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Study of efficacy and compliance of iron sucrose in iron deficiency anaemia in pregnancy

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Abstract
A prospective study conducted at Apollo Medical College & Hospital to study the intravenous iron sucrose efficacy in moderate iron deficiency anemia in pregnancy in patients between 14-34 weeks of gestational age.100 patients with moderate iron deficiency anemia with hemoglobin between 7 -10 gm/dl and serum ferritin less than 15mg/ltand peripheral blood picture showing microcytic hypochromic anemia were included in the current study. Majority patients were multiparous with a mean age of 22.9 years and gestational period of 30-34weeks. 60% were vegetarians and 40% non -vegetarians in the present study. Out of100 patients, 70% were from rural area whereas 30% were from urban area. In the present study the mean change of pre-treatment and post- treatment heamoglobin level is found to be 1.6460 which is statistically significant. The median of pre-treatment and post treatment serum ferritin level is found to be 132.2680 which is statistically significant. Largely Iron sucrose can be a treatment of choice with no serious side effects and is indicated for correction of anemia in pregnancy or restoring maternal iron stores. Hence intravenous iron sucrose treatment will certainly help to reduce risk of homologous blood transfusions and correction of anemia.

Keywords: IDA- Iron Deficiency Anemia
APH - Antepartum Hemorrhage
HB - Hemoglobin
MEH - Mean Corpuscular hemoglobin
MCHC - Mean Corpuscular hemoglobin concentration
MCV - Mean Corpuscular Volume
PCV - Packed Cell Volume
TIBC - Total Iron Binding capacity
ISC - Iron Sucrose Complex
IPC - Iron Polymaltose Complex

Introduction
Iron deficiency anemia in pregnancy is the most common problem in developing nations. About 70% of the pregnant women in south East Asian region suffer from nutritional anemia which is mainly caused by iron deficiency. Anemia effects the lives of people either directly or indirectly, severe anemia may lead to cardiac failure, infections, post-partum hemorrhage, pre-term labor, puerperal sepsis. Pregnancy leads to tremendous changes in hematological system and physiological changes including anemia. According to WHO 500,000 maternal deaths per year and 20,000,000 morbidity cases are attributed to anemia. The prevalence of iron deficiency anemia in pregnancy in developing countries is 56%(range 35-75%)and in developing countries it is 18% whereas prevalence of anemia is low socio-economic group in first, second and third trimester is 9%, 14% and 37% respectively.

Pregnancy is well known to increase oxidative stress, Anemia causes oxidative stress due to inadequate tissue oxygen supply and thus causes intra uterine growth retardation, preterm labor, preeclampsia, maternal sepsis, low birth weight babies, neonatal anemia, and it is also associated with poor APGAR scores and impaired neurological development of the babies. Although oral iron supplementation is given during pregnancy, not all patients respond adequately to oral iron therapy, as it has several side effects like gastrointestinal discomforts thus lead to poor compliance and poor efficacy. Whereas the blood transfusion remains a last resort due to patient choice of accepting it and is also associated with risks of transfusion reactions, mismatched transfusions, infections particularly Hepatitis, HIV, and transfusion related lung injury. Thus the need for parenteral administration intra venous iron sucrose offered and showed better

compliance and tolerance, high efficacy and safety profile. Intravenous iron can be used for rapid repletion of iron stores and correction of anemia during pregnancy.

Objective: To study efficacy of intravenous iron sucrose in moderate iron deficiency anemia (7-10 gm/dl) in pregnancy between 14-34 weeks of gestational age.

Material and methods

Study population: 100 pregnant women with moderate anemia between 14-34 weeks of gestational age, attending OPD in Apollo Medical College and Hospital during period of February 2020- May 2021.

Inclusion criteria: All cases of moderate iron deficiency anemia in pregnancy who met the following diagnostic criteria: Hemoglobin between 7-10gm/dl, Serum ferritin less than 15ug/lt, peripheral blood picture showing microcytic hypochromic anemia.

Exclusion criteria: Pregnancy with history of eczema, asthmaorother atopic allergy. Women in the first trimester of pregnancy with known hypersensitivity to Iron sucrose. Anemia not attributable to iron deficiency.

