

Efficacy of parenteral iron sucrose in treatment of pregnancy associated iron deficiency anemia with special reference to body iron stores

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Abstract

Worldwide Iron deficiency anemia (IDA) affects 25% population and in India it affects 80% of pregnant. Prospective interventional study was conducted to know the efficacy of intravenous (IV) iron sucrose in the management of IDA in pregnant women. Pregnant women with singleton pregnancy with gestational age more than 20 weeks and IDA (Hemoglobin <10 gm % and serum ferritin <15ng/dl) were enrolled in the study. Women divided in two treatment groups using lottery system division. Among these two groups, one group received oral iron treatment and another group received IV iron sucrose according to a predesigned standard treatment protocol. Hemoglobin and serum ferritin levels were studied one months after completion of treatment it was observed that in IV iron sucrose treatment group there is statistically significant improvement in Hb and serum ferritin on day 30 after completion of treatment (p value < 0.0001).

Keywords: Pregnancy, Iron deficiency anemia, Hemoglobin, serum ferritin, Iron sucrose.

1. Introduction

Overall 20% of world's population is Iron deficient and Iron deficiency anemia (IDA) is the most common type of anemia met in clinical practice [1]. A crude estimate is that 500 million women between 15-49 years of age worldwide are anemic [2]. In developing countries IDA in pregnancy affects over half of pregnant women. Prevalence of IDA in first trimester ranges from 3.5% to 7.4% and this rate increases up to 15.6 to 55% in third trimester [3]. In India IDA affects 80% of pregnant women.

Oral iron therapy has been effective in correcting IDA in most cases [4]. Its efficacy however is limited in many women especially in pregnancy because of dose-dependent side effects, poor compliance and insufficient absorption. [5]-[7] Considering inadequate effects of oral iron therapy, particularly in later months of pregnancy, it was pertinent to try an alternative treatment for IDA to achieve optimum health of mothers without risk.

Various parenteral Iron preparations like sodium ferric gluconate are considered safer than iron dextran but study [8] reported 74 adverse events attributed to ferric gluconate complex and was reported to WHO. Therefore, considering significant adverse reaction to iron dextran and other similar molecules iron sucrose has been considered as an effective alternative in the management of IDA.[9]-[11]

Since early 1990s, many obstetric clinics have been using only IV iron sucrose for management of IDA during pregnancy and puerperium.[7]

Iron sucrose molecule is a type II iron complex of intermediate stability and strength. It is rapidly metabolized and readily available for erythropoiesis in the bone marrow. Complex stability and unique iron distribution profile makes iron sucrose clinically safe. Moreover, as complexes contain no biological polymers, anaphylactic reactions are unlikely and makes these preparations safe to use in pregnancy[12][13] and rate of blood transfusions reduced to 1% of patients per year[14]. IDA in pregnancy had immense need to review treatments offered to mothers with in light of emerging research evidence and to assess current practice in order to build on strengths, share lessons learnt and identify gaps. These perceptions of IDA during pregnancy were considered and this research was undertaken with the objective to evaluate the efficacy of parenteral iron (Iron sucrose) versus oral iron therapy (Carbonyl iron) in the management of Iron deficiency anaemia (IDA) in pregnancy, with special reference to body iron stores.

2. Material and Method

Present prospective interventional study was carried out at Kasturba hospital Sevagram a tertiary care rural hospital in central India. The study was conducted over a period of two years. Pregnant women with singleton pregnancy with gestational age > 20 weeks and IDA (Hb <10 gm %) were selected. Informed written consent was taken. Ethical clearance was taken from institutional ethical committee (IEC). Women having other type of anemia, asthma, liver diseases, renal diseases, multiple pregnancy and suspected acute infection were excluded from the study.

In pregnant women IDA was estimated by measuring hemoglobin (Hb), RBC count, MCHC and PCV and body iron store was estimated by serum ferritin levels. Women with Hb < 10 and serum ferritin levels < 15 ng/ml were selected for the study. Other investigations including urine routine and culture sensitivity, renal function tests, liver function test, stool examination for ova and cyst were also done.

Women were randomly divided into two groups with the help of computer generated random allocation system. One study group received IV iron sucrose. Dose of IV iron sucrose was calculated by formula given below:

Total iron dose (in mg): {2.4 X (target Hb-Actual Hb) X Prepregnancy Wt. (in kg)} + 1000

Total dose of iron sucrose in mg was given in 3 divided doses over a week on alternate days. 200 mg iron sucrose was diluted in 200 ml of isotonic sodium chloride solution to be given over period of 4 hour during each dose. For first injection, 25 mg (25 ml) was given slowly at a rate of 1ml/min and the women were monitored for 30 minute for any adverse symptoms and signs of anaphylactic reaction. For first dose women were admitted in ward where emergency cardiopulmonary resuscitation facilities were available. Other 2 doses were given on OPD basis in one day care treatment ward.

