

COMPARATIVE STUDY BETWEEN INTRAVENOUS IRON SUCROSE VS ORAL IRON THERAPY

Swetha R Vernekar¹, Shonali Agarwal²

¹Senior Resident, Consultant Obstetrician and Gynaecologist, JGMM Medical College Hubli, Karnataka, India

²Associate Professor, Department of Obstetrics and Gynaecology, SSG Hospital, Govt Medical College, Vadodara, Gujarat, India

Received : 18/04/2023
Received in revised form : 22/05/2023
Accepted : 15/06/2023

Keywords:

Intravenous iron sucrose, Oral iron therapy, Anemia, Pregnancy.

Corresponding Author:

Dr. Swetha R Vernekar,

Email: swethatejaskulkarni@gmail.com

DOI: 10.47009/jamp.2023.5.3.375

Source of Support: Nil,

Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5(3); 1894-1898



Abstract

Background: Anemia is a major health problem in the antenatal clinics all over the world. In the poor and developing countries, factors like lower socio economic status, inadequate hygiene, recurrent pregnancies, poor quality diet add to the already existing burden of physiologic anemia in pregnancy and make the scenario even worse. The objective is to compare the changes in hemoglobin, serum ferritin and total iron in the pregnant women treated with oral ferrous sulphate and intravenous iron sucrose. **Materials and Methods:** This prospective study to compare the effects of oral ferrous sulphate and intravenous iron sucrose in pregnant women was carried out between June 2010 to October 2011 among antenatal patients attending OPD of SSG hospital Vadodara. **Result:** A clear increase in hemoglobin was observed in both the groups, arising from 7.87gm/dl to 10.69gm/dl after 3 months in the iv group and from 8.43gm/dl to 9.84gm/dl in the per oral group. The two group showed no difference in the rate of rise in hemoglobin level. (F test was applied , f value >0.05) There was statistical difference in the ferritin levels between two groups (p value <0.05). Iron stores were rapidly replenished in the IV iron sucrose group. There was no statistical difference in the rate of rise in reticulocyte count between the two groups. (p value >0.05). In the IV group only 4 patients developed low grade fever which lasted for one day. In the oral group 80% developed nausea and 4% developed constipation. There was no significant difference in the mean birth weight of oral therapy (2275gm) and in IV therapy group (2384gm). **Conclusion:** I.V iron sucrose compared to oral iron administration is more efficient in rapid replenishment of iron stores. Overall iron sucrose appears to be treatment of choice with no serious side effects.

INTRODUCTION

In India incidence of anemia varies approximately between 40-80%. Among the different types of anemia seen in pregnancy, the Iron deficiency type is the commonest. Maternal mortality & morbidity rates are higher in anaemia. Anaemia is also an indirect contributor to other pregnancy related complications like antepartum or post-partum hemorrhage, preterm labour, PIH etc. Also fetal complications like prematurity, IUGR, perinatal mortality & morbidity are also higher in children born to anemic mothers. The only good thing about anemia is that it is a condition that can be easily diagnosed and has simple and effective treatment.^[1] Iron supplement is the main stay in the treatment of iron deficiency anaemia. Iron can be given orally or parenteral. Oral administration is safest mode of administration as serious complications are least. (0.5%) There is no hematological benefit in giving

parenteral as opposed to oral iron. The majority of women can tolerate the cheaper preparation with no significant side effects. These side effects are shown to be related to quantity administered. If daily dose is reduced to 100 mg, side effects are rare with any preparation. Still some women will have gastric upset & constipation which could be easily overcome by simple measures. Relatively no side effects claimed by generally more expensive slow release preparation has been attributed to very little release of iron in intestines. This means that increased dose may have to be given to cover the requirements & there by further increasing the expense. As majority of women can tolerate cheaper preparation with minimum side effects & in the interest of economy these should be tried first.^[2]

The primary objective of this review is to compare the effect of oral and parenteral iron supplementation for anemia in pregnancy. It compares treatment outcomes between the use of using either IV iron

sucrose in comparison with oral ferrous sulfate for the treatment of iron deficiency anaemia.

Intravenous iron administration with iron sucrose has been available for several years and is routinely used in a number of European countries to treat severe anemia. Iron sucrose has an excellent safety record, unlike older IV formulations such as ferrous dextran, which has been associated with a significant risk of anaphylactoid reactions.

Intravenous iron sucrose can be administered as an infusion in small doses (about 200mg) over a 30-minute time period.

A new IV iron preparation, ferric carboxymaltose, has been recently developed. It provides rapid replacement of iron storage and can be administered in higher single doses of up to 1000mg during a minimum administration time of less than 15 minutes.

