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Comparison of the use of intravenous iron sucrose with intravenous ferric Carboxymaltose for treatment of iron deficiency anaemia in pregnant patients

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ABSTRACT

BACKGROUND & OBJECTIVE: Iron deficiency results in major disabilities and death all over the world, about two billion people are suffering from anaemia at the moment. To compare intravenous iron sucrose with intravenous ferric carboxymaltose in terms of mean change in hemoglobin level and mean corpuscular volume (MCV) for treatment of iron deficiency anaemia in pregnant patients.

METHODOLOGY: Prospective comparative study was conducted at the department of Obstetrics/ Gynecology of POF Hospital Wah Cantt and HIT Hospital Taxila Cantt. The study duration was 2 years, from January 2017-December 2018. A total of 80 patients were included in the study. Patients were randomly divided into two groups; in Group-A; 40 patients were given intravenous iron sucrose, and in Group B, 40 patients were given intravenous ferric carboxymaltose. Patients were observed for hemoglobin level and mean corpuscular volume (MCV). Data analysis was done with SPSS version 24. An Independent t-test was applied, and results with p-value ≤0.05 were found significant.

RESULTS: Post-treatment hemoglobin means level in the iron sucrose group was 9.90±0.4SD, and in the intravenous ferric carboxymaltose group, post-treatment hemoglobin was 10.71±0.9SD (p≤0.001). In the iron sucrose group, the post-treatment mean corpuscular volume mean level was 81.94±6.0SD and in the intravenous ferric carboxymaltose group mean post-treatment mean corpuscular volume was 88.08±7.1SD (p≤0.001)

CONCLUSION: Treatment with intravenous iron caboxymaltose is superior to intravenous iron sucrose with respect to hematological response, which seems to be safe, as very few severe side effects were observed.

KEYWORDS: Anemia, Intravenous sucrose, Iron deficiency.

INTRODUCTION

Changes in maternal physiology, i.e., increased red blood cell mass and increase in blood volume, and increased needs for fetal growth, lead to the marked increased iron requirement in pregnancy[1,2]. World Health Organization defines iron deficiency anemia as a decrease in hemoglobin resulting from a deficiency of iron stores[3]. World Health Organization consider anemia as a diagnosis during pregnancy when hemoglobin levels are< 11 g/dL[4].

Iron Deficiency Anemia (IDA) is in high prevalence in different regions of the world (12-43%)[5]. Iron deficiency results in major disabilities and death all over the world, about two billion people are suffering from anaemia at the moment[6]. In developing countries like Pakistan, the prevalence of anemia is already very high and increasing with time. All socio-economic groups have been affected by anemia during pregnancy [7]. In one study, microcytic hypochromic anemia was seen in 76% of women, out of which 64% of patients never used iron supplements [8].

Previously iron deficiency anemia was treated through oral iron therapy because of its high efficacy, safety, and less cost. The use of oral iron supplements in up to 40% of patients has reported adverse effects secondary to its use. These side effects increase as dosage has been increased in patients resulting in non-compliance and prolonged duration of treatment required for recovery of all such patients, sometimes unable to treat patients at all. In recent years gynecologists have considered intravenous (i.v.) iron administration in pregnant women with severe iron

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deficiency anemia (Hb < 9.0 g/dL), and patients with marked adverse effects due to oral iron supplements. In advanced pregnancy iron deficiency leads to complications occurring in maternal and fetal health, which can be prevented by rapid iron reserve replacement through I/V supplements [8].

A newer compound of iron, i.e., Ferric carboxymaltose (FCM) is a chemically stable Type I polynuclear iron (III) hydroxide carbohydrate complex which has been regularly used in Europe since 2007 for the treatment of severe iron deficiency anemia. Other iron compounds i.e., sodium ferric gluconate and iron sucrose, were used previously, but biochemically and structurally, Ferric carboxymaltose has been found to be more effective and stable, so a high level of a single dose of ferric carboxymaltose over short time duration can be administered as compared to sodium ferric gluconate or iron sucrose resulting in a decreased number of dosage and high patient compliance when FCM has been administered in anemic patients [9].

Several large clinical trials have been carried out regarding FCM's clinical efficacy and safety regarding other diseases, including chronic kidney disease and chronic heart failure, and patients were followed up for one year, which showed promising results [10]. Iron deficiency is the leading cause of mortality in developing countries like Pakistan. Our study is conducted to provide knowledge in choice of iron deficiency anemia management in resource-limited areas. The present study was planned to compare intravenous iron sucrose with intravenous ferric carboxymaltose in terms of mean change in hemoglobin level and mean corpuscular volume (MCV) for the treatment of iron deficiency anemia in pregnant patients.

