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Original Research Article

Intravenous verses oral iron supplementation for anaemia of pregnancy in the arid region of Western India: a retrospective cohort study

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ABSTRACT

Background: India has a high prevalence of anemia in pregnant females, resulting greater risk of blood transfusion and its associated complications during the peripartum period. Administration of intravenous iron sucrose may reduce such a risk. Due to a greater prevalence in western arid region of India, this study was planned to compare efficacy and safety of intravenous iron sucrose and oral ferrous ascorbate in the treatment of iron deficiency anemia of pregnancy in a community health center of rural Jodhpur.
Methods: A retrospective cohort study was conducted in Community Health Center of Jodhpur to review the heamoglobin values of pregnant females in 28 to 37 weeks of gestation, treated with either intravenous iron sucrose or oral iron ascorbate. Cohorts were matched based on parity and age, and the hemoglobin values after 2, 4 and 6 weeks of start of therapy were compared using independent t-test.
Results: Of the 152 pregnant females' records included in the study, 82 were provided intravenous therapy and 70 were given oral iron therapy. Both the modes of administration showed marked increase in heamoglobin values, with statistically more significant rise through parenteral route at each point of measurement. Overall change in mean heamoglobin was 2.43 g/dl through iv route and 0.61 g/dl through oral route ($p<0.001$). Adverse events following therapy were reported by 9 females from intravenous group and 31 women from oral group.
Conclusions: The study provided evidence that parenterally administered iron sucrose elevated hemoglobin and restored iron stores better than oral ferrous ascorbate with lesser adverse reactions.

Keywords: Pregnancy, Peripartum period, Anemia, Iron sucrose, Ferrous ascorbate, Western India

INTRODUCTION

The WHO defines anemia in pregnancy as hemoglobin concentration below the 11 g/dl.[1] Across the world, it is considered to be one of the leading causes of disability and is thus a serious global public health issue.[2] While the prevalence of anemia in pregnancy varies considerably because of the different difference in social-economic conditions, lifestyles and health seeking behaviors, across the world, it inadvertently affects all pregnant women ranging from 23% in the developed world to a staggering 52 % in developing countries.[3,4] Some of the common causes of anemia include poor nutrition, iron and micronutrients deficiency, malaria, schistosomiasis, HIV infection and hemoglobinopathies. Amongst these, iron deficiency is the major cause of anemia followed by folate deficiency.[2,4,5] The high prevalence of iron and other micronutrients deficiency among women in developing

countries is a cause of considerable perinatal morbidity and mortality.[6] As per the WHO estimates South Asian countries have a much higher prevalence in comparison to other countries, amongst which, with a contribution of 80% of the maternal deaths due to anemia, India holds the highest country specific prevalence.[7,8] According to the National Family Health Survey (2005-2006) incidence of anemia in pregnant women in India is 54.6% in urban and 59% in rural areas.[4,9]

Almost a thousand severely affected young women are reported to die every week because of inability to cope with the stress of childbirth.[10] Anemia is associated with an increased need of blood transfusion and its risks during the peripartum period and iron therapy before delivery may reduce the transfusion rate for iron deficient women.[11] Iron sucrose preferred for the intravenous administrations has iron similar in structure to that of physiologically occurring ferritin.[12,13] Further, due to a large molecule size, its renal elimination is prohibited. It is a stable complex that does not release ionic iron under physiological conditions. Due to the absence of dextran, chances of anaphylaxis are also negligible. With a terminal half-life of approximately 5-6 h, the molecule is readily cleared from the serum and this rate of iron delivery to marrow is a determining factor in regulation of marrow proliferation. Thus, it is more rapidly available for erythropoiesis.[14,15]

Ferrous ascorbate iron salt is the drug of choice for oral administration. The molecule has the highest bio-availability in the range of 26.4-50.4% due to prevention of formation of insoluble and unabsorbable forms of iron by the salt.[8,16] Thus, more mineral is available in ferric state, required for uptake by duodenal and proximal mucosal cells of the small intestine.[17]

Previous studies have shown a greater prevalence of micronutrient deficiency and related disorders in western arid regions of India than the national average.[18,19] The aim of the study was to compare the efficacy and safety of intravenous iron sucrose and oral ferrous ascorbate in the treatment of iron deficiency anemia of pregnancy amongst females attending a rural community health center of rural Jodhpur.

