

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20183298>

Original Research Article

## Can oral iron tablets be replaced by the intravenous iron sucrose in antenatal period? A new thought

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**Received:** 13 March 2018

**Accepted:** 23 June 2018

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### ABSTRACT

**Background:** Anaemia is the commonest medical disorder that contributes significantly to maternal morbidity and mortality, preterm delivery, intrauterine growth restriction. Pregnant women are particularly vulnerable to anaemia because they have dual iron requirements both for their growth and growth of foetus. A high proportion of women in both industrialized and developing countries become anaemic during pregnancy. Intravenous iron therapy is safe convenient and effective than oral iron therapy in prevention of iron deficiency anaemia when compliance is the problem. The aim of this study is to compare the efficacy, safety and acceptability of intravenous iron Vs oral iron in prevention of iron deficiency anaemia during pregnancy. The objective of the present research was to study the efficacy, safety and acceptability of oral iron (ferrous fumarate) versus intravenous iron (iron sucrose) for the prevention of iron deficiency anaemia during pregnancy.

**Methods:** It was a prospective comparative case control study without blinding including 400 registered antenatal women in SKNMC and GH, Narhe, Pune. Results were based on collection and analysis of data from samples within study population.

**Results:** There was no significant difference in mean haemoglobin rise between oral group and IV group but there is significant difference between mean ferritin levels between oral group and IV group. In IV group ferritin levels at 36 weeks were almost 1.8 times more than oral group. Acceptability and convenience of IV iron was significantly more than oral iron.

**Conclusions:** Intravenous iron therapy in the form of three divided doses, one in each trimester can be safely used in the antenatal woman as an alternative to prophylactic iron tablets for prevention of iron deficiency anaemia especially in women who are non-compliant or does not tolerate oral iron tablets.

**Keywords:** Ferritin, Iron deficiency anaemia, IV iron therapy

### INTRODUCTION

It may not be possible to set up the blood banks in every remote corner of the country, but it is certainly possible to make blood bank in woman's body by building up her haemoglobin. Anaemia is the commonest medical disorder that contributes significantly to maternal morbidity and mortality. The most common cause of anaemia worldwide is iron deficiency, resulting from

prolonged negative iron balance, caused by inadequate dietary iron intake or absorption, increased needs for iron during pregnancy or growth periods, and increased iron losses as a result of menstruation and helminth (intestinal worms) infestation.<sup>1</sup> Anaemia is the commonest haematological disorder that may occur in pregnancy, others being rhesus isoimmunisation and blood coagulation disorders.<sup>2,3</sup>

A high proportion of women in both industrialized and developing countries become anaemic during pregnancy. Estimates from the World Health Organization report that from 35% to 75% (56% on average) of pregnant women in developing countries, and 18% of women from industrialized countries are anaemic.<sup>4</sup> Pregnant women are particularly vulnerable to anaemia because they have dual iron requirements, for their own growth and the growth of the foetus.<sup>5-11</sup>

Currently the standard treatment for prevention of iron deficiency anaemia is oral iron supplementation. However, this is limited by patient non-compliance and gastrointestinal symptoms such as nausea, vomiting, diarrhoea. Absorption of oral iron is influenced by the dosage, the patient's iron storage, the proximity of taking medication relative to mealtime.<sup>12</sup> According to WHO 30 to 60 mg of elemental iron with 0.4 mg of folic acid should be supplied to pregnant women for the prevention of iron deficiency anaemia. According to National nutritional Anaemia control programme pregnant mother should receive 100 mg of elemental iron and 0.5 mg of folic acid every day.<sup>13-15</sup> In the studies conducted later it was found that 70% pregnant women are anaemic as per National Family Health Survey III, and only around 22.4% pregnant women consume 100 iron and folic acid (IFA) tablets during pregnancy according to the District Level Household Survey (DLHS) III, 2007-2008. Increasing consumption of IFA tablets is a big challenge, especially among rural pregnant women who come for antenatal check-up to Auxiliary Nurse Midwife on Village Health Nutrition Day or those visiting government health facilities. Whole host of reasons have contributed to failure of IFA program including partial coverage of population, inadequate dosing of the iron supplement, short supplies, defective absorption, diets which contain high levels of iron chelators, problems with formulation, inadequate consumption or poor compliance by the beneficiaries, failure to replenish the stocks at the beneficiary level and lack of effective health education and supervision.<sup>16-18</sup>

As compliance to oral therapy is very poor and also results are unpredictable, parenteral iron therapy might be better option to treat such patients.