Study method: Pregnant women in the age group of 18-30 years attending the antenatal clinic were screened for anemia. Detailed history was taken about the geographical place and diet pattern. These women were subjected to following tests**:** Complete hemogram, peripheral blood smear, complete urine examination, stool for occult blood and ova cyst, Serum ferritin, Serum Iron, TIBC. 400mg intravenous Iron sucrose in two divided doses was used for treatment on these women in outpatient basis. Oral Iron was stopped 3 days prior to infusion. Iron sucrose was administered over 20minsafter dilution with isotonic saline solution and patients were monitored for an hour for any adverse reactions. As the aim of the study is to response of uniform dose over a range of pre treatment hemoglobin, optimal dose of Iron sucrose was not calculated and patient was called after 1 month and repeat hemoglobin and ferritin level was assessed for improvement i.e. drug efficacy.

Results

The present study was carried out in Department of Obstetrics and Gynecology, Apollo Medical College and Hospital, Chittoor.

The age distribution was as per Table 1 and the mean age of the patients who were involved in the study is 22.9000 as per Table 2.

Table 1: Age Distribution

Age	Frequency	Percent
18-21	30	30
22-24	42	42
25-30	28	28
Total	100	100

Table 2: Maximum, Minimumand Mean age in Cases

	Frequency	Minimum	Maximum	Mean	Standard deviation
Age of years	100	18.00	28.00	22.9000	2.63609

About 26%patients are primi, 46% are second gravida, 24% are third gravida and 4% are fourth gravid (Details in Table 3)

Chi Square=17.68

P value =0.001 which is significant

Table 3: Distribution of parity

Parity	Frequency	Percent
G1	26	26
G2	46	46
G3	24	24
G4	4	4
Total	100	100

Dietary history is presented in the following Table 4.

Table 4: Dietary History

Diet	Frequency	Percent
Vegetarian	60	60
Non vegetarian	40	40

Chi square =2.00

P value =0.157 which is not significant

Discussion

Anemia can be identified by measurement of serum hemoglobin concentration or hematocrit which are the primary screening lists. Measurement of the serum ferritin levels has highest sensitivity and specificity for diagnosing iron deficiency anemia. Levels< 10-15ug/l confirms iron deficiency anemia.

Iron deficiency anemia in pregnancy is the major problem throughout the world ranging from 15% pregnant women in developed countries to an average of 56% in developing countries. Although oral iron supplementation is the first line treatment for anemia due to its poor patient compliance and poor absorption leading to severe gastro intestinal side effects, it remained a challenge to increase the iron restores and in correction of anemia efficiently. 58%of pregnant women in India are anemic and anemia is the underlying cause of 20-40% of maternal deaths in India and 80% in South America.

For pregnant women requires 100 mg of elemental iron and 500 mcg of folic acid daily for 100 days. For treating mild anemia 200 mg elemental iron per day is required.

Treatment of mild anemia in pregnancy with intravenous iron sucrose increases the safety and efficacy. Parenteral iron therapy would be a good substitute to oral iron therapy in treating mild anemia in pregnancy and postpartum period. Though parental iron therapy previously had many adverse reactions on patient the recent change of molecules like intravenous sucrose, ferric gluconate had decreased the adverse reactions and increased the efficacy.

Treatment of anemia in pregnancy and postpartum period using iron sucrose is safe and feasible with high patient compliance (Tan and site, 2008). The safety and efficacy of intravenous sucrose had been demonstrated in many clinical trials and thus it is safe and cost effective with high patient compliance for restoration of body iron stores and hemoglobin.

The iron sucrose is well tolerated and has got the least antigenic reactions as it is a polynuclear iron III complex analogous to ferritin with apoferritin replaced by sucrose.

Following intravenous administration, intravenous sucrose is

dissociated into iron and sucrose. The sucrose component is mainly eliminated by urinary excretion. The iron is transported as a complex with transferrin to target cells including erthyroid precursor cells. The iron in precursor cells is incorporated into the hemoglobin as the cells mature in to red blood cells.

In the present study intravenous iron sucrose injections given to 100 pregnant women with hemoglobin <9gm/dl are reported. Those women on average required 1800mg of Iron Sucrose which translates into 18 IV injections (each containing 100mg of elemental Iron). Their response in terms of improvement in serum Iron, ferritin and hemoglobin levels was satisfactory. There were minor side effects and in one case thrombophlebitis.

Hemoglobin baseline change was significantly higher in the intravenous group than the oral. During each measurement, the changes with respect to subsequent hemoglobin were significantly higher on 14 and 28 days. Pregnant patients receiving intravenous Iron throughout the pregnancy has higher Ferritin values. Serious adverse reactions were not observed.

