COMPARATIVE STUDY OF INTRAVENOUS IRON SUCROSE VS ORAL FERROUS SULFATE THERAPY FOR UNCOMPLICATED IRON DEFICIENCY ANEMIA

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Abstract:

Background: Iron deficiency anemia (IDA) is one of the most frequent nutritional deficiency leading to morbidity and mortality in whole world. Oral iron therapy as well as intravenous (IV) iron therapy can be given to treat the IDA patients.

Objective: To compare the efficacy and hematological changes of Oral and IV iron preparation in patients with uncomplicated iron deficiency anemia.

Method: An interventional, prospective study in patients with uncomplicated IDA anemia receiving IV iron sucrose and Oral iron ferrous sulfate were included. Clinical history, baseline hemoglobin, anemia indices data were recorded in a case record form. A total number of 80 patients were enrolled in this study. 40 patients (Group A) were treated with IV iron sucrose and another 40 patients (Group B) were treated with oral iron ferrous sulfate. After therapy Hemoglobin level, RBC indices and adverse drug reactions (ADRs) were observed.

Place and period of Study: Study was carried out in the Department of Hematology at Dhaka Medical College Hospital (DMCH), from July 2015 to June 2016.

Results: The mean age of total participants was 35.77 ± 16.08 (range of 13 – 75 years). In this study female (72.5%) is predominant than male (27.5%). Oral and IV iron preparations significantly (P<0.0001) improved mean hemoglobin, anemia indices at the end of study. However, mean increase in hemoglobin were significant (P<0.0001) with IV iron sucrose (7.6 ± 2.9) gm/dl, as compared to Oral ferrous sulfate (6.4± 2.2)gm/dl, after 2 months of therapy. In this study Hemoglobin increases in group A (IV iron arm) almost 1mg/kg/week and in group B (oral iron arm) 0.8 mg/dl/week).Surprisingly, ADRs were more in patients treated with oral ferrous sulfate (38%) compared to iron sucrose (26%).

Conclusion: IV iron sucrose improves hemoglobin, anemia indices and replenish iron stores rapidly and is well tolerated than oral iron preparations.

Key words: Iron deficiency anemia, Intravenous iron sucrose, Hemoglobin concentration.

Introduction:

Iron deficiency is the most common nutritional deficiency in the world[1]. In the United States iron deficiency most commonly occurs in toddlers, adult and adolescent fe males[1,2]. Patients with iron deficiency anemia (IDA) may be asymptomatic, or may have signs and symptoms such as headache, fatigue, tachycardia, exertional tachypnea[2].

One of the most common causes of iron deficiency in adult Americans is acute blood loss,like gastrointestinal (GI) bleeding, trauma,

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surgery and postpartum bleeding , other causes include malnutrition, decreased iron absorption, celiac disease, use of erythroid stimulating agents (ESAs), chronic illness, gastric bypass surgery, and congenital iron deficiency[1,2]. IDA is associated with an increased susceptibility to infections, decreased work productivity and slower cognitive and motor development in children[3,4]. In addition, there is an association between low hemoglobin and preterm birth as well as lower birth weight[5,6].

The available intravenous iron formulations include iron dextran, iron sucrose, sodium ferric gluconate and iron carboxymaltose[7]. Iron sucrose and sodium ferric gluconate seem to have a lower incidence of anaphylaxis[7,8], can safely given in small dosages or as an infusion of larger dosages[8,9]. For past half a century the standard therapy for iron deficiency anemia has been ferrous salts[10]. Ferrous sulfate and gluconate are effective in the correction of iron deficiency anemia, though prolonged duration of treatment is required to correct anemia and replenish iron stores, it is cheap and no history of anaphylactic reaction[10].

So, the present study was done to compare the hematological response and observe ADRs after therapy with IV iron sucrose and oral iron ferrous sulfate therapy in uncomplicated iron deficiency anemia.

