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PREVENTING IRON DEFICIENCY ANAEMIA IN ANTENATAL WOMEN

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ABSTRACT

Iron deficiency anemia accounts for 75–95% of anemia in pregnancy. Adherence to daily iron supplementation still faces challenges. So, we had planned to compare the efficacy of oral iron with single dose parenteral iron sucrose as prophylaxis of anemia.

Prospective interventional cohort study was conducted in Department of Obstetrics & Gynecology JNMCH, Aligarh between Oct 2013-15. Non-anemic women between 14- 26week GA were allocated into two groups. Group A was supplemented with oral iron 100 mg once a day till term. Group B was administered single dose iron sucrose infusion of 500 mg. Pre supplementation and pre delivery hemoglobin and serum ferritin were noted. T-test and Chi-square were used for data analysis.

Mean increase in serum ferritin levels in Group B patients was 4.35±4.02ng/ml and by 1.06±2.9ng/ml in Group A patients. ($t = 5.96$, p value<0.001).

Single dose iron sucrose may be effective in prophylaxis of iron deficiency anemia.

BACKGROUND

Anemia is one of the most common medical disorders of pregnancy defined by the World Health Organization as hemoglobin levels of ≤ 11 g/dl. However, in India and most of the other developing countries the lower limit is often accepted as 10 g/dl [1,2,3]. According to the Nutrition Impact Model Study's 2011 estimates, the worldwide prevalence of anemia in pregnant women was 38% [4]. Developing nations have a very high prevalence of anemia in the world with almost 58 percent of pregnant women in India being anemic [5]. Antenatal Iron deficiency anemia accounts for 75–95% of cases [6]. Anemia results in an increased number of preterm, low birth weight, impaired cognitive development of children, postpartum hemorrhage, postpartum depression and reduced adult work productivity [7].

The total iron requirement during entire pregnancy of a 55-kg woman is nearly 1000 mg [7]. Iron requirements are highest for pregnant women –1.9 mg/1,000 Kcal of dietary energy in the second trimester and 2.7 mg/1,000 Kcal in the third trimester [5]. A woman must enter pregnancy with iron stores of ≥ 500 mg if she is to meet her requirements fully [8].

According to Ministry Of Health and Family Welfare of India, pregnant women should receive standard daily dose of 100 mg of elemental iron with 500µg folic acid for 100 days starting after the first trimester, at 14- 16 weeks of gestation and to be repeated for 100 days post partum [5].

Daily oral supplementation in pregnant women has been a long-standing recommended intervention. However, adherence to daily iron and folic acid supplementation still faces challenges as its effectiveness is largely compromised by lack of absorption, poor compliance, increased adverse effects such as nausea, vomiting, constipation, diarrhea (up to 56%), and discontinuation of treatment (up to 20%)[9].

Therefore, we had planned to conduct a study to establish the efficacy of single dose iron sucrose as a prophylactic supplementation during pregnancy. The study aims to compare the efficacy, side effect profile and overall maternal and neonatal outcome of oral iron supplementation with single dose iron sucrose administration during pregnancy.

PROCEDURE

This hospital based prospective interventional cohort study was conducted in the Department of Obstetrics and Gynecology OPD and Ward of JNMC Hospital, AMU, Aligarh between October 2013- October 2015 in collaboration with the Department of Pathology after the approval from the Ethical Committee of the Institution. The inclusion criteria of the study consisted of non-anemic (hemoglobin ≥10gm%) antenatal women between 14 to 28 weeks gestational age with singleton pregnancy non- smoker, non- alcoholic and who were willing to participate in the study were randomized using simple random sampling into 2 groups with a written consent. As per MOHFW, women in Group A were started on 100mg elemental iron as supplied by government of India, in form of ferrous sulphate for 100 days starting between 14 to 28 weeks [5]. Group B women were given single dose iron sucrose 500 mg as infusion transfused between 14 to 28 weeks of gestation. The exclusion criteria included multiple pregnancy and intrauterine growth restriction, women with other associated medical conditions such as diabetes, tuberculosis, women with pre eclampsia or eclampsia, women with anemia, women who had any form of prior blood transfusion, parenteral iron therapy or oral iron therapy for anemia during current pregnancy. Pre therapy serum ferritin was calculated using ELISA Reeder and Washer technique (RFCL Calbiotech) and hemoglobin percent was calculated using cyanmethemoglobin method. Complete history and detailed examination for each patient was done in addition to the mentioned investigations. All women were followed up with regular ANC visits and hemoglobin percent was repeated at each ANC visit made by patient. It was planned that Group B women would be given a second dose intravenous iron sucrose in case the hemoglobin falls during the follow up period, while the Group A women would continue with the oral iron therapy. All women were monitored for adverse reactions. At term or immediately before delivery, serum ferritin and hemoglobin percent were repeated. All the laboratory values were documented.