Other group received two tablets of carbonyl iron containing elemental iron 60 mg each for 4 weeks. Compliance was checked on a compliance calendar and involvement of ASHA (Accredited social health activist) worker. Women were asked to come for follow up every 7 days with compliance calendar and ASHA to be given as supervised dose. Five milligram of folic acid and tablet Albendazol 400 mg 2 doses 1 week apart was given orally to both groups.

Post therapy evaluation at end of four weeks for both treatment groups was done with estimation of Hb and serum ferritin. In both groups Hb estimation was done on 7th day and Hb and serum ferritin estimation on 30th day after completion of treatment. Statistical evaluation was done using Epi6 software. P value<0.5 was taken as significant.

3. Results and Observations

241 mothers registered in study of which 193 (80.08%) women came for follow up of Hb and serum ferritin. 7 women came for follow up with personal efforts making sum of 200. In each group 100 women were included. Efficacy of oral and injectable iron was compared by comparing Hb rise on day 7 and Hb and serum ferritin rise on day 30. Following observations were made on day 30.

3.1 Increase of Hb in both treatment group.

In oral treatment group, on **day 1** baseline Hb in 3% pregnant women was <7gm%, 71% women had Hb between 7-8gm% and 26% women had Hb between 8-9 gm%. In injectable group, baseline Hb was <7 gm % in 26%, 7-8 gm% in 59%, 8-9 gm% in 13% and 2% women had Hb between 9-10gm%.

On **day 7** of completion of treatment in both groups, there was no significant shift of Hb % in oral treatment group but in injectable treatment group, out of 26 women with Hb <7 gm% and 56 women with Hb 7-8 gm%, only one woman in each group remained severely anemic. On day 7 of therapy 17% women had Hb level of 8-9 gm %, as compared to 26 (13%) on day 1 reflecting 4% shift of women from lower Hb to Hb between 8-9 gm%. 44% women shifted to Hb group 9-10 gm%, 30% shifted to Hb group 10-11gm% and 5% shifted to Hb above 11-12gm% group in comparison none of mothers in oral group improved Hb above 9 gm%.

On **day 30** of treatment, in oral group no women had Hb <7gm%, 3% women had Hb 7-8gm%, maximum (70%) were in Hb group of 8-9 gm% and 27% shifted to Hb group 9-10gm%. However no mother could improve Hb above 10gm% in oral group.

In contrast, there was significant shift of Hb concentration in injectable group. After injectable iron therapy no women had severe anemia. Only 3% had Hb between 8-9 gm %, 12% had Hb 9-10gm%, 39% had Hb 10-11 gm%, 32% women were in Hb group 11-12 gm% and 14% study women had Hb rise more than 12gm% in injectable treatment group. (Figure A1 and A2)

Figure A1: Changes in hemoglobin in oral iron group (n=100)

