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Research Article

A Comparative Study on efficacy and safety of intravenous iron sucrose and intramuscular iron sorbitol in pregnancy anaemia

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Abstract: Iron deficiency is a leading cause of anaemia in pregnancy. The present study aimed to compare the efficacy of intramuscular and intravenous iron therapy in improving iron deficiency anaemia in pregnancy and restoring iron stores, compare the obstetric outcome in the two groups and evaluate the safety of intravenous iron sucrose. This was a prospective study, where 200 anemic antenatal women with hemoglobin 5-9 g%, and serum ferritin <15 µg/l, were randomized into two groups. In group A (n=100), iron sucrose was given in divided doses of 200 mg twice weekly by slow intravenous infusion and Group B(n=100) received iron sorbitol. Primary outcome measure was treatment efficacy, assessed by measurement of hemoglobin and red blood cell indices on 2, 4wks and at delivery, and of ferritin at delivery. Any side-effects of treatment and the neonatal outcome were studied as secondary outcome measures. At the beginning, mean Hb was 7.42 ± 0.72 g% in group A, and 7.63+0.42 g% in group B. The mean Hb after tretmet was 11.52+0.65g% and10.56+0.52g% respectively in group A and group B. Serum ferritin level also increased in both groups. There was a statistically significant difference in increase of hemoglobin levels and ferritin levels between the two groups after treatment. The adverse effects from iron treatment were mild in both groups. Neonatal outcome was comparable in the two groups. It is concluded that intravenous administration of iron sucrose was a safe treatment for correction of anaemia in pregnancy, without serious side-effects.
Keywords: Intravenous iron, Intramuscular iron, Haemoglobin, Anaemia, Pregnancy.

INTRODUCTION

India has always been a country with a high prevalence of anaemia. Indian obstetricians and nutrition scientists earlier documented that pregnant women were the most vulnerable group for anaemia. They reported adverse health consequences of anaemia in pregnancy on mother and child [1]. Estimates from the World Health Organization report that from 35% to 75% (56% on average) of pregnant women in developing countries were anaemic, However, many of these women were already anemic at the time of conception, with an estimated prevalence of anaemia of 43% in non pregnant women in developing countries [2]. At least half of all anaemia cases have been attributed to iron deficiency [3]. The prevalence of iron deficiency is far greater than the prevalence of anaemia and iron deficiency (low serum ferritin and sparse or absent stainable iron in bone marrow) often develops during the later stages of pregnancy even in women who enter pregnancy with relatively adequate iron stores [4].In many developing countries endemic problems such as malaria and helminth infections, together with the problem of poor nutrition make anaemia one of the most common pathologies in pregnancy. 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 in Indian population [5].

Iron deficiency anaemia in pregnancy is a risk factor for preterm delivery and subsequent low birth weight, and possibly for inferior neonatal health. Even for women who enter pregnancy with reasonable iron stores, iron supplements improve iron status during pregnancy and for a considerable length of time postpartum, thus providing some protection against iron deficiency in the subsequent pregnancy [2].

WHO defines anaemia as haemoglobin [Hb] <11 g % 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. In absence of interfering factors, serum ferritin <12-15 µg/l is considered as iron deficiency [6].

In India oral iron tablets for anaemia have been distributed since many years, but there has been no significant change in the burden of anaemia. In theory, parenteral administration of iron provides quick and certain correction of the total iron deficit because it not only corrects the anaemia but also builds up iron stores. Parenteral administration of iron can be achieved by either an intramuscular or an intravenous route. In 2013 Government of India has released guidelines for treatment of iron deficiency anaemia in pregnancy; suggested intramuscular iron was the treatment of choice in moderate anaemia in pregnancy [1]. 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 [7].The injection can be given without test dose [8].

