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Comparison of Intravenous Iron Infusion or Oral Iron for Treatment of Moderate Postpartum Anemia

Orta Düzey Postpartum Anemi Tedavisinde İntravenöz ve Oral Demir Tedavi Yöntemlerinin Karşılaştırılması

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ÖZ

Amaç: Çalışmamızda, orta düzey postpartum anemisi olan ve klinik olarak stabil olan hastalarda intravenöz ve oral demir tedavi seçeneklerinin hematolojik etkinliğini karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Doğum sonrası taburcu olmadan hemen önce hemoglobin değerlerini 8-9.5 gr/dl olan 180 postpartum olgu iki gruba ayrıldı. 1. grup oral fe +2 (n = 127, %70.6), diğer grup ise intravenöz ferrik karboksmaltoz (n = 53, %29.4) ile tedavi edildi. Grup 1 oral demir tedavisi yaklaşık 8 hafta aldı. Grup 2'ye 1 hafta ara ile iki kez intravenöz ferrik karboksmaltoz replasmanı yapıldı. Geç postpartum (doğumdan 8 hafta sonra) hemoglobin düzeyleri toplandı ve kaydedildi.

Bulgular: Postpartum maternal hemoglobin seviyeleri açısından grup 1 ve grup 2 arasındaki fark istatistiksel olarak anlamlı bulunmuştur (sırasıyla, 10,52±1,26 g/dl, 11,82±1,06 g/dl, P değeri 0,021). Grup 2' de intravenöz demir tedavisi sonrası hb seviyelerinde artış oranı grup 1'le karşılaştırıldığında anlamlı olarak yüksek bulunmuştur. (sırasıyla, 1,51±0,72 g/dl, 2,90±0,46 g/dl, P değeri 0,01).

Sonuç: Anemik postpartum vakaların klinik değerlendirmeleri genel tedavi ve hasta takip yaklaşımlarımızın bir parçası olsada, orta ve derin anemik olgular hızlı hematolojik iyileşme için 3. jenerasyon intravenöz demir formları ile tedavi edilmelidir.

Anahtar Kelimeler: Postpartum anemi, demir eksikliği, demir preparatları

ABSTRACT

Aim: In our study, we aimed to compare the hematological efficacy of intravenous and oral forms of iron treatment in clinically stable patients with moderate postpartum anemia.

Material and Methods: One hundred and eighty postpartum cases, who had pre-discharge hemoglobin evaluation levels between 8-9.5 g/dl, were allocated into two groups. The 1st group was treated with oral fe +2 (n = 127, 70.6%), and the other group was treated with intravenous ferric carboxymaltose (n = 53, % 29.4). Group 1 received oral iron treatment for approximately 8 weeks. Also, in Group 2, intravenous ferric carboxymaltose iron replacement was performed twice with 1-week intervals. Late postpartum (8 weeks after delivery) hemoglobin levels were collected and recorded.

Results: Difference between group 1 and group 2 in terms of late postpartum maternal hemoglobin levels were found statistically significant (respectively, 10,52±1,26 g/dl vs 11,82±1,06 g/dl, P-value 0,021). After intravenous treatment, an increased rate of hemoglobin in group 2 was found statistically significant when comparing within group 2. (1,51±0,72 g/dl vs 2,90±0,46 g/dl, P-value 0,01).

Conclusion: Although clinical evaluations and stability of anemic postpartum cases are part of our overall treatment and patient follow-up approaches, moderate and deeper anemic cases should be treated with 3rd generation intravenous iron forms for rapid hematologic improvement.

Keywords: Postpartum anemia, iron deficiency, iron preparations

INTRODUCTION

Postpartum anemia is a serious and common problem around the world. (1,2). The prevalence of postpartum anemia is higher in developing countries, and it is considered among the most common causes of maternal mortality and morbidity (3,4,5). The most common causes of postpartum anemia are iron deficiency anemia in the antepartum period and excessive bleeding in labor; bleeding during labor is also the most important cause of acute change in the hematological status (6).

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Postpartum anemia and postpartum hemorrhage, which is often the cause of the former, may disrupt the formation of newborn-mother relationships in the early period and cause dyspnea, lethargy, tachycardia and infectious conditions in the mother. In the long-term, anemia can cause emotional instability, increased risk for postpartum depression, including impaired quality of life, poor cognitive performance and decreasing lactation, iron deficiency in breast milk, etc. (1,7). As we leave the labor behind, this turns into a severe issue for women in the reproductive period.

Postpartum anemia should be treated by filling the body iron stores orally or intravenously. Depending on the severity of anemia, iron should be supplied fast and effectively to minimize the anemia complications mentioned above.

In our study, we aim to compare the hematological efficacy of i.v. and oral forms of iron therapy in clinically stable patients with moderate postpartum anemia.

MATERIAL AND METHODS

The article was designed as a retrospective study evaluating the efficacy of oral iron therapy and i.v. iron therapy in women diagnosed with anemia on postpartum control hemogram. Regional Ethical Board ap proved the study (protocol no. 29/09/2018-09), and it was carried out between January 2015 and September 2017.