METHODOLOGY

A prospective comparative study was carried out at the department of Obstetrics/ Gynecology of POF Hospital Wah Cantt and the Department of Obstetrics/Gynecology of HIT Hospital Taxila Cantt. The study was carried out for 24 months, from January 2017- December 2018. A sample size of 82 patients (rounded off to 80) was calculated using μ1=32, μ2=29, SD=5.0, Power of study 80%, and significance level 5%10. Ethical approval was taken from the ethical review board of the hospital (ERC=12-2016/D). Patients were selected through non-probability consecutive sampling. Patients were divided into two equal groups (computer-generated numbers).

In Group-A; 40 patients were given I/V iron sucrose, and in Group-B, 40 patients were given I/V ferric carboxymaltose. Non-probability consecutive sampling was done, and patients were allocated group through the lottery method. Hemoglobin (Hb) less than 10.5 gm/dl and mean corpuscular volume (MCV) less than 76 flwere considered diagnostic of iron deficiency anaemia. Women diagnosed with anemia other than iron deficiency, hemoglobinopathies, a history of allergy to parenteral iron preparations, allergic bronchospasm, and rheumatoid arthritis were excluded from the study. Women with obstetric complications like multi-fetal pregnancy, antepartum hemorrhage, and hypertensive disorders were also excluded.

Patients with iron deficiency anaemia diagnosed through Blood CP performed in the hospital laboratory were given treatment through I/Viron sucrose and I/V ferricCarboxymaltose.I/V iron supplements were given in dosage of once daily infusion for 3 weeks, and ferric carboxymaltose injection was given intravenously in dose of 500 mg. Response to treatment was assessed through Blood CP performed after 3 weeks of treatment, and findings were recorded in pre-formed proforma. Data analysis was done with SPSS version 24. An Independent t-test was applied, and results with p-value ≤0.05 were found significant.

RESULTS

A total of 80 patients were included in the study. Patients were divided into two groups. Descriptive statistics of age in group A showed mean age was 28.92±3.61 years, and group B showed mean age was 27.53±2.12 years. In group A, the mean gravidity was 3.66±0.97, and in group-B mean gravidity was 3.37±0.74. The mean parity was 2.5+0.88 in group A, and mean parity was 2.2±0.65 in group B.

In the iron sucrose group, the mean gestational age was 32.9±1.48 weeks. In I/V carboxmaltose group, the mean gestational age was 33.28±1.15 weeks, as shown in table-I.

Pre-treatment hemoglobin mean level in the iron source group was 8.69±0.53 g/dl and in I/V ferric carboxymaltose group was 8.60±0.68 g/dl, independent sample t-test was applied, which shows that both means are statistically non-significant as p-value is 0.542. Pre-treatment MCV mean level in the iron source group was 72.06+4.06 fL/red cell and in I/V ferric carboxymaltose group was 75.88+0.68 fL/red cell, independent sample t-test was applied, and which shows that both means are statistically different as p-value is ≤0.001 that difference is not by chance as shown in table-II.

Post-treatment hemoglobin mean level in the iron source group was 9.90±0.41 g/dl and in I/V ferric carboxymaltose group was 10.71±0.95 g/dl, independent sample t-test was applied, which shows that both means are statistically different as p-value is ≤0.001 that difference is not by chance. Post-treatment MCV mean level in the iron source group was 81.94±6.00fL/red cell and in I/V ferric carboxymaltose group was 88.08+7.19fL/red cell, independent sample t-test was applied, which shows that both means are statistically different as p-value is ≤0.001 that difference is not by chance table-III.

In I/V iron sucrose group, 07 patients developed skin rash with treatment as a side effect of treatment however, no major side effects were seen during the treatment. In I/V ferric carboxymaltose group; 02 patients developed rash with injection, and no major side effects other than skin rash were seen in group B post-treatment (as shown in the figure:I-II).

Table-I: Descriptive statistics distribution in both interventional groups.

Descriptive statistics	Group-A (Iron sucrose)	Group-B (Ferric carbocxymaltose)
Age	28.92±3.61	27.53±2.12
Gravidity	3.66±0.97	3.37±0.74
Parity	2.5±0.88	2.2±0.65
Gestational age	32.9±1.48	33.28±1.15

Table-II: Pre-treatment Hemoglobin level and mean capsular volume comparing both groups.

Pretreatment Hemoglobin level Mean±SD (g/dl)		p-value
Group A (Iron sucrose) n=40	8.69±0.53	0.542
Group-B (Ferric carbocxymaltose) n=40	8.60±0.68 g/dl	
Pretreatment MCV Mean±SDfL/red cell		
Group-A (Iron sucrose) (g/dl)	72.06±4.06	≤0.001
Group-B (Ferric carbocxymaltose) fL/ red cell	75.88±0.68	

Table-III: Post-treatment hemoglobin level and meancorpuscular volume level comparing both groups.

