# Assessment of the Efficacy and Safety of Intravenous Iron Sucrose in Treatment of Adult Patients with Iron Deficiency Anemia

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**Abstract**

**Background:** Iron deficiency is the most common cause of anemia worldwide. The treatment for iron deficiency anemia consists of replacement of iron either orally or parenterally. Patients with iron deficiency anemia (IDA) who need intravenous iron are normally treated with iron dextran. One of the major side effects of iron dextran is severe (sometimes fatal) anaphylactic reaction. On the other hand, iron sucrose another intravenous iron preparation that has improved safety and ease of administration. This preparation is being used in dialysis patients with very good results. But this has never been formally evaluated in non-dialysis-dependent patients.

**Objective:** To assess the efficacy and safety of intravenous iron sucrose in treatment of adult patients with iron deficiency anemia.

**Patients & Methods:** Between August 2009 and August 2011, one hundred fifty eight patients with iron deficiency anemia who were seen at the out-patient clinic at the national center of hematology with hemoglobin level < 11 g/d, or inadequate response to iron oral therapy were included in this study. Written informed consent was obtained from all patients. The main laboratory tests done were: complete blood count and blood film, reticulocyte count, serum iron, total iron-binding capacity, serum ferritin. After testing dose, patients received a weekly dose of iron sucrose diluted in 500 mL of 0.9% sodium chloride solution administered intravenously for 3 to 4 hour. The dose was calculated according to special formula. Treatment continued until a hemoglobin level equal or more than 12 g/dL for women and 13 g/dL for men or until full administration of the total dose of parenteral iron recommended for each patient.

**Results:** Mean age of the patients studied was 33 years (ages ranging from 17 to 66 years). One hundred thirty nine patients (88%) were females while 19 patients (12%) were males. The most common cause of iron deficiency anemia was abnormal uterine bleeding observed in 68% of the female patients (95 out of 139) and gastrointestinal causes observed in 63% of the male patients (12 out of 19). Correction of anemia was obtained in 144 out of 158 patients (91%). The mean hemoglobin and ferritin values were 8.09 g/dl and 6.20 ng/ml (before treatment) and 12.42 g/dl and 88.78 ng/ml (after treatment) ($p < 0.001$), respectively. In general the average increase of hemoglobin was 3.74 g/dl, ranging from 1.30 to 7.60 g/dl. . Among all the patients studied, only 8 patients (5%) had mild reactions related to intravenous iron.

**Conclusion:** The use of intravenous iron sucrose is an effective and safe option in the treatment of adult patients with iron deficiency anemia lacking satisfactory response to oral iron therapy. This treatment option should be considered mainly for patients with severe anemia in order to obtain rapid increase of the hemoglobin level and avoid blood transfusion.

***Keywords:*** *Efficacy, iron sucrose, iron deficiency anemia*

## Introduction:

Iron deficiency anemia (IDA) is the most widespread nutritional problem, and affects over two billion people [(1)]. It is a particularly common disorder among infants, preschool aged children, young women and older people, but it can occur at all ages and in any region. A high demand for iron during rapid growth, pregnancy and lactation, accompanied by dietary deficiencies and menstrual blood loss, are the most common causes of iron deficiency in children and young women[(2)]. Anemia is associated with a low work capacity, a poor pregnancy outcome, as well as lasting effects on learning and cognitive function, attention, behavior, health and growth. Several studies have been conducted to evaluate the effects of IDA on psychomotor development and cognitive functions [(3, 4)].

Although nutritional deficiencies of folate and vitamin B12, infectious diseases, such as the human immunodeficiency virus, hookworm, malaria and other chronic diseases, may account for anemia, according to the literature, more than 50% of cases of anemia in young children and pregnant women in developing countries are related to iron deficiencies[(1,5)].

The treatment for iron deficiency anemia consists of replacement of iron either orally or parenterally [(7)]. The efficacy of oral iron, however, is limited by many factors, including gastrointestinal side effects, poor gastric absorption and noncompliance. Intramuscular injection is not an attractive alternative as this may result in skin necrosis, skin pigmentation and abscess. Intravenous iron is usually reserved for those patients who have failed a trial of oral iron therapy due to gastrointestinal intolerance, failure to absorb the oral iron, or if the rate of iron loss exceeds the rate of iron replacement. Although parenteral infusion is available, concern about its potential side effects limits its widespread acceptance [(8)].

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 [(9)].