Despite its advantages, this treatment option is not readily available as it is currently not FDA approved.

Intravenous iron treatment with iron sucrose is available and is already in use in our hospital free of cost to all the pregnant and postpartum mothers. It is possibly the only therapy near ideal; i.e. maximum benefits with minimum side effects. The above observation led us to study the response and adverse effects of these two modes of iron administration in iron deficiency anaemia in pregnant women.

MATERIALS AND METHODS

The present study consists of 100 cases of iron deficiency anaemia with hemoglobin level between 5 – 10 gm/dl, and pregnancy of 16 – 36 weeks.

Patients attending the antenatal clinic or admitted in obstetrics ward of SSG hospital, Baroda were selected for this prospective study.

The study was carried out between June 2010 to October 2011.

Inclusion Criteria

- HB between 5 to 10 gm/dl
- Gestational age between 16 to 36 weeks.
- Mean corpuscular volume <100fl
- Ferritin <50microgm/l

Exclusion Criteria

- Anaemia not linked to iron deficiency.
- Asthma
- Cirrhosis
- Viral hepatitis
- Multiple pregnancy
- Risk of premature birth
- Suspected acute infection
- Intolerance to iron derivatives.
- Sickle cell disease.

The patients fulfilling the above criteria were selected randomly for this prospective study.

Patients were investigated as follows:

A detailed history according to well-planned proforma was taken.

- A detailed physical examination was done.

- Iron deficiency anaemia was confirmed by laboratory investigations.
- Diagnosis of iron deficiency anaemia was made from history, clinical examination and laboratory investigations.
- Patients were divided at random into two groups according to mode of iron administration.
- Group A: oral iron
- Group B: Intravenous iron
- Group A: This group consisted of 50 patients. They were given oral ferrous sulphate tablets. 200 mg tabs were given two times a day, equivalent to 120 mg of elemental iron daily.

In the intravenous group, the total iron sucrose dose to be administered as calculated from the following formula:

$\text{Weight(kg)} \times (\text{target HB}-\text{Actual HB}) \times 0.24 + 500\text{mg}$
rounding was done to the nearest multiple of 100 mg. Target hemoglobin set as 11 gm/dl patients.

A maximum of 200mg (2 ampoules) was diluted in 200ml normal saline and given over 30 mins. For initial 10 minutes, the infusion was given slowly to see for any hypersensitivity reactions. The total calculated dose was divided and given as 2 ampoules on alternate days

After completion of the total calculated dose, the patient was asked to come for follow up after 3 weeks and 3 months.

The group receiving oral treatment received 120 mg of elemental iron per day. 5 mg of folic acid was given in both the group per day, to prevent an eventual folic acid deficiency.

The two groups were followed up after 3 weeks and after 3 months.

Both groups were monitored both clinically and biologically. On each visit, adverse reactions linked with or likely to be linked with the treatment were identified. All incidents were noted, such as arterial hypotension during injections, tachycardia, hyperthermia, arthralgia, abdominal pain, a sensation of chest tightness, headache, vertigo, digestive problems, skin eruptions, allergic reactions and a strange taste during injection.

On inclusion, the following measurements were recorded: hemoglobin, reticulocyte count, mean corpuscular volume, serum iron, serum ferritin and sickling.

Iron sucrose infusions were administered as an outpatient setting, and all patients were observed for 1 hour after the infusions.

The primary outcome measure: was hemoglobin concentration after 3 weeks and 3 months.

The secondary outcome measures included ferritin levels, the recorded adverse effects and fetal birth weight.

RESULTS

Maximum numbers of patients were in the age group 25-35 years in both the group. Most of the patients came from low socio-economic status in

both the group. 80% of women in oral therapy and 75.5% of IV iron sucrose group were illiterate. Maximum patients were of 26-36 gestational weeks.44% in oral therapy and in iv group 59.1%. Prevalence of anaemia was more among the multigravida. Maximum patients in both the group had hemoglobin level between 8-10gm/dl.

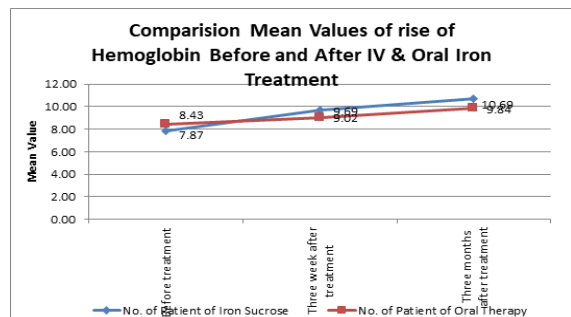


Figure 1: Comparison Mean Values of rise of Hemoglobin Before and After IV & Oral Iron Treatment