MATERIALS AND METHODS

The prospective study was conducted in the department of Obstetrics and Gynaecology, Mamatha medical college Khammam from January 2013 to June 2015. Ethical clearance for the study protocol was taken from the Ethics Committee of the institute. Informed written consent was taken from all the patients before starting the therapy. A total of 300 women presenting in antenatal clinic with gestational age of 14-32 weeks, haemoglobin between 5-9 g% , serum iron level less than 60ug/dl were screened and included in study. But this study analysed 200 people who completed the total iron therapy to avoid statistical errors. After completion of baseline investigations including liver and kidney function tests, urine [routine microscopy and culture sensitivity], stool examination [for ova and cyst] women were included in study. Group A [n=100] received intravenous iron sucrose therapy. Iron sucrose was given in a dose of 200 mg intravenously twice weekly in 200 ml normal saline over a period of 1 hour to the total calculated doses were completed. Group B received intra muscular injection of iron sorbitol 2.5ml [150mg] twice monthly till total calculated doses by means of z technique. The target Hb level was≥11g%. Patients were observed for side effects and anaphylactic reactions.

The primary outcome measures, haemoglobin measured after 4 and 8 wks and at delivery and serum ferritin measured after completion of iron therapy. Adverse effects and perinatal outcome like period of gestation at the time of delivery, type of birth, postpartum haemorrhage, need of blood transfusion and fetal birth weight were also noticed.

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%).Chi-square test was used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

The mean age of women was 26.4± 3.9(range 21-34) yr and mean period of gestation at the time of diagnosis was 22.52 ± 4.82 (14-32) wk. There is no significant difference between 2 groups in age, parity and gestational age.

At the beginning, mean Hb was 7.42 ± 0.72 g% in group A, and 7.63+0.42in group B. The mean Hb after tretmet was 11.52+0.65 and10.56+0.52 respectively in group A and group B. Hb levels at different intervals were given in table 1.The target Hb achieved in 88% women in group A and 52% in group B at the time of delivery. The mean duration to achieve haemoglobin level more than 11 g% was 6.2 ± 1.5 wk. Haematological parameters and effect of iron therapy on the parameters were given in table 2.

Serum ferritin from 9.39 ± 2.8 µg/L raised to 32.78 ± 4.6 µg/L. All women were followed treatment till delivery. Among these, 28% in group A and 37% in group B underwent cesarean section and the remaining delivered vaginally. Mean period of gestation at delivery was 39.2 ± 1.0 [37-41] wk. Only one woman had postpartum haemorrhage and required blood transfusion in group B. The mean birth weight of babies was 2.7+0.32Kg in group A and 3.1+0.25Kg in group B.

In group A seven women complained of nausea, four had vomiting, one had thrombophlebitis, one had mild giddiness and restlessness, three women complained of mild fever after the first dose of injection and all of them were normal on subsequent doses. In group B side effects like Rash, itching, mild pain and mild skin staining were observed in most of women. Severe body pain in four cases, vomiting in 8, fever in 6, head ache in 7 and athralgia in two members were observed, there was no allergic or anaphylactic reactions.

Table- 1: Hb levels at different intervals in two groups

Hb level	No. found Group A[I/V]				No. found Group B[I/M]			
	Before	2wk	4wk	At delivery	Before	2wk	4wk	At delivery
5-7	32	14	0	0	33	24	10	
7.1-9	42	34	18	0	48	66	42	2
9.1-11	26	52	78	12	19	10	48	46
>11	0	0	4	88	0	0	0	52
Mean Hb	7.42	8.32	10.04	11.52	7.64	7.74	8.84	10.56

Table 2: Effect of iron therapy on Haemotological parameters

parameter	Group A[I/V]		Group B[I/M]	
	Before	after	Before	After
Haemoglobin (g%)	7.42 ± 0.72	11.52+0.65	7.63+0.42	10.56+0.52
Haematocrit pcv %	25.6+3.51	36.56+5.47	26.5+3.11	32.7+2.22
Serum ferritin (ug/l)	9.39 ± 2.8	32.78 ± 4.6	7.5+1.82	22.4+2.12

DISCUSSION

Iron is an essential micronutrient that plays an important role in critical cellular functions in all organ systems. The human body operates several hundred iron-containing metallo enzymes in which iron is indispensable. Amongst the most important is ribo nuclotide reductase, being necessary for DNA synthesis and cell proliferation, the cytochromes, being involved in electron transport and ATP synthesis. Important iron containing proteins are haemoglobin (Hb), which provides transport of oxygen from the lungs to the body tissues and myoglobin, which serves as an oxygen reserve in the muscles. Consequently, iron is important for a normal function of all cells and organs in the human body[4].It is vital for early brain growth and function because it supports neuronal and glial energy metabolism, neurotransmitter synthesis, and myelination [9]. Low iron stores at birth and Iron Deficiency Anaemia in infants may also adversely influence cognitive, emotional, motor, and neuro physiological development in humans, with short- and long-term consequences that are not corrected by iron therapy [10, 11].

