ORIGINAL ARTICLE

Comparison for Effects of Intravenous versus Oral Iron Therapy for Postpartum Anemia

AMBREEN MUMTAZ, FAREEHA FAROOQ

ABSTRACT

Objectives: The aim of our study was to compare the effects of intravenous ferrous sucrose versus oral ferrous sulphate on postpartum iron deficiency anaemia.

Material and methods: This prospective randomized study was conducted in Obstetrics and Gynaecology Department of Alkhidmat Teaching Hospital Mansoorah Lahore and in the Obstetrics and Gynaecology Department of Akhtar Saeed Trust Hospital in 2009. The study included 80 postpartum patients. The inclusion criteria was Hs<9 gm/dl and serum ferritin of <15 µg/l at 24-48 hours post-delivery. The exclusion criteria was intolerance to iron derivatives, peripartum blood transfusion or a history of asthma, thromboembolism, seizure, alcohol, drug abuse, renal or hepatic dysfunction. Women were divided into two groups consisting of forty patients in each group by randomization. The group I received 2 doses of intravenous ferrous sucrose 200 mg given in day 2 and 4 as an infusion in 100 ml of 0.9% sodium chloride for more than 30 minutes. In group II patients were advised to take 200 mg of ferrous sulphate twice daily together with meals for 6 weeks. Blood samples were measured on day 0, 7, 14 and at 40 days for Haemoglobin levels, hematocrit, red-cell indices, serum ferritin and serum iron levels were measured. All analysis was conducted using SPSS for Windows, version 10.0.

Results: On day 7 in group 1, haemoglobin rises from 8.4 to 11 g/dl whereas in group II, Hb rises from 7.8 to 8.3 g/dl. The rise in haemoglobin level is rapid in intravenous group and in the oral group it is a gradual rise but at 40 days the result showed no significant difference in between the two groups. As far as the iron stores are concerned, serum ferritin in group I rose rapidly and remained at higher level where in group II, rise in serum ferritin is comparatively less than the intravenous group. Similarly the results are same in the case of serum iron.

Conclusion: Intravenous iron sucrose is efficacious and a successful method for raising the level of iron stores as compared to oral iron supplements.

Keywords: Intravenous iron, oral iron, postpartum anaemia.

INTRODUCTION

Anaemia is the commonest medical disorder in pregnancy and has a varied prevalence, aetiology and the degree of severity in different population being more common in non-industrialized countries[1].

The WHO definition for diagnosis of anaemia in pregnancy is a Hb concentration of less than 11g/dl and a hematocrit of less than 0.33[2]. The overall prevalence of anaemia is estimated to be about 40% of the world's population. The prevalence is 35% for non-pregnant women and 51% for pregnant women globally[3]. Anaemia affects about 18% of women during pregnancy in industrialized countries while in non-industrialized countries, prevalence varies between 35-75% with the average being 56%[4].

The prevalence is very high in Central Asia also as shown by demographic and health surveys in Kazakhstan and Uzbekistan where the incidence was80%[5]. About half of the global total number of anaemic women live in the Indian sub-continent and in India alone, the prevalence of anaemia during pregnancy may be as high as 88%[5,6].

Postpartum haemoglobin levels of less than 10 g/dl are observed in up to 30% of women, with more severe anaemia that is less than 8 g/dl seen in 10% of women[7]. Iron deficiency is the principle cause, this is partly attributable to an iron deficit during pregnancy caused by the increased iron demands of the feto-placental unit and an increased maternal red cell mass[8]. Irrespective of mode of delivery, blood loss is a contributing factor, with 5% of deliveries involving loss of more than one litre[9,10].

Postpartum can lead to a variety of morbidities such as lethargy, palpitations, fatigue, lactational failure and postpartum depression[11].

The routine management of iron deficiency anaemia is oral iron supplementation and transfusion is reserved for severe and symptomatic cases. Blood transfusion has a number of hazards like transfusion reaction, infections, anaphylaxes, lung injury which can be very dangerous for a young mother. The

Obstetrics and Gynaecology Department of Alkhidmat Teaching Hospital Mansoorah Lahore
Correspondence to Dr. Ambreen Mumtaz

compliance of oral iron supplementation is bad, due to its gastrointestinal side effects and its role in the treatment of severe anaemia is limited[13].