Out of various iron compound available iron sucrose gives better results due to quick binding of iron to transferrin and quick travel to bone marrow resulting in early rise in Hb. Iron sucrose is administered as an IV infusion of 200 mg over 30 min period. Iron sucrose complex is effective because of the rapid removal from the plasma and the availability of iron for erythropoiesis. After a bolus dose of iron sucrose, the plasma peak occurs in 10 minutes. Twenty-four hours after administration, the plasma level is negligible, indicating rapid bone marrow uptake as has been shown by positron emission tomography studies. Studies have shown that 70-97% of the iron is used for erythropoiesis, with only a

4-6% elimination rate.<sup>19</sup> Anaphylactic reactions are virtually unknown with iron sucrose.<sup>20</sup>

Hb levels and serum ferritin values is the current gold standard for checking for IDA. Ferritin is a protein that stores iron and releases iron as needed. It is a representative of iron stores. By the time patient develops iron deficiency anaemia they have already depleted iron storage.<sup>21</sup>

In this study the efficacy, safety and acceptability of oral iron (ferrous fumarate) versus intravenous iron (iron sucrose) is compared for the prevention of iron deficiency anaemia during pregnancy.

## METHODS

It was a prospective case control study. The place of the study was Smt. Kashibai Navale Medical College and General Hospital, Narhe, Pune, Maharashtra.

### Sample size

400 well motivated pregnant women attending antenatal clinic fulfilling the inclusion criterion were selected. Before including detailed history, clinical examination and informed consent was taken. The initial iron status of the patient was assessed by clinical and laboratory examination (Hb, Sr. Ferritin). All these women were registered in the first trimester had Hb  $\geq$ 10 gm%. They were given single dose of 400mg of Albendazole for deworming at 16 weeks and were randomly divided into 2 groups.

### Inclusion criteria

- Pregnant patients with Hemoglobin level of 10gm% or more, registered in the antenatal clinic and ready to give consent were included in the study.

### Exclusion criteria

- Pregnant patients with hematological disorder
- suffering from chronic illness like renal, cardiac, hepatic or immunological disorders
- known hypersensitivity to injectable iron compounds
- Pregnant patients with gestational age less than 12 weeks
- Patients who not given consent or not likely to follow up.

Group A (200 patients) received 100 tablets, each containing 100 mg of ferrous fumarate and 0.5 mg of folic acid starting at 16<sup>th</sup> week. No other iron supplement was given. Compliance was checked by counting remaining tablets in each follow up visit. Nausea, vomiting, constipation was noted.

Group B (200 patients) received total of 1000 mg of intravenous iron sucrose. The dose was divided into three

parts. 1<sup>st</sup> dose of 400 mg was given between 16 to 18 weeks. 2<sup>nd</sup> dose of 400 mg was given between 24 to 26 weeks of pregnancy. Third dose of 200 mg was given in 34<sup>th</sup> weeks of pregnancy. All the doses were given in the OPD in the form of intravenous infusion of 200 mg of iron sucrose diluted in 100ml normal saline over 30 minutes by scalp vein in any of the forearm vein. In case of 400 mg dose, 2 doses were given at the interval of 48 hours. Single observer observed the patient. All emergency drugs were kept ready for management of anaphylactic reaction. Check list was kept for minor and major reactions like myalgia, thrombophlebitis, fever, hypotension, chest pain, breathlessness. Oral 5 mg of folic acid was given to the patients in this group throughout pregnancy. In the follow up Haemoglobin was checked at 20<sup>th</sup>, 28<sup>th</sup> and 36<sup>th</sup> week of pregnancy. Serum Ferritin was repeated at 36<sup>th</sup> week.

Post-test satisfaction questionnaire was given in the form of exit interview from which level of acceptance, convenience and time consumption between the two groups were assessed.