ELIGIBILITY CRITERIA

In the postpartum period, patients with moderate iron-deficiency anemia during the postpartum period and patients who were found to be hemodynamically stable and had iron replacement therapy were included in our study.

Patients who were not anemic, who had metabolic illnesses such as severe or extensive anemia (hb: less than 8 g/L), acute systemic infection, vitamin B12 or folate deficiency, hepatitis, HIV, severe asthma, patients who are allergic to iron, who had undergone a change in the form of iron therapy for intolerance or any other reason, who had weight gain over 15 kg and who gained less than 5 kg in pregnancy were determined as the exclusion criteria. Also, those still having specific dietary patterns (i.e., who are vegetarian or under a vegetarian diet) or any dietary restrictions (i.e., allergies or food intolerance) were excluded from the study. In the follow-up of the patients in both groups, the respiratory rate did not increase, and there was no tachycardia, blood pressure was normal, no hypotensive attack, no dizziness; these were uneventful clinical follow-ups.

ALLOCATION OF CASES

All of the patients included in the study, had prepartum anemia while the blood samples measured at admission were slightly anemic (9.5-12 g/dl). Patients within the hb level of 8-9.5 g/dl during the evaluation before the postpartum patients were discharged were selected for treatment and study group.

Patients were allocated into one of the two treatment groups randomly via the medical records. Group 1, is the group that received oral iron (II) sulfate (Gynofero, Koçak Farma, Turkey) treatment and the second group is the one that received i.v. iron carboxymaltose (Ferinject, Abdi İbrahim, Turkey). The group receiving oral treatment received 160 mg/day iron replacement in 2 equal daily doses for an average of 8 weeks. The second group receiving i.v. the therapy received a total of 1500 mg of iron carboxymaltose at one-week intervals. The first dose of 1000 mg out of 1500 mg iron carboxymaltose was administered before the patient was discharged by i.v. infusion with 250 ml of 0.9% sodium chloride solution in a way to be completed in 15 minutes. The second dose, 500 ml, was administered with 100 ml of 0.9% sodium chloride solution in 10 minutes.

Venous blood samples were collected and recorded three times, at the time of prepartum (hospital admission), postpartum (before being discharged, early postpartum) and late postpartum (approximately eight weeks after delivery) periods. For the 1st blood sampling (prepartum), 873 cases were examined. It was observed that there were 471 slightly anemic (9.5-12 g/dl) cases, then, via the 2nd sampling, the early postpartum moderate anemia cases were determined and excluded. Third blood sampling was used in an attempt to evaluate the response to the treatment. The difference between the hemoglobin (hb) values of the blood received during early and late postpartum periods was used as a comparison criterion for oral and i.v. iron regarding the treatment and also as the increments of hb.

Demographic characteristics, age, body mass index (BMI), maternal weight during the postpartum period, maternal weight change during the pregnancy and average treatment time for oral iron support were recorded.

STATISTICAL ANALYSIS

All statistical analyses were performed using the SPSS ver. 15.0 (SPSS Inc., Chicago, IL, USA). The consistency of the data with the normal dispersion has been evaluated by the Kolmogorov-Smirnov test. It has been observed that none of the data groups are consistent with the normal dispersion. The difference between the groups was investigated by the Mann-Whitney U test because there were two groups and they were not consistent with normal dispersion. Numerical variables were shown as the mean ± standard deviation (mean ± SD). $P < 0.05$ has been accepted as statistically significant.

RESULTS

One hundred and eighty pregnants with moderate postpartum anemia were divided into two groups, 70,6% (n=127) group 1 (orally iron II sulfate), 29,4% (n=53) grup 2 (intravenous ferric carboxymaltose).

In all two groups were similar regarding maternal age, body mass index (BMI), maternal weight, weight gain, maternal hb levels before delivery, hb levels after delivery, hb control time after delivery, hb control time late postpartum period. Although these parameters differed between the groups, no statistical significance was found. After intravenous treatment, an increased rate of hemoglobin in group 2 was found statistically significant when comparing with in group 2 ($p < 0,01$), (Table I).

Table I. Comparison of demographic characteristics of two groups.

	Orally iron II sulphate group 1 n=127 (70,6)	İntra venous ferric carboxymaltose group 2 n=53 (29,4)	*P* value*
Maternalage (year)*	31,42±2,16	31,10±3,49	NS
Maternal weight (kg)*	68,48±4,67	67,78±3,18	NS
Maternal BMI at firsttrimester*	26,14±1,87	26,61±1,55	NS
Materal weight gain (kg)*	12,83±2,41	13,46±1,21	NS

Maternal haemoglobin before delivery (g/dl)*	11,21±1,43	11,01±1,21	NS
Maternal haemoglobin after delivery (g/dl)*	9,01±0,54	8,92± 0,60	NS
Maternal haemoglobin control time after delivery (h)	21,75±2,57	22,55±3,04	NS
Maternal haemoglobin late postpartum period (g/dl) *	10,52±1,26	11,82±1,06	0,021
Maternal haemoglobin control time late postpartum period (d)	57,21±3,45	56,82±3,21	NS

kg, kilogram; BMI, body mass index; g/dl, gram per deciliter; h, hour; d, day.

