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COMPARATIVE STUDY BETWEEN TOTAL DOSE OF IRON INFUSION AND INTRAMUSCULAR IRON ADMINISTRATION IN TREATMENT OF IRON DEFICIENCY ANEMIA IN PREGNANT WOMEN

By

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ABSTRACT

Background: Iron deficiency anemia (IDA) is the most common problem of nutritional deficiency in pregnant women worldwide. There is a concern about the high prevalence of iron and other micronutrient deficiencies among women during pregnancy in developing countries, and maternal anemia continues to cause significant perinatal morbidity and mortality.

Objective: To compare between total dose of iron infusion and intramuscular iron administration from 12-32 weeks in pregnant women with moderate iron deficiency anemia.

Patients and Methods: The study was held on 100 patients in the Obstetrics and Gynecology Department at Al-Hussien University Hospital Al- Azhar University on pregnant women at 12-32 weeks gestation attending the antenatal care unit from September 2019 to March 2020.

Results: Group A was received I.V iron, Hb (pretherapy) ranged from 7.1-9 g%, elevated to 10.1-12 g%, the ferritin ranged from 15-30 ng/ml, elevated to 32-49 ng/ml. **Group B** was received I.M-iron, Hb (pretherapy) ranged from 7-9 g%, elevated to 8.5-10.9 g%, and ferritin ranged from 16-29ng/ml, elevated to 24-35ng/ml.

Conclusion: Intravenous iron showed high effectiveness in the treatment of iron deficiency anemia during pregnancy. No side effects were detected and thus, it can be considered as a useful and alternative formulation for the treatment of iron deficiency.

Keywords: Iron infusion; Intramuscular iron; Iron deficiency anemia; Pregnant Women.

INTRODUCTION

Pregnant women are the most vulnerable to iron deficiency anemia because of the increased iron requirements during pregnancy *(Munoz et al., 2019)*.

Serum ferritin may be a better indicator of iron status, as it is impractical to examine iron stores in bone marrow *(Hoffman et al., 2018)*.

In pregnancy, the WHO defines anemia as Hb levels below 11g / dL. The majority of women start their pregnancy with iron reserves partially or completely depleted *(Bridwell et al., 2019)*.

During pregnancy, there is an increase in both red cell mass and plasma volume to accommodate the needs of the growing uterus and fetus *(Von Wowern et al., 2019).*

The volume of plasma increases more than the red cell mass does, leading to a decrease in the Hb concentration in the blood, in spite of the increase in the total number of red cells. This decrease in Hb concentration reduces the viscosity of the blood and is thought to boost placental perfusion, providing better maternal-fetal gas and nutrient exchange *(Baradwan et al., 2018).*

However, the relevance of this physiological hemodilution of pregnancy is controversial for women and their babies, as is the Hb level at which they would benefit from the treatment of iron *(Haman et al., 2019).*

The maternal body requirements for iron increase to approximately 1000 mg on average during pregnancy. During pregnancy severe anemia results in adverse maternal and fetal outcomes. Preterm labor, preeclampsia, sepsis, postpartum hemorrhage and increased blood transfusion are adverse maternal outcomes *(Haman et Al., 2019).*

The fetal adverse outcome is a high rate of fetal mortality in the third trimester of gestation *(Khan, 2019).*

In addition, moderate degree IDA will influence children and adolescents' motor and mental development *(Ahmed et al., 2018).*

The aim of this work was to compare between total dose of iron infusion and intramuscular iron administration from 12-32 weeks in pregnant women with moderate iron deficiency anemia.

PATIENTS AND METHODS

This study is an interventional randomized study, comparing the effect of intravenous and intramuscular iron therapy on pregnant women with moderate anemia. The study was held on 100 patients in the Obstetrics and Gynecology Department at Al-Hussien University Hospital, Al-Azhar University on pregnant women at 12-32 weeks gestation attending the antenatal care unit. The study was approved by the Ethics Board of Al-Azhar University.

Inclusion criteria: Pregnant women between 12 weeks and 32 weeks of gestational age. Iron deficiency anemia. Primigravida and multigravida. And hemoglobin level from 7-9 gm /dl. Exclusion criteria: Women suffering from liver disease, kidney disease, dimorphic anemia, hemolytic anemia, all infectious diseases, multi-fetal gestation, extreme anemia (Hb < 7gm%) and those who had previously undergone blood transfusion or the treatment with parenteral iron, treatment with Erythropoietin within 8 weeks before the screening visit and scheduled elective surgery during the study.

