

## Research Article

# Efficacy and safety of intravenous iron sucrose therapy in a group of children with iron deficiency anemia

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## ABSTRACT

**Background:** Iron deficiency anemia is common problem in children, though the oral iron therapy is the main stay of treatment, but most of children not responding to it due to non-compliance. So the parental iron therapy is the treatment of choice for it.

**Methods:** Fifty children between the age group of 1-17 years of age were selected for this study diagnosed as iron deficiency anemia. Iron sucrose given by IV according to their weight and age. CBC performed before starting of study and after receiving Iron sucrose intravenously i.e. after 4, 10 and 30 days of iron sucrose.

**Results:** Among the red cell indices, mean corpuscular volume and mean corpuscular haemoglobin in this study we got mark improvement in both the parameters along with improvement in PCV and finally increase in haemoglobin level. All the parameters having P value highly significant i.e. <0.001 along with minimal side effects.

**Conclusions:** Iron sucrose can be safely used in children.

**Keywords:** Iron deficiency anemia, Iron sucrose, Haemoglobin

## INTRODUCTION

Iron deficiency is the most common cause of anemia due to nutritional deficiency.<sup>1,2</sup> In industrialized countries 17% of children under 5 years old suffer from iron deficiency anemia.<sup>3</sup> A recent study from Israel showed a prevalence of 15.5% in infants aged 9-18 months.<sup>4</sup>

Many factors predispose children to iron deficiency anemia, including nutritional deprivation, intestinal malabsorption and blood loss. Another cause is ingestion of intestinal iron absorption inhibitors, such as phytates or cow's milk protein, which may lead to iron deficiency.<sup>5</sup> The treatment of iron deficiency anemia

consists of improved nutrition along with oral, intramuscular or intravenous iron administration. Currently, several intravenous iron preparations are available for use, including iron dextran, iron gluconate and iron sucrose. Treatment with these intravenous iron preparations leads to an increase in hemoglobin blood levels and to restoration of iron stores.<sup>6</sup> However, the use of iron dextran is associated with side effects that include anaphylactic reactions (immune and dose-related) in approximately 1% of treated patients.<sup>7,8</sup> In addition, serum iron and ferritin blood levels remain significantly elevated for a long time after iron dextran administration.<sup>9</sup> The administration of iron gluconate is also associated with adverse effects, but these are usually

mild and no fatal allergic reaction following the use of this preparation has been reported.<sup>10</sup> The use of iron gluconate or iron sucrose has fewer side effects compared to iron dextran.<sup>10</sup> In fact, iron gluconate was successfully administered to patients who previously had shown severe reactions, including anaphylaxis, to iron dextran.<sup>11</sup> In contrast, iron sucrose treatment is effective<sup>12</sup> and may be given safely to predialysis and hemodialysis patients with or without erythropoietin therapy.<sup>13-15</sup> Pregnant women have also been treated with iron sucrose without untoward effects.<sup>16</sup>

We conducted a retrospective study in which infusions of iron sucrose were administered to pediatric patients with iron deficiency anemia who failed to respond to oral iron treatment.

## METHODS

The study was approved by the local ethics committee of the institute, Mahatma Mission hospital and medical college. It is a prospective study patient attained pediatrics OPD and received iron sucrose therapies from 1/7/13 to 30/12/13 were included in this study. Patients were stay in OPD side room when they receiving the iron sucrose therapy. In this study we included 1-15 years of children. The diagnosis of iron deficiency was defined as hemoglobin level lower than 2 standard deviations below the normal 15.5%. Blood level corrected for age. Non-compliance in children was defined as a child not taking

iron treatment, administered in the form of at least two different oral preparations, for a minimum period of 3 months. The oral preparations that were administered to the patients were polymaltose iron complex, ferrous gluconate, ferrous lactate or ferrous sulfate at a dose of 6–7 mg/kg/day of elemental iron given two to three times daily. 50 children were included in this study. All patients were initially treated with oral iron for at least 3 months, except for one patient who suffered from short gut syndrome and was given intravenous iron as the initial treatment. Fortynine patients did not receive the oral iron treatment and thus were defined as non-compliant. Detail history of patients was recorded in OPD case paper. Causes of iron deficiency anaemia obtained from OPD case paper. The following laboratory tests were performed: complete blood count, including and reticulocyte count.

