INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

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RESEARCH ARTICLE

USE OF INTRAVENOUS IRON SUCROSE THERAPY FOR ANAEMIA IN PREGNANCY

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ARTICLE INFO

Article History:
Received 16th February, 2016
Received in revised form 24th March, 2016
Accepted 23rd April, 2016
Published online 28th May, 2016

Key words:

intravenous iron sucrose, pregnant women, anaemia, haemoglobin, serum ferritin

ABSTRACT

Aim: To test the efficacy and safety of Intravenous Iron Sucrose therapy in pregnant women with anaemia.

Material and method: A total of 212 pregnant women with Hemoglob in (Hb) 6-8.6g/dl were prospectively given intravenous sucrose iron therapy between September 2014 to February 2016. All the patients were underwent Hemoglob in levels, MCV, MCH, MCHC, Serum iron levelsm, Serum Ferritin levels and Reticulocyte counts before therapy and repeated at 3rd week, 6th week after the therapy. The relative changes in these parameters were analysed. The relevant statistical analysis were done using SPSS software version 16.

Results: Out of 200 patients majority of the patients 92 were in the age group of 18-22 years and 78 women were in 28-32 weeks of gestation. The level of Mean Hb (g %), Serum Iron (ng/dl), Serum Ferritin level (µg/l), Reticulocute counts (%) , MCV (fl), MCH (pg) and MCHC (g/dl) were 8.80±0.61g (%),11.5±3.90 (ng/dl), 1.50±0.50(%),67.45±4.0(fl), 22.1±1.9(pg) and26.2±1.5(g/dl) before tansfusion; 8.80±0.61(g %), 49.94±9.3 (ng/dl),21.23±8.00 (ng/dl), 4.8±2.1(%),78.4±4.5 (fl), 26.34±3.4 (pg) and 33.54±3.3 (g/dl) at 3 week post therapy ($p<0.001$) ; 9.61±0.80(g %), 58.41±10.11 (ng/dl), 30.34±10.23 (ng/dl), 5.2±1.8(%),82.34±2.3 (fl), 36.87±2.9 (pg) and 42.44±3.4 (g/dl)($p<0.001$) at 6 weeks post therapy respectively. No patients were developed severe adverse reaction during therapy.

Conclusion: Intravenous iron sucrose therapy is effective and safe in treating moderate anaemia in pregnant women.

INTRODUCTION

Indian pregnant women have always been a vulnerable group with a high prevalence of anaemia due to various socio-economic reasons and Indian research studies have reported adverse health consequences of anaemia in pregnancy on mother child.[1,2].

According to WHO, the prevalence of iron deficiency anaemia(IDA) is about 18 per cent in developed countries and 35-75 per cent (average 56%) in developing countries[1]. Globally, the prevalence of anaemia is 55.9 per cent with variations between developed and developing countries. In India, prevalence ranges between 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]. Many programmes have been introduced and implemented to reduce the burden of anaemia in the country but the decrease is lower than other South Asian countries[4]. Various surveys [National Family Health Survey (NFHS), District Level Household Survey (DLHS),

Indian Council of Medical Research (ICMR) Micronutrient Survey] have been conducted to calculate the prevalence of anaemia in India. During 10th Five Year Plan (2002-2007)[4], a study conducted by ICMR[5] showed that the prevalence of anaemia was highest among pregnant women (50-90%) and that of moderate (<8 g%) and severe anaemia (<5 g%) was persistently high. Prevalence was high in all States of the country with considerable variations in moderate to severe anaemia[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 in Indian population[7].

WHO defines anaemia as haemoglobin (Hb) <11 g %[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.

During 1970s they showed that *(i)* daily oral iron folate therapy (60 mg of elemental iron and 500 µg of folic acid) prevented fall in haemoglobin (Hb) levels seen in pregnancy and resulted in some improvement in birth weight, and *(ii)* daily administration of two or maximum tolerated dose of oral iron folic acid (60 mg of elemental iron and 500 µg of folic acid) from the time of diagnosis of anaemia till delivery succeeded in correction of mild anaemia provided the compliance was good[3,4,5].