Since the availability of Parenteral iron administration in the form of ferrous sucrose, a good and a safe option is available and routinely used in a number of European countries. Ferrous sucrose has an excellent safety record unlike previous formulation like ferrous dextran which was associated with a significant risk of anaphylactoid react.0ons. Hence the aim of our study was to compare the efficacy of treatment with either oral ferrous sulphate or intravenous ferrous sucrose on postpartum iron deficiency anaemia.

METHODS

A prospective randomized study was conducted in the obstetrics and Gynaecology Department of Alkhidmat Teaching Hospital Mansoorah Lahore attached with University of Lahore and in the Obstetrics and Gynaecology Department of Akhtar Saeed Trust Hospital. The study included 80 postpartum patients. About 76 patients underwent caesarean section and 4 patients underwent vaginal deliveries. Informed consent was taken from the patients included in the study.

The criterion of selecting patients in the study was Hb < 9mg/dl and serum Ferritin of < 15mg/dl at 24-48 hours post-delivery. The exclusion criterion was intolerance to iron derivatives, peripartum blood transfusion or a history of asthma, thromboembolism, seizure, and alcohol or drug abuse. Women with signs of infection or evidence of renal or hepatic dysfunction were also excluded from the study.

Women were divided into two groups consisting of 40 patients in each group. In group 1, patients received two doses of intravenous ferrous sucrose, 200 mg given in day 2 and 4 as an infusion in 100 ml of 0.9% sodium chloride for more than 30 minutes. This group received no further iron supplementation. Patients were advised to note any symptoms or side effect of treatment. The dose of ferrous sucrose used in this study was based on pooled data from different studies using cumulative doses of 100-800mg.[12] In group II, the patients were advised to take 200mg of ferrous sulphate twice daily together with meals for 6 weeks. Women were advised to document treatment compliance and symptoms. Intravenous sucrose was administered in hospitals where facilities for monitoring and resuscitation were available.

Blood samples of patients were taken at the day of recruitment into the study (day 0) and the rest of the samples were taken in day 7, day 14, day 40 after the start of the treatment. The timing of these samples was based on pooled data from different studies12. detect any difference in the speed of restoration of Haemoglobin and iron stores. Hemoglobin, hematocrit, red cell indices, mean corpuscular volumes and mean corpuscular hemoglobin levels were measured. Iron status markers measured were serum ferritin & serum iron.

RESULTS

Initially 86 patients were recruited into the study. But due to non-compliance and complications like infection, secondary postpartum hemorrhage etc., and 6 patients were excluded and only 80 patients were included in the study that completed the treatment and tests advised to them.

Table 1: Data at recruitment into the study

Characteristic	**Group I (n=40)**	**Group II (n=40)**
Age (years)	24.6 (3.7)	25.1 (3.3)
Hb (before delivery)(g/dl)	11.2 (0.7)	10.9 (0.7)
Hb (after delivery)(g/dl)	8.4 (0.3)	8.1 (0.5)
Hematocrit %	25.4 (1.4)	24.0 (0.8)
Ferritin (microgram/l)	11.3 (0.9)	11.9 (1.0)
Serum Iron (nmol/l)	6.2 (0.3)	5.6 (0.7)

Data are given as mean (SD)

Table 2: Data after treatment with Iron

	Group I (n=40)	**Group II (n=40)**
Hb g/dl		
Day 0	8.4	7.8
Day 7	11.0	8.3
Day 14	11.4	9.0
Day 40	12.4	11.8
Ferritin (µg/l)		
Day 0	9.5	9.7
Day 7	46.5	13.0
Day 14	40.0	18.0
Day 40	43.5	16.7
Serum Iron (nmol/l)		
Day 0	6.4	6.1
Day 7	14.5	8.7
Day 14	25	13.5
Day 40	29.5	18

Data are given as mean

Table 3: Complications

Group 1	
Metallic taste	5 (25%)
Facial flushing	4 (20%)
Local inflammatory reaction	1 (5%)
Muscular cramps	3 (15%)
Group II	
Dyspepsia	1 (5%)
Nausea	1 (5%)
Abdominal Cramps	1 (5%)
Constipation	2 (10%)
Diarrhea	2 (10%)

Haemoglobin level increased from baseline in both treatment groups at days 7, 14 and 40. The higher levels of hemoglobin were seen in patients who received intravenous iron especially at day 7 and 14 (Fig.1). The mean increase in Hb Level from baseline at day 7 was 2.6 g/dl in group 1 and 0.5 g/dl in group II, although at the end of the study by day 40 there was no significant difference in haemoglobin levels between the treatment groups but it can be clearly seen in Fig.1 that the rise of haemoglobin level is more rapidly achieved in the intravenous group.