### Iron treatment

Iron was administered intravenously as iron sucrose complex (Venofer) according to the protocol provided by the manufacturer, in the pediatric OPD. Venofer is supplied in ampules containing 100 mg of elemental iron in 5 ml. The total amount of iron administered was calculated according to the patient's weight and hemoglobin using the following formula:<sup>17</sup>

$$\text{The total amount of iron administered} = \frac{\text{Normal hemoglobin for age} - \text{Initial hemoglobin}}{100} \times \text{Blood volume (ml)} \times 3.4 \times 1.5$$

Where 3.4 converts grams of hemoglobin into milligrams of iron and factor 1.5 provides extra iron to replace depleted tissue stores.<sup>18</sup>

### Daily dosage

Daily dosage was calculated as 5 mg Fe<sup>+++</sup> per kilogram per day. The number of days was calculated by dividing the total dose by the daily dose. The iron preparation was diluted to 1 mg Fe<sup>+++</sup> in 1 ml of NaCl 0.9%, and administered at an infusion rate of 1-1.3 ml/minute three times a week. All patients underwent a test where a quarter of the dose that was planned for the first infusion was administered at a rate that did not exceed 0.5 ml/minute.<sup>19</sup>

### Follow-up tests

According to this study hemoglobin level, reticulocyte count were determined immediately before the iron administration, 4 days 10 days and 30 days after the iron dose following completion of therapy.

### Statistical analysis

The data were collected and analyzed by the SPSS 11 for Windows software package.

To assess the effect of changes in hemoglobin concentration and Paired t-tests were performed to compare between the groups. P <0.05 was considered significant in all comparisons.

## RESULTS

The study comprised 50 paediatric patient (n=50) showing iron deficiency anemia. The age wise distribution presented in Table 1 indicates that the highest number (40%) of patients belonged to age group between the age of 16-17 years, followed by 1-5 years and 6-10 years of age, making 30% and 118%, respectively.

The haemoglobin concentration before treatment in different patients depicted in Table 2 indicate that the number of patients with Hb level between 6-7 g/dL was 23 (46%) followed by range 7-8 g/dL accounting for 18

(36%) patients and the number of patients whose Hb level between 5-6 was only 6 (12%). The changes in haematological parameters following administration of I/V iron sucrose are presented in Table 3.

Our study demonstrated that administration of iron sucrose caused increase in all the estimated haematological parameters. On the 30<sup>th</sup> day after treatment, average Hb level, hematocrit, RBC count increased from  $6.95 \pm 0.72$  g/dl to  $12.10 \pm 0.69$  g/dl,  $21.19 \pm 2.33\%$  to  $37.33 \pm 2.45\%$ ,  $3.48 \pm 0.37 \times 10^6$  cell/cu.mm to  $5.56 \pm 0.41 \times 10^6$  cell/cu.mm, respectively.

The red blood cells indices also showed increasing trends after the administration of iron sucrose. On the 30<sup>th</sup> day, the MCV increased from  $65.62 \pm 3.04$  fL to  $87.92 \pm 7.03$  fL and the MCH values also increased from  $23.85 \pm 2.6$  pg to  $35.58 \pm 6.56$  pg.

**Table 1: Age wise distribution of patients.**

| Age group (years ) | No. of patients | Percentage of patients (%) |
|--------------------|-----------------|----------------------------|
| 1-5                | 15              | 30                         |
| 6-10               | 9               | 18                         |
| 11-15              | 6               | 12                         |
| 16-17              | 20              | 40                         |

**Table 2: Range of haemoglobin concentration in different patients before treatment.**

| Range of Hb (g/dL) | No. of patients | Percentage of patients (%) |
|--------------------|-----------------|----------------------------|
| 5-6                | 6               | 12                         |
| 6-7                | 23              | 46                         |
| 7-8                | 18              | 36                         |
| 8-9                | 3               | 6                          |

