of anemia was found 26% and 47% in non-pregnant women of aged 15 to 44 years living

in urban and rural areas respectively. Another survey was conducted in antenatal clinics of large tertiary care units of Karachi and results were very similar for pregnant women living in urban areas i.e. anemia was found in 29% to 50% women.[9]

It is estimated that about ¼ one fourth of the women who were not anemic during pregnancy develops anemia during postpartum period in United States.[10] Postpartum anemia is associated with high morbidity and mortality rates depending on how much the blood loss. In 1995, 515000 maternal death were reported worldwide among them anemia was recognized as a cause in 20% cases.[11] To make a diagnosis of iron deficiency anemia both Hb level and serum Ferritin levels are currently used gold standards.[12] In presence of inflammation serum ferritin levels are falsely raised. It is reported in National pregnancy Nutrition Surveillance System that 29.8% of women develop anemia in postpartum period who were previously have normal Hb levels.[13]

According to WHO the period between one hour from the delivery of placenta till 42 days or six week is known as postpartum period or puerperium.[14] Fatigue, depression, disturbance in cognitive behavior, anxiety and stress are recognized consequences of anemia. Failure of lactation, delayed wound healing (episiotomy or caesarean), and decrease immunity that leads to increased susceptibility to mastitis, ductitis and urinary tract infections are other features associated with postpartum anemia.[15,16] Mother and child relationship is also disturbed in postpartum anemia. Previous studies have shown developmental delay in infants of anemic mother. Women with postpartum anemia are less responsive to their child and shows negative behavior.[17]

There is intense psychological and physical stress found in postpartum period. High cost, longer hospital stay, and need for appropriate medical therapy are also the effects of anemia along with its other consequences. Patients treated only with oral iron supplementation takes 2 months to recover their iron stores.[18]

Oral iron therapy is the current standard of treatment for patients with anemia. Gastrointestinal irritation manifest as diarrhea, constipation, nausea and vomiting and non-compliance of the patient are the major limitations of its use.[19] Intravenous (i/v) iron therapy and blood transfusion are alternate treatment options for anemia. High risk of allergic reaction and transmission of blood borne diseases is associated with blood transfusion and it is not cost effective.[12]

Iron dextran was the only compound available for intravenous use previously. Severe anaphylactic reactions were reported with this compound, so not in use now days. Comparatively safe with low side effect profile new compound iron sucrose is available for intravenous use.[20]

Locally the comparative trials of treatment efficacy are very rear, and if done are not available, further clinical trials with adequate sample size are warranted to evaluate the efficacy and tolerable profile of the drugs used to treat postpartum iron deficiency anemia.

AIMS & OBJECTIVE

To study and compare the effects of ferrous sulfate (orally) and iron sucrose complex (intravenous) on various hematological parameters in the treat of postpartum iron deficiency anemia & to observe the adverse effects encountered by the administration of either of the drug.

Study Design

This was a comparative, randomized, open-labeled, prospective study conducted in the department of pharmacology and therapeutics, Hamdard College of Medicine & Dentistry, Hamdard University, Karachi in collaboration with the department of Obs/ Gyne JPMC, Karachi between January to December 2015.

METHODOLOGY

Grouping of Patients

A total of 40 patients will be enrolled and will be divided into two treatment groups,

Group A: (20 patients) includes those patients that were treated with oral 525 mg tablets of ferrous sulfate (Tab. Iberet, Abbot Pharma) together with meals, once daily for 12 weeks.

Group B: (20 patients) includes those patients that were treated with doses of intravenous iron sucrose complex 200mg (venofer, RG Pharma).

Inclusion Criteria

- Women aged 18 years or more with Hb level of less than 9 gm/dl or less after delivery, whether vaginal or cesarean.
- Women with mean corpuscular volume less than 100 fl.