For all the recruited pregnant female the following was done:

i. Informed written consent was given by each patient.

ii. Detailed history (personal, present, past histories, family, obstetric and menstrual (first day of LMP).

iii. Investigations: complete blood count, serum ferritin level estimation, liver function test, kidney function test.

iv. Ultrasound and Doppler study: trans abdominal ultrasound was performed to all patients and Biometric measurement to assess gestational age and fetal growth.

v. General and local examination:

Women were randomly assigned into two equal groups: Group A received intravenous full correction with total dose intravenous infusion of iron dextran. The drug that used was (Cosmofer 50mg/ml). Each 2ml ampoule of Cosmofer contains 100mg elemental iron as Iron Dextran. Total dose infusion of iron dextran was calculated according to the formula, (weight in kg x hemoglobin deficient x 0.024+500mg). Hemoglobin deficient (target hemoglobin-actual hemoglobin) (in single dose) *(El Aal et al., 2019)* Group B received intramuscular iron administration of Hydroxide polymaltose complex. The drug that used was Heamojet (50mg/ml). Each 2ml ampoule of Heamojet contains 100mg elemental iron as Ferric Hydroxide Polymaltose complex. Total iron requirement in intramuscular administration was calculated by the formula (0.3 x W x D + 500mg) where W was the weight of patient in kg. D was deficiency in hemoglobin percentage (target Hb- actual Hb). 500 mg was the iron for replenishing stores.

Follow-up was for Hb and serum ferritin 4 weeks after last dose of therapy.

Statistical analysis:

Comparison between numerical data was performed using unpaired t-test or Mann Whitney U test in the two groups studied; while a comparison was made between pre and post iron intake in the same group, the paired t-test was used. Using Fischer's exact test, comparison was made between categorical data. The data analysis was carried out using SPSS computer program (version 19 windows. Statistically, data were described as mean± standard deviation or number (%). For comparison between both groups, a difference in variables was expressed by P value where P value $\leq$ 0.05 was significant.

RESULTS

In comparison between two groups before treatment regarding age, parity, weight and gestational age No significant difference between two groups according to age, parity, weight and gestational age **(Table 1)**.

Table (1): Comparison between two groups according to age, parity, weight and gestational age using Mann-Whiteny U test

Parameters \ Groups		Group A (n=50)	Group B (n=50)	P. value
Age (year)	Range	22 – 33	21 – 32	0.124
	Mean ± SD	27.12 ± 3.75	26.14 ± 2.43	
Parity	Range	0 – 3	0 – 3	0.646
	Mean ± SD	1.81 ± 0.93	1.72 ± 1.02	
Weight (kg)	Range	61 – 82	60 – 80	0.199
	Mean ± SD	70.25 ± 6.72	68.53 ± 6.59	
Gestational age (year)	Range	12 – 30	13 – 32	0.161
	Mean ± SD	20.58 ± 5.81	21.23 ± 6.17	

In groups A comparison between pretreatment and post treatment regarding age, parity, weight and gestational age there was a significant difference between pretreatment and posttreatment according to age, parity, weight and gestational age **(Table 2)**.

Table (2): Comparison between pretreatment and posttreatment according to Hb, MCV, HCT, MCHC and ferritin in group A

Parameters \ Group A	Pre (n=50)	Post (n=50)	P. value
Hb (g/dl)	7.1 – 9.0	9.85 – 13.26	0.001
	8.18 ± 0.50	11.15 ± 0.61	
MCV (cell/l)	61 – 82	60 – 91	0.001
	70.32 ± 6.06	80.16 ± 5.73	
HCT (%)	17 – 21.8	23.17 – 35.62	0.001
	19.35 ± 1.42	27.59 ± 2.10	
MCHC (g/dl)	13 – 29	20.65 – 31.65	0.001
	20.44 ± 4.30	26.81 ± 4.56	
Ferritin (ng/ml)	15 – 30	32.58 – 46.23	0.001
	21.84 ± 5.12	39.54 ± 5.67	

In groups B comparison between pretreatment and post treatment regarding age, parity, weight and gestational age there was a significant difference between pretreatment and post treatment according to age, parity, weight and gestational age **(Table 3)**.

