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Original Research Article

A Comparative Assessment of Efficacy of Intravenous Iron Sucrose (IVIS) Versus Oral Iron in Treating Anemia among the Antenatal Mothers

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Abstract

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**.**

Material & Methods: This study was carried out at the Department of Obstetrics & Gynecology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India over a period of 1year**.** 120 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.

Results: There was statistical significance of difference in the mean Hb levels between the two groups at 4 and 8 weeks of treatment. A statistically significant difference was observed between the two groups after 4 weeks (P = 0.01) and 8 weeks (P = 0.01) of iron therapy. Statistical significance of difference between the two groups with respect to rise in PCV was also observed as well.

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

Introduction

Iron deficiency anemia (IDA) is one of the most widespread of all nutritional deficiencies in pregnancy. Estimates from the World Health Organization (WHO) report that from 35% to 75% of pregnant women in developing countries are anemic. [1]

It is a direct cause of 20% of maternal mortality in India [2] and indirect cause in 20 to 40% of maternal deaths [3]. Anemia interferes with the normal intrauterine growth leading to fetal loss and perinatal deaths. It is associated with increased preterm labor (28%), preeclampsia (31%) and maternal sepsis [4].

Over the past years, various oral, intramuscular and intravenous preparations of iron have been used for correction of IDA (Iron Deficiency Anemia) in pregnant patients [5]. The first choice in the treatment of iron deficiency anemia for almost all patients is oral iron replacement because of its effectiveness, safety, and lower cost [5].

Oral iron is the most commonly prescribed therapy for pregnant women with mild-to-moderate anemia; [6-7] however, compliance to oral iron is poor because of gastrointestinal side-effects. [8-9] In several countries, parenteral iron preparations such as iron dextran, iron sucrose, sodium ferric gluconate, and ferric carboxymaltose are recommended as an alternative treatment modality for pregnant women who fail to respond to oral therapy. [10-11] In cases of severe anemia, blood transfusion remains the mainstay treatment. [9, 11]

Intravenous iron sucrose was initially used for the treatment of refractory anemia in patients with chronic kidney disease after its safety and effectiveness was established by several randomized controlled trials. [12-13] Several small experimental studies in pregnant women have shown improvements in hematological indices with intravenous iron sucrose. [14-19] A Cochrane review [10] of two trials (137 women in total) reported the pooled weighted mean difference in hemoglobin concentration between intravenous iron sucrose and oral iron groups to be 0・60 g/dL (95% CI 0・33–0・87). In another systematic review of six trials (576 women in total),[20]significant increases in hemoglobin concentration (weighted mean difference 0・85 g/dL, 95% CI 0・31–1・39) and ferritin concentration (63・32 ng/mL, 39・46–87・18) were observed in the intravenous group compared with the oral iron group. There were fewer mild adverse events in the intravenous group than in the oral iron group (risk ratio 0・50, 95% CI 0・34–0・73). [20] 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.

Material & Methods:

This study was carried out at the Department of Obstetrics & Gynecology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India over a period of 1year

120 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.

A meticulous clinical examination along with laboratory investigations, i.e., hemoglobin (Hb), packed cell volume (PCV), and peripheral smear, was carried out before recruitment of the patients.

Patients included in the study were randomized into two groups of 60 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 [21]. The target Hb was 11 g/dL. 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), pruritis, 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 nonnominal 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: 9.7 ± 0.79 (oral) versus 8.68 ± 0.70(IVIS) and PCV: 28.61 ± 1.52(oral) versus 28.42 ± 1.81(IVIS). [Table 1]

Table 1: Demographic profile of the study cases

Parameters	Oral iron group [n=60]	IVIS group[n=60]
Mean gestational age (weeks)	25.40±3.73	27.88±1.30
Parity (%)		
Primi	37 (61.6%)	35 (58.3%)
G2	16 (26.6%)	12 (20%)
G3	7 (11.6%)	13 (21.6%)
Mean maternal weight (kg)	51.72 ± 0.88	52.20 ± 1.23
Mean hemoglobin (g %)	9.7 ± 0.79	8.68 ± 0.70
Mean PCV (%)	28.61 ± 1.52	28.42 ± 1.81