Administration of iron sucrose infusion: All Group B women were given a standardized single dose of 500 mg of iron sucrose as infusion on day care basis after a test dose (of 25 mg i.e. 1 ml diluted up to 10 ml was injected very slowly and followed by a 15 minute window period). If no reactions occurred, rest of the dose was administered. Iron sucrose complex was administered as 500 mg elemental iron in 500 ml 0.9% normal saline infusion over three to four hours.

STATISTICAL ANALYSIS: The data collection was done using Microsoft Excel and the results were presented in mean standard deviation and percentages. Chi-square test, unpaired t- test and paired t- test were used to compare categorical variables, independent means and mean before and after treatment respectively. The relative risk with its 95% confidence interval (CI) was also calculated. P value <0.05 was considered as significant. All the analysis was carried out using SPSS 21.0 version.

RESULTS

The baseline characteristics are enumerated in Table I. A total of 28 (46.7%) women were booked in the antenatal out patient department between 14 to 20 weeks of gestational age (early second trimester). 53.3% women (32) had either of the intervention between 15 – 20 weeks of gestational age.

As mentioned in Table II, out of 15 cases in Group A, 6 women had a combination of the mentioned side effects such as nausea, vomiting and constipation. In Group B, 3 women had side effects, which included pain at the injection site and rashes. There was a significant association observed between side effect and intervention groups. Neither any fatal adverse effect was observed in either of the study group cases, nor at any point of time during the study, the intervention required to be discontinued.

As elaborated in Table III, among women who received oral iron, there was not a significant increase in mean hemoglobin 0.1±0.3051 mg (p value = 0.083). Also, there was decrease in mean serum ferritin of 1.060±2.9106 ng/ml, which was not significant (p value = 0.056). Among women who received parenteral iron sucrose, there was a significant increase in mean hemoglobin of 0.333±0.3556 mg% (p value<0.001) and in serum ferritin of 4.3523±4.027 ng/ml (p value<0.001).

This study found that women, who received single dose iron sucrose, had a significant change in hemoglobin and serum ferritin levels compared to women who received oral iron supplementation. ($t(58) = 2.728$, $p = 0.008$) and ($t(58) = 5.966$, $p < 0.001$) respectively which is enumerated in Table IV.

In our study, we had 75% (45) vaginal deliveries, which included 12 preterm and 33 term deliveries. 25% women had cesarean section. In our study, 53.3% (32) women had the babies in the weight ranging from 2.5-3 kgs. There was no significant difference among the neonatal weight when compared between cases and controls. The mean baby weights of Group A and Group B were 2.819±0.374 and 2.837±0.375 kgs respectively.

DISCUSSION AND CONCLUSION

Placebo-controlled studies have consistently shown that pregnant women using iron supplements [10] have significantly higher iron status compared to women taking placebo. WHO has formulated dose of oral iron according to the prevalence of anaemia in pregnant women, which if <40%, a dose of 60 mg iron and 400 µg folic acid daily for 6 months is considered and if the duration of supplementation is shorter, a higher dose (120 mg) is recommended. In areas with a higher prevalence of anaemia, it is recommended that supplementation continue for three months postpartum [11].

Although oral iron improves hematological response, associated non-compliance and side effects make them unpopular. Parenteral iron sucrose is a safe preparation and now being used worldwide for correcting anemia.

The mean age of all primigravida in our study was 23.89±2.67 years, which is close to 26.4±4.01 years as reported by Gharoro EP et al (2000) [12]. In our study, 15% women were illiterate and 85% women were literate. A total number of 44 women (73.3%) enrolled in the study belonged to an urban background. 42 (86.7%) women belonged to middle class background. Gharoro EP et al (2000) [12] reported that social classes 1 and 2 constituted 52.1% of the routine antenatal population, while 1.85% of the patients belonged to social class V and all women in their study had completed the primary level of education. Our study shows a bias towards the literate and urban population, which could be possibly due to non-anemic status among the same. A total of 28 (46.7%) women were booked between 14 to 20 weeks of gestational age (early second trimester) and 12 (20%) women were booked between 21 to 26 weeks of gestational age (late second trimester). Mean gestational age of booking in our study was 16.55±5.69 weeks. This booking gestational age is earlier from 23.7 weeks gestation as reported by Gharoro EP et al (2000) [12]. Mean hemoglobin in our study was 10.967±0.3781 mg%, which is close to 10.6±1.5 mg% as reported by Menon KC et al (2013) [13]. In Group A, 15 controls had side effects, most common being nausea, vomiting and constipation, which is higher in comparison to as reported by Al-Momen et al (1996) wherein, 4 (6%) of the oral iron group could not tolerate ferrous sulfate, 18 (30%) complained of disturbing gastrointestinal symptoms and 18 (30%) had poor compliance [14]. In our study in Group B, 3 cases had side effects, which included pain at the injection site and rashes, though no episodes of thrombophlebitis were observed. In terms of compliance, no cases of Group B required follow up with respect to supplementation, which adds to its advantage. In Group A, 22 controls (36.7%) were compliant with regular intake of iron tablets, 6 controls (10%) gave history of on and off intake of iron tablets due to forgetfulness, 1 control (1.7%) took oral iron on alternate days for a period of 100 days and 1 control (1.7%) missed numerous doses of oral iron due to side effects such as nausea, vomiting and diarrhea. In a study conducted in U.S.A. reasons for non-compliance with iron deficiency treatment included: inadequate program support (lack of political commitment and financial support); insufficient service delivery (poor provider-user dynamics; lack of supplies, access, training, and motivation of health care professionals); and patient factors (misunderstanding instructions, side effects, frustration about the frequency and number of pills taken, migration, fear of having big babies, personal problems, nausea that accompanies pregnancy, and the subtlety of anemia which makes demand for treatment low) [15]. Iyengar et al (1970) reported a rise in hemoglobin in 29% women who were started on 30 mg oral iron from 24 weeks gestational age till delivery, whereas there was a decrease in hemoglobin in 60% women who took placebo [16]. Markides et al (2003) elaborated significant fall in serum ferritin and hemoglobin when no supplementation was given [17]. Siega Riz A.M. et al (2006) also compared 30 mg oral iron with placebo for minimum of sixteen weeks of supplementation in antenatal women and it was observed that in all cases there was a fall in serum ferritin values [18] suggestive of ineffectiveness of oral iron to increase the stores of iron in the body. Similarly, in our study, we observed a decrease in mean serum ferritin levels in cases receiving oral iron as a form of supplementation. Possible reasons could be due to low compliance, dietary methods followed in developing countries like India, where tannins, phytates are included high in diet which decrease absorption of oral iron significantly. Our study found that the patients who received single dose iron sucrose, had a significant change in hemoglobin and serum ferritin levels compared to Group A controls, who received oral iron supplementation. ($t(58) = 2.728$, $p = 0.008$) and ($t(58) = 5.966$, $p < 0.001$) respectively. With best of our efforts we were not able to find any literature after thorough searching to prove the efficacy of single dose iron sucrose in non-anemic antenatal population. When compared in terms of cost effectiveness, implementation of single dose iron sucrose as prophylaxis proved to be more beneficial, wherein the mother who would regularly take oral iron for 100 days antepartum and post partum, would have a total burden of Rs.1600 to Rs.2000 per mother per pregnancy (approximately Rs. 8 per Fe tablet) as compared to Rs.1100 to Rs.1200 which included entire cost of single dose iron sucrose transfusion. It gave advantage of a single day therapy as compared to oral iron wherein, women had to take the doses daily. Apart from increasing the hemoglobin values, iron sucrose also increased the iron stores in the body, rendering the post-partum period of the mother protective from clinical complication such as infections. Further if women experiences side effects of oral iron, it would lead to low compliance thereby causing ineffectiveness and more requirement of iron, thus creating a vicious cycle and increasing the cost of healthcare. Collectively, healthcare expenses spent by women in Group A were higher than Group B. Altogether, we inferred from our study that iron sucrose is more effective than oral iron as prophylaxis but we had limitations in our

study such as the total number of cases were less. Often many women were not ready for multiple tests to be carried out during the study period. Oral iron tablet was thought to be a nutritional supplement by most of the women and many women and their family members considered iron sucrose infusion for a diseased condition. Thus, many antenatal women were not ready for enrollment in the study. We did not include dietary factors, which could be a confounding factor in our study.

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Conflicting Interest (If present, give more details): Nil

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TABLES

Table I. Baseline Characteristics

Parameters	Mean/ Percentage Group A	Mean/ Percentage Group B
Age group	23.93±2.599	24.20±2.784
Literacy status		
Literate	41.7%	43.3%
Illiterate	8.3%	6.7%
Locality		
Rural	10%	16.7%
Urban	40%	33.3%
Socioeconomic status		
Lower class	6.7%	6.7%
Middle class	43.3%	43.3%
Parity		
Primigravida	36.7%	38.3%
Multigravida	13.3%	11.7%
Presupplementation hemoglobin	10.933±0.3144	11.00±0.4355

Table II Comparison of Side effect profile of both Groups

SIDE EFFECTS	GROUP A	GROUP B
Constipation	4	-
Nausea	14	-
Vomiting	4	-
Metallic taste	1	-
Diarrhea	1	-
Pain at injection site	-	3
Rashes	-	1

Table III. Change observed with oral iron supplementation and single dose iron sucrose supplementation

PAIRED SAMPLE T TEST FOR GROUP A								
PARAMETERS	MEAN	STAND-ARD DEVIATION	STANDAR D ERROR MEAN	95% CONFIDENCE INTERVAL		T	DF	P
				LOWER	UPPER			
CHANGE IN HEMOGLOBIN	0.1	0.3051	0.0557	-0.0139	0.2139	1.795	29	0.083
CHANGE IN SERUM FERRITIN	-1.060	2.9106	0.5314	-2.146	0.0268	1.995	29	0.056
PAIRED SAMPLE T TEST FOR GROUP B								
CHANGE IN HEMOGLOBIN	0.3333	0.3556	0.0649	0.2006	0.4661	5.135	29	<.001
CHANGE IN SERUM FERRITIN	4.3523	4.0270	0.7352	2.8486	5.8560	5.920	29	<.001

Table IV. Comparison of efficacy of oral iron versus single dose iron sucrose

INDEPENDENT SAMPLE T TEST					
PARAMETERS		GROUP A	GROUP B		
CHANGE IN HEMOGLOBIN					
	MEAN	0.1	0.3333		
	STD DEVIATION	0.3051	0.3555		
T-TEST FOR QUALITY OF MEANS	T	DF	P	CONFIDENCE INTERVAL	
EQUAL VARIANCES ASSUMED	2.728	58	0.008	0.06210	0.40457
EQUAL VARIANCES NOT ASSUMED	2.728	56	0.008	0.06201	0.40466
CHANGE IN SERUM FERRITIN					
	MEAN	-1.0600	4.3523		
	STD DEVIATION	2.9106	4.0270		
T-TEST FOR QUALITY OF MEANS	T	DF	P	CONFIDENCE INTERVAL	
EQUAL VARIANCES ASSUMED	5.966	58	<.001	3.5964	7.2282
EQUAL VARIANCES NOT ASSUMED	5.966	52	<.001	3.5926	7.2320

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