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Iron prophylaxis in pregnancy – intravenous versus oral route

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ABSTRACT

Objective: A. To assess the response of intravenous iron sucrose with that of oral ferrous sulphate in the prophylaxis of iron deficiency anemia in pregnancy.
B. To compare the efficacy and safety of two and three doses of intravenous iron sucrose with daily oral ferrous sulphate in the prophylaxis of gestational anaemia in pregnant women.
C. To compare the acceptability, efficacy and side effects of injectable iron sucrose over oral ferrous sulphate in the prophylaxis of anaemia in pregnancy.
Materials and method: 300 women with singleton pregnancy who met inclusion criteria were randomized into either the intravenous iron group or the oral iron group. Of 200 women in the intravenous iron group, 100 women received two doses of 200 mg iron sucrose and 100 women received three doses of 200 mg iron sucrose. The first dose was administered between the 21st and 24th gestational weeks, the second between the 28th and 32nd and the third between the 34th and 36th. The women of the oral group were given 100 tablets of oral ferrous sulphate 100mg once daily for 3months between 20 to 36 weeks. This treatment was supplemented with folic acid, to all the three groups. All women were given Tab albendazole 400mg in the second trimester before starting iron therapy.
Results: There was a non-significant trend to a higher frequency of responders (haemoglobin ≥ 11 g/dl) in the intravenous iron group (75 vs. 80%). There was no significant difference in terms of packed cell volume, mean corpuscular volume. No differences were observed in regard to maternal and perinatal outcomes.
Conclusions: Intravenous iron sucrose could be a better alternative to oral ferrous sulphate in the prophylaxis of iron deficiency anemia in pregnancy so as to reduce the maternal mortality and morbidity.

KEYWORDS Iron deficiency anemia, Hemoglobin, packed cell volume, mean corpuscular volume, Iron sucrose, Oral ferrous sulphate.

Introduction

Anemia is a major public health problem. Anemia (defined by the WHO as hemoglobin of <11 g/dl) is one of the world's leading cause of disability and thus one of the most serious global public health issues [1].

The prevalence of anemia in pregnancy varies considerably because of the differences in social conditions, lifestyles, and health seeking behaviors across different cultures. Anemia affects all pregnant women in the world—52 % in developing countries compared with 23 % in the developed world. The most common causes of anemia are poor nutrition, deficiencies of iron, micronutrients, malaria, hookworm infestation and schistosomiasis, HIV infection and hemoglobinopathies [1,2].

Anemia is one of the most prevalent nutritional deficiency problems affecting pregnant females. Iron deficiency is the major cause of anemia followed by folate deficiency. Prevalence of anemia is higher in India as compared to other developing countries. Prevalence of anemia in South Asian countries is the highest among the other countries in the world. WHO estimates that even among the South Asian countries, India has the highest prevalence of anemia. India contributes to about 80 % of the maternal deaths due to anemia. The high prevalence of iron and other micronutrients deficiency among women in developing countries is of concern and maternal anemia is still a cause of considerable perinatal morbidity and mortality [3].

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].

Anemia is responsible for adverse obstetric outcome in a large number of women in developing countries. Almost one thousand severely affected young women are reported to die every week because of inability to cope with the stress of childbirth.

Anemia leads to increased risk of blood transfusion during the peripartum period. Iron therapy before delivery may reduce the transfusion rate for iron deficient women.

The aim of this study was to compare the efficacy and safety of two and three doses of intravenous iron sucrose and oral ferrous sulphate in the treatment of iron deficiency anemia of pregnancy.

Materials and Methods

An experimental randomized study was conducted in the department of obstetrics and gynecology, institute of social obstetrics, Kasturba Gandhi hospital, Chennai between December 2011 and December 2012. All antenatal women attending antenatal OP who fulfi;; the inclusion/ exclusion criteria were randomly selected and included in the study. Eligible participants were singleton pregnant women between 20-35 years of age, 20 - 36 weeks of gestation with established iron deficiency anemia who had hemoglobin levels > 10 g%.

Exclusion Criteria were: history of allergy to iron, allergic condition or bronchial asthma, multiple pregnancy, cirrhosis, viral hepatitis, h/o hematological disease, history of bleeding tendency.