PCV: Packed cell volume

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. A statistically significant difference was observed between the two groups after 4 weeks ($P = 0.01$) and 8 weeks ($P = 0.01$) of iron therapy. Statistical significance of difference between the two groups with respect to rise in PCV was also observed 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 51 [85%] (oral) versus 57 [95%] (IVIS). [Table 2]

Table 2: Comparison of study parameters

Parameter	Oral iron group	IVIS group
Mean pretreatment Hb (g %)	9.5 ± 0.80	8.40 ± 0.78
Mean Hb at 4 weeks (g %)	10.90 ± 0.54	11.42 ± 0.64
Mean Hb at 8 weeks (g %)	11.11 ± 0.45	12.21 ± 0.50

Mean pretreatment PCV (%)	27.34 ± 1.69	28.38 ± 1.84
Mean PCV at 4 weeks (%)	32 ± 0.8	33 ± 0.5
Mean PCV at 8 weeks (%)	35.73 ± 0.60	38.54 ± 0.89
Number of women achieving target Hb (11 g %) at 4 weeks	51 (85%)	57 (95%)

Hb: Hemoglobin, PCV: Packed cell volume

Discussion:

In a study in Danish women, daily iron supplements at a dose of 20 mg per day was found to be adequate to cover the iron needs of the neonates because further increases did not affect iron status or clinical outcomes. [22]

Intravenous iron sucrose reduced the requirement of blood transfusion among pregnant women with severe anemia. Although this was a post-hoc subgroup result, this finding has implications for the health system. Blood transfusion is mandated in severe anemia (hemoglobin concentration<5 g/dL any time in pregnancy and <6 g/dL if a woman presents after 36 weeks of gestation). As per the Federation of Obstetric & Gynecological Societies of India 2011 good clinical practice guidelines6 for treatment of severe anemia, blood transfusion is indicated in case of abnormal fetal oxygenation, postpartum anemia with shock, severe acute blood loss following spontaneous delivery or caesarean section, or maternal decompensation resulting from severe anemia during pregnancy. [7]

In a study by Dede et al. [17] in 2004, 50 patients were included in the I.V iron sucrose group (200 mg in 100 ml normal saline daily till total dose was met) and 25 patients were included in oral ferrous sulphate group (300 mg tablet containing 60 mg elemental iron thrice daily). Blood samples were taken to evaluate levels of Hb, serum ferritin, serum iron, CRP (C - reactive protein), MCV (Mean corpuscular volume), and TIBC (Total iron binding capacity) before the start of therapy and at days 7 and 28. It was shown in the study that intravenous iron therapy with an iron sucrose complex significantly increased serum ferritin levels within a short time with fewer adverse effects than oral iron therapy in women with postpartum iron deficiency anemia.

Al Momentet al., observed that the IVIS group achieved significantly higher hemoglobin level (P value ≤ 0.001) in a shorter period (P value ≤ 0.001). [24] In a study done by Al et al., hemoglobin was different for patients in the OI and IVIS groups across time in each individual group as well as at any given point of time. The hemoglobin level was significantly higher in the IVIS group. [25]

Our study also elucidated 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 etal. and Gupta etal., where no side effects were reported in the women who received parenteral iron therapy [26-28].

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. Similarly, Neeru et al. reported better tolerability for parenteral iron in their study [14].

Conclusion:

IVIS was found to be more effective than oral iron therapy in treating antenatal anemia with no serious adverse drug reactions. Intravenous iron sucrose can be viewed as an alternative treatment for severe anemia in pregnant women as part of the national programme in India and other similar settings. It is already in use

by many practitioners in both public and private sectors, for all categories of anemia, albeit with no defined protocol. Therefore, introduction of this intervention in health programmes will not be a gross deviance from the current practice.

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