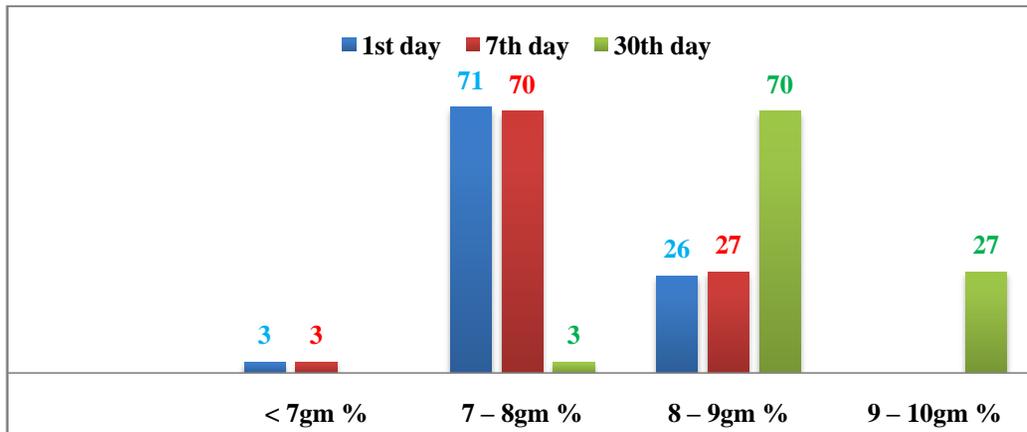
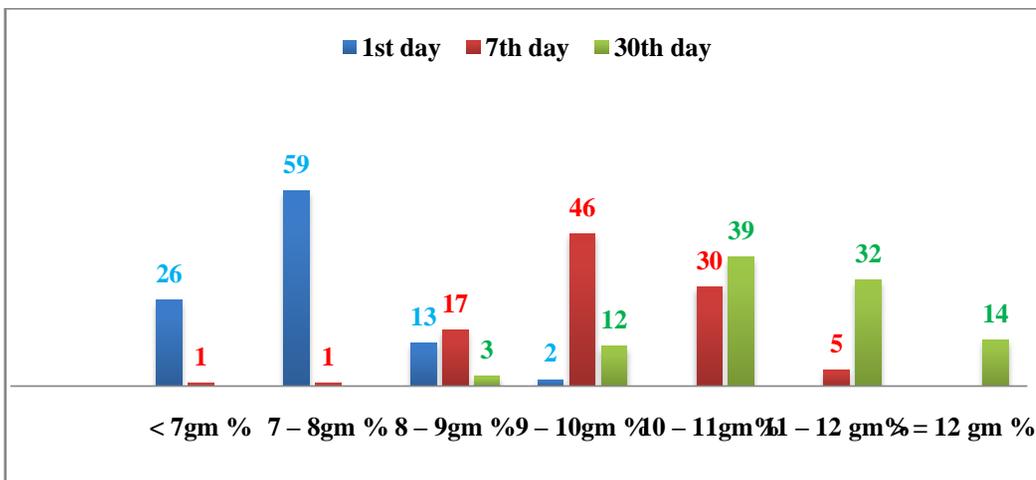


Figure A2: Change in Hb in IV iron sucrose group (n=100)

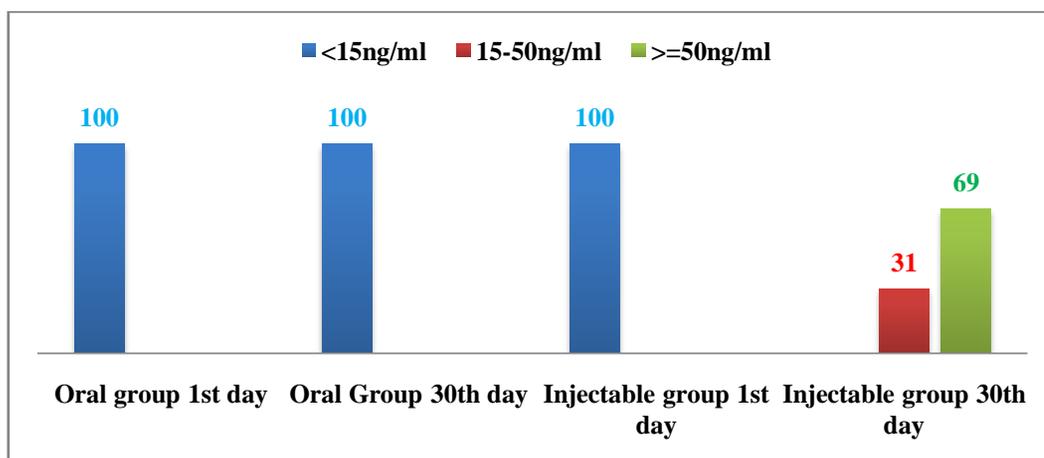


3.2 Increase of serum ferritin (body iron stores) in both treatment groups

In oral treatment group there was no improvement in body iron store, whereas in injectable iron treatment group, 31% women improved iron stores up to 15-50 ng/ml of serum

ferritin and 69% improved body iron stores indicated by serum ferritin ≥ 50 ng/ml on day 30 after completion of treatment. Thus this study reflects role of iron sucrose in improving body iron stores significantly. (Figure B)

Figure B: Changes in serum ferritin in both treatment group (in %)