**Table 3: Changes in haematological parameters following intravenous administration of iron sucrose (n=50).**

| Parameters                       | 0 day            | 4 day            | 10 day           | 30 day             | Mean increase on 30 <sup>th</sup> day | P value |
|----------------------------------|------------------|------------------|------------------|--------------------|---------------------------------------|---------|
| Hb (g/dL)                        | $6.95 \pm 0.72$  | $7.75 \pm 0.74$  | $9.67 \pm 0.77$  | $12.10 \pm 0.69^*$ | $5.15 \pm 0.55^*$                     | <0.001* |
| PCV (%)                          | $21.19 \pm 2.33$ | $23.65 \pm 2.41$ | $29.59 \pm 2.71$ | $37.33 \pm 2.45^*$ | $16.14 \pm 2.16^*$                    | <0.001* |
| RBC ( $\times 10^6$ cells/cu.mm) | $3.48 \pm 0.37$  | $3.88 \pm 0.38$  | $4.81 \pm 0.43$  | $5.56 \pm 0.41^*$  | $2.08 \pm 0.55^*$                     | <0.001* |
| MCH (pg)                         | $23.85 \pm 2.6$  | $26.26 \pm 3.2$  | $34.00 \pm 5.07$ | $35.58 \pm 6.56^*$ | $11.73 \pm 5.52^*$                    | <0.001* |
| MCV (fL)                         | $65.62 \pm 3.04$ | $68.98 \pm 2.61$ | $79.56 \pm 5.51$ | $87.92 \pm 7.03^*$ | $22.30 \pm 5.62^*$                    | <0.001* |

The values presented are Mean  $\pm$  SD; \*Significant (using paired “t” test)

The study demonstrated that following administration of iron sucrose, increase in the base line level of all the estimated haematological parameters was observed (Mean increase in Hb was  $5.15 \pm 0.55$  g/dL, hematocrit was  $16.14 \pm 2.16\%$ , RBC count was  $2.08 \pm 0.55 \times 10$  cell/cu.mm, MCV was  $22.30 \pm 5.62$  fL, MCH was  $11.73 \pm 5.52$  pg). The results were analysed by paired ‘t’ test method and the difference was found to be statistically significant (P <0.001). And also the high rate of reticulocytosis following I/V administration of iron sucrose.

The reticulocyte count increased to  $7.18 \pm 1.29$  cells on day 4 from initial  $1.78 \pm 0.77$  cells, and on day 10<sup>th</sup> the reticulocyte count was  $2.80 \pm 0.76$ , indicating accelerated erythropoiesis in the treated patients. The overall sense of well-being in all the patients improved dramatically from the 3rd day onwards.

There were no serious reactions to the treatment except a few patients complaining of moderate abdominal pain and skin staining (Table 4).

**Table 4: Adverse effects in both the groups.**

| Adverse effects         | Number | Percentage |
|-------------------------|--------|------------|
| Local phlebitis         | -      | -          |
| Shivering and weakness  | -      | -          |
| Moderate abdominal pain | 1      | 2          |
| Local pain              | -      | -          |
| Skin staining           | 1      | 2          |
| Headache                | -      | -          |
| <b>Total</b>            | 2      | 4          |

## DISCUSSION

Iron deficiency anemia is a very common problem in the pediatric population and is usually treated by oral iron administration. Most patients tolerate the therapy well. However, a number of patients fail to respond to oral iron treatment. In our patients the most common reason for oral treatment failure was lack of compliance. For these patients, intravenous iron sucrose treatment is recommended. Two patients who responded only partially to the treatment were found to have concomitant

beta-thalassemia minor so they are omitted from this study. After nutritional deficiency *H. pylori* gastritis, a well-known cause for iron deficiency anemia.<sup>20</sup> *Helicobacter pylori* gastritis should be treated concurrently with iron supplementation. Very few studies on intravenous iron supplementation in children have been published. Iron dextran was found to be effective when given to children with inflammatory bowel disease. Nevertheless, 14% of these patients developed immediate hypersensitivity reactions, which fortunately were not life threatening.<sup>21</sup> Iron sucrose was found to be more effective than oral iron in restoring postoperative hemoglobin following spinal surgery in children,<sup>22</sup> or in rapidly increasing hemoglobin concentration in pediatric candidates for elective surgery.<sup>23</sup> Intravenous iron sucrose may be safely administered to preterm infants. However, the small number of patients in the study precludes exact statistical analysis.<sup>24</sup> The blood ferritin level was a dependable marker for iron storage, increasing quickly within 10 days following the treatment and decreasing after 6 months. This effect could be explained by the fact that the hemoglobin and ferritin levels are not reciprocally linear. Hemoglobin and ferritin levels post-treatment reflect erythropoietic recovery on the one hand, followed by a reactive decrease in ferritin due to feedback at the mRNA level on the other.<sup>25</sup> In our study we not included the ferritin level because it is very costly investigation, and our hospital mostly serving poor peoples, so it is not affordable to patients and hospital also, so we include only basic investigation for these patients, and we found that, Iron sucrose administration was found to be a safe treatment with few, transient and reversible side effects, even in small children. Further research involving a larger population specially below the one year age of patients is needed to determine the safety and efficacy of intravenous iron therapy in small age group children.

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