Material And Methods:

Study design, study setting and study period:

This interventional, prospective study was carried out in the Department of Hematology at Dhaka Medical College Hospital (DMCH), conducted from July 2015 to June 2016 for a period of one (01) year.

Study participants, sample size, sampling:

Study participants were classified in two groups. Total 80 study population were taken purposively.40 patient is in group A at any age, diagnosed as iron deficiency anemia with hemoglobin <9 gm/dl, given IV iron sucrose with an optimum duration of therapy of 01 to 02 weeks. Another 40 patient in group B with hemoglobin <9 gm/dl, treated with oral iron ferrous sulfate for consecutive 2 months.

Exclusion criteria: a) Anemia not linked to iron deficiency. b) History of asthma, thrombo-embolism, seizures or drug abuse. c) Signs of infection or evidence of renal or hepatic dysfunction

Methods of data collection: The study participants were selected from indoor and outpatient hematology department of DMCH after fulfilling the selection criteria. After careful history taking, clinical examination and minimal investigations for other causes of anemia were ruled out. The initial iron status was assessed by the clinical and laboratory examinations (complete blood picture, reticulocyte count and serum iron profile). Who are fulfilling above criteria were included in the study. They were randomly divided into two groups. For group A, the amount of IV iron needed by an individual is calculated by the following formula[11].

Body weight (kg) × 2.3 × (15-patient's hemoglobin, g/dl) +500 or 1000 mg (for stores).

For group B oral ferrous sulfate given 200 mg (65 mg elemental iron) twice daily for 2 months (total elemental iron 3900 mg X 2 months).

All patients are randomly enrolled for group A and group B in this study. Prior to the commencement of this study, the research protocol was approved by the ethical committee of the Dhaka Medical College Hospital, Dhaka. Informed consent was taken from the participants prior to interview.

Adverse effects were observed after therapy like dyspepsia, diarrhea, local discomfort, skin rash, fever, headache, arthralgia, hypertension, lymphadenopathy, anaphylactic reactions, hypotension, body pain and others. The follow up schedule was before therapy, 2 weeks, 1 month and 2 months after therapy.

Statistical analysis: All data were recorded systematically in preformed data collection form (questionnaire) and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using Microsoft Office Excel 2016. Probability value (P) <0.05 was considered as level of significance.

Results

Table-I

Age & Sex distribution of the respondents

Parameter	Mean± SD	Range (years)
Age	35.77 ± 16.08	13-75
Sex	Frequency	Percent
Male	22	27.5
Female	58	72.5

Table-III

Response of Peripheral Blood Film (PBF) before and after iron therapy in Both A and B group

PBF	Findings
Before Therapy	Iron deficiency anemia
2 weeks After Therapy	Dimorphic anemia
1 month After Therapy	Normal Study
2 months After Therapy	Normal Study

Table-IV
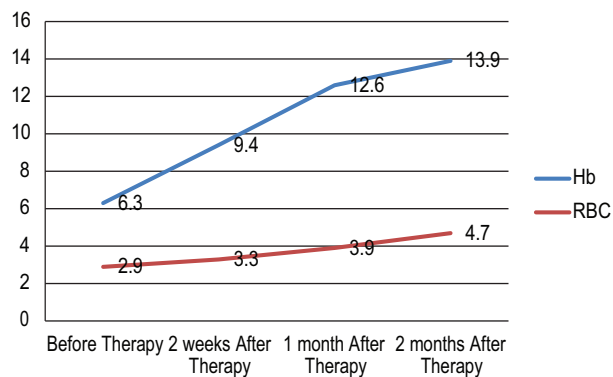
Changes of Hemoglobin and RBC count after IV iron therapy