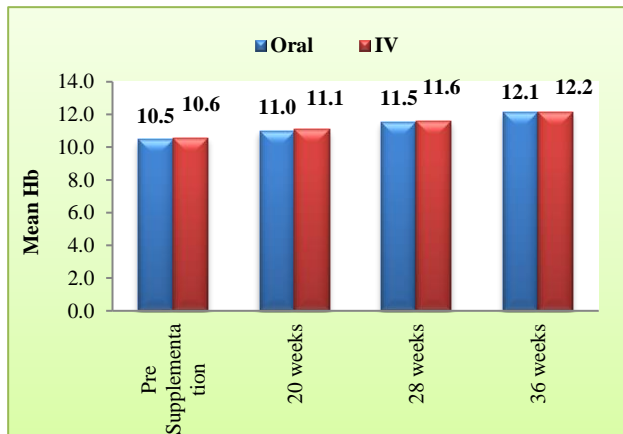
**RESULTS**

In this study 56% patients were primigravida and 46% were multigravida. There was no significant difference between distribution of parity in oral group and IV group (Table 1).

**Table 1: Gravida wise distribution of patients.**

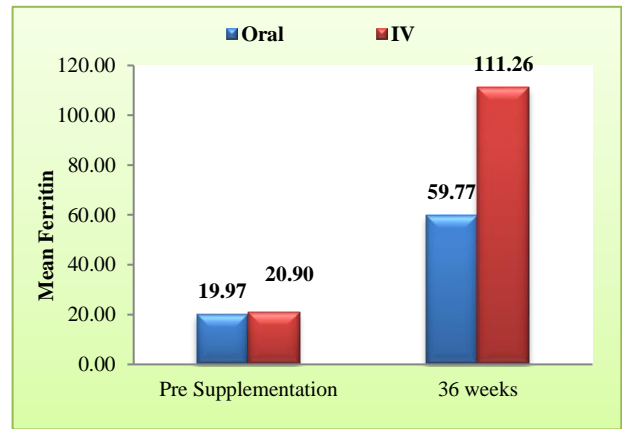
Parity	Treatment group		Total	P-value
	Oral	IV		
Primigravida	109	114	223	0.687
Multigravida	91	86	177	
Total	200	200	400	

Even though the patients included in this study had Haemoglobin level more than 10 gm%, it was seen that the levels of serum ferritin which is indicative of iron storage were less (20.43±0.5 ngm/ml) in them.



**Figure 1: Comparison of haemoglobin levels between both the groups.**

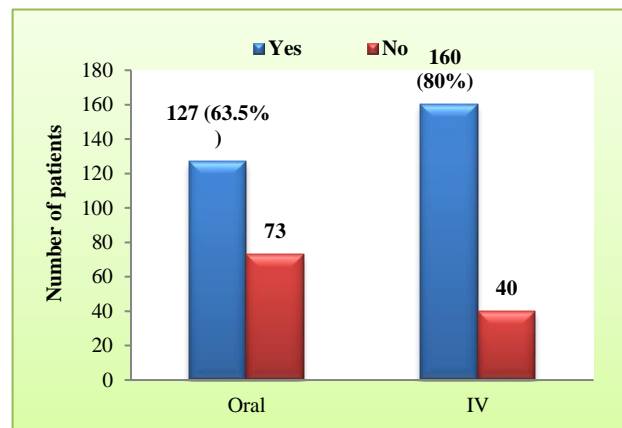
By using 2 independent sample t-test p-value >0.05 therefore there is no significant difference in mean haemoglobin rise between oral group and IV group at different gestational age.



**Figure 2: Comparison of serum ferritin levels between both the groups.**

By using 2 independent sample t-test p-value < 0.05 therefore there is significant difference between mean ferritin levels between oral group and IV group at 36 weeks. Rise in ferritin levels in intravenous group is around 1.8 times more as compared to the rise in oral group at 36 weeks.

Rise in haemoglobin was compared between the oral and IV group at 20 weeks, 28weeks and 36 weeks and it was found that there is no significant difference in mean haemoglobin rise between oral group and IV group (Figure 1) but there was significant difference in mean ferritin levels between oral group and IV group (Figure 2). In IV group serum ferritin levels at 36 weeks were almost 1.8 times more than oral group and it was found to be statistically significant.