A total of 300 patients were studied. All were randomly assigned to either intravenous or oral group. During the antenatal visit, for all the women attending the outpatient department, the following investigations were done:

1. Hemoglobin
2. Packed cell volume
3. Mean corpuscular volume.

Those who fulfill the criteria were enrolled in the study after getting informed consent. Detailed history and complete clinical examination was done.

Group A were given two doses of 200mg iron sucrose between 20-24 weeks and 28-32weeks and oral iron was not given to this group.

Group B were given three doses of 200mg iron sucrose between 20-24 weeks, 28-32weeks and 34-36weeks. oral iron was not given to this group.

Group C was give 100 tablets of oral ferrous sulphate 100mg once daily for 3 months between 20-36 weeks.

This treatment was supplemented with folic acid in all three grouos. All women were given tab albendazole 400mg in second trimester before starting iron therapy.

In each infusion the maximum total dose administered was 200 mg elemental iron in 100 ml of normal saline infused over 20–30 min, given. Each ampoule was of 2.5 ml containing 50 mg of elemental iron. The ampoules were diluted with normal saline immediately before the infusion. No test dose was given. Treatment was completed after administration of the calculated dose. Additional iron was not administered during the study.

Laboratory evaluation was performed at the time of inclusion in the study. The response to treatment was monitored by hematological indices (hb, pcv, mcv) at 4 weeks, 8 weeks and at term. The results were statistically analyzed using SPSS software.

Results And Discussion

Among 300 women studied, 157 women (52.3%) belong to age group between 20-24 years, 110 (36.7%) women belong to age group between 25-29 years and only 13 (11%) belong to age group between 30-35 years. 239 women (79%) belong to class IV socioeconomic status, 39 (13%) women belong to class V socioeconomic status and only 22 (7.3%) belong to class I socioeconomic status. None of them belong to class I and class II socioeconomic status.

Among 300 women in our study, 185 women (61.7%) were primipara. 115 women (38.3%) were multipara, this suggests that anemia is common in multipara due to previous pregnancy events.

TABLE 1: HB VALUES

	GROUP A		GROUP B		GROUP C	
HB	MEAN	SD	Mean	SD	Mean	Sd
BEFORE	10.644	0.3942	10.756	0.4222	10.705	0.3812
4WKS	11.091	0.2896	11.208	0.3871	11.062	0.3212
8WKS	11.314	0.2425	11.444	0.3767	11.274	0.3111
AT TERM	11.613	0.1715	12.357	0.2717	11.433	0.2756

Table 2: CHANGE IN HB:

	GROUP A		GROUP B		GROUP C	
HB	MEAN	SD	MEAN	SD	MEAN	SD
BEFORE	10.644	0.3942	10.756	0.4222	10.705	0.3812
AT TERM	11.613	0.1715	12.357	0.2717	11.433	0.2756
CHANGE IN HB	0.969	P<0.005	1.599	P<0.002	0.729	P<0.001

- In group A, the mean pretreatment hemoglobin was 10.64 and the standard deviation was 0.3942 and at term the mean hemoglobin was 11.613 with standard deviation of 0.1715 after giving two doses of iron sucrose. There is a mean rise in hemoglobin of about 0.969. there is a statistically significant rise in hemoglobin with p value <0.005

- In group b, the mean pretreatment hemoglobin was 10.756 and the standard deviation was 0.4222 and at term the mean hemoglobin was 12.357 with standard deviation of 0.2717 after giving three doses of iron sucrose. There is a mean rise in hemoglobin of about 1.599. there is a statistically significant rise in hemoglobin with p value <0.002

- In in group c, the mean pretreatment hemoglobin was 10.705 and the standard deviation was 0.3812 and at term the mean hemoglobin was 11.433 with standard deviation of 0.1715 after taking oral iron tablets. There is a mean rise in hemoglobin of about 0.729. there is a statistically significant rise in hemoglobin with p value <0.001

TABLE 3: PCV VALUES

	GROUP A		GROUP B		GROUP C	
PCV	MEAN	SD	MEAN	SD	MEAN	SD
BEFORE	34.62	1.0324	34.82	0.9974	34.76	1.0284
4WKS	35.54	1.005	35.24	0.0064	34.24	0.1006
8WKS	35.28	0.9680	35.76	0.7328	35.54	0.7818
AT TERM	35.70	0.6540	36.20	0.3426	35.72	0.4326