Exclusion Criteria

- Women with intolerance to iron derivatives
- Women with peripartum blood transfusion
- Women with abnormal renal or hepatic functions
- Women with hypersplenism disorder
- Women with asthma, thrombo-embolism, convulsive disorder, alcohol or drug abuse and cardiovascular diseases.
- Women with all types of anemia other than iron deficiency.

Investigations

Blood samples were taken before start of therapy that is day 0 and then at day 45 and day 90th of treatment. Following parameters were assessed during the study.

- Hemoglobin (Hb)
- Hematocrit (Hct)
- Mean Corpuscular Volume (MCV)

RESULTS

This is a comparative prospective study conducted Between January to December 2015. 40 patients with postpartum anemia were randomized and divided into two equal groups. Group A was treated with 525mg tablet of ferrous sulfate orally once daily for 12 weeks while group B patients were treated with intravenous iron sucrose complex according to hemoglobin deficit.

Baseline characteristics of study subjects are shown in Table-I and Figure-1. Oral iron group was found younger with mean age 31±6 years as compare to parenteral iron group. The mean hemoglobin concentration in group A was 9.93 ± 1.00 while that of group B was 9.54 ± 0.64 at initiation of therapy. BMI was found similar in both the groups. Hemoglobin and other red cell indices were followed at 6 and 12 week of the treatment. Table-I shows the baseline characteristics of the patients enrolled in the study.

Characteristic	Oral Iron Group (N=20)	Parenteral Iron Group (N=20)
Age (years)	31±6	32±5
BMI	24±2	23±2.4
Hemoglobin (Hb)	9.93 ± 1.00	9.54 ± 0.64
Hematocrit (Hct)	31.9 ± 2.04	30.3 ± 1.80
Mean Corpuscular Volume (MCV)	70.6 ± 0.99	69.4 ± 3.36

Table-I. Base line characteristics of the patients

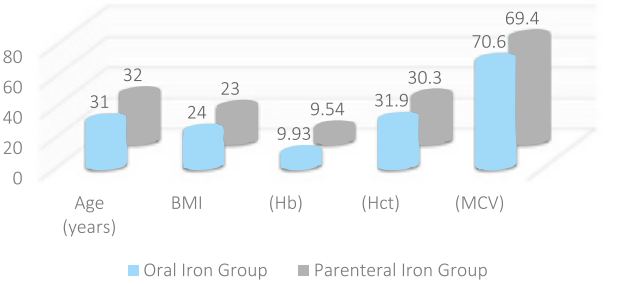

Figure-1. Base line characteristics of the patients

HB RESPONSE

Hb concentration increased in both groups at days 45 and 90. Patients treated with parenteral iron therapy shows higher levels. In patients treated oral therapy mean increase in Hb at day 45 and day 90 was 1.19 g/dl and 2.57 g/dl respectively. While in parenteral therapy group there is 2.94 g/dl and 3.51 g/dl increase in Hb level at 6 and 12 weeks of treatment. Hb level increase by 25.85% and 36.71% in both treatment groups i.e. group A and B as shown in Table-2 and Figure-2.

CHANGE IN HAEMATOCRIT

Mean haematocrit of group A at day 45 and 90 was found 33.5 ± 1.24 and 37.15 ± 1.98 respectively. Group B at day 45shows mean haematocrit of 35.3 ± 2.56 while at day 90 it is 40.7 ± 2.81. Statistically significant difference (P

Groups	Day 0	Day 45	Day 90	P – value			% Change
				D 0–45	D 45–90	D 0–90	
Group A	9.96	11.15	12.535	t = -9.2	t = -8.81	t = 11.77	25.85
	±1.02	±0.81	±0.62	p <0.0001	p < 0.002	p < 0.002	
Group B	9.546	12.485	13.05	t = -14.61	t = -4.43	t = -19.95	36.71
	±0.65	±0.54	±0.49	p < 0.002	p < 0.0001	p < 0.0001	
A VS B				t = -6.13		t = -2.94	
				p < .001		p < 0.001	

Table–II. Changes in HB Concentration

<.002) was found between group A and B. At day 90th of treatment group B shows 17.86% better performance.

