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# Comparison Between Parenteral And Oral Iron Replacement Therapy In Anemic Iraqi Female Patients

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## ABSTRACT

Anemia is the universal complication affected to the women's health more than the men resulting to diminish the quality of women life. The deficiency of iron occurs in females during menstrual blood losses and there is a significant correlation for the reduction in hemoglobin concentration. The therapy of iron deficiency is faced with many challenges such as; the most important thing is to discover and treat the main cause of iron deficiency anemia, then, select the suitable product for iron which meets the patients' needs.

The present study was to compare Intravenous iron and oral iron supplementation. It is included 90 patients in this study, ages between 20 to 65 years of women with anemia. Anemia is detected through the level of hemoglobin with less of 12 g/dL, and serum ferritin below 30 ng/dl. Pregnancy, Hemoglobinopathy, Diabetes, renal, heart, and hepatic diseases are excluded from this study .

The efficacy of oral iron is diminished when it is uptake through the gut is impaired. Patient compliance is decreased due to the side effects of oral iron. It was observed that oral iron therapy is a less efficient therapy of iron deficiency anemia compared to intravenous iron therapy.

**Keywords:** comparison, Iron deficiency anemia, ferrous sulfate, iron sucrose

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## INTRODUCTION

Anemia is a universal health problem influence the countries income and social life. Anemia reduces the female's health leading to raise the danger of maternal and a new baby.

Iron deficiency anemia (IDA) is a form of anemia and this disease occurs due to the low levels of iron that lead to producing unhealthy red blood cells. Many reasons are leading to iron deficiency anemia, for example; blood loss, gut malabsorption, and micronutrients inadequate (1).

The prevention and medication of iron deficiency (ID) are the considerable health target, especially in kids, females, and individuals in low-income society (2). It is urgent to treat anemic patients to diminish the subsequent risks of anemia. There are two therapeutic methods to increase the levels of hemoglobin (Hb) in the clinical practices; oral iron and intravenous (IV) iron sucrose, to improve or maintain their quality of life (3).

The first option of IDA therapy is oral iron as ferrous sulfate. Some issues are found when the patients are having the iron orally such as difficulties to tolerate, stuck in the mouth, or might be the treatment is not respond to the iron orally (4)(5). In this case, the oral iron is replaced with intravenous (IV) iron preparations, such as ferric carboxymaltose, iron dextrans, iron gluconate or iron sucrose. They are used to raise iron levels and increase hemoglobin in anemic patients with or without chronic kidney disease (CKD) (6)(7).

According to the FDA in 2009, iron dextrans injection is required for iron therapy for low doses (100 mg) with the full treatment course 1 g. The doses of infusion are administrated to the patient are dependent on the body weight and the time; for example, the labeling of the UK permits 20 mg / Kg (iron/body weight) over 4 – 6 hours (7).

Some medical practices have a reluctance to utilise iron dextrans as IV. Thus, this is because it maybe is an unsafe and not effective treatment with the previous doses as well

the high incidence of adverse effects (9, 10). The properties of Iron dextrans are unsteady and weak molecule, and the consequence of that is releasing the ions of plasma iron. The releasing ferric ions with the low concentrations are deposit in many organs especially in the liver, while the high concentrations of iron ions are deposit in the renal. Besides, there is a consideration of the increasing risk of adverse interactions of iron dextrans preparations due to the existence of Biological polymers in iron dextrans solution (8).

Another IV injection for anemia treatment is Ferumoxytol, it was confirmed by the FDA in 2009. The nature of Ferumoxytol is a colloidal superparamagnetic ferric oxide. Ferumoxytol is used to treat IDA and anemia in CKD. The suitable dose for administration is 510 mg with twice injections (8)(9). Ferumoxytol is used to treat IDA patients which unable to have iron orally as well as it has efficacy and safety when compared to iron sucrose (3).

The common IV iron compound is iron sucrose; it is used as an infusion to correct the levels of Hb. The utilised permit dosage is between 200 – 300 mg by 2 hours infusion without adverse effects. Side effects have been observed when increased the dose over 400 mg such as; low blood pressure, nausea and dizziness (10). Both iron sucrose and iron gluconate have fewer side reactions when compared to iron dextrans (11). However, iron sucrose was found to be less side effect and effective with good safety even in childhood and pregnancy with mild non-serious side effect although was reported anaphylactic reactions (immune and dose-related) in approximately 1% of treated patients (10)(12)(13). Iron sucrose also could be given in the safe method to the patients suffering hemodialysis in anemia of chronic kidney disease (14)(15).

## PATIENTS AND METHODS

## Comparison Between Parenteral And Oral Iron Replacement Therapy In Anemic Iraqi Female Patients

The project was achieved in the College of Medicine - Anbar University from February to May 2019. The selected persons recruited are patients who visiting Ramadi Teaching hospital in Anbar Governorate, west of Iraq, and it approved by independent ethics committees.