A random prospective open study with individual benefit was performed involving 50 patients with hemoglobin levels between 8 and 10ug/dl and a ferritin value of<50ug/l conducted by Francoise Bayoumeu, MD, Carole subiran-buisset, MD, Anour-eddine baka, MD, a *et al*. an increase in hemoglobin was observed, rising from 9.6-+ 0.79g/dL to 11.11+_1.3 g/dl on day 30. Their study concluded that iron sucrose appears to be a treatment without serious side effects indicated in correction of pregnancy anemia or iron stores depletion similar to the results of this study (Amjobstetgynecol 2002; 186; 518-22).The Cochrane review for iron deficiency anemia in pregnancy shows that iron sucrose had minor adverse effects including a metallic taste, flushing of the face and pain at injection site occurred in 0.5 percent of cases. The high tolerance of drug has been partly attributed to slow release of iron complex and also due to low allergenicity of sucrose.

In a prospective cohort study on effectiveness, safety and feasibility of the intravenous iron sucrose in antenatal anemic women, Shrivastava included all women with hemoglobin of 6-8 gm% from 20 weeks to 48 hours postpartum. They studied hemoglobin PCV, MCV, MCHC on days 1,7,14 and 21. This study concluded iron sucrose elevates hemoglobin and iron stores faster. Iron sucrose also decreased the need for the blood transfusion in the peripartum period.

In the present study hemoglobin and ferritin levels are used to monitor the response of hemopoietic system to iron sucrose because of their relative importance in the hemodynamics of the pregnant woman. Though bone marrow study is gold standard for iron deficiency anemia, it is invasive and impractical to use in pregnancy. Due to hemodilution in pregnancy there is a decrease in hemoglobin, hematocrit and red blood cell count but MCV remains unaffected. Accordingly, serial monitoring is useful in differentiating dilutional anemia from progressive iron deficiency anemia. Serum ferritin is most sensitive and specific test though its level initially rises and later gradually falls to about 50% of pre pregnancy level by late second trimester, currently low serum ferritin levels are regarded as the best for confirmation of iron deficiency anemia. In second and third trimester serum ferritin level drastically falls because of hemodilution effect.

In the present study, iron sucrose efficacy has been observed after giving fixed dose of 400 mg of iron sucrose infusion, so the mean increase in hemoglobin was 1.6460 gm/dl, compared to study by Vandana S *et al*. infused 600 mg of iron sucrose in their study and observed an increase of hemoglobin 2.446 gm/dl.

In the present study the increase in the mean hemoglobin is 1.6460 which is compared to the studies by David B *et al*. observed a rise of 2g/dl Deepthi Shrivastava *et al*. study (2.3g/dl), Avantika Gupta *et al*. study (1.4 g/dl).

In this present study, the mean rise in Hemoglobin levels was 1.6460gm/dl which is compared with studies by Breymann C etal had seen a rise of 1.7 gm/dl. Ragip *et al*. had seen a rise of 1.2 gm/dl, Kriplani *et al*. 2.27gm/dl and Gupta *et al*. had seen a rise of 2gm/dl. The observed finding almost correlated with findings of the studies of Dewen Bhupesh *et al*. (2.2gm/dl), Lakshmi *et al*. (2 gm/dl), Hallak M *et al*. (2.3gm/dl).There is difference when compared to few studies, in this present study the rise of mean hemoglobin showed the study of efficiency after fixed dose of 400mg of iron sucrose therapy as in the Table 5.

Table 5: Comparison of rise in mean Hb of different studies

Study	Rise in mean Hb
Divakar H *et al*.	1.31gm /dl
T.Mays and Mays	1.9gm /dl
Shafi *et al*.	2.1gm /dl
Ragip *et al*.	1.2gm /dl
Kriplani *et al*.	1.27gm /dl
Dewanbhupesh *et al*.	2.2gm /dl
Lakshmi *et al*.	2 gm /dl
Hallak M *et al*.	2.3gm /dl
Gupta *et al*.	2gm /dl
Breymann C *et al*.	1.7gm /dl
Present Study	1.6460gm/.dl