In group A and B there is significant change in difference with P<.001 was found from baseline to day 90 of the treatment. Group A shows 16.46% increase in haematocrit while group B gives 34.32% increase in haematocrit. (Table-III, Figure-3)

MEAN CORPUSCULAR VOLUME

Table-IV shows mean corpuscular volume of group A and B at day 45 i.e. 73.95 ± 2.54 and 77.55 ± 2.91 and at day 90 of study i.e.79.65 ± 4.75 and 84.05 ± 2.63. After 12 week treatment statistically significant difference with P <.001 was found among two groups.

Intra- group difference in group A and B from day 0 to 90 of the treatment showed significant change (P<.001) as shown in figure 4. There is12.82% and 21.11% change was found in group A and B respectively from baseline to final day of treatment. Both groups' shows increase in mean corpuscular volume at the end of treatment but group B give promising results i.e. 8% better than group A.

MEAN CORPUSCULAR VOLUME

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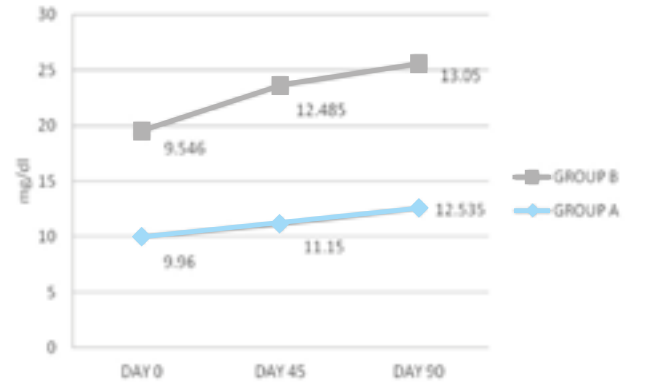
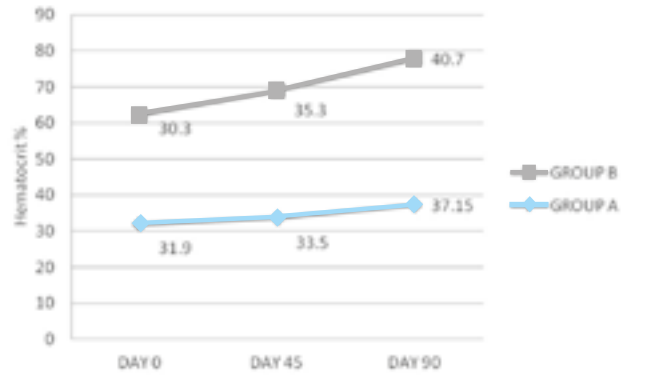
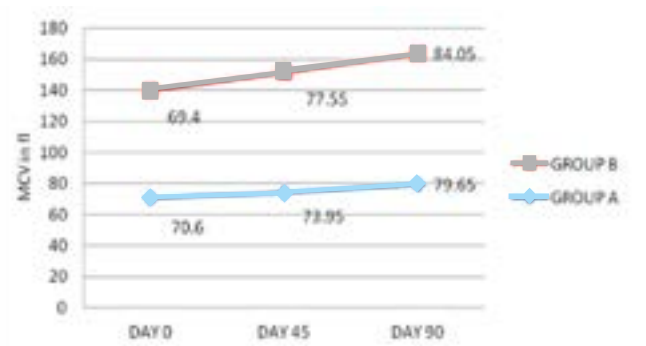


Figure–2. Changes in HB concentration



Figure–3. Changes in haematocrit



Figure–4. Changes in MCV

Intra- group difference in group A and B from day 0 to 90 of the treatment showed significant change (P<.001) as shown in figure 4. There is12.82% and 21.11% change was found in group A and B respectively from baseline to final day of treatment. Both groups' shows increase in mean corpuscular volume at the end of treatment but group B give promising results i.e. 8.3% better than group A.