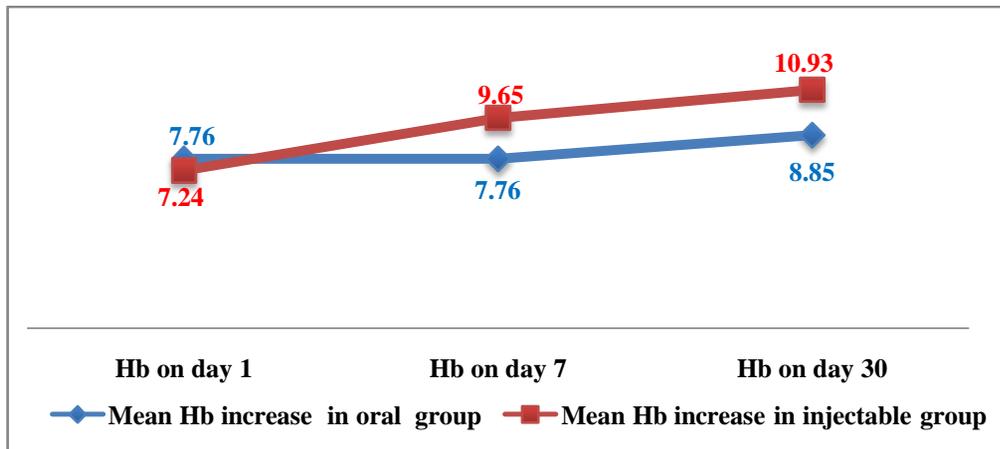


3.3 Mean increase of hemoglobin in both study groups (n=200)

There was no increase in mean Hb on day 7 in oral treatment group. In contrast in injectable treatment group increase in mean Hb was from 7.24±1.02 g/dl to 9.65±0.88 g/dl on day 7 which was statistically significant (p<0.05). On comparing day 30 Hb, in oral group there was significant increase of Hb from 7.76±0.45 g/dl to 8.85 ±0.52 g/dl (p

value < 0.05) and in injectable group this mean rise of Hb was noted from 9.65±0.88 g/dl to 10.93±0.92 g/dl which was significant (p value < 0.0001). If we compare day 1 and day 30, rise in Hb was from 7.76±0.45 g/dl to 8.85±0.52 g/dl in oral group as compared to rise of Hb from 7.24±1.02 g/dl to 10.93±0.92 g/dl in injectable treatment group which was statistically significant (p<0.0001) (Figure C)

Figure C: Mean increase in Hb in both treatment groups (in gm%)

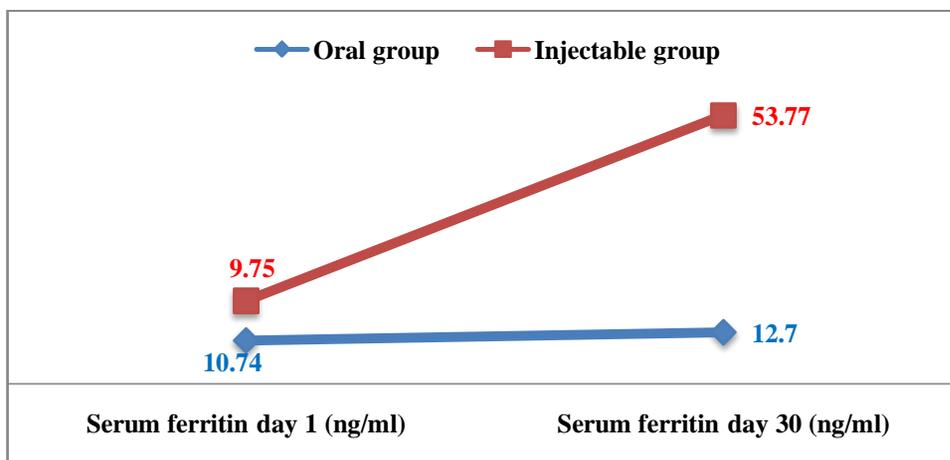


3.4 Mean increase of serum ferritin in both study groups (n=200)

In oral treatment group there was an increase in mean serum ferritin from 10.74 ng/ml ±2.00 to 12.70 ±1.43 ng/ml (p value <0.05) which was statistically significant but body iron stores did not reach to necessary levels for pregnancy i.e. >50ng/ml. In injectable treatment group, serum

ferritin level improved from 9.75±2.15 ng/ml to 53.77±6.53 ng/ml (p value < 0.0001) which is statistically significant. Moreover mean level of serum ferritin level was more than 50 ng/ml, which is sufficient for demands of pregnancy.(Figure D) Thus injectable iron sucrose was found to increase body iron stores significantly to a considerable extent so as to meet increased demands of pregnancy.