The total requirement of iron during pregnancy is approximately 1000 mg [500 mg for developing foetus and placenta and similar amount for red cell increment]. Usually, this iron is mobilized from iron stores [12]. However, women with poor iron stores become iron deficient during pregnancy. Diet alone cannot supply, the increased demands of body were supplemented.

Transfer of iron from the mother to the fetus is supported by a substantial increase in maternal iron absorption during pregnancy and is regulated by the placenta. Serum ferritin usually falls markedly between 12 and 25 wk of gestation, probably as a result of iron utilization for expansion of the maternal red blood cell mass. Most iron transfer to the fetus occurs after week 30 of gestation, which corresponds to the time of peak efficiency of maternal iron absorption. When maternal iron status is poor, the number of placental transferring receptors increases so that more iron is taken up by the placenta. Excessive iron transport to the fetus may be prevented by the placental synthesis of ferritin [13, 14].

In this study at the beginning, mean Hb was 7.42 ± 0.72 g% in group A, and 7.63+0.42g% in group B. The mean Hb after tretmet was 11.52+0.65g% and10.56+0.52g% respectively in group A and group B. The target Hb achieved in 88% women in group A and 52% in group B at the time of delivery. wali *et al.;* [15] observed mean Hb in i/v group was 11.3 g/dl was achieved 70% at the time of delivery. Kriplani et al [16] reported mean Hb raised to 11.20 ± 0.73 g% and 67 % achieved Hb ≥11 g%. Similar increase in hemoglobin and ferritin levels observed [17, 18, 19, 20]. The significant raise in hemoglobin and ferritin also observed in intramuscular iron sorbitol [3, 21]. The mean birth weight of babies was 2.7+0.32Kg in group A and 3.1+0.25Kg in group B but Neonatal outcome was comparable in the two groups [17].

In our study only one woman had postpartum haemorrhage and required blood transfusion in group B. wali et al [15] mentioned two [2.2%] women had postpartum haemorrhage and required blood transfusion. In other study blood transfusion rate was 1.9% [20].

Intravenously administered iron can cause anaphylactic shock, and all safeguards, such as hospital admission with resuscitation equipment available by the bedside, the use of correct techniques, and correct infusion rate as advised by the manufacturer, should be followed [22].Comparison of treatments showed that intravenous iron administration was associated with risk of venous thrombosis than intramuscular administration, but the IM route resulted in pain at the injection site more frequently. There were minor side effects observed in our study. Concurrent reports were observed in others [15-20]. Perewunsnyk *et al.; [*23] reported minor general adverse effects including a metallic taste, flushing of the face and burning at the iron sucrose injection site occurred in 0.5 per cent cases. Breymann treated about 500 anaemia women with Intravenous iron sucrose according to the calculated dose as either iv push over 5-10 min or iv infusion over 20-30 min. All injections were given on outpatient basis without any test dose [24].Above all studies emphasizes on the safety of iron sucrose injection. Devasenapathy et al*. ;* [25] mentioned that standard protocols and guidelines for intravenous iron usage are lacking. These need to be formulated before scaling it up across public health facilities in India.

CONCLUSION

Anaemia is one of the major leading nutritional deficiencies in India. The response in terms of improvement in serum ferritin and Hb levels was satisfactory in both groups. Intravenous iron sucrose is safe, convenient and faster acting than intramuscular iron sorbitol for treatment of moderate to severe anaemia. However, to keep the risk of severe side effects within acceptable limits, parenteral iron

injections must be given in hospital settings, where resuscitation facilities are available to deal with any adverse events.

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