In both groups, the ferritin levels at baseline were almost similar in the start of the treatment. There was significant increase in ferritin levels in group 1 by day 7 and the ferritin levels remained elevated in this group (Fig.2). In comparison only slight increase in ferritin levels was seen with oral iron supplementation. Serum Iron levels also increase in both groups, but levels were significantly higher in group I at day 14 and 40 (Fig.3). The results in our study are comparable to a similar study conducted by N. Bhandal and R. Russell in 2006 BJOG[13].

No serious adverse effect was reported. In group I, ten women (25%) complained of metallic taste during the infusion of the drug. This was transient in nature and resolved immediately after the infusion was complete. Eight women (20%) complained of facial flushing as a warm tingling sensation, one patient due to extravasation of injection had a local inflammatory reaction and six women complained of muscular cramps (15%). There were no hemodynamic disturbances observed either during infusion or after infusion.

In group II, fourteen women (35%) complained of adverse effects. These were all of a gastrointestinal nature ranging from dyspepsia, nausea, abdominal cramps, constipation and sometimes diarrhea. These patients needed emotional support and counseling.

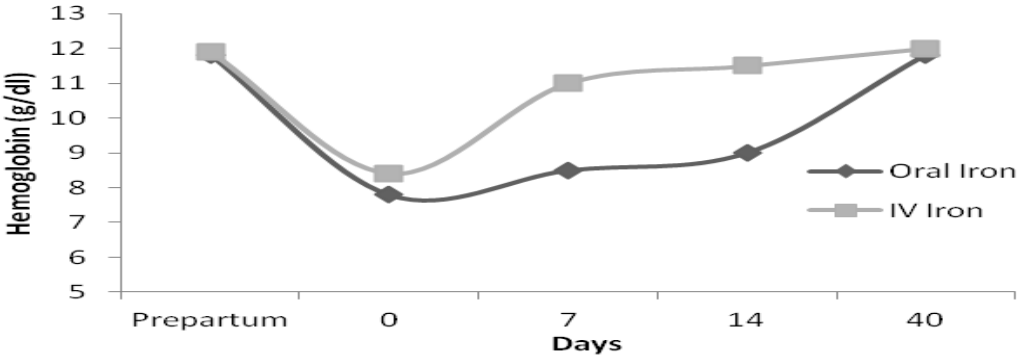

Fig.1. Response of Hb to intravenous and oral iron therapies.

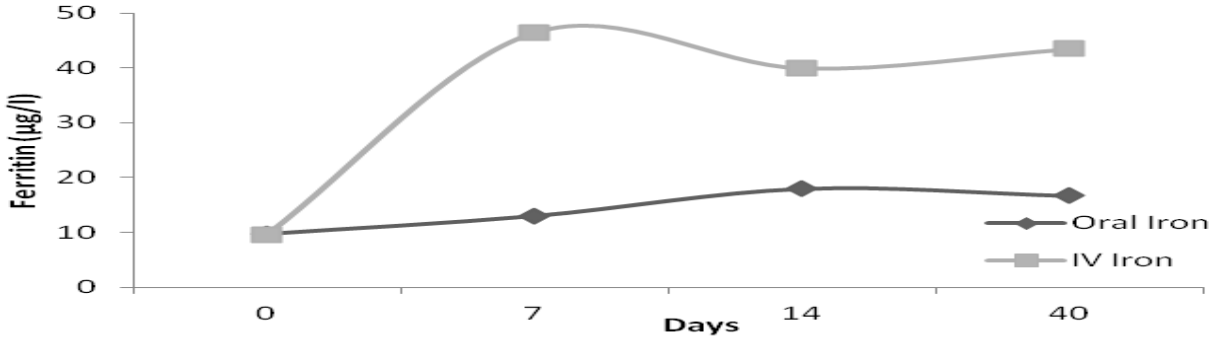

Fig.2. Response of Ferritin to intravenous and oral iron therapies.

