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The role of intravenous iron sucrose treatment in patients with iron deficiency anemia in pregnancy: A prospective controlled cohort study

Gebelikte demir eksikliği anemisi olan hastalarda intravenöz demir sükroz tedavisinin rolü: Prospektif kontrollü kohort çalışması

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Abstract

Aim: Iron deficiency anemia is the most common nutritional disorder in pregnancy and approximately 40% of all pregnant women are complicated with perinatal morbidity and mortality. In this work, the efficacy of intravenous iron sucrose and oral iron hydroxypolymaltose is compared in third-trimester pregnancies with iron deficiency anemia.

Methods: A prospective cohort study is planned. A total of 140 pregnant women were enrolled in the study in two groups. The first group consisted of patients who could not tolerate oral iron therapy and were treated with intravenous iron sucrose and the second group was composed of patients who used oral iron III hydroxy polymaltose for anemia treatment in third trimester.. The treatment effects of blood count parameters were compared between groups.

Results: Demographic and baseline characteristics were similar in both groups. Mean hemoglobin levels before treatment were 9.03±0.47 g/L in the intravenous treatment group and 8.82±0.39 g/L in the oral treatment group. 30 days after treatment, the mean hemoglobin levels were 10.7±0.55 g/L in the intravenous treatment group and 10.9±0.58 g/L in the oral treatment group. Before delivery, the mean hemoglobin levels were 11.38±0.56 g/L in the intravenous treatment group and 11.35±0.47 g/L in the oral treatment group. There was no significant difference between groups for hemoglobin levels before treatment, 30 days after treatment, and before delivery (p=0.355, p=0.513, and p=0.975, respectively). The mean mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) levels were not statistically different between groups before treatment, 30 days after treatment, and before delivery.

Conclusions: Intravenous administration of iron sucrose is an alternative to blood transfusion for the treatment of pregnant women with iron deficiency anemia during the third trimester.

Keywords: Iron sucrose, Iron deficiency anemia, Third-trimester pregnancy

Öz

Amaç: Demir eksikliği anemisi gebelikte en sık görülen beslenme bozukluğudur ve tüm gebelerin yaklaşık% 40'ı anemi nedeni ile perinatal morbidite ve mortalite ile komplikedir. Bu çalışmada, demir eksikliği anemisi olan üçüncü trimester gebeliklerde intravenöz demir sukroz ve oral demir hidroksipolizmaltozun etkinliği karşılaştırıldı.

Yöntemler: Prospektif bir kohort çalışması planlandı. Çalışmaya iki grupta toplam 140 hamile kadın alındı. Birinci grup oral demir tedavisini tolere edemeyen ve intravenöz demir sukroz ile tedavi edilen ve ikinci grup üçüncü trