Research Article

A study to assess the effect of Intravenous iron sucrose therapy in pregnant women with moderate anaemia

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Abstract

Background: Iron deficiency anaemia (IDA) is the most common nutritional deficiency in pregnancy. Prophylactic oral iron is recommended during pregnancy to meet the increased requirement. In India, women become pregnant with low baseline haemoglobin level resulting in high incidence of moderate to severe anaemia in pregnancy where oral iron therapy cannot meet the requirement. Pregnant women with moderate anaemia are to be treated with parenteral iron therapy. **Objectives:** This study was undertaken to evaluate the response and effect of intravenous iron sucrose given to pregnant women with IDA. **Methods:** This study was conducted in between January 2010 to December 2011. One hundred pregnant women with haemoglobin between 7-9 gm% with diagnosed iron deficiency attending antenatal clinic were given intravenous iron sucrose in a dose of 200 mg twice weekly schedule after calculating the dose requirement. **Result:** Mean heamoglobin raised from 7.63 to 11.20 gm% (P<0.001) after eight week of therapy. There was significant rise in serum ferritin levels (from 11.2 to 69 µg/l) (P<0.001). Reticulocyte count increased significantly after two week of starting therapy (from 1.5 to 4.6). Other parameters including serum iron levels and red cell indices were also improved significantly. No major side effects or anaphylactic reactions were noted during study period. **Conclusions:** Parenteral iron therapy was effective in increasing haemoglobin, serum ferritin and other haematological parameters in pregnant women with moderate anaemia. Intravenous iron sucrose can be used as it can replace intramuscular therapy due to injection related side effects.

Keywords: Anaemia, Ferritin, Iron deficiency, Iron sucrose, Haemoglobin, Parenteral iron therapy.

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INTRODUCTION

Iron deficiency anaemia (IDA) is the most common nutritional deficiency in pregnant women. According to World Health Organization (WHO), the prevalence of IDA is about 18 per cent in developed countries and 35-75 per cent (average 56%) in developing countries[1]. In India, prevalence ranges from 33-89 per cent[2]. About half of the global maternal deaths due to anaemia occur in South Asian countries; India contributes to about 80 per cent of this mortality ratio[3]. A study conducted by Indian council of Medical Research (ICMR) [4] showed that the prevalence of anaemia was highest among pregnant women (50-90%) and that of moderate (<8 gm%) and severe anaemia (<5 gm%) was persistently high. Prevalence was high in all States of the country with considerable variations in moderate to severe anaemia[5,6]. Other factors responsible for high incidence of anaemia in our country include early marriage, teenage pregnancy, multiple pregnancies, less birth spacing, phytate rich Indian diet, low iron and folic acid intake and high incidence of worm infections[7]. WHO defines anaemia as haemoglobin (Hb) level <11 gm% [1]. In India, the ICMR classification of iron deficiency anaemia is: 8-11 g% as mild, 5-8 g % as moderate and <5 g% as severe anaemia.[4]

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In absence of interfering factors, serum ferritin <12-15 µg/l is considered as iron deficiency[4]. The first choice for prophylaxis and treatment of mild iron deficiency anaemia in pregnancy is oral iron therapy. But in patients with moderate and severe anaemia, oral therapy takes long time and compliance is a big issue in our country. Thus, pregnant women with moderate anaemia should be better treated with Parenteral iron therapy and/or blood transfusion depending upon individual basis. Various Parenteral iron preparations are available in the market which can be given either intravenously or intramuscularly. Initially, iron dextran and iron sorbitol citrate was started. But test dose was required to be given before these injections as severe anaphylactic reactions were reported with intravenous iron dextran. Iron sucrose has been reported to be safe and effective during pregnancy[8]. The injection can be given without test dose[9]. The present study principally aims to evaluate the response and effect of intravenous iron sucrose given to pregnant women with IDA.

MATERIAL AND METHODS

A prospective study was conducted in Government hospital in urban area of Pune Maharashtra from January 2010 to December 2011. Study population included all pregnant women presented in antenatal clinic. A total of 100 women with haemoglobin between 7-9 gm% were screened. Women with diagnosed iron deficiency anaemia and given informed consent were included in study. Exclusion criteria were causes other than iron deficiency anaemia, multiple pregnancies, high risks for preterm labour and recent blood transfusions, thalasaemia another medical disorders. Red cell indices, peripheral blood smear and detailed serum iron studies were also conducted. Baseline investigations including liver and kidney function tests, urine (routine microscopy and culture sensitivity), stool examination (for ova and cyst) were done. All women were given antihelmenthic therapy with tablet mebendazole 100 mg twice daily for three days. Folic acid tablets were given to all women during therapy. The formula used for calculation of iron sucrose dose was as follows: Required iron dose (mg) = (2.4 × (target Hb - actual Hb) × pre-pregnancy weight (kg)) + 1000 mg for replenishment of stores [10]. The required iron dose varied depending upon index Haemoglobin level and pre-pregnancy weight. Average dose requirement was 1777 ± 168.5 mg (1400-2160 mg). Mean duration to complete total therapy was 4.5 ± 1.0 (3.5-5.5 week). Iron sucrose was given in a dose of 200 mg intravenously twice weekly in 200 ml normal saline over a period of 15-20 min. First dose was given in the ward where equipment for cardiopulmonary resuscitation was available. The following doses were given on outpatient basis. Patients were observed for side effects or anaphylactic reactions. Any minor or major side effects were documented. All parameters were repeated at 2 weeks interval till 8 weeks. The primary outcome measures were haemoglobin and serum ferritin levels after 4 and 8 weeks. Secondary outcome measures were improvement in serum iron levels, Reticulocyte count, any adverse effects and peri-natal outcome [period of gestation (POG) at the time of delivery, type of birth, postpartum haemorrhage, need of blood transfusion and foetal birth weight]. All the selected pregnant women were followed till delivery for their peri-natal outcome assessment. Statistical analysis: The data was entered in Microsoft Office excel. The data was analyzed using SPSS (Software package for social sciences) software version 20 at Community medicine department of MGM Medical Collage. ANOVA of repeated measures was applied to assess significant difference due to intervention at various levels of time interval.

RESULTS

The mean age of participants were 27.8 ± 3.9 years (range 21-34 years), mean parity was 1.3, and mean period of gestation (PDG) at the time of diagnosis was 25.69 ± 4.82 weeks (14-32 weeks). At the beginning, mean Haemoglobin level was 7.63 ± 0.61 gm%. 32% women had mild anaemia (>8 gm%) and 68% had moderate anaemia (5-7.9%). After completion of therapy, mean Haemoglobin level raised to 11.20 ± 0.73 gm%. Of the total women, 67% achieved Hb ≥11 gm%. The mean duration to achieve haemoglobin level more than 11 gm% was 6.5 ± 2.3 weeks. Table I shows the baseline haematological parameters and effect of iron sucrose therapy on all the parameters. Complete dosage schedule was done in all women.

Table 1: Baseline haematological parameters and effect of iron sucrose therapy

Parameters	Baseline	2wk	4wk	8wk	P value
Mean Hb (gm %)	7.63	7.89	9.9	11.2	0.001
Serum iron (ug/dl)	32.72	42.94	59.11	82.42	0.001
TIBC(ug/dl)	354.2	328.8	320.96	315.5	0.001
Serum ferretin(ug/l)	11.2	17.64	25.60	69	0.001
Reticulocytecount(%)	1.50	4.6	4.8	5.5	0.001
MCV (fl)	67.24	76	79.3	85	0.001
MCH(pg)	22.3	24	34	44	0.001
MCHC(gm%)	26.5	31	40	56	0.001

Peri-natal outcome: Out of total included female, 9% delivered before 37 week POG. Table II shows the associated antenatal complications in the included women. The remaining 90 women delivered after 37 weeks. Of these, 28 (31.2%) underwent emergency or elective cesarean section and the remaining 62 (68.8%) delivered vaginally. Mean period of gestation at delivery was 38.5 ± 1.0 (37 - 41) week. 2.2% women had

postpartum haemorrhage (blood loss >500ml) and required blood transfusion. Intrapartum and postpartum period of the remaining was uneventful. The mean birth weight of babies was 2762 ± 355 gm.

Table 2: Associated obstetrical complications in the study population

Associated medical and obstetrical complications	Occurrence (%)
Preeclampsia	10
Intrauterine growth restriction	12
Preterm labor	8
Preterm Premature rupture of membranes	3
Gestational diabetes mellitus	4
Intrahepatic cholestasis of pregnancy	3
Abruption	1

Side effects: Five women complained of nausea and three had vomiting after first dose. One woman had diarrhea after the second dose. One had thrombophlebitis after second dose, one had mild giddiness and restlessness at first dose which subsided spontaneously and did not recur on subsequent doses. Two women complained of mild fever after the first dose which did not recur on further dosing. One woman had hemetemesis after first dose. She was evaluated by the gastroenterologist and no cause was found. Iron sucrose was restarted after one week and she completed the full course without any further side effects. All other women well tolerated the injections. There were no major side effects and no allergic or anaphylactic reaction.

DISCUSSION

The total requirement of iron during pregnancy is approximately 1000 mg (500 mg for developing fetus, placenta and similar amount for red cell increment)[11]. Usually, this iron is mobilized from iron stores. However, women with poor iron stores become iron deficient during pregnancy. Studies have shown that Haemoglobin levels < 8 gm% (moderate to severe anaemia) in pregnancy is associated with higher maternal morbidity [3, 11, 12]. Haemoglobin less than 5 gm% is associated with cardiac decompensation and pulmonary edema. Blood loss of even 200 ml in third stage of labour can cause sudden shock and death in these women[3,11,12]. As compared to western women whose iron stores are sufficient and they need 30-40 mg elemental iron per day for anaemia prophylaxis in pregnancy [13, 14]. The stores in Indian women are deficient and they need 100 mg elemental iron per day for prophylaxis[14]. For treatment of anaemia, dose recommended is 200 mg elemental iron per day[14]. In the present study, 5-9 gm% Haemoglobin level was taken as cut-off. Intravenous iron is superior to oral iron with respect to faster increase in Haemoglobin and faster replenishment of body iron stores[15]. Also, it reduces the need of blood transfusions[16], and it can be given at outpatient basis. In a study to compare the clinical efficacy and safety of intravenous iron sucrose with intramuscular iron sorbitol citrate, it was found that rise of Haemoglobin was more in intravenous group[17]. This study emphasized the superiority of intravenous iron therapy to intramuscular therapy in terms of rise of Haemoglobin and also safety profile. According to study of Perewunsnyk *et al* [18] out of 400 women (who received a total of 2000 ampoules of iron sucrose), only 0.5 per cent cases had minor general adverse effects including a metallic taste, flushing of the face and burning at the injection site. The high tolerance of the drug has been partly attributed to slow release of iron from the complex and also due to the low allergenicity of sucrose. Till date, one death has been reported with intravenous iron sucrose injection[19]. The explanation given for this was because of very slow infusion (1-2 hours)[19]. The cause of death may be free radicals released from the iron sucrose [19]. The injection should be given within 15-20 minutes or up to 200 mg can be given as slow intravenous push over 2-3 minutes. This case has not been mentioned in the literature but is available on clinical trial registry site[19]. In the present study, no major side effect was reported. Breymann C.[20] treated more than 500 antenatal women diagnosed with iron deficiency anaemia. Intravenous iron sucrose was given according to the calculated dose as either intravenous push over 5-10 minutes or intravenous infusion over 20-30 minutes[20]. All injections were given on outpatient basis without any test dose [20]. This study also emphasizes on the safety of iron sucrose injection. In the present study, the first dose was given in ward where facilities for emergency care were available. All subsequent doses were given on OPD basis. None of the patients required any emergency care. In other studies[17,21], target Haemoglobin for calculation of required dose has been taken 11 gm/dl and for replenishment of stores 500 mg has been added. Keeping in mind very low iron stores in Indian women, we took 14 gm/dl as index Haemoglobin level and added 1000 mg for replenishment of stores. Even with this, maximum mean serum ferritin level after 8 weeks of starting therapy was 69 µg/l, which was well within normal range. As compared to previous studies[17, 20], ferritin levels in our study women showed a lesser increase. The reason can be due to severely depleted iron stores in Indian women. Hookworm is one of the well established causes of anaemia in developing countries[21]. Routine antihelminthic therapy in pregnancy is not recommended[21]. But due to high prevalence in developing countries including India, it is advisable to give antihelminthic therapy to pregnant women presenting with anaemia [21]. A study conducted to evaluate the safety and efficacy of iron sucrose in dialysis patients

who were sensitive to iron dextran, demonstrated the safety of intravenous iron sucrose injections[22]. In a study to assess and compare the efficacy of two and three doses of intravenous iron sucrose with oral iron therapy, there was higher frequency of responders (Hb > 11 gm%) in intravenous group (75 vs. 80%)[23]. There was a significant difference of repleted iron stores before delivery (ferritin >50 mg/l) in the group with three intravenous iron doses in comparison to the oral iron group (49 vs. 14%; P <0.001)[23]. No differences were observed in maternal and perinatal outcomes. The study did not conclude any significant benefit of parenteral iron therapy over oral iron therapy. However, in practice, noncompliance is very common with oral iron therapy. This study showed that intravenous iron sucrose therapy was effective to treat moderate anaemia in pregnant women. Intramuscular preparations are known to be associated with local side-effects. Iron sucrose complex intravenous therapy was associated with negligible side effects. It caused rapid rise in haemoglobin level and the replacement of stores was faster. Long term comparative studies are required to assess if it can be used at peripheral level.

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