˚ Data are given as n (%).

* Data are given as mean standard deviation (SD)

*Mann Whitney U test

In our study, the comparison of the difference between the levels of hb increase in the groups after the treatment are summarized in Table 2. Hb increase was statistically significant in Group 2 (P-value 0.01).

Table II. Comparison of mean hemoglobin increases of two groups.

	Orally iron II sulphate group 1 n=127 (70,6)	İv ferric carboxymaltose group 2 n=53 (29,4)	*P*value*
Mean haemoglobin increase (gr/dl) *	1,51±0,72	2,90±0,46	<0,01

g/dl, gram per deciliter.

˚ Data are given as n (%).

* Data are given as mean standard deviation (SD)

*Mann Whitney U test

The limitations of the study were the fact that it was retrospective, and that it is unknown when appropriate anemic hematologic parameters were acquired.

DISCUSSION

There are a few official guides in the literature regarding the treatment of postpartum iron deficiency anemia (IDA). These are Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe and the Network for Advancement of Transfusion Alternatives (8,9). Table 3 is shown.

Table III. Guidelines for treatment of postpartum IDA associated with blood losses

	Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe	Network for Advancement of Transfusion Alternatives
Slight IDA=hemoglobin 95–120 g/l	Oral iron 80–200 mg/day	
Moderate IDA=hemoglobin 80–95 g/l	I.v. iron 500–1,000 mg	I.v. iron 500–1,000 mg Consider erythropoietin 10,000–20,000 U subcutaneously
Severe IDA=hemoglobin <80 g/l	I.v. iron 500–1,000 mg Consider erythropoietin 10,000–20,000 U subcutaneously	
Very severe IDA=hemoglobin <60 g/l		Consider blood transfusion

In the literature, it is a consensus that the oral iron treatment should be the first option in women with mild to moderate IDA (hb levels of 95–120 g/l) (10). This group should be treated with ferrous iron 100–200 mg/day (8,9). After the two weeks of treatment, the therapeutic response should be controlled by hb measurement. If the hb level is higher than ≥10 g/l, oral iron treatment should be continued at 200 mg/day for eight weeks. When the hb reaches >12 g/dl level, the iron dose may be reduced to 100 mg/day. It should be noted that after the successful treatment of oral iron therapy with IDA, it takes a long time to regenerate body iron stores and obtain the ideal serum plasma ferritin level (10).

In the i.v. iron treatment, 3rd generation iron preparations with proven efficacy have been used. These preparations vary according to their ability to bind iron; while iron sucrose and low-molecular-weight iron dextran are in the 2nd generation group, ferric iron carboxymaltose and ferric iron isomaltoside, which have higher activity rates, are in 3rd generation iron group. (11,12,13,14,15)

In postpartum IDA, several studies have demonstrated the efficacy of the use of i.v. In studies comparing the i.v. and oral use of iron therapy, superiorities were found in the use of i.v. when it comes to hb and ferritin levels. Intravenous iron provides a faster and higher increase in hb concentration than oral iron. (16,17). It is emphasized by the manufacturers that side effects may be observed only at the rate of 0.5% in the use of i.v. iron. Many manufacturers even advocate the need that the i.v. iron should be provided In the literature, it is a consensus that the oral iron treatment should be the first option in women with mild to moderate IDA (hb levels of 95–120 g/l) (10). This group should be treated with ferrous iron 100–200 mg/day (8,9). After the two weeks of treatment, the therapeutic response should be controlled by hb measurement.

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In the trial of Iyoke et. al. it is stated that single total-dose intravenous iron for treatment of puerperal iron-deficiency anemia was as effective as daily single doses of ferric iron tablets. In this study, although it didn't reach a statistical significance, there was, in fact, a minor difference between the posttreatment hb levels in favor of iv treatment group of which results were similar to ours (21).

In a systematic review, published by Sultan P. in 2018, among women with postpartum anemia, hemoglobin concentrations at 6 weeks postpartum were almost 1 g/dL higher in women who received IV iron compared to oral iron. The safety profile of IV iron was also reassuring. Given the weaker hemoglobin response and a higher risk of gastrointestinal side effects with oral iron use, its findings suggest that IV iron be considered as a viable treatment option for postpartum iron deficiency anemia (22). Similar to the aforementioned results in our study hemoglobin concentrations at late postpartum period was almost 1,4 g/dL higher in women who received IV iron compared to oral iron.

CONCLUSION

Although the clinical evaluations and the stability of the anemic postpartum mother are part of our general treatment and patient follow-up approaches, the 3rd generation i.v. the iron form should be preferred at the first step with a moderate side effect profile in terms of rapid hematological improvement in moderate and more profound.

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