The experience with the use of iron dextran, especially in the '70s and '80s, has generated strong fear in the indication of treatment with parenteral iron due to the high incidence of adverse reactions and severe complications after administration of iron-dextran [(20,22)].

These complex preparations consist of weak and unstable molecules resulting in release of plasma iron ion, with rapid saturation of transport proteins with deposition particularly in liver tissue and higher concentrations of iron in the kidneys. Furthermore, the presence of Biological polymers in the preparations of iron-dextran significantly increases the risk of side effects [19]. Iron sucrose administration was found to be a safe treatment with few, transient and reversible side effects, even in children 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 [10,11]. 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 [13]. In contrast, iron sucrose treatment is effective [14] and may be given safely to predialysis and hemodialysis patients with or without erythropoietin therapy [15,16]. Pregnant women have also been treated with iron sucrose without untoward effects [17].

The aim of this study was to assess the efficacy of intravenous iron sucrose in treatment of adult patients with iron deficiency anemia

**Patients and Methods:**

From august 2009 to august 2011, one hundred fifty eight patients treated at the national center of Hematology, Baghdad, Iraq were included in this study. Written informed consent was obtained from all patients prior to receiving treatment of iron sucrose, All patients had a diagnosis of iron deficiency anemia (Hb <10.0 g / dL for women, Hb <11.0 g / dL for men and serum ferritin <12.0 ng / mL).

Exclusion criteria included: patients aged ≤ 15 years, pregnant women in first trimester of pregnancy, patients with anemia other than iron deficiency anemia e.g. thalassemia, hemolytic anemia, hypersplenism, liver or renal disease, and patients with a history of hypersensitivity to iron sucrose,

All patients underwent the following procedures: complete history (including questions about back ground menstrual and obstetric, chronic loss of blood, donation of blood, blood transfusion, use of drugs as aspirin, non-steroidal anti-inflammatory drugs etc.). And physical examination.

collection of blood sample done for the following laboratory tests: complete blood count done by Abbott auto analyzer, reticulocyte count, serum iron, total binding capacity done by standard laboratory technique, and serum ferritin done by (enzyme linked immune sorbent assay ELISA), other tests like Hb-electrophoresis and occult blood in the stool done whenever there were indication.

The transferrin saturation index (TSI) was calculated from the formula:

Serum Iron/ total iron binding capacity x 100.

Patients diagnosed with iron deficiency anemia received iron sucrose complex. Total dose of Iron sucrose was calculated and administered in a weekly successive session in which total dose in each session did not exceed 500 mg elemental iron in 500 ml 0.9% normal saline infusion over 3-4 hour . A test dose of 2.5 mL of iron sucrose was diluted in 100 mL of 0.9% sodium chloride and administered over 30 min prior to the first administration. The doses were calculated according to the patient's body weight and the total iron deficit calculated as follows

Iron deficit (mg) = (target Hb – actual Hb) x weight (kg) x 2.2

Plus 1000 mg for male and 600 mg for female to replenish storage [18]

Hemoglobin level, reticulocyte count and MCV level were determined immediately before the iron administration, then after 2 weeks after the first iron dose and monthly for the first 3 month following completion of therapy, while serum ferritin was determined before starting therapy and then after 1 month , 3 month, and 6 month

Allergic reactions were graded as grade I and grade II and they are described as following. A

Grade I reaction was mild to moderate in nature, settled with an anti-allergic drug but not requiring discontinuation of the infusion. A grade II reaction was severe in nature, threatening the patient's life and requiring discontinuing of infusion

**Statistical analysis:**

The data were collected and analyzed by the SPSS 17 for Windows software package. To assess the effect of changes in hemoglobin concentration and ferritin levels, comparisons were used for hemoglobin and ferritin concentrations between samples. Paired *t*-tests were performed to compare between the groups. $P < 0.05$ was considered significant in all comparisons

**Results:**

The characteristics of the one hundred fifty eight patients according to age, sex and etiology of IDA shown in Table 1.

