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Original Research

A comparative study to evaluate oral iron and intravenous iron sucrose for treatment of anemia in pregnancy in South India

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ABSTRACT:
Introduction: The prevalence of anemia during pregnancy is as high as 80% in some sections of the Indian population. In our study we aim to evaluate the efficacy of intravenous iron sucrose (IVIS) versus oral iron in treating anemia among the antenatal mothers attending a tertiary care center of South India. **Materials and Methods:** One hundred women between 18 and 28 weeks of gestation with diagnosed iron-deficiency anemia and hemoglobin (Hb) of 7–10.9 g/dL were enrolled to be administered either oral ferrous sulfate 200 mg twice daily or requisite dose of IVIS 100 mg in 100 ml normal saline on alternate days. Hb and hematocrit were measured at the time of enrollment, 4th week, and 8th week of therapy. Acceptability of both the drugs based on like and dislike after interviewing the study participants was recorded. Adverse drug reactions, gestational age at delivery, and neonatal birth weight were also noted in both the groups. The results were analyzed by Student's *t*-test and Chi-square test. **Results:** Hb and hematocrit values were found to be increased in both the groups at 4th and 8th weeks. When both the groups were compared, the rise in the values was higher in the iron sucrose group (at 4th week $P = 0.01$ and at 8th week $P = 0.00$). The number of participants who reached target Hb levels at 4 weeks was 41 (82%) with oral iron and 48 (96%) with iron sucrose. In the iron sucrose group, no adverse effects were observed, suggesting its safety, and the acceptability and newborn birth weight were noted to be higher. **Conclusion:** IVIS was found to be more effective than oral iron therapy in treating antenatal anemia with no serious adverse drug reactions.
Keywords: Iron- deficiency anemia, Iron sucrose, Oral iron therapy

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INTRODUCTION

Anemia is the most common medical disorder in pregnancy, being more rampant in the developing countries with varied incidence, etiology, and severity [1]. In India, more than 90% of anemia cases are estimated to be due to iron deficiency, because of vegetarian dietary patterns [2]. The high frequency of iron-deficiency anemia during pregnancy in the developing world has substantial health and economic costs and is of concern and a cause of considerable morbidity and mortality [3].

The second National Family Health Survey-11 in 1998–1999 showed that 54% of rural women of childbearing age were anemic compared with 46% in

urban areas [4]. South Indian state of Kerala had only 23% prevalence of anemia [4].

Treating nutritional anemia in pregnancy with oral iron is staggering due to its associated side effects, resulting in noncompliance for the same. Parenteral iron therapy is therefore considered an alternative for oral iron defaulters, which can also reduce the need for blood transfusion in antenatal period. The present study was aimed at comparing the efficacy and safety of iron sucrose and oral iron for the treatment of iron-deficiency anemia in pregnancy and to know the acceptability of both the therapies among patients in terms of their like and dislike.

MATERIALS AND METHODS

This study was carried out at the Department of Obstetrics and Gynaecology, in a tertiary care center of South India for a period of one year after the institutional ethical committee approval. One hundred consenting women with singleton pregnancy and gestational age between 18 and 28 weeks, with iron-deficiency anemia confirmed by a peripheral smear and Hb of 7–10.9 g/dL, were included in the study. Patients with hematological disease other than iron-deficiency anemia, hypersensitivity to iron, prior blood transfusion in current pregnancy, and anemia in failure and those with multiple pregnancy and obstetrical complications were excluded from the study. Patients included in the study were randomized into two groups of 50 each. The first group (intravenous iron sucrose [IVIS] group) comprised of patients who were given IVIS 100 mg in 100 mL of normal saline on alternate days after a test dose. A minimum dose of 100 mg iron sucrose/day and up to a maximum of 300 mg/week was administered. The following formula was used for the calculation of requisite dose of iron sucrose: Body weight in kg × (target Hb – initial Hb) × 2.4 plus 500 mg [5]. A test dose of 15 ml of iron sucrose infusion was administered slowly and followed by a 15 min halt during which the patient was observed for anaphylactic reactions. If no reactions occurred, the rest of the infusion was administered. The second group (oral group) comprised of patients who were given 200 mg oral ferrous sulfate tablets twice daily each containing 60 mg elemental iron. Both the groups received equal amount of folic acid. The patients were asked to report after 4 and 8 weeks for estimation of Hb and PCV and to inquire about any side effect. Pre- and post-treatment mean values of Hb and PCV were compared individually and between the two groups. The acceptability of both the drugs was assessed based on "like" and "dislike" after interviewing the study participants during follow-up. Adverse effects such as gastrointestinal (nausea, vomiting, constipation, and diarrhea), pruritus, fever, myalgia, hypotension, local extravasation, metallic taste, and anaphylactic reactions were noted. The severity of the adverse reactions was graded based on patient's response as following: mild defined as adverse effect that did not require medical intervention; moderate defined as adverse effect that required medical intervention; and severe defined as adverse effect that required medical intervention and intensive care unit admission. The patients were followed up to their delivery, and the gestational age at the time of delivery and the newborn birth weight were recorded and compared between the two groups. Statistical analysis was carried out using unpaired *t*-test to compare non-nominal parameters (hemoglobin and PCV) between the two groups. Chi-square test was used for binominal variables (side effects), and $P < 0.05$ was considered statistically significant.