**Figure 3: Comparison of convenience in both the groups.**

From the questionnaire given to the patients it was analysed that acceptability and convenience of IV iron

was significantly more than oral iron. Almost 80% patients found the IV method convenient as compared to 63.5% patients in oral group (Figure 3). Also 80% patients in Group B well accepted the IV route of iron as compared to 61.5% in oral group (Figure 4).

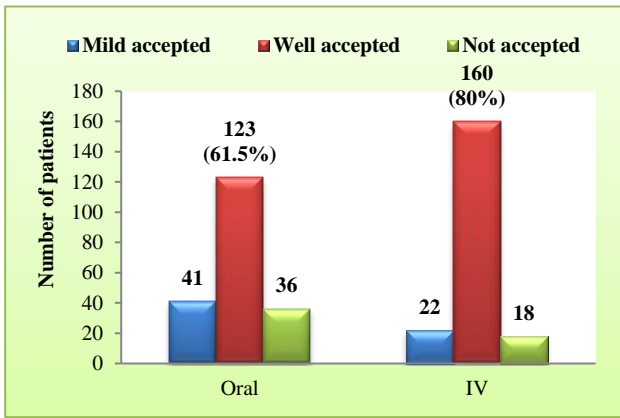


Figure 4: Comparison of level of acceptance between both the groups.

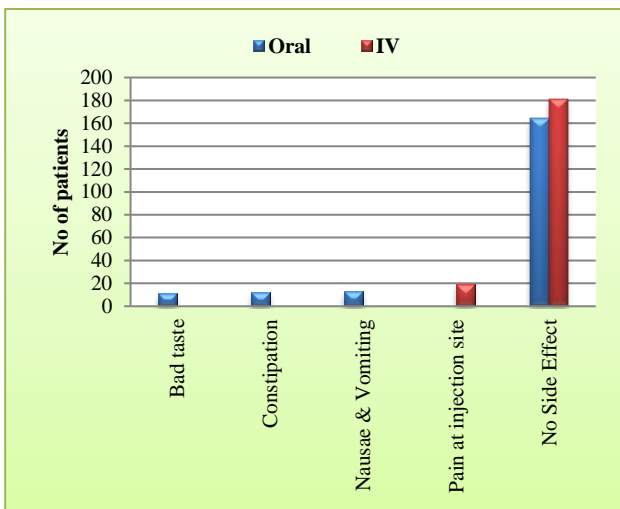


Figure 5: Minor side effects between both the groups.

There was no significant minor or major side effects in both the groups (Figure 5 and 6). There were no episodes of anaphylaxis or hypotensive shock. There were no patient withdrawals and no drug discontinuation caused by drug related adverse events in the intravenous group. Commonest side effect in the intravenous group was pain at IV site (n=19). Other adverse effects were breathlessness (n=1), chest pain (n=1) and fever (n=1).

In the oral group gastrointestinal symptoms were experienced by 36 women. 11 women had complaints of bad metallic taste, 12 suffered from constipation and 13 women had nausea and vomiting. All of them were managed by symptomatic treatment. No women discontinued the drug because of gastrointestinal symptoms. In the IV group 86% patients found injectable

iron treatment is less time consuming as compared to 66% patients in oral group (Figure 7).

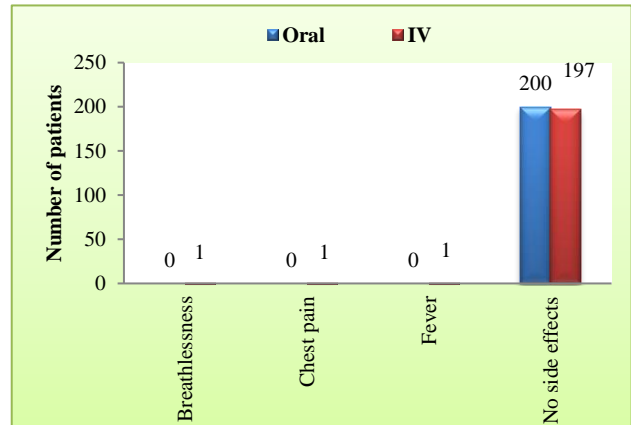


Figure 6: Major adverse effects between both the groups.