Hemoglobin (gm/dl)	Therapy	Mean ± SD	Range (Min – Max)
	Before Therapy	6.3 ± 1.1	4.60 - 8.70
	2 weeks After Therapy	9.4 ± 1.4	7.20 - 11.70
	1 month After Therapy	12.6 ± 0.5	11.60 - 14.20
	2 months After Therapy	13.9 ± 0.7	12.10 - 15.70
RBC (number x 10^{12}/L)	Before Therapy	2.9 ± 0.2	2.07 - 3.01
	2 weeks After Therapy	3.3 ± 0.9	2.81 - 3.40
	1 month After Therapy	3.9 ± 0.1	3.40 - 4.01
	2 months After Therapy	4.7 ± 0.5	4.03 - 5.94

Data was expressed as Mean ± SD
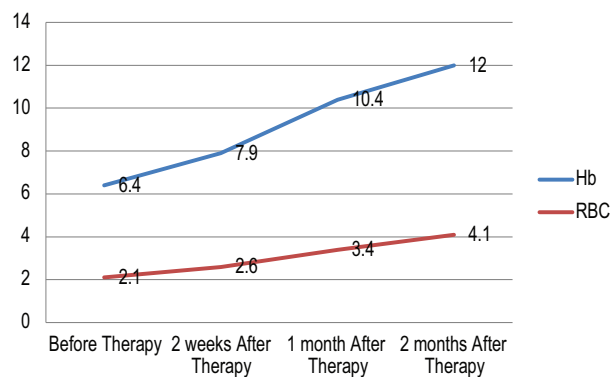
Table-V

Changes in Hemoglobin and RBC count after Oral iron therapy

Hemoglobin (gm/dl)	Therapy	Mean ± SD	Range (Min – Max)
	Before Therapy	6.4 ± 1.5	4.30 - 8.80
	2 weeks After Therapy	7.9 ± 0.7	6.90 - 9.10
	1 month After Therapy	10.4 ± 0.6	9.20 - 11.20
	2 months After Therapy	12.0 ± 0.6	11.10 - 13.22
RBC (number x 10^{12}/L)	Before Therapy	2.1 ± 0.07	2.01 - 2.21
	2 weeks After Therapy	2.6 ± 0.2	2.31 - 2.80
	1 month After Therapy	3.4 ± 0.2	3.10 - 3.71
	2 months After Therapy	4.1 ± 0.2	3.91 - 4.40

Data was expressed as Mean ± SD

**Fig.-1:** *Hemoglobin and RBC count increment to response of IV iron*

**Fig.-2:** *Hemoglobin and RBC count increment to response of oral iron*

Table-VI

Response of RBC indices after IV iron and Oral iron therapy

MCV (fl)	Therapy	Mean ± SD	Range (Min - Max)	
	Before Therapy	63.6 ± 4.8	58.00 - 71.00	
	2 weeks After Therapy	72.9 ± 3.6	66.20 - 76.10	
	1 month After Therapy	79.0 ± 2.7	75.10 - 82.30	
	2 months After Therapy	81.9 ± 2.4	78.40 - 86.30	
MCH (pg)	Before Therapy	16.8 ± 1.6	12.60 - 18.20	IV iron
	2 weeks After Therapy	22.5 ± 2.2	18.70 - 25.01	sucrose
	1 month After Therapy	26.6 ± 1.5	25.10 - 30.02	
	2 months After Therapy	28.8 ± 1.6	27.01 - 33.03	
MCHC (g/dl)	Before Therapy	26.5 ± 1.9	21.10 - 28.00	
	2 weeks After Therapy	29.6 ± 1.5	26.10 - 31.70	
	1 month After Therapy	31.4 ± 1.5	28.40 - 34.00	
	2 months After Therapy	32.7 ± 0.7	32.10 - 36.10	
MCV (fl)	Before Therapy	66.4 ± 4.5	59.00 - 72.00	
	2 weeks After Therapy	71.6 ± 2.0	68.20 - 74.10	
	1 month After Therapy	77 ± 1.9	74.10 - 80.30	
	2 months After Therapy	79.3 ± 1.8	76.40 - 82.30	
MCH (pg)	Before Therapy	15.7 ± 0.8	14.60 - 17.20	Oral iron
	2 weeks After Therapy	21 ± 2.1	17.70 - 24.01	ferrous
	1 month After Therapy	25.8 ± 1.2	24.10 - 28.02	sulfate
	2 months After Therapy	28.6 ± 1.6	26.01 - 32.03	
MCHC (g/dl)	Before Therapy	22.6 ± 1.7	20.10 - 25.00	
	2 weeks After Therapy	24.9 ± 2.2	22.10 - 28.70	
	1 month After Therapy	28.6 ± 1.2	26.40 - 30.30	
	2 months After Therapy	29.8 ± 1.2	28.10 - 32.10	