Table (3): Comparison between pretreatment and posttreatment according to Hb, MCV, HCT, MCHC and ferritin in group B

Group B / Parameters	Pre (n=50)	Post (n=50)	P. value
Hb (g/dl)	7 – 9	8.34 – 12.32	0.001
	8.12 ± 0.42	10.01 ± 0.61	
MCV (cell/l)	60 – 82	65 – 83	0.002
	69.76 ± 6.57	73.52 ± 5.29	
HCT (%)	17.2 – 21.5	20.71 – 25.76	0.001
	19.25 ± 1.26	22.91 ± 1.31	
MCHC (g/dl)	13 – 30	18.94 – 29.67	0.013
	21.48 ± 4.95	23.85 ± 4.35	
Ferritin (ng/ml)	16 – 29	23.76 – 36.74	0.001
	20.84 ± 3.29	29.46 ± 4.12	

In comparison between two groups after treatment regarding age, parity, weight and gestational age there was significant difference between two groups according to age, parity, weight and gestational age **(Table 4)**.

Table (4): Comparison between two groups according to Hb, MCV, HCT, MCHC and ferritin post treatment

Groups / Parameters		Group A (n=50)	Group B (n=50)	P. value
Hb (g/dl)	Rang	9.85 – 13.26	8.34 – 12.32	0.001
	Mean ± SD	11.15 ± 0.61	10.01 ± 0.64	
MCV (cell/l)	Rang	60 – 91	65 – 83	0.001
	Mean ± SD	80.16 ± 5.73	73.52 ± 5.29	
HCT (%)	Rang	23.17 – 35.62	20.71 – 25.76	0.001
	Mean ± SD	27.59 ± 2.10	22.91 ± 1.31	
MCHC (g/dl)	Rang	20.65 – 31.65	18.94 – 29.67	0.001
	Mean ± SD	26.81 ± 4.56	23.85 ± 4.35	
Ferritin (ng/ml)	Rang	32.58 – 46.23	23.76 – 36.74	0.001
	Mean ± SD	39.54 ± 5.67	29.46 ± 4.12	

There was significant difference between two groups according to pain, Anaphylactic reaction and Brown pigmentation at injection site but non-significant difference between two groups according to other side effects **(Table 5)**.

Table (5): Comparison between two groups according to side effects

Groups / Side effects	Group A (n=50)		Group B (n=50)		P. value
	N	%	N	%	
Myalgia	0	0	2	4	0.153
Anaphylactic reaction	5	10	0	0	0.022
Local thrombophlebitis	1	2	2	4	0.558
Upper digestive troubles	0	0	1	2	0.315
Diarrhea	0	0	1	2	0.315
Nausea	1	2	0	0	0.315
Constipation	0	0	1	2	0.315
Tachycardia and Dyspnea	3	6	0	0	0.079
Fatigue	0	0	1	2	0.315
Pain	0	0	4	8	0.041
Brown pigmentation at injection site	0	0	4	8	0.041
delayed reaction	1	2	2	4	0.558

DISCUSSION

In this study, at the beginning of iron administration, women 12-32 weeks of gestational age were chosen as women 12 weeks of gestational age and those that were > 32 weeks of gestational age may not have enough time to restore the hemoglobin deficiency through other means than blood transfusion, but transfusions have risks and costs of their own. So, some intramuscular or intravenous iron may also still be useful, because in the postpartum period, iron can be used. Iron dextran and iron hydroxide polymaltose complex have different pharmacokinetic properties. Iron dextran has a 3–4-day serum half-life, which has long stability and strength of approximately 5–6 hours compared with iron Hydroxide polymaltose complex, with a short half-life. It is quickly cleared of serum. The total required iron is calculated and administered, thus confirming full dose administration and making it convenient for the patient as it is single dose. Besides that, the objective of iron therapy, i.e. providing enough iron to correct the hemoglobin deficiency as well as replenishing supplies, is accomplished without the need for more iron therapy during pregnancy and possibly afterwards. For intravenous group 10 % of women had adverse effects and intramuscular group 28 % of participants had adverse effects. Such adverse effects were mild and symptomatic managed. Neither group required discontinuation of treatment. None of the women had adverse effects of grade II. Side effects are mild to moderate reactions; do not require discontinuation of treatment for e.g. local area pain and Myalgia. Side effects such as severe anaphylactic reactions are life-threatening reactions requiring discontinuation of treatment. Limitations of intravenous iron may occur in cases of acute blood loss, as in these cases blood transfusion is preferred due to volume issues, but in such patients iron stores may be intact, but in patients with chronic anemia and without contraindication to its use, intravenous iron therapy in patients who have sufficient time left till delivery could be a better option.