The cases in our study were 90 females with ages between 20-65 years old. The criteria of containment were anemia patients due to iron deficiency, which indicates through the levels of hemoglobin that is less than 12 mg/dL with iron profiles. Criteria of exclusion are Pregnancy, thyroid dysfunction, heart and cancer disease, renal and hepatic diseases.

Blood samples obtained from subjects and collected in two test tubes; one of them with ethyl diamine tetraacetic acid (EDTA) anticoagulant for estimation hemoglobin and PCV using (ERMA PCE-210-Full automatic blood cell counter/Japan). Another test-tube for collecting blood samples is without EDTA anticoagulant, it is used to estimate serum iron, serum ferritin and TIBC. Hormonal assay Ferritin is determining with the reagent kit available in the markets using Minividas (a compact automated immunoassay system based on the Enzyme-Linked Fluorescent Assay (ELFA) principles/France). Other investigations were done like Hb electrophoresis and Thyroid function tests whenever there was any indication. Hematology and iron status (CBC and serum ferritin), were determined at baseline levels (pre-treatment) and post-treatment follow-up.

We divided patients into 2 groups depending on Hb level group A more than 9 gm /dl and group B Hb less than 9 gm/dl anemia. We started iron therapy to group A by ferrous sulfate (200 mg by 3) and group B anemia with iron sucrose infusion upon its total need depend on this equation; (Target Hb - actual Hb) (g/l) x (Bodyweight/kg) x 0.24) + 1000 mg iron for iron stores (16). Treatment and follow up for 2 months, then the response and comparison were evaluated between patients who took oral iron and others took infusion iron.

### Statistical analysis

The statistical analysis was performed with IBM SPSS Statistics software (version 23.0). Data distribution was assessed. Variables displaying a normal distribution were distinct as mean ± SD. ANOVA was used for the comparison of variables among anemic females. Pearson correlation coefficients were calculated for the whole study as appropriate to detect associations between age, Hb, and serum ferritin. The levels of Statistical significance were set when the p-value was less than 0.01, 0.05, 0.001 respectively (two-tailed).

### RESULTS

Serum ferritin concentrations were (10.13 ± 11.39), (8.57 ± 9.86) and (28.41 ± 47.52) µg/dL (P = 0.008) for the age groups 20-29, 30-39 and 40-65, respectively. The mean ferritin concentration was 13.01 ± 24.04 in anemic females was a significantly positive correlation with Hb level as shown in table 1.

**Table 1: Parameter levels among women of different age groups**

	20-29	30-39	40+	Total	p-value
<b>Age number (%)</b>	27 (30)	45 (50)	18 (20)	90 (100)	
<b>Age mean (±SD)</b>	26.11 (2.00)	34.31 (2.87)	54.28 (7.52)	35.84 (10.71)	< 0.001*
<b>Hb</b>	9.06 (1.32)	8.93 (1.57)	8.57 (1.38)	8.89 (1.45)	NS**
<b>PCV</b>	29.32 (3.08)	28.92 (4.63)	26.433 (3.87)	28.51 (4.14)	< 0.05*
<b>Ferritin</b>	10.13 (11.39)	8.57 (9.86)	28.41 (47.52)	13.01 (24.04)	< 0.01*

\*The correlation is significant at the (0.01, 0.05, 0.001 respectively) level (2-tailed). ANOVA test was used to calculate f & p-value

\*\*NS, not significant.

**Table (2): Haematological characteristics of women according to anemia status**

		Pre Treatment	Post Treatment	P-value
<b>Group A</b>	<b>(Hb ≥9)</b>		<b>By Oral</b>	
Hemoglobin	Mean (±SD)	9.83(±0.79)	11.26(±1.11)	< 0.001*
	NT(Range)	43(9.0-11.9)	(9.7-13.0)	
	NN (Mean±SD Pre-Post)	28(9.69±0.61)	(10.55±0.60)	
	NR (Mean±SD Pre-Post)	15(10.11±1.01)	(12.59±0.25)	NS**
Ferritin	Mean (±SD)	17.9(±4.73)	21.68(±5.87)	< 0.001*
	NT(Range)	43(13.1-29)	(14.9-30.4)	
	NN (Mean±SD Pre-Post)	28(15.33±1.01)	(17.48±0.91)	
	NR (Mean±SD Pre-Post)	15(22.71±5.17)	(29.52±0.80)	< 0.05*
<b>Group B</b>	<b>(Hb &lt;9)</b>		<b>By Infusion</b>	
Hemoglobin	Mean (±SD)	7.10(±0.79)	12.59(±0.25)	< 0.001*
	NT(Range)	47(6.1-8.9)	(12.0-13.1)	
	NR (Mean±SD Pre-Post)	47(7.10±0.79)	(12.59±0.25)	< 0.001*
Ferritin	Mean (±SD)	6.92(±2.60)	54.1(6±6.32)	< 0.001*
	NT(Range)	47(4.2-12.9)	(45.7-70.2)	
	NR (Mean±SD Pre-Post)	47(6.92±2.60)	(54.16±6.32)	< 0.001*

\*The correlation is significant at the (0.01, 0.05, 0.001 respectively) level (2-tailed). T-Test paired Samples Correlations.