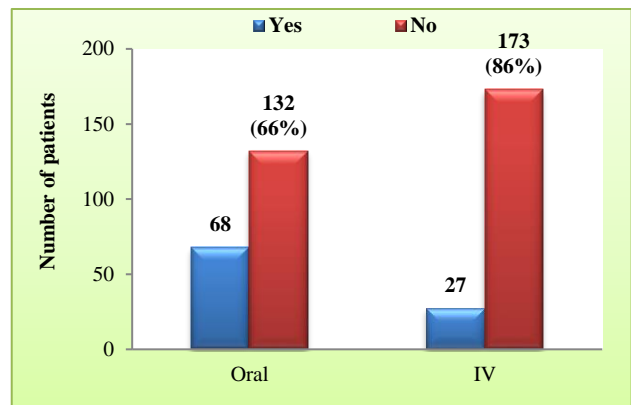


Figure 7: Comparison of time consumption between both the groups.

## DISCUSSION

In present study there was no significant difference in mean haemoglobin rise between oral group and IV group at different gestational age. This was comparable with a study done by Bencaivo et al.<sup>22</sup> Their study assessed and compared the efficacy and safety of intravenous iron sucrose to oral ferrous sulfate. There was a non-significant increase in hemoglobin in the intravenous group but the repleted iron stores (serum ferritin) were significantly higher in IV group than in the oral group. These results were also comparable with a similar study by Neeru et al.<sup>24</sup> In a study by Devasenapathy et al, haemoglobin levels, MCV and PCV at recruitment, 2<sup>nd</sup> and 4<sup>th</sup> week and at term were taken into account.<sup>26</sup> They found that mean difference in haemoglobin at recruitment and at 2<sup>nd</sup> week were significant statistically when 2 groups were compared but the mean differences of MCV and PCV were not significant. In their study improvement of haemoglobin in iron sucrose group was much better than that of oral iron group at 2<sup>nd</sup> week, 4<sup>th</sup> week and at term. This difference in the results with

present study may be because of difference in the study population and differences in the haemoglobin level at the time of enrollment of the patients. In present study patients with Hb  $\geq 10$  gm% in the first trimester were only included in the study.

In a similar study by Al et al intravenous iron sucrose was compared with oral iron polymaltose complex (300 mg elemental iron per day).<sup>27</sup> They found that the change in hemoglobin from baseline was significantly higher in the intravenous group than the oral group at each measurement. Serum ferritin levels were also higher in the intravenous group, than in the oral group at each point of measurement. In the oral group it was  $11 \pm 11$   $\mu\text{g/l}$  compared to  $28 \pm 26$   $\mu\text{g/l}$  in the intravenous group ( $P < 0.001$ ) at the fourth week and  $18.1 \pm 11$   $\mu\text{g/l}$ , compared with  $23.7 \pm 13.8$   $\mu\text{g/l}$  ( $P = 0.04$ ) at birth in oral and intravenous group, respectively. This study is comparable to present study because there was a significant rise in ferritin levels in intravenous group compared to oral group.<sup>27</sup> This study was also comparable with a similar study by Gupta et al.<sup>25</sup> All these old studies showed that there was no significant adverse effect of IV iron sucrose and it can be safely used in pregnant patients for treatment of iron deficiency anaemia.

## CONCLUSION

Present study concluded that intravenous iron therapy is safe. It restores iron levels faster and more effectively than oral iron. There is irrefutable evidence that compared to oral iron, iv iron sucrose results in a much more rapid resolution of iron deficiency anaemia. It is more convenient, well accepted, less time consuming and also achieves optimal results. Majority of women receiving IV iron accepted the mode of treatment well, they found taking IV iron was easier than taking one tablet of oral iron daily thus it circumvents the problems of compliance. The adverse reactions were also minimal, so it can act as a suitable alternative to oral iron in those patients who can not tolerate oral iron therapy.

If all pregnant women receive parenteral iron along with folate therapy, it could be possible to prevent iron deficiency anaemia in pregnant women which will lead to improvement of overall pregnancy outcome. Therefore, Intravenous iron sucrose could be the Holy Grail in the prevention and eradication of IDA in pregnancy in a setting, such as India.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Tate SS, Shirsath AS, Risbud NS. Can oral iron tablets be replaced by the intravenous iron sucrose in antenatal period? A new thought. *Int J Reprod Contracept Obstet Gynecol* 2018;7:3103-8.