Figure D: Mean increase in serum ferritin in both treatment groups (in ng/ml)



4. Discussion

Baseline mean Hb level in oral treatment group was 7.76±0.45 g/dl and in injectable treatment group was 7.24±1.02 g/dl. After completion of therapy on day 7 there was no change in Hb level in oral group but there was

significant rise in mean Hb level in injectable group. Mean Hb rise occurring in injectable group was from 7.24±1.02 g/dl to 9.65±0.88 g/dl (p value <0.05). On comparing day 30 Hb levels in oral group there was significant increase of Hb from 7.76±0.45 g/dl on day 1 to 8.85±0.52 g/dl on day 30 (p value < 0.05) and in injectable group mean rise of Hb was noted

from 9.65 ± 0.88 g/dl on day 7 to 10.93 ± 0.92 g/dl on day 30th which was statistically significant (p value < 0.05). After analysis it was concluded that mean rise in Hb in oral group was 1.09 ± 0.07 g/dl and 3.69 ± 0.10 g/dl in injectable group on day 30 after completion of treatment ($p < 0.05$). Significant rise in Hb was found in oral group on the 30th day of completion of treatment but in injectable group, there was significant increase in mean Hb on day 7 too after completion of the treatment.

If we compare day 1 and day 30 in both groups, rise of Hb was from 7.76 ± 0.45 g/dl to 8.85 ± 0.52 g/dl ($p < 0.05$) in oral group as compared to rise of Hb from 7.24 ± 1.02 g/dl to 10.93 ± 0.92 g/dl which is statistically significant ($p < 0.0001$). Moreover no woman in oral group had Hb rise above 9 gm% whereas 14% of women in injectable group had Hb rise > 12 g/dl.

While comparing body **iron stores replenishment** in oral group from 10.74 ± 2.00 ng/ml to 12.70 ± 1.43 ng/ml (p value < 0.05) which was statistically significant but body iron stores did not reach to necessary levels i.e. > 50 ng/ml in any mother after 30 days of completion of oral therapy whereas in injectable group, serum ferritin level improved from 9.75 ± 2.15 ng/ml to 53.77 ± 6.53 ng/ml. (p value < 0.05) Mean level of serum ferritin level was more than 50 ng/ml in this group being sufficient for demands of pregnancy.

In a study [15] it was found that iron sucrose group achieved significantly higher Hb level (128.5 ± 6.6 g/l vs. 111.4 ± 12.4 g/l in control group $P < \text{or} = 0.001$) in a shorter period (6.9 ± 1.8 weeks vs. 14.9 ± 3.1 weeks in control group, $P < \text{or} = 0.001$) and concluding that iron sucrose is safe and effective in treatment of IDA during pregnancy.

IV iron sucrose becomes therapeutic mainstay for severely iron-deficient mothers when they are unable to take oral preparations [16]. In practice, physician often face poor compliance, justified by digestive side effects leading to worsening of anemia. In these cases parenteral iron sucrose of administration are indicated.[17]

Researchers found that serum ferritin levels were significantly higher in injectable than oral treatment group ($p < 0.001$). They also suggested that total dose infusion is able to replenish iron stores more efficiently, completely and at a faster rate than oral iron therapy [18][19]. Another observation [20] recommended that in pregnant mothers IV iron sucrose therapy is recommended if serum ferritin falls below 100ng/ml. IV iron sucrose supplementation represents practical alternative to oral iron and can be safely administered to the mothers in an outpatient setting [21]. Compared with daily oral iron therapy, IV iron supplementation was better tolerated and resulted in superior Hb levels and body iron stores replenishment [22].

Schroder et al[23] suggested that injectable iron sucrose led to rise in serum ferritin concentration. Although being equal in short term efficacy and overall tolerability, their results suggests a better gastrointestinal tolerability for iron sucrose. Another trial ($n=100$) in Singapore supported

that higher Hb values at end of pregnancy were found with IV iron treatments compared with oral iron.[24] Similar observations were also made by many others.[25][26]

Hence, considering demographic, social, economical and religious background in poor clinical set ups and scanty health facilities including facilities for blood transfusion one may consider estimation of serum Hb along with serum ferritin as an accurate way to diagnose IDA in general population as well as in pregnant women. With same philosophy injectable iron sucrose provides us with an effective, alternative and safe form of treatment for iron deficiency anemia. Apart from improving hematological indices, iron sucrose also helps to improve clinical as well as maternofetal outcome of pregnancy. Also in various studies also it has been proved that IV administration of iron sucrose is a safe treatment for correction of anemia in pregnancy (antenatal and postnatal), without serious side-effects.[27]-[29]

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