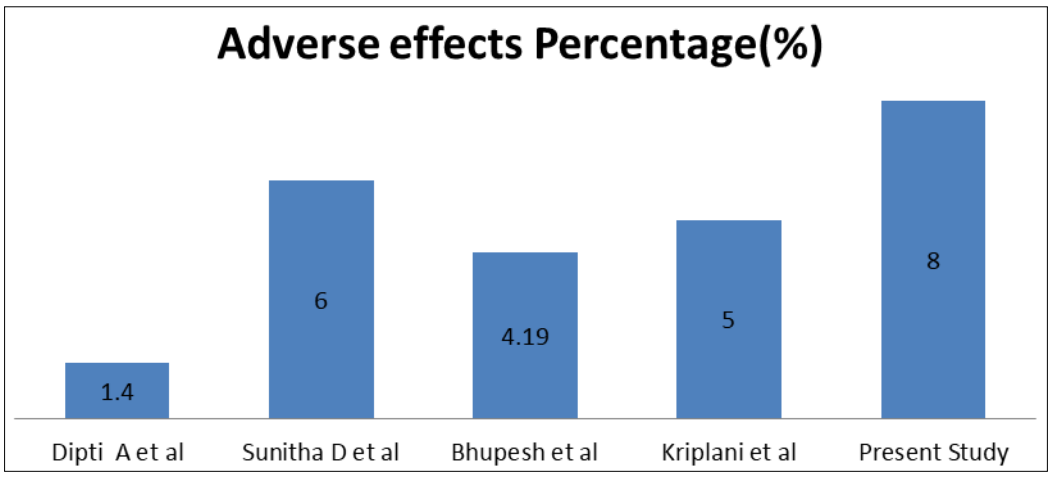
Increased incidence of thrombosis (9/41, 22%) has been reported with a single intravenous iron sucrose. Infusion associated thrombosis was not observed when 6 small doses of intravenous iron sucrose was administered over a three-week period, 45 pregnant women were administered intravenous iron sucrose in 5 daily doses and they also tolerated well.

RaheelaFarhat, MahnaazRoohi *et al*. reported that intravenous group achieved a increased hemoglobin level in a shorter period and no major side effects observed whereas (80%) of patients in oral iron therapy developed gastrointestinal symptoms. So, intravenous iron sucrose is safe and effective in treatment of iron deficiency anemia during pregnancy.

In the study done by Bhndal N (2006), there were no serious adverse effects reported, but 23% of them complained of metallic taste during infusion. 18% of them had facial flushing and pain at the injection site. Percentage of adverse effects of Iron sucrose is shown in Table 6 and graphical comparison with other studies is shown in Graph 1.

Table 6: Showing the percentage of adverse effects of Iron Sucrose in different studies

Studies	Adverse effects in percentage (%)
Dipti A *et al*.	1.4%
Sunitha D *et al*.	6%
Bhupesh *et al*.	4.19%
Kriplani *et al*.	5%
Present Study	8%



Graph 1: Comparison of adverse effects with other studies

In the present study about 26% of cases are Gravida1, 46% of cases are Gravida 2, 24% of cases are Gravida 3,4% of cases are Gravida 4.

Majority of the patients were multipara (77%). In the study by Khurshid R *et al*. shows comparable results as the present study. This shows that multiparity is an important etiological factor in iron deficiency anemia. Repeated short interval pregnancies predisposes the pregnant woman to suffer from iron deficiency anemia as increased demand in pregnancy is not met with the supply due to faulty dietary habits.

A total dose of therapy with the iron sucrose complex (inclusive of storage) costs between Rupees 2500/- to 6000/-.In country like India the majority of the pregnant women suffering from iron deficiency anemia belong to middle to lower socioeconomic status and to purchase a complete dose of parenteral iron therapy is an economic burden for them. However, the present study showed that the increase in all laboratory parameters was significant after the fixed dose of 400 mg of iron sucrose therapy.

Though intravenous Iron sucrose increased serum ferritin significantly, patients were not followed up in the post natal period to find out whether hemoglobin levels were maintained during lactation. Serum ferritin was not repeated at the end of pregnancy nor during the post natal check-up to see how long the stores last and this was limitation to this study.

Conclusion

Iron deficiency anemia is a major problem in pregnancy. Though it was treated with oral iron supplements or blood transfusion or both it has many drawbacks like noncompliance and gastrointestinal side effects, whereas blood transfusions have transfusion reaction, immunologic impact and risk of infections. As anemia is concomitant with increased maternal mortality & morbidity, during pregnancy for treatment of iron deficiency the modern alternate is to treat with intravenous iron because it is well tolerated &restores iron stores rapidly which is effective and safe.

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