Moderate anaemia (seen in about 15-20% of Indian pregnant women did not respond well to oral iron therapy because *(i)* one or two tablets a day was insufficient to raise the Hb levels beyond 11 g/dl; *(ii)* attempts to increase the dose resulted in increased side effects and reduced compliance; and *(iii)* increased dose also increased gut motility and reduced iron absorption[6,7]. As a result, oral iron therapy was not found useful for treatment of moderate anaemia. Therefore the need for I.V iron therapy.

MATERIALS AND METHODS

This is a prospective study conducted in the department of Obstetrics and Gynaecology, BGS Global Institute of Medical Sciences, Bangalore, India from September 2014 to February 2016. A total of 212 women with gestational age between 20-36weeks presenting in antenatal clinic with haemoglobin between 6-9 g% were included in the study after obtaining an informed written consent. Exclusion criteria were causes other than iron deficiency anaemia, multiple pregnancy, and high risk for preterm labour and recent blood transfusions, thalasaemia and other medical disorders.

Three part analyser using impedance method was used for haematological analysis of blood, Haemoglobin levels, Red blood cell counts, red cell indices and peripheral blood smear were conducted. Three women with other causes were excluded from the study, one had haemolytic anaemia and two women had chronic renal disease. Nine women could not be followed up and therefore were excluded from study. Therefore, 200 women were recruited for intravenous iron sucrose therapy in this study. Ethical clearance was taken from the Ethics Committee of the institute. Informed written consent was taken from all the patients before starting the therapy. 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.

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].

Iron sucrose was given in a dose of 200 mg intravenously twice weekly in 100 ml normal saline over a period of 15-20 min. All infusions were given on inpatient basis equipment with emergency drugs being kept ready with facilities for cardiopulmonary resuscitation being available Patients was observed for side effects or anaphylactic reactions. Any minor or major side effects were documented. . Maternal pulse, blood pressure, respiratory rate was taken every ten minutes during infusion and foetal heart rate was assessed before and after infusion. The primary outcome measures was haemoglobin levels after 3 and 6 wks. Secondary outcome measures were improvement in Red blood cell indices, reticulocyte count, any adverse effects, maternal and perinatal outcome.

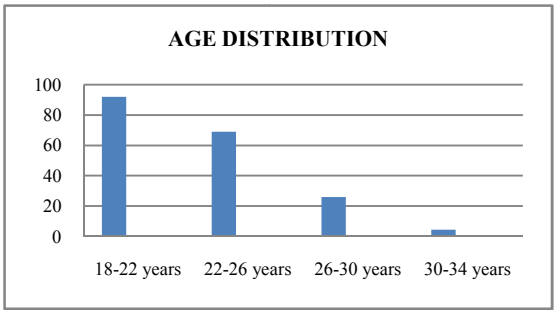
The statistical analysis was done using SPSS version 16 (SPSS Inc., USA).

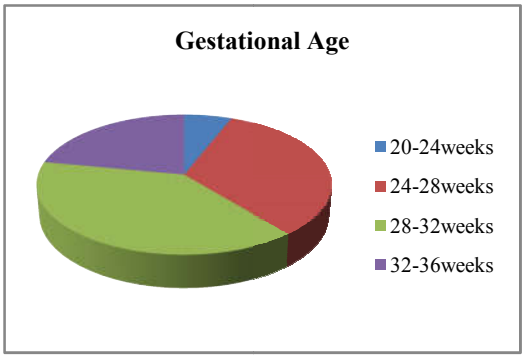
RESULTS

The Demographic characteristics of the women included in the study is outlined in Graph 1 and 2

Age Distribution(Graph 1)- In the study(n=200), 92 women were in between 18-22 years, 69 women in 22-26 years age group, 26 women were in 26-30 years age group, and 13 women in the 30-34 years age group.

Gestational Age (Graph 2) - In the study group (n=200), 12 women were between 20-24weeks gestational age, 66 women in 24-28weeks gestation, 78 women in 28-32weeks gestation, 44 women in 32-36weeks gestation.