Data was expressed as Mean ± SD
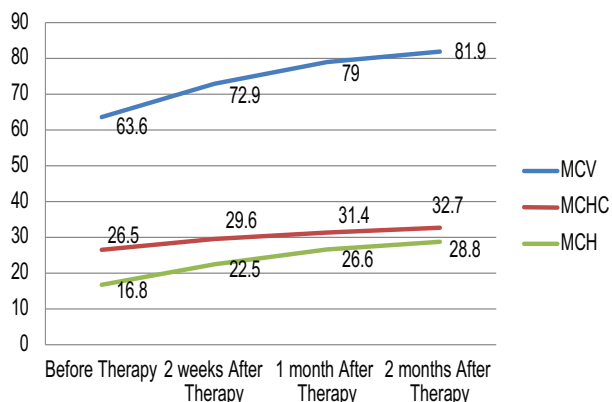
Fig.-3: *Changes of RBC indices after IV iron therapy*
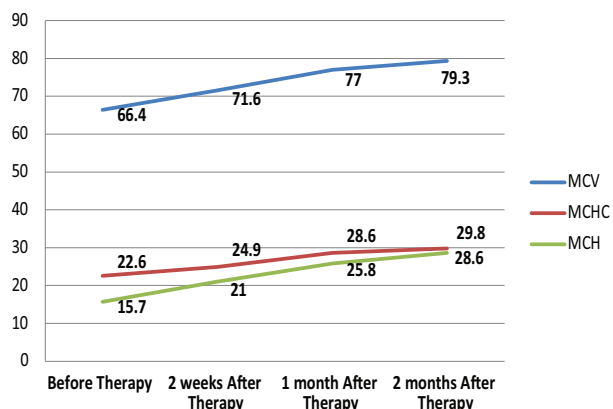
Fig.-4: *Change of RBC indices after oral iron therapy*

Table VII

*Changes of Hemogram before and 60 days after therapy with IV iron*

Hemogram	Before Therapy	60 days after therapy	p-value
HB	6.3 ± 1.1	13.9 ±0 .7	.001
RBC	2.9 ± 0.2	4.7 ± 0.5	.001
MCV	63.6 ± 4.8	81.9 ± 2.4	.001
MCH	16.8 ± 1.6	28.8 ± 1.6	.001
MCHC	26.5 ± 1.9	32.7 ± 0.7	.001

p value 0.001

Table-VIII

Changes in Hemogram before and 60 days after therapy with oral iron

Hemogram	Before Therapy	60 days after therapy	p-value
HB	6.4 ± 1.5	12.0 ± 0.6	.001
RBC	2.1 ± 0.07	4.1 ± 0.2	.001
MCV	66.4 ± 4.5	79.3 ± 1.8	.001
MCH	15.7 ± 0.8	28.6 ± 1.6	.001
MCHC	22.6 ± 1.7	29.8 ± 1.2	.001