**Table 1:** Major characteristics of patient in this study

| Characteristic | (n=158) |
|---|---|
| Sex (M:F) | 19:139 |
| Median age (yr)(range) | 33 (17-66) |
| Etiology of iron deficiency | No. (%) |
| Nutritional causes | 27(17) |
| Gynecological blood loss | 95(60) |
| Gastrointestinal blood loss | 19((12) |
| Combined etiology | 10(6.3) |
| Pregnancy | 7(4.7) |

**Table 2**: Distribution of patients according to age

| Age (years) | No (%) |
|---|---|
| 15-24 | 44 (27.8) |
| 25-34 | 86 (54.4) |
| 35-44 | 14 (8.8) |
| 45-54 | 6 (3.7) |
| 55-64 | 5 ( 3.1) |
| > 65 | 3 (1.8) |
| Total | 158 100 |

**Table 3:** Comparison of the results of the main laboratory variables used at the beginning and after 1 month of treatment with IV iron sucrose (IS) administered to 158 patients with iron deficiency anemia

| Variable | Before treatment | | After treatment | | P value |
|---|---|---|---|---|---|
| | Mean (SD) | Min-Max | Mean (SD) | Min-Max | |
| Hemoglobin(g/dl) | 8.09(1.79) | 5.9-10 | 12.42(1.45) | 9.3-13.6 | <0.001 |
| MCV (fl) | 65.42(8.33) | 56-78 | 77.95 (6.10) | 73.4 -91.2 | <0.001 |
| Iron (mg / dl) | 8.67(10.65) | 2.70-59 | 59.20(23.76) | 13 -120 | <0.001 |
| Ferritin(ng/ml) | 6.20 (4.10) | 3.80-14.8 | 88.78 (83.22) | 6.30 380 | <0.001 |

SD = standard deviation, Min = minimum, Max = maximum

**Discussion:**

The oral iron replacement has been universally accepted as treatment of choice for patients with iron deficiency anemia.

However, treatment with intravenous iron is an effective alternative option, which may be indicated in certain situations where oral iron replacement is not enough to obtain the normalization of hemoglobin levels and / or storage of normal body iron due to malabsorption, poor tolerability by the patient or, when it is necessary for rapid correction of circulating hemoglobin[10,12]

In this study, we analyzed 158 patients with iron deficiency anemia whose mean age was 33 years, ranging from 17 to 66 years, 139 (88%) were females and 19(12%) of patients were males. Regarding age group about 62% of patients fall between 25 and 44 years.

It is estimated that about 10% to 40% of patients have adverse reactions to iron which administered orally.

The most common reactions are gastrointestinal in nature, as nausea, abdominal pain, vomiting, diarrhea or constipation; such symptoms are due, mostly, to dose rather than the compound itself, although the slow-release preparations provide better tolerability. Some of these symptoms may be minimized by administering the iron along with meals or reducing the dose administered. However, persistence of these adverse effects results in less patient adherence to treatment and consequently low effectiveness of therapy [12,23]

The most common cause of iron deficiency anemia in women in this study was abnormal uterine bleeding was observed in 95/193 (68%). In women of reproductive age, blood loss in menstruation is often responsible for the increase in the iron requirements.

For women of reproductive age, anemia whose intensity is disproportionate to menstrual blood loss indicates that the patient is probably need investigation to know the possible cause or aggravating factor related to the condition of iron deficiency anemia, in absence of gynecological problems [11]. The most common cause of iron deficiency anemia in males was gastrointestinal causes which were observed in 12/19 (68%) which is similar to previous reported studies [11, 24]

Intramuscular injections use is not an attractive option because of discomfort, pain, staining of the skin, tissue necrosis, bleeding, tissue atrophy with ulceration and development of sarcoma at the injection site [8].

In this study, all patients had significant increase in serum iron, hemoglobin and ferritin level. The increased mean hemoglobin was 2.91 g / dL for females and 3.83 g / dL for males after an average relatively short period of treatment, i.e. six weeks. The correction of anemia in general was observed in 144/158 (91%) of all patients, 128/139 (92%) in female patients and in 16/19 (84.2%) of male patients. Data obtained in this study are consistent with results published in literature [22-26]. Of the 158 patients, none received RBC transfusion during or after the treatment.

Regarding the safety of the drug used, no serious adverse reaction observed in any patient during and after taking intravenous iron sucrose in this study, only eight of the 158 patients (5%) had mild side effects which were treated with antihistamine and paracetamol; 4 patients had mild leg edema, 2 patients had mild itching at the site of infusion and the other 2 patient has mild hypotension. Side effects were limited in the present study because the total dose of intravenous sucrose complex was administered at intervals and it was given in diluted form and slowly, the results observed in current study confirm the data reported in previous studies [12, 15, 23, 26]

**Conclusion:**

The use of intravenous iron sucrose is an effective and safe in the treatment of adult patients with iron deficiency anemia who do not respond to oral iron therapy. This treatment option should be taken into consideration especially in patients with more severe degrees of anemia, in order to obtain rapid increase in hemoglobin values and avoid the use of blood transfusion

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