The mean Hb levels prior to transfusion was 7.55±0.60, which increased to 8.80±0.61, 3weeks after transfusion and 9.61±0.80 6weeks after transfusion. The complete hematological parameter analysis is shown in Table1.

Table 1 Baseline hematological parameters and its effect post iron sucrose transfusion

Parameters	Pre infusion levels	3weeks post transfusion	6weeks post transfusion	P value
Mean Hb (g %)	7.55±0.60	8.80±0.61	9.61±0.80	0.001
Serum Iron(ng/dl)	32.72±5.00	49.94±9.3	58.41±10.11	0.001
Serum Ferritin levels(µg/l)	11.5±3.90	21.23±8.00	30.34±10.23	0.001
Reticulocyte Count (%)	1.50±0.50	4.8±2.1	5.2±1.8	0.001
MCV(fl)	67.45±4.0	78.4±4.5	82.34±2.3	0.001
MCH(pg)	22.1±1.9	26.34±3.4	36.87±2.9	0.001
MCHC(g/dl)	26.2±1.5	33.54±3.3	42.44±3.4	0.001

Table 3 Associated Obstetric complications

Pre-eclampsia	11 (0.055%)
Intra uterine growth restriction	23 (0.115%)
Preterm labour	09 (0.045%)
Preterm premature rupture of membranes	02 (0.010%)
Gestational diabetes mellitus	15 (0.075%)
Intrahepatic cholestasis of pregnancy	06 (0.030%)
Abruption	02 (0.010%)

During the study, 10 women had local adverse side effects and 32 women experiencing mild systemic side effects like pruritis (13 women), hypotension (3 women), nausea/vomiting (14 women), headache (2 women). There were no incidents of

Table 2 Adverse Effects during the transfusion

Local- Burning sensation/ Extravasation	**10 (0.050%)**
Systemic-1. Pruritis	13 (0.065%)
2. Hypotension	03 (0.015%)
3. Nausea/ Vomiting	14 (0.070%)
4. Headache	02 (0.010%)
5. Anaphylaxis	00

DISCUSSION

Iron is required in pregnancy for both the mother and the developing fetus, the total requirement of iron during pregnancy is approximately 1000 mg[11]. Normally, this iron requirement is mobilized from maternal iron stores. But, in women with poor iron stores, this requirement is not met and they become iron deficient during pregnancy. Moderate to severe anaemia in pregnancy are associated with higher maternal and fetal morbidity[3,11,12]. Haemoglobin less than 5 g% is associated with cardiac decompensation and pulmonary oedema.

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 iv iron therapy to intramuscular therapy in terms of rise of Hb and also safety profile.

Perewunsnyk ***et al***[18] studied 400 women who received a total of 2000 ampoules of iron sucrose. Minor general adverse effects including a metallic taste, flushing of the face and burning at the injection site occurred in 0.5 per cent cases. 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 h). The cause of death may be free radicals released from the iron sucrose. The injection should be given within 15-20 min or up to 200 mg can be given as slow iv push over 2-3 min. 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[20] treated more than 500 antenatal women diagnosed with iron deficiency anaemia. Intravenous iron sucrose was given 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. 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 Hb for calculation of required dose has been taken 11 g/dl and for replenishment of stores 500 mg has been added.

In our study treatment with intravenous iron therapy showed statistically significant rise in haemoglobin levels and all other red cell indices at 3 and 6th week post transfusion with no significant adverse effects.

CONCLUSION

Intravenous iron sucrose therapy is effective to treat moderate anaemia in pregnant women with minimal side effects compared to intramuscular preparations which are associated with more significant side-effects.