This study proved that treatment with intravenous iron was more effective than

intramuscular therapy. Iron therapy in moderate anemia treatment, according to these main results: - Group A who received I.V iron, Hb (pretherapy) ranged from 7.1-9 g %, elevated to 10.1-12 g %, and ferritin ranged from 15-30 ng/ml, elevated to 32-49 ng/ml. - Group B who received I.M-iron, the Hb (pretherapy) ranged from 7-9 g %, elevated to 8.5-10.9 g%, and ferritin was ranged from 16-29 ng/ml, elevated to 24-35ng/ml. The study findings were consistent with those reported by *El Aal (2019)* conducted a study to compare efficacy, safety and compliance of intravenous iron sucrose (group A), and intramuscular iron sorbitol (group B) during pregnancy with iron deficiency anemia. The results reported by *El Aal (2019)* in mean Hb in group was 8.9+0.7 g/dl and in group B was 8.0+1 g/dl in group B. After iron therapy, Hb has shown an average rise of 2.8 g/dl in group A and 1.6 g/dl in group B. Another study reported by *Singh et al. (2013)* in mean pretherapy Hb was 6.49 g / dl in group A and 6.48 g / dl in group B. In group A, the increase in Hb was 3.52 g / dl after 4 weeks of therapy and in group B was 2.33 g / dl. The difference was statistically significant between group A (IV iron) and group B (IM iron). A similar study to ours was by *Wali et al (2010)* who reported mean hemoglobin was 8.0 ± 1.1 g / dl and 8.9 ± 0.7 in group A and group B, respectively. Initial hemoglobin in group A and B evaluated 3 weeks post-treatment, with an average increase of 2.8 g/dl (group A) and 1.9 g/dl (group B) and a second evaluation of hemoglobin before delivery showing a total increase of 3.8 g/dl (group A) and 2.4 g/dI (group B). Pre delivery mean hemoglobin was 11.8 g / dl and 11.3 g / dl respectively in group A and B. A similar study to our was by *Gaikwad et al. (2017)* who reported mean hemoglobin rise was 7.48, 7.947 and 8.616 respectively after 7, 21 and 30 days of initiation of intramuscular therapy. The rise in mean hemoglobin level in the intravenous group was 8.154, 9.567 and 10.568 respectively after 7, 21 and 30 days. A similar study to our was also done by *Qassim et al. (2019)* who reported use of intravenous iron polymaltose for iron deficiency treatment during pregnancy. They found that women treated with intravenous iron had greater increase in hemoglobin from treatment until delivery. The results of our study proved that the intravenous iron, showed high effectiveness in the treatment of iron deficiency anemia during pregnancy. No side effects were detected and thus, it can be considered as a useful and alternative formulation for the treatment of iron deficiency.

CONCLUSION

Intravenous iron infusion is preferred to multiple intramuscular doses since the risk of anaphylaxis is present with either route of therapy and because of the ease of administering intravenous therapy as opposed to multiple intramuscular injections. The response to parental iron appeared to be faster than that for oral iron because of the greater amount of iron made available for hemoglobin synthesis in the bone marrow. So, IV iron preparations can be used safely to treat iron deficiency anemia during pregnancy, especially for rapid anemia improvement and rapid replacement of the storage of iron.

Conflict of interest: No conflict of interest in declared by the authors.