RESULTS

The demographic data for both the groups are presented in Table 1. The gestational age, parity, and maternal weight between the two groups were comparable. The mean Hb level (g/dL) and PCV (%) in the two study groups were as follows: Hb: 9.6 ± 0.74 (oral) versus 8.84 ± 0.66 (IVIS) and PCV: 29.56 ± 1.36 (oral) versus 29.73 ± 1.36 (IVIS). As demonstrated in Table 2, there was statistical significance of difference in the mean Hb levels between the two groups at 4 and 8 weeks of treatment. The mean Hb (g/dL) after treatment at 4 weeks was 10.96 ± 0.46 (oral) versus 11.20 ± 0.51 (IVIS) and at 8 weeks it was 12.51 ± 0.47 (oral) versus 12.87 ± 0.41 (IVIS). A statistically significant difference was observed between the two groups after 4 weeks ($P = 0.01$) and 8 weeks ($P = 0.00$) of iron therapy. The mean differences of rise of Hb level (g/dL) in the oral group after 4 and 8 weeks of therapy were 1.6 g/dL and 2.91 g/dL, respectively. However, in the IVIS group, after 4 weeks, Hb rise was 2.12 g/dL; after 8 weeks, it was 4.03 g/dL. The mean difference of rise in PCV (%) after 4 weeks was 3.44% (oral) versus 4.27% (IVIS). After 8 weeks, it was 7.13% (oral) versus 8.59% (IV), thereby demonstrating statistical significance of difference between the two groups with respect to rise in PCV as well. In the present study, it was observed that the number of cases who attained the target Hb level at the end of 4 weeks was 41 (oral) versus 48 (IVIS). It was also observed that side effects occurred only in cases on oral therapy, whereas no adverse reaction was seen in the IVIS group. Among the oral therapy group, 28% of cases had no side effects, whereas the remaining had the following: nausea 16%, vomiting 8%, dyspepsia 16%, constipation 6%, diarrhea 6%, metallic taste 16%, myalgia 2%, and pruritus 2%. Of 36 cases who experienced adverse effects in the oral group, 26 had mild, 10 had moderate, and none had severe adverse effects. It was observed that acceptability for IV therapy was higher than oral therapy based on like and dislike of cases after interviewing them at 4 and 8 weeks. It was noted that 78% of cases who were on oral iron liked the therapy, whereas 86% of cases on IVIS liked the same. However, this difference was not statistically significant as the *P*

value observed was 0.298. The mean gestational age (in weeks) at delivery in the oral group was 37.40 ± 0.65 versus 37.95 ± 0.70 in the IVIS group (P = 0.000). The mean neonatal birth weight (in kg) was 2.67 ± 0.05 (oral) versus 2.79 ± 0.89 (IVIS), thereby demonstrating statistical significance of difference between oral therapy and intravenous therapy based on neonatal outcome (P = 0.00).