References

1. Dutta Dc. Text book of obstetrics including perinatology & contraception. 6th ed. Calcutta: New Central Book Agency (P) Ltd; 2004. Anaemia in pregnancy; pp. 262–7.
2. Ezzati M, Lopus AD, Dogers A, Vander HS, Murray C. Selected major risk factors and global and regional burden of disease. Lancet. 2002; 360:1347–60.
3. Toteja GS, Singh P, Dhillon BS, *et al*. Prevalence of anemia among pregnant women and adolescent girls in 16 districts of India. Food Nutr Bull. 2006; 27:311–5.
4. Kalaivani K. Prevalence & consequences of anaemia in pregnancy. Indian J Med Res. 2009; 130:627–33.
5. Nutrition. New Delhi: Government of India; 2002. [accessed on December 12, 2012]. Planning Commission. Government of India. Tenth Five- Year Plan 2002-2007. Sectoral Policies and Programmes. Available from: Planningcommission.nic.in/plans/ planrel/fiveryr/10th/10defaultchap.html .
6. DLHS on RCH. Nutritional status of children and prevalence of anaemia among children, adolescent grils and pregnant women 2002-2004.
7. Toteja GS, Singh P. New Delhi: Indian Council of Medical Research; 2004. Micronutrient profile of Indian population.
8. Silverstein SB, Rodgers GM. Parenteral iron therapy options. Am J Hematol. 2004;76:74
9. Charytan C, Levin N, Al-Saloum M, Hafeez T, Gagnon S, Van Wyck DB. Efficacy and safety of iron sucrose for iron deficiency in patients with dialysis-associated anemia: North American clinical trial. Am J Kidney Dis. 2001; 37:300–7.
10. Adamson JW. Iron deficiency and other hypoproliferative anemias. In: Braunwald E, Fauci AS, Kasper DL, editors. Harrison's textbook of internal medicine. 17th ed. New York: McGraw Hill; 2008. pp. 628–33.
11. Rome: FAO; 1988. FAO/WHO Joint Expert Consultation Report. *Requirements of vitamin A, iron, folate and vitamin B12* (FAO Food and Nutrition series 23)
12. Prema K, Neela Kumari S, Ramalakshmi BA. Anaemia and adverse obstetric outcome. Nutr Rep Int. 1981; 23:637–43.
13. Milman N. Iron prophylaxis in pregnancy - general or individual and in which dose? Ann Hematol. 2006; 85:821–8.

14. Milman N, Bergholt T, Eriksen L, Byg KE, Graudal N, Pedersen P, *et al*. Iron prophylaxis during pregnancy - how much iron is needed? A randomized dose- response study of 20-80 mg ferrous iron daily in pregnant women. Acta Obstet Gynecol Scand. 2005; 84:238–47.
15. Bashiri A, Burstein E, Sheiner E, Mazor M. Anaemia during pregnancy and treatment with intravenous iron: review of the literature. Eur J Obstet Gynecol Reprod Biol. 2003; 110:2–7.
16. Hallak M, Sharon A, Duikman R, Auslender R, Abramovici H. Supplementing iron intravenously in pregnancy. A way to avoid blood transfusions. J Reprod Med. 1997; 42:99–103.
17. Wali A, Mushtaq A, Nilofer. Comparative study - Efficacy, safety and compliance of intravenous iron sucrose and intramuscular iron sorbitol in iron deficiency anemia of pregnancy. JPMA. 2002; 52:392–7.
18. Perewusnyk G, Huch R, Huch A, Breymann C. Parenteral iron therapy in obstetrics: 8 years experience with iron-sucrose complex. Br J Nutr. 2002; 88:3–10.
19. Breymann C. The use of iron sucrose complex for anemia in pregnancy and the postpartum period. Semin Hematol. 2006; 43:S28–S31.
20. Brooker S, Hotez PJ, Bundy DAP. Hookworm-related anaemia among pregnant women: A systematic review. PLoS Negl Trop Dis. 2008; 2:e291.
21. Van Wyck DB, Cavallo G, Spinowitz BS, Adhikarla R, Gagnon S, Charytan C, *et al*. Safety and efficacy of iron sucrose in patients sensitive to iron dextran: North American clinical trial. Am J Kidney Dis. 2000; 36:88–97.
22. Bencaiova G, von Mandach U, Zimmermann R. Iron prophylaxis in pregnancy: Intravenous route versus oral route. Eur J Obstet Gynecol Reprod Biol. 2009; 144:135–9.