METHODS

A retrospective cohort study was designed to include pregnant females attending the antenatal clinic of Community Health Center of Jodhpur (rural). The females in 28 to 37 weeks of gestation and with established iron deficiency anemia (hemoglobin levels between 6 and 10 g/dl) attending the clinic between March and September 2017 were included in the study.

Females with anemia due to causes other than iron deficiency, multiple pregnancies, previous blood transfusion and history of hematological disease were excluded from the study. Cohorts of women were developed based ongoing treatment with intravenous iron sucrose intake or oral ferrous ascorbate supplementation while matching key characteristics such as parity (1) and age (20-27 years). Heamoglobin values were from the available hospital records were reviewed at 2, 4 and 6 weeks of the administration and the results were analysed using independent t-test. Additionally, information about incidences of adverse drug reactions were also gathered from the available hospital records and compared for the two modes of iron administration. Independent t-test was used to compare mean heamoglobin values of both cohorts at 2-, 4- and 6-weeks using SPSSv23 and p value less than 0.05 was considered statistically significant.

RESULTS

A total of 152 pregnant women with iron deficiency anemia meeting the inclusion criteria of the study visited the antenatal clinic of identified CHC during the study period. Amongst these, 82 patients were found to be administered intravenous iron sucrose and 70 patients were administered oral ferrous ascorbate. The mean age of all the females was 23.6 years (SD=1.51), with the mean age of 23.3 years (SD=1.50) in intravenous group and 23.9 years (SD=1.47) in the oral group (Table 1).

It was observed that in each intravenous infusion the maximum total dose administered was 200 mg elemental iron in 100 ml of normal saline infused over 20-30 min, given on alternate days. Each ampoule was of 2.5 ml containing 50 mg of elemental iron, diluted with normal saline immediately before the infusion. Treatment was completed after administration of the calculated dose. Additional iron was not administered.

In the oral administration, women were instructed to take two tablets (ferrous ascorbate with 100 mg of elemental iron per day with 1.1 mg of folic acid) twice daily throughout the pregnancy either empty stomach or 2 h before or after their meals. The tablets were counted back during the follow ups visits to ensure compliance.

Weekly laboratory evaluation was performed by the health center staff along with CBC and peripheral smear, however, Hb values after 2, 4, and 6 weeks from start of therapy were recorded and analyzed for the study objectives.

An increase in hemoglobin was observed from baseline to 6 weeks in both the groups, however the overall increase in mean hemoglobin values in intravenous iron sucrose group was more than oral ferrous ascorbate group at each point of measurement ($p<0.001$) (Table 2 and Figure 1).

The difference in hemoglobin values from baseline in the intravenous group was 1.72±0.484 (g/dl) at 2 weeks, 2.18±0.865 (g/dl) at 4 weeks, 2.89±0.5989 (g/dl) at 6 weeks compared to oral iron, which is 0.5750±0.456 (g/dl) at 2 weeks, 1.39±0.4402 (g/dl) at 4 weeks, and 1.9±0.3020 (g/dl) at 6 weeks. On comparison of the mean in all the three scenarios using independent t-tests the p

value obtained was less than 0.001, indicating a high statistical significance. Moreover, the change in mean heamoglobin from baseline to 6 weeks after intravenous and oral therapy was found to be 1.82 g/dl which shows that the increase in hemoglobin levels was more in the intravenous group in comparison to the oral group. Upon exploration of episodes of adverse reactions, no episodes of anaphylaxis or hypotensive shock were reported by the pregnant women during the course of treatment as per the hospital records. Minor events such as hot flushes (2), arthralgia (1), dizziness (1) and nausea (5) were reported by the women getting intravenous therapy; while in the oral group, gastric disturbances were experienced by 31 women. Amongst these, 20 women had upper gastrointestinal symptoms including pyrosis (15), nausea (8) and vomiting (4), while 5 women suffered from diarrhea. The adverse events were managed by symptomatic treatment by the hospital staff and no reports of women discontinuing the therapy were found.