TABLE 4: CHANGE IN PC

	GROUP A		GROUP B		GROUP C	
PCV	MEAN	SD	MEAN	SD	MEAN	SD
BEFORE	34.62	1.0324	34.82	0.9974	34.76	1.0284
AT TERM	35.7	0.6540	36.20	0.3426	35.72	0.4326
CHANGE IN PCV	1.08	P<0.047	1.28	P<0.004	34.76	1.0284

- In group A the mean PCV before starting treatment and t term was 34.62 and 35.70 respectively. The mean change in PCV is 1.08 which is statistically significant with P<0.047

- In group B the mean PCV before starting treatment and term was 34.82 and 36.20 respectively. The mean change in PCV is 1.28 which is statistically significant with P<0.004

- In group c before starting treatment and t term was 34.76 and 35.72 respectively. The mean change in PCV is 0.96 which is statistically significant with P=0.000

There were no serious adverse drug reactions recorded. 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. Adverse events in the intravenous group were local pain in (2) patients, giddiness (two), rashes (one), chest discomfort (one), and palpitation (four).

In the oral group gastrointestinal symptoms were experienced by 25% women. 15 women had upper gastrointestinal symptoms including epigastric discomfort, nausea and vomiting and 2 women suffered from diarrhea which was managed by symptomatic treatment. No women discontinued the drug because of gastrointestinal symptoms.

Our study confirmed that parenterally administered iron sucrose elevated hemoglobin and restored iron stores better than oral ferrous sulphate.

Al Momen et al. [5], in their study compared 52 women treated with intravenous iron sucrose and 59 women treated with 300 mg oral iron sulfate. Intravenous iron sucrose complex group achieved significantly higher hemoglobin levels 128.5 ± 6.6 versus 111.4 ± 12.4 g/l in the oral iron group *(P < 0.001)* in a shorter period 6.9 ± 1.8 versus 14.9 ± 3.1 weeks in control group *(P ≤ 0.001)*. Iron sucrose complex group showed no major side effects while 4 (6 %) of the control group could not tolerate ferrous sulfate, 18 (30 %) complained of disturbing gastrointestinal symptoms, and 18 (30 %) had poor compliance. The authors concluded that iron sucrose was a safe and effective alternative in the treatment of iron deficiency anemia during pregnancy [6]. This study is comparable to our study in that hemoglobin concentration was higher in the intravenous group in a shorter period of time.

In the study done by Bayoumeu et al. [7], involving 50 women intravenous iron sucrose was compared with oral ferrous sulfate. In the intravenous group an increase in hemoglobin was observed rising from 9.6 ± 0.79 to 11.11 ± 1.3 g/dl on day 30 and from 9.7 ± 0.5 to 11 ± 1.25 g/dl on day 30 in the oral group which was not significant. Ferritin values were higher in intravenous group, on day 30 *(P < 0.0001)* and at delivery P = 0.01 which was significant. This study slightly deviates from our study because sample size was small and iron sucrose was given over 21 days [7].

Conclusion

Iron sucrose is an effective alternative to oral ferrous sulphate in the treatment of iron deficiency anemia of pregnancy. Intravenous iron sucrose produces a more rapid increase in hemoglobin concentration and serum ferritin levels than oral ferrous sulphate.

Intravenous iron therapy is a safe alternative for the treatment of anemia, being able to reduce the need for blood transfusion and its concomitant side effect such as anaphylactic shock, febrile and hemolytic reactions, infections (hepatitis B, C, HIV, protozoan and bacterial) alloimmunization and graft versus host disease. During pregnancy and puerperium it helps to rebuild iron stores, helping the symptoms of anemia to subside at a faster rate and reduces the risk of developing anemia in subsequent pregnancies. Major advantages are safety, efficacy, compliance, simple mode of administration in an outpatient setting and cost effectiveness because admission is not needed in all cases.

Normally blood transfusion is an option in the cases of moderate and severe anemia in the third trimester of pregnancy. The given Iron sucrose intravenously may reduce the need for blood transfusion because of its faster action. Therefore, it can be considered as an alternative to blood transfusion in the treatment of pregnant women with moderate iron deficiency anemia during the third trimester.

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