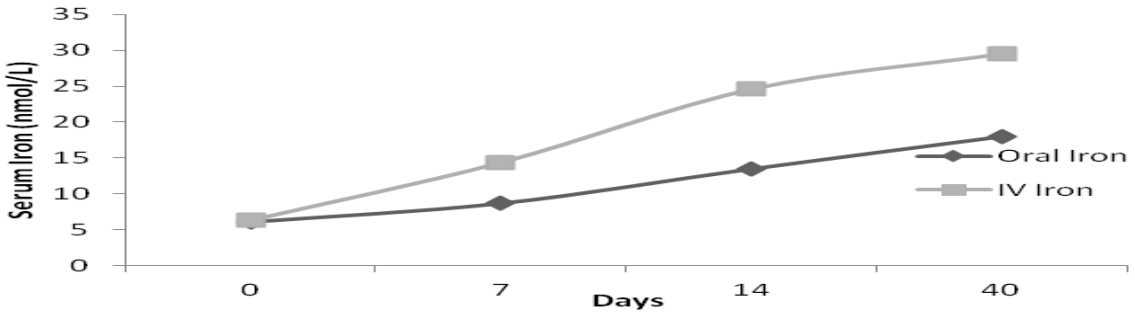

Fig.3. Response of Serum Iron to Intravenous and Oral Iron therapies

DISCUSSION

Anaemia is a condition of low circulating haemoglobin and the two most common causes of anaemia in pregnancy and the puerperium are iron deficiency and acute blood loss. Anaemia antedates pregnancy, is aggravated by increased requirement during pregnancy and blood loss at delivery, infections in the antenatal and postnatal periods, and the early advent of next pregnancy perpetuates it.

This study was done in postpartum anaemic patients to compare the effects of intravenous ferrous sucrose versus oral iron supplementation on haemoglobin concentration and iron stores (i.e. serum ferritin and serum iron).

In our study the rise in haemoglobin level is seen in both treatment groups. In group I patients who received two doses of 200 mg intravenous ferrous sucrose, there is a significant increase in haemoglobin levels within 7 days with a mean increase from baseline of 2.6 g/dl. In group II patients who received oral ferrous sulphate the rise in haemoglobin in 7 days is about 0.5 g/dl. As we can see in Fig. 1 that the rise of haemoglobin is more rapidly achieved in group I, but after 40 days haemoglobin levels were similar in both the groups. These figures are comparable with international studies[18,13].

In our study serum ferritin and serum iron were used as indicators of iron storage in the body. In the pregnancy because of hemodilution serum ferritin levels are low as compared to actual level in the body but serum ferritin levels remain a reliable indicator of iron deficiency, where a cutoff level of < 15 microgram/l is used[14.15].

In our study in both groups, the ferritin levels at the base line were almost similar in the start of treatment. There was significant increase in ferritin levels in group I by Day 7 and ferritin levels remained elevated in this group (Fig. 2). In comparison only slight increase in ferritin levels was seen with oral iron supplementation. Serum iron levels also increased in both groups but the levels were significantly higher in group I on Day 14 and 40. The results of our study are almost closer to similar international study conducted in 2006[13].

This shows that the intravenous iron not only cause rapid rise in haemoglobin but improves the iron storage in the body more effectively. Hence it is the ideal method of improving the haemoglobin levels in anaemic patients. Many studies conducted on renal patients with severe iron deficiency anaemia have shown that when intravenous ferrous sucrose was given for treatment, 70-97 % of iron is used for erythropoiesis, with only 4-6 % elimination. This has been shown by positron emission tomography studies, which show immediate incorporation into the bone marrow while the plasma level falls[16].

Previously other iron preparations have been used like ferrous dextran (Imferon) which can be given intramuscularly or intravenously and iron sorbitol citrate (Jectofer) which can only be given intramuscularly and it is quite painful locally. Due to high anaphylactoid risk of iron dextran and other risks, there is considerable hesitancy to use them.

In our study intravenous ferrous sucrose was well tolerated and not associated with any serious side effects. This fact is supported by previous larger studies that have investigated the safety profile of intravenous ferrous sucrose, both during pregnancy and in the postpartum period[13].