Table 1: Age distribution of the study participants

Cohort	Number	Mean age (years)	SD
Intravenous group	82	23.3	1.50
Oral group	70	23.9	1.47
Total	152	23.6	1.51

Table 2: Heamoglobin values before and after administration of oral and intravenous iron.

Parameters	Intravenous group	Oral group	P value
Mean heamoglobin baseline (g/dl)	7.10	7.92	
Mean heamoglobin 2 weeks (g/dl)	7.79	8.21	0.006
Mean heamoglobin 4 weeks (g/dl)	8.54	8.42	0.033
Mean heamoglobin 6 weeks (g/dl)	9.43	8.52	0.000
Change in mean (g/dl)	2.43	0.61	0.000

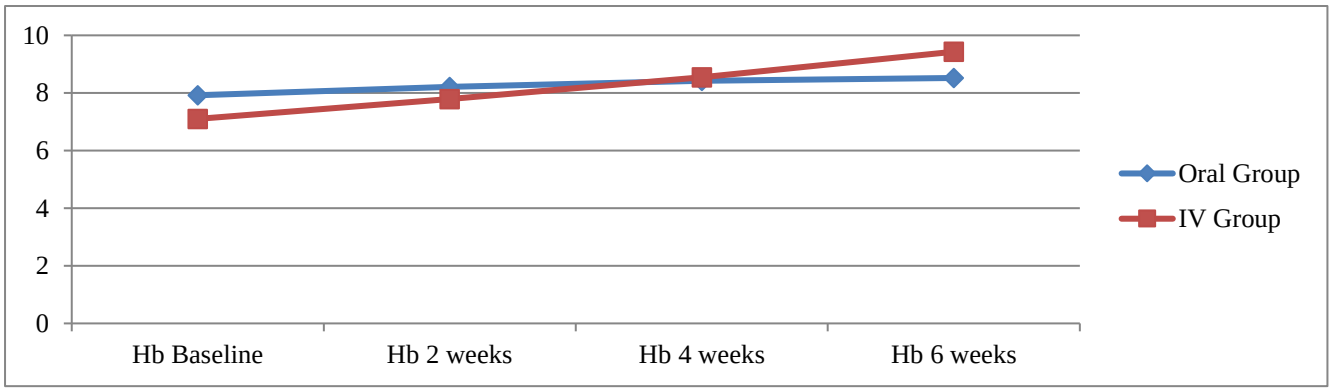

Figure 1: Trend in change of mean heamoglobin values due to oral and intravenous iron supplementation over the course of 6 weeks of therapy.

DISCUSSION

The study results asserted that the rise in heamoglobin levels were significantly more upon administration of intravenous iron sucrose. Numerous such studies have been conducted in various parts of the world; however, this study is first of its kind to be conducted in the Western Rajasthan region, which comes with it's own set of challenges, being the gateway to Thar Desert region. However, despite poor iron intake as described by Ruchi et al, the findings were found to be generalizable in context to the regional population.[19]

Similar findings in context to heamoglobin increase and iron uptake were described in other studies conducted by Shafi et al, Momen et al and Bayoumeu et al involving administration of intravenous iron sucrose and oral ferrous sulfate.[7,20,21] However, the study findings deviate from the findings of Bencaivo et al while assessing the efficacy and safety of intravenous iron sucrose to oral ferrous sulfate, in which, the though ferritin levels were significantly raised, increase in hemoglobin in the intravenous group was found to be non-significant.[22]

Another significant finding of the study was decreased incidence of adverse events in cohort getting intravenous therapy than in the cohort with oral iron therapy. Similar findings were described in a systematic review conducted by Bonovas et al and Rizvi et al while intravenous iron was suggested as an attractive and safe option for patients unable to tolerate oral iron by Loughery et al.[23-25]

Since the present study was a hospital-based study, further studies are needed involving more healthcare centres for

establishing greater generalisability and validity of findings.

CONCLUSION

The study provided evidence that parenterally administered iron sucrose elevated hemoglobin and restored iron stores and produces a more rapid increase in hemoglobin concentration, better than oral ferrous ascorbate with lesser adverse reactions even in the harsh climatic conditions associated with arid regions. Thus, intravenous iron sucrose can be considered as an effective alternative to oral ferrous ascorbate in the treatment of iron deficiency anemia of pregnancy.

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

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