There was no difference between the mean rise of hemoglobin between the two groups. F-test was applied and there was no statistical difference between the two groups ($p > 0.05$)

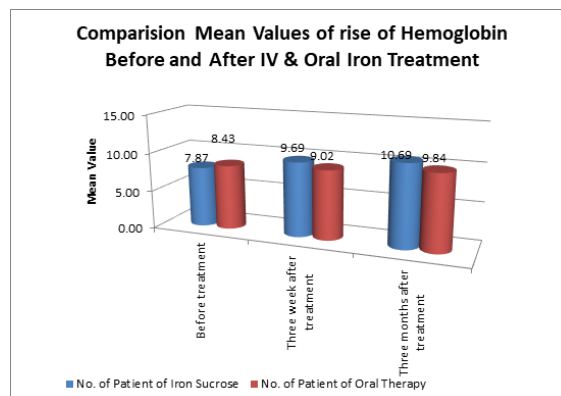


Figure 2: Comparison Mean Values of rise of Hemoglobin Before and After IV & Oral Iron Treatment

Table 1: Distribution of Anaemia

Haemoglobin(gm/dl)	Degree of Anaemia	Oral therapy	IV Therapy
<6	SEVERE	0(0)	5(10.2)
6-8	MODERATE	17(34)	16(32)
8-10	MILD	33(66)	28(57.1)

Majority of the patients were mildly anemic. Only 4 developed minor reaction like low grade fever. None developed major anaphylactic reaction. Majority of the patients had nausea as adverse effect.

Table 2: Distribution of Delivered Patients

Delivery	No. of Patient of Iron Sucrose	%age n=49	No. of Patient of Oral Therapy	%age n=50
Vaginal	37	77.08	38	88.37
LSCS	11	22.92	5	11.63
Total (out of 49)	48	97.96	43	86.00

There was no statistical difference in the birth weight of babies delivered in oral and iv iron sucrose therapy. ($p > 0.05$).

Table 3: Comparison Mean Values of rise of Reticulocyte Count Before and After IV & Oral Iron Treatment

Reticulocyte Count	Patient of Iron Sucrose (n=49)	Patient of Oral Therapy (n=50)
Before treatment	0.77	0.65
Three week after treatment	0.98	0.71
Three months after treatment	1.25	0.98

There was no statistical difference in the rate of rise in reticulocyte count between the oral and iv iron group. ($p > 0.05$).

Table 4: Distribution of Mean Values Of Ferritin Between The Two Groups

Ferritin (mg/l) mean values	Patient of Iron Sucrose (n=49)	Patient of Oral Therapy (n=50)
Before treatment	20.50	14.01
Three week after treatment	61.27	17.56
Three months after treatment	97.23	20.06
F-Test Two Sample for Variance (P-Value)	0.006	

There was statistical difference in the rise of ferritin levels between the two groups. ($p < 0.05$)

Table 5: Distribution of mean values of rise of serum iron between the two groups

Serum Iron mean	No. of Patient of Iron Sucrose	No. of Patient of Oral Therapy
Before treatment	54.56	59.36
Three week after treatment	87.02	64.89
Three months after treatment	112.00	68.29
F-Test Two Sample for Variance (P-Value)	0.024	

Comparison Mean Values of rise of Serum Iron Before and After IV & Oral Iron Treatment.

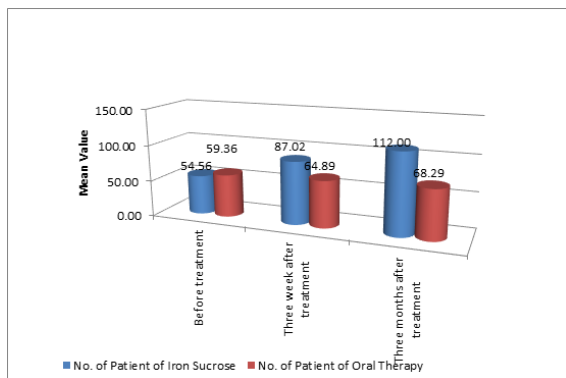


Figure 3: Comparison Mean Values of rise of Serum Iron Before and After IV & Oral Iron Treatment

This table shows that there was statistical difference in the rise of serum iron between the two groups ($p < 0.05$)

DISCUSSION

Iron deficiency anemia during pregnancy is common and deserves special attention because of its potential consequences.

In our study iron sucrose appears to restore iron reserves in case of severe deficiency with a statistical difference at any time of the treatment period. In a similar study, it was a random, prospective open study involving 50 patients with hemoglobin 8-10 gm/dl, Ferritin <50microgm/l.^[3]

There was highly significant difference in ferritin levels between the two groups (oral vs iv sucrose therapy) and no statistical difference in the rise of hemoglobin.