\*\*NS, not significant.

NT, Number of the total; NR, Number of response; NN, Number of patient not response.

The results were obtained from oral iron supplementation within 2 months of treatment for mild IDA from 43 patients; 16 patients only response to ferrous sulfate while 27 patients

did not reach the target for Hb 9.7 gm/dl and just reach to (10.1 gm/dl) and serum ferritin (21.68 ng/dl).

However, 47 patients with Hb below 9 gm /dl were treated by iron sucrose infusion (first testing dose 50 mg put in 500 ml normal saline within one hour) then four doses of 200 mg with four non-successive days over 14 days) and followed for

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8 weeks. It was observed that all patients are significantly increasing the levels of Hb and serum ferritin from 7.1 mg/dl to 12.6 mg/dl and 6.9 ng/dl to 54 ng /dl, respectively. Also, no serious adverse events occurred apart from mild nonserious side effects (mild leg swelling, itching) which could be treated with an antihistamine.

### DISCUSSION

Iron deficiency anemia in females is a public health problem and deserves specific concern due to the subsequent dangers. The treatment of ID in women patients through the oral iron without symptomatic is narrow, in case of the various factors such as intolerance, weak absorption and need a long period time for the response (2). However, the limitations have been concluded with the treatment through oral iron, for example; low obligation to the medication, slow response especially in women who suffer a loss of blood during menstruation and gastrointestinal adverse effects.

On the other hand, the levels of Hb are raised with a good response when used intravenous iron treatment in patients with symptomatic anemia. (3)(10) This may be indicated when oral iron therapy is not enough to correct low hemoglobin and iron body store due to poor tolerability by the patient, delay responses and malabsorption. Many research works have been concluded that the replacement of intravenous iron, particularly with iron sucrose, allowed treating the deficiency of iron effectively and safely. (3)(10)(12)(17)

Iron sucrose increases in iron stores and it has a significant benefit over oral iron, indicate that iron infusion has an advantage in patients with severe anemia (10)(12). During parenteral iron therapy, work up such as hemoglobin concentration, serum ferritin, MCV, MCH and hematocrit value were chosen to investigate, because they are commonly preferred by physicians in clinical practice and give a better idea for diagnosis, prognosis as well as the evaluation of the therapy (18).

In this study, we have evaluated 90 patients, ages between 20 to 65 years of women with iron deficiency anemia. The mean age was 35.84(±10.71). 43 patients 48% with mean Hb was 9.8 gm/dl and serum ferritin was 17.9ng/ml. The other 47 patients 52% with mean Hb was 7.1 gm/dl and serum ferritin was 6.9 ng/ml. The first group of the patients treated by oral ferrous sulfate and the second group treated by iron sucrose infusion .patients who received oral iron has only 16 from 43 patients (37%) have increased in serum iron, hemoglobin and serum ferritin while the remaining 27 from 43 patients (63%) no response to oral therapy. The second group of patients 47 all had a significant increase in Hb, Serum ferritin and serum iron with a short period of treatment 8 weeks. This study consistent with the result of Breymann C, et al 2001(18)(19).

By utilising the iron sucrose infusion in week 8, the levels of Hb are significantly recovered with an extent greater than ferrous sulfate (P=0.001). Moreover, the normalised of the levels of Hb (Hb  $\geq$ 11.0 g/dL) with the intravenous iron sucrose treatment is significantly effective and rapid as well as a significant effect to replenish iron stores (18).

With the consideration of intravenous iron sucrose therapy, it was observed no significant of adverse drug reactions to all anemic females in the present study which having intravenous iron sucrose. Only 2 from the 47 females patients (4.2%) are suffering skin itching (pruritus) at the infusion area, and mild leg edema which was treated with antihistamine medications. The side effects in the present study were limited due to many reasons; for example, the overall dosage of intravenous iron sucrose was no very high and the iron complex was delivered to the patients in slowly

and diluted preparation. The results were obtained in our study were similar to the concluded results in previous studies (14)(20)(21).

### CONCLUSIONS

The results obtained from our study display the effectiveness of infousin of iron sucrose. The rapid enhancement of anemia with the increase in the levels of hemoglobin, as well as restore the iron store, are shown in female patients, those patients are suffering iron deficiency with a low level of hemoglobin. All women patients are accomplished and restored to the normal level of Hb. Despite oral iron is still the public therapy for the deficiency of iron which advice from physicians, the results obtained in the present work are concluded that intravenous iron sucrose could present as the effectiveness and safe replacement to the oral iron if the oral iron can not be utilised or does not tolerate. To sum up, the results target are supporting to normalise the levels of hemoglobin as well as preserve the normal levels of iron status.

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