Table 1: Demographic profile of the study cases

Parameters	Oral iron group	IVIS group
Mean gestational age (weeks)	25.40±3.73	27.88±1.30
PARITY(%) Primi	33 (66)	32 (64)
G2	13 (26)	11 (22)
G3	4 (8)	7 (14)
Mean maternal weight (kg)	51.25±0.85	52.93±1.06
Mean hemoglobin (g %)	9.6±0.74	8.84±0.66
Mean PCV (%)	29.56±1.36	29.73±1.36

Table 2: Comparison of pre- and post-treatment levels of hemoglobin and packed cell volume

Parameter	Oral iron group	IVIS group
Mean pretreatment Hb (g %)	9.6±0.74	8.84±0.66
Mean Hb at 4 weeks (g %)	10.96±0.46	11.20±0.51
Mean Hb at 8 weeks (g %)	12.51±0.47	12.87±0.41
Mean pretreatment PCV (%)	29.56±1.36	29.73±1.36
Mean PCV at 4 weeks (%)	33±0.9	34±0.6
Mean PCV at 8 weeks (%)	36.69±0.66	38.32±0.85
Number of women achieving target Hb (11 g %) at 4 weeks	41 (82)	48 (96)

DISCUSSION

The total maternal need for extra iron averages close to 800 mg (elemental iron), of which about 300 mg is for the fetus and the placenta and the rest is for maternal hemoglobin mass expansion [6, 7]. Therefore, iron supplementation during pregnancy is recommended universally even in nonanemic women. Supplementation of iron can be done through various methods such as oral iron therapy, parenteral therapy, or blood transfusion. Oral iron is an easy and cost-effective method of iron replenishment; however, it has certain disadvantages [8]. On the other hand, parenteral iron presents as a useful therapeutic option, especially in patients who do not tolerate oral iron, patients who are noncompliant, or patients with proven mal-absorption [9]. Blood transfusion, although an effective and rapid method of iron replenishment, is associated with the risk of transmission of infectious agents such as HBV, HCV, and HIV [10]. In our study we found that there was a greater rise in Hb and PCV levels in the parenteral group as compared to the oral group at the end of 4 and 8 weeks of therapy, respectively. A statistically significant difference was observed between the two groups after 4 (P = 0.01) and 8 weeks (P = 0.00). The mean difference of rise in PCV after 4 weeks in oral was 3.44% and in IVIS was 4.27%. After 8 weeks, rise in PCV was 7.13% (oral) and 8.59% (IVIS), showing a statistical significance of difference between the two groups with respect to rise in PCV percentage among study cases. These findings were similar to that reported by Tripathi and Pradhan, who in their study showed a higher rise in Hb in women receiving parenteral iron sucrose [11]. They demonstrated that the mean increase in total serum iron following iron sucrose was 40.20 ± 5.11 g/dL compared to an increase of 33.56 ± 3.39 g/dL with oral ferrous sulfate, which was statistically highly significant (P < 0.0001). It was also noted that the target Hb taken as 11 mg/dL was achieved by a larger proportion of women belonging to the parenteral iron group. A total of 41 (82%) women in the oral versus 48 (98%) women in the parenteral group reached target Hb level at the end of 4 weeks of therapy. Similar findings were reported by Parmar *et al*., showing that parenterally administered iron sucrose elevated hemoglobin and restored iron stores earlier and also led to the reduction in the rate of blood transfusion rate [12]. Our study also exposed that side effects occurred only in cases on oral therapy, whereas no adverse reaction was seen in the parenteral group. A similar picture was seen in the studies conducted by Dubey *et al*. and Gupta *et al*., where no side effects were reported in the women who received parenteral iron therapy [13,14]. It was observed that acceptability for IV therapy was higher than oral therapy based on like and dislike of cases after inter- viewing them at 4 and 8 weeks. It was noted that 78% of cases who were on oral iron liked the therapy, whereas 86% of cases on IVIS liked the same. Similarly, Neeru *et al*. reported better tolerability for parenteral iron in their study [15].

Another noteworthy finding of our study was the favorable neonatal outcome in terms of birth weight, which was found to be higher in the parenteral therapy group. The mean neonatal birth weight (in kg) was 2.67 ± 0.05 (oral) versus 2.79 ± 0.89 (IVIS), thereby demonstrating statistical significance of difference between oral therapy and intravenous therapy based on neonatal outcome ($P = 0.00$).

CONCLUSION

The present study reveals that parenteral iron therapy is superior in terms of tolerability and correction of anemia when compared to its oral counterpart. It also yields a quicker rise in Hb as well as a higher neonatal birth weight with no adverse effects. This makes parenteral iron a better option to administer to the pregnant women.

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