The dose of oral ferrous sulphate used in our study was well tolerated. The compliance with oral treatment was satisfactory and was reinforced with regular visits. Gastrointestinal adverse effects are usually dose related; a study conducted by AlMomen et al described gastrointestinal adverse effects with a frequency of up to 30%. In our study adverse effects occurred in 35 % of women but were not severe enough to affect compliance.

In our study, intravenous ferrous sucrose appeared to provide a rapid restoration of both hemoglobin and iron stores for women with postpartum IDA. Treatment with intravenous iron is superior to oral iron with respect to hematological response. If used appropriately, intravenous ferrous

sucrose may help in reducing the need for blood transfusion and its hazards and is especially important in the safety of women who for various reasons oppose blood transfusion.

REFERENCES

1. Schwartz W. Tharnau G.R. Iron deficiency anemia in pregnancy Clin Obstet Gynecol 1995;38: 443-454
2. *Report of a WHO group* of *experts* on *nutritional anemias*. *Technical report* series no. 503. Geneva, WHO, 1972.
3. *World Health Organization* (WHO). The *prevalence of Anaemia in women: a tabulation* of available information. Geneva, Switzerland: WHO; 1992.
4. *World Health Organization* (WHO). Global Database Geneva, WHO 1997.
5. Abel R. Rajaratnam J Sampath Kumar V. Anemia in pregnancy, Impact of Iron, Deworming and IEC RUSHA Dept. Tamil Nadu, CMC, Vellore. 1999.
6. Barbin L, Nicholas S, Gogate A, Karandea A. High prevalence of Anemia among women in Mumbai India. Food nutrition bulletin 1998, 19:205-209.
7. Aggelt. Iron and women in their reproductive years. The British Nutrition Foundation Task Force Editors. Iron Nutritional and Physiological Significance. First Edition London: Chapman and Hall: 1995 Pg. 110-118.
8. Baker W. Iron deficiency in pregnancy, obstetrics and gynecology. *Hematol Oncol Clin North Am* 2000;14:1061–77.
9. Gulmezoglu AM, Villar J, Ngoc NT, Piaggio G, Carroli G, Adetoro L, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. *Lancet* 2001;358:689–95.
10. Kotto-Kome AC, Calhoun DA, Montenegro R, Sosa R, Maldonado L, Christensen MD. Effect of administering recombinant erythropoietin to women with postpartum anemia: a meta-analysis. *J Perinatol* 2004;24:11–15.
11. Alkinson LA, Bexley EG. Post-partum fatigue. American Family Physician 1994. 50:113-118.
12. Perewunsnyk G, Huch R, Huch A, Breymann C. Parenteral iron therapy in obstetrics: 8 years experience with iron-sucrose complex. *Br J Nutr* 2002;88:3–10.
13. Bhandal N, Russell R. *Intravenous versus* oral *iron therapy for postpartum* anaemia. *BJOG 2006*; 113:1248–1252.
14. Mei Z, Cogswell ME, Parvanta I, Lynch S, Beard JL, Stoltzfus RJ, Grummer-Strawn LM. Haemoglobin and ferritin are currently the most efficient indicators of population response to iron interventions: an analysis of nine randomised controlled trials. *J Nutr* 2005; 135:1974–80.
15. Van den Broek NR, Letsky EA, White SA, Shenkin A. Iron status in pregnant women: which measurements are valid? *Br J Haematol* 1998;103:817–24.
16. Beshara S, Lundqvist H, Sundin J, Lubberink M, Tolmachev V, Valind S, et al. Pharmacokinetics and red cell utilization of iron (III) hydroxide-sucrose complex in anaemic patients: a study using positron emission tomography. *Br J Haematol* 1999;104:296–302.
17. Hallberg L, Ryttinger L, Solvell L. Side effects of oral iron therapy. A double-blind study of different iron compounds in tablet form. *Acta Med Scand Suppl* 1966;459:3–10.
18. Al Momen AK- al Meshan A, al Nuaim L, Saddique A, Abuttalib Z Khashogji, et al. Intravenous iron sucrose complex in the treatment of Iron Deficiency Anemia during pregnanacy, Eur J Obstet Gynecol Reprod Biology 1996:69:121-4.