A study conducted by Al, Rapig et al,^[1] it was a randomised study to compare the efficacy of IV iron to oral iron in anemia in pregnancy. In this study 90 women of hemoglobin levels between 8-10.5gm/dl were randomly assigned to receive either oral iron (n=45) or intravenous iron (n=45).

The results showed the change in hemoglobin from baseline was significantly higher in the intravenous group than the oral group at each measurement. Ferritin values were also higher in the intravenous group than the oral group.

Oral iron usually should be given in dose of about 200mg of elemental iron per day. Once iron is started it takes about 6-10 wks for hemoglobin to return to normal level. However in iron deficiency anaemia, iron stores are exhausted and need to be replenished. Replenishment of iron stores begins only after hemoglobin returns to normal. Absorption of iron diminishes after hemoglobin returns to normal and hence replenishing iron stores is a very slow process and takes about 3-4 months. hence iron therapy should be continued for 5-6 months.^[4]

As seen in our study there is rapid replenishment of iron stores in case of iv iron sucrose therapy.

Intravenous iron sucrose was considered occasionally necessary to patients intolerant or

unresponsive to oral iron therapy, non-compliance of the patient or patient near term with severe anaemia.

We agree that oral iron supplement is the ideal way to replace iron stores as it uses the normal body mechanism. But the short coming is the gastrointestinal tracts limited capacity for iron absorption. Only about 2-3mg of elemental iron is absorbed even though 50-100mg are presented to gut lumen. Hence replenishing 1000mg iron deposit may take a long time. Most of the patients fail to comply with such a prolonged oral iron replacement therapy and replacement of stores with oral iron becomes a nearly impossible task.

Intravenous iron sucrose has the potential for eradicating iron deficiency anaemia because it overcomes the problem of compliance and absorption and has an excellent safety record.

Over the last one decade, the efficacy and safety of intravenous iron sucrose therapy has been well studied. The tolerance is excellent and adverse reactions are in frequent.

There were concerns about the release of free iron during iv iron infusions, because the capacity of available apo transferrin to bind the free iron can be exceeded. Free iron is known to increase the toxicity of free radicals and other reactive oxygen products that are normally found in body contributing to oxidative stress.

But according to the study conducted by Van Wyck DB et al, a scientific approach to intravenous iron therapy (2004) reported that regardless of increasing use of intravenous iron, the availability of iron sucrose has eliminated most of the side effects and more importantly, no intravenous iron sucrose compound generated detectable free iron.

Prospective randomized study states that Iron sucrose cannot be given intramuscularly. Also it cannot be given as total dose single day infusion. It can be either administered as slow intravenous bolus of 50 – 100mg 2-3 times in a week, or even as a short infusion of 100-200mg over 2-3 hours once or twice a week. No test dose is indicated and hence there is no black box warning.

Side effects of iron sucrose: serious life-threatening anaphylaxis was around 0.002%, hypersensitivity reactions around 0.005% and mild adverse reactions was up to 35%.

Through infusion of iron sucrose it is possible to eradicate the iron deficiency anaemia which is the most common medical disorder in pregnancy thereby dramatically reducing maternal morbidity and mortality, while improving the quality of life of women in the developing world.^[5]

CONCLUSION

I.V iron sucrose compared to oral iron administration is more efficient in rapid replenishment of iron stores. Overall iron sucrose appears to be treatment of choice with no serious side effects.

REFERENCES

1. Ragip A, Unlubilgin E, Kanderim O, Yalvac S, Cakir L, Haberal . (2005) A. Intravenous versus oral iron treatment of anemia in pregnancy: randomized trial. *Obst Gynecol*
2. Petewusnyk G, Huch R, Huch A, Breymann C. . (2002) Parenteral iron therapy in obstetrics: 8 years experience with iron-sucrose complex. *Br J Nutr*;88:3–10.
3. Breymann C, Major A, Richter C, Huch R, Huch A. Recombinant human erythropoietin and parenteral iron in the treatment of pregnancy anemia: a pilot study. *J Perinat Med* 1995; 23:89-98
4. Santolaya-Forgas J, Vengalil S, Duval J, Gottmann D, Meyer W, Gauthier D, et al. Use of recombinant human erythropoietin (EPO-alfa) in a mother alloimmunized to the Js(b) antigen. *J Matern Fetal Med* 1999;8:141-5.
5. Hercberg S, Galan P, Prual A, Preziosi P. Epidemiology of iron deficiency and iron deficiency anemia in the French population. *Ann Biol Clin* 1998;56:49-52.