p value 0.001
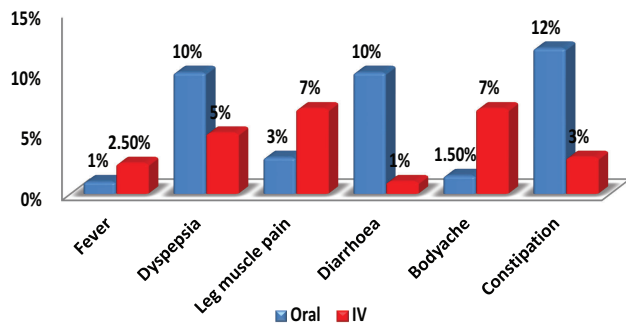
Fig.-5: *Compare the adverse effects after IV iron and Oral iron therapy*

Discussion:

Iron is critical for the growth of all human cells, that's why IDA independently increases morbidity and mortality significantly [1]. There are an estimated 3.5 billion iron deficient people worldwide, the vast majority is in developing countries and remarkably, iron deficiency is also the most common cause of anemia in the United States [2].This study Intravenous iron sucrose was given to group A participants and oral iron ferrous sulfate was given to group B participants.

In this study, the mean age of the respondents was 35.77 ± 16.08 which ranges from 13 – 75 years (Table-1). Similar result was published by Zhu et al. (2010)[11] and Edward Litton et al. (2013)[12], mentioned that IDA remains extremely common in the adult population.

Regarding sex, females were 72.5% and males were 27.5% (Table-1) which indicates females were predominant than male. Similar finding was supported by Alleyne et al. (2008) [13], Ho et al (2008) [14], these studies explained the reason and mentioned that females generally have lower levels of iron than males because of the iron is lost during menses, pregnancies and lactation and detected that IDA is more prevalent among female which is consistent with the present study.

Another similar study done by Alleyne *et al.*, hemoglobin was different for patients in the oral iron and IV iron sucrose groups across time in each individual group as well as at any given point of time. The hemoglobin level was significantly higher in the IV iron sucrose group[13]. Iron sucrose is costlier than Oral iron and requires a hospital setting for administration[15]. Al Momen *et al.*, observed that the intravenous iron sucrose (group A) achieved significantly higher hemoglobin level (*P* value ≤0.001) in a shorter period (*P* value ≤0.001) [15].

The mean hemoglobin concentration in group A (IV iron arm) before therapy was 6.3 ± 1.1 with a range of 4.60 - 8.70 gm/dl and two month after therapy the mean hemoglobin concentration was 13.9 ± 0.7, with a range of 12.10 to 15.70 gm/dl. The mean Hemoglobin concentration in group B (Oral iron arm) before therapy was 6.4±1.5 with a range of 4.30 to 8.80 gm/dl and two month after therapy the mean hemoglobin concentration was 12.0 ± 0.6 with a range of 11.10 to 13.22 gm/dl.

The study by Breymann C *et al.* showed a mean rise in the hemoglobin level was 1.7 g/dl, 25 days after the iron sucrose therapy. Also a study by Wali *et al.* showed the hemoglobin level rise of 2.6 g/dl after 3.6 weeks[16]. Similar result was reported by Alleyne et al (2008)[13] and mentioned that patients with iron deficient anemia should manifest a response to iron by an increase in hemoglobin in 2-4 weeks. The

study also added that theoretically, 500 mg of absorbed iron should produce 500 cc of packed cells, the amount in about 2 units of blood, or raise the hemoglobin about 2 g/dL.

Conclusion:

Though Oral Iron preparation is safe but associated with gastric side effects resulting in poor compliance. In group B more than 30% of participants stop iron intake due to related side effects. Several studies have proved the safety & efficacy of iron sucrose, it is tolerated well & has no major side effects, therefore can be used as a substitute for oral preparations [17, 18]. In our study there were no major side effects with iron sucrose & had better compliance so can be safely used in any age and an alternative to blood transfusion in the treatment of severe iron deficiency anemia. Yet larger trials are required to conclude that parental preparation can be substituted for oral preparations.

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