Groups	Post-treatment Hemoglobin level	p-value
Iron sucrose (g/dl)	9.90±0.41	
Ferric carbocxymaltosefL/ red cell	10.71±0.95	0.001
-	Post-treatment MCV level	-
Iron sucrose (g/dl)	81.94±6.00	
Ferric carbocxymaltosefL/ red cell	88.08±7.19	0.001

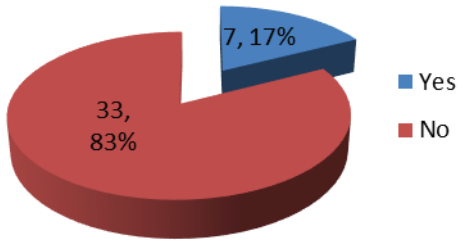

Figure-I: Presence of body rash in intravenous Iron sucrose group.

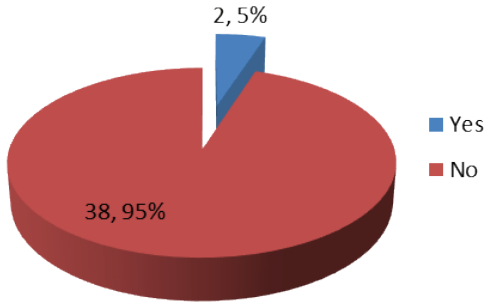

Figure-II: Presence of body rash among patients of the intravenous ferric carboxymaltose group.

DISCUSSION

Iron deficiency anemia is a very common condition, overall, throughout the world, 40% suffer from IDA [11]. IDA results in high mother death rates and morbidity. The most common morbidities encountered include peripartum hemorrhage, preterm delivery, and low birth weight [12]. All these complications increase in iron deficiency anaemia patients. IDA is globally the third most common reason for years lived with disability (YLDs) since 1990. If the last two decades results are reviewed, iron deficiency anemia remains the same. The most widely prescribed drug for oral iron supplementation has a composition of a ferrous salt. Ferrous salt has got low and variable absorption rate[13].

Newer type II and III iron complexes have been developed over the past few years, which have been reported by patients as highly recommended and better tolerated. These salts have been used for the fast restoration of iron stores. Evidence exists that a single dose of IV iron sucrose results in a high occurrence of thrombosis (9/41, 22%)[14]. However, 6 small doses of intravenous iron sucrose, which were given during 3 weeks time period resulted in no thrombosis[15].

A study on ferric carboxymaltose was done over one year; results depicted that the use of FCM during the second and third trimesters resulted in good patient compliance and the same complication rates. For FCM group adverse effects rate was8%, while for iron sucrose group adverse effects rate was 11%[16]. Froessler et al. included 65 pregnant women suffering from anemia in a prospective control study. Patients were given ferri ccarboxymaltose. In this patient group, hemoglobin levels increased highly after FCM administration and 66% of women improved after the administration of FCM. No complications and adverse effects occurred after the administration of FCM. Minor side effects were reported in 13 patients (20%). All were managed conservatively, and only one patient required medicine to control nausea and vomiting [17].

In multi-center clinical trials, a total of 4,903 doses of ferric carboxymaltosewere administered to 2,065 patients without major adverse drug effects. The mean maximum single dose administered was 800 mg. Ferric carboxymaltose complex results in how same efficacy of IV iron administration. Benefits of FCM include no multiple infusions administered, no prolonged time duration for administration and less adverse GI effects[18].In one study, injection site discoloration was observed more in I/V iron sucrose group patients (1.8%) as compared to I/V iron carboxymaltose group patients (1.6%)[19].

A study performed in 2014 on I/V iron carboxymaltose use among iron deficiency anemia patients showed that hemoglobin levels improved in 66% of patients[20]. Previous studies showed that I/V iron sucrose was associated with rapid absorption into bone marrow however, with advent of I/V iron carboxymaltose, even faster improvement in hemoglobin levels has been observed[21]. Ferric carboxymaltose complex has the same efficacy as other IV

iron administration however, single-dose administration without prolonged infusion times and less risk of adverse drug effects have resulted in better patient compliance and satisfaction.

CONCLUSION

Iron is essential to man, and an adequate body iron balance is crucial. Treatment with intravenous iron caboxymaltose is superior to intravenous iron sucrose with respect to hematological response, which seems to be safe, as very few severe side-effects were observed and may result in hastened recovery from anemia and lower transfusion requirements.

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Author's Contribution:

Khir-Un Nisa: Substantial contributions to the conception and design of the work.
Rukhsana Shaheen Afzal: Acquisition, analysis, and interpretation of data for the work
Faiza Safdar: Analysis and interpretation of data.
Noreen Majeed: Data collection, and manuscript writing.
Shabana Kalsoom: Data collection, and revising the manuscript critically.
Irum Mushtaq: Conception, analysis, interpretation, and drafting of the article.

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