REFERENCES

1. **Ahmad MS, Farooq H, Maham SN and Qayyum Z. (2018):** Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. Pediatrics, 107(6):1381–1386.
2. **Baradwan S, Alyousef A and Turkistani A. (2018):** Associations between iron deficiency anemia and clinical features among pregnant women: a prospective cohort study. J Blood Med., 9: 163–169.
3. **Bridwell RE, Carius BM and Long BJ. (2019):** Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Physiol., 256(4 Pt 2):1060–1065.
4. **El Aal Al-Omda FA, El Sayed Al Naggar W and Al Sayed Al-Morsi MA. (2019):** Comparative study-efficacy, safe and compliance of intravenous iron sucrose and intramuscular of sorbitol in iron deficiency anemia of pregnancy. The Egyptian Journal of Hospital Medicine; 74 (4): 905-913.
5. **Gaikwad HS, Sindhu A and Sarda N. (2017):** Comparison of efficacy and safety of intravenous iron sucrose and intramuscular iron sorbitol therapy in patients with anemia during pregnancy in a developing country. Asian Journal of Medical Sciences; 8(5): 31-35.
6. **Hamm RF, Blauvelt C and Wang EY. (2019):** Intravenous versus oral iron for treatment of anemia in pregnancy: a randomized trial. Obstet Gynecol., 106(6):1335–1340.
7. **Hoffman R, Benz EJ, Silberstein LE, Heslop H, Jeffrey I and Sebastian M. (2018):** Hematology: Basic Principles and Practice. 7th ed.Pbl New York: Churchill Livingstone, Inc,; p. 2374.
8. **Khan M. (2011):** Effect of maternal anaemia on fetal parameters. J Ayu Med Coll Abbottabad., 13(2):38–41.
9. **Muñoz M, Stensballe J, Ducloy-Bouthors AS, Bonnet MP, De Robertis E and Sara G. (2019):** Impact of parturition on iron status in non anaemic iron deficiency. Eur J Clin Invest.; 33: 919-23.
10. **Qassim A, Gergis RG, Jeffries B, Grivell RM and Grzeskowiak LE. (2018):** Use of intravenous iron polymaltose in the management of iron deficiency in pregnancy: A retrospective cohort study. Australian and New Zealand Journal of Obstetrics and Gynaecology; 58(2): 163-169.
11. **Singh S, Singh S and Singh PK. (2013):** Efficacy and safety of intravenous iron sucrose and intramuscular iron sorbitol therapy for anemia during pregnancy. J Obstet Gynaecol India; 63(1): 18-21.
12. **Von Wowern E, Källén K and Olofsson P. (2019):** Early pregnancy changes in hemodynamics and volume homeostasis are consecutive adjustments triggered by a primary fall in systemic vascular tone. Am J Obstet Gynecol., 169(6):1382–1392.
13. **Wali A and Mushtaq A. (2010):** Comparative study--efficacy, safety and compliance of intravenous iron sucrose and intramuscular iron sorbitol in iron deficiency anemia of pregnancy. Journal of Pakistan Medical Association; 52(9): 392.

دراسة مقارنة بين جرعة الحديد عن طريقة التقطير الوريدي والحقن العضلي في علاج أنيميا نقص الحديد في النساء الحوامل

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خلفية البحث: يعد فقرالدم بسبب نقص الحديد هو الأكثر انتشارا والذي يؤثر على السيدات الحوامل في جميع أنحاء العالم. ولا يزال فقر الدم سبباً في حدوث معدلات كبيرة للوفيات خلال فترة الولادة.

الهدف من البحثِ: علاج الانيميا المتوسطة عن طريق مقارنة للحقن الوريدي والحقن العضلي للحديد من حيث الاكثر فاعلية وأمانا والأقل تاثيرا جانبيا.

المريضات وطرق البحث: تم اختيار 100من السيدات الحوامل اللاتي تم حجزهن بعيادات النساء والتوليد بمستشفي الحسين الجامعي وسيدي سالم العام، وقد تم تقسيم السيدات الحوامل إلي مجموعتين متساويتين: المجموعة الاولي تم علاجهن بالحديد عن طريق الحقن الوريدي والمجموعة الثانية تم علاجهن بالحديد عن طريق الحقن العضلي.

نتائج البحث: أظهر حقن الحديد عن طريق الوريد فعالية عالية مقارنة بحقنه العضلي في علاج فقر الدم بسبب نقص الحديد خلال فترة الحمل، بالاضافة الي قلة الأثار الجانبية الناتجة عن الحقن العضلي كما أثبتت النتائج أن حالات نقص الحديد الشديدة ينتج عنها مضاعفات خطيرة كالنزيف ما بعد الولادة، الولادة المبكرة وقلة وزن حديثي الولادة.

الاسستنتاج: أفضل وسيلة للحد من نقص الحديد لدى االسيدات الحوامل في يكون عن طريق اعطاء مكملات الحديد أثناء فترة الحمل وبين كل حمل والآخر.