Groups	Day 0	Day 45	Day 90	P – value			% Change
				D 0–45	D 45–90	D 0–90	
Group A	31.9	33.5	37.15	t = -3.94	t = -9.3	t = -10.25	16.46
	±2.05	±1.54	±1.98	p < 0.002	p < 0.0001	p < 0.002	
Group B	30.3	35.3	40.7	t = -7.26	t = -11.17	t = -14.83	34.32
	±1.81	±2.56	±2.81	p < 0.0001	p < 0.0002	p < .001	
A VS B				t = -2.70		t =-4.62	
				p < 0.0001		p < 0.002	

Table–III. Changes in Haematocrit

Groups	Day 0	Day 45	Day 90	P – value			% Change
				D 0–45	D 45–90	D 0–90	
Group A	70.6	73.95	79.65	t = -6.58	t = -8.5675	t= -9.21	12.82
	±0.99	±2.54	±4.75	p < .001	p < 0.001	p < .001	
Group B	69.4	77.55	84.05	t = -8.32	t= -2.6079	t = -5.17	21.11
	±3.36	±2.91	±2.63	p <0.002	p < 0.0001	p <0.001	
A VS B				t = -4.17		t = -3.63	
				p < .001		p < .001	

Table–IV. Changes in mcv

DISCUSSION

In women with postpartum iron deficiency anemia we compare the results of intravenous iron with conventional oral iron therapy with regard to improvement in Hb concentration and other hematological parameters like MCV and Hematocrit. Intravenous iron therapy was found more effective in improving hemoglobin level as compared to oral iron treatment. The reason being rapid clearance and utilization of ferrous sucrose from plasma which makes it more effective for the process of erythropoiesis. A peak plasma level of iron sucrose is achieved after 10 minutes of bolus dose and within 24 hours these levels become negligible.

In our study an average of three doses of 200 mg of i/v ferrous sucrose shows significant increase in HB levels with a mean increase of 3.51 g/dl from baseline. At the end of therapy both groups have similar HB levels. Parenteral therapy i.e. ferrous sucrose appeared more effective in improving hemoglobin concentration during study period. These findings are consistent with results of Bhandal and Russell who found a mean hemoglobin concentration increase of 2.5 g/dl and 0.7 g/dl in intravenous and oral iron therapy groups respectively. The study done by Broche et al. in 2005 also shows similar results. He found a mean increase in Hb of 1.9 g/dl within 7 days of therapy and 3.1 g/dl after 14 days of intravenous iron sucrose therapy. Similar results were also found by Jain Geeta in 2006, she found increase of 2.4 g/dl and 1.2 g/dl in intravenous and oral iron groups respectively.

CONCLUSION

According to our study intravenous infusion of iron sucrose provides a rapid resolution of hemoglobin and other hematologic parameters in women having iron deficiency anemia in postpartum period. Oral iron therapy is associated with a high rate of adverse effects and low compliance that may result in failure of therapy. In future large randomized control trials are needed to observe the risk and benefits of two treatment groups over each other.

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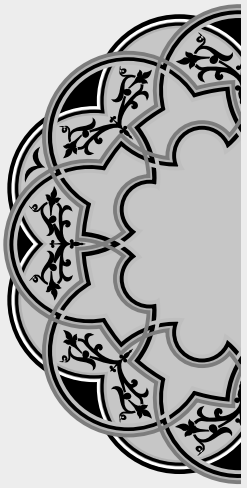
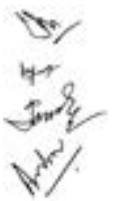


"Quiet people have the loudest minds."

Stephen King

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Syed Mohsin Turab	All authors have equal contribution in this article	
2	Dr. Muhammad Furqan		
3	Dr. Shah Nawaz Jamali		
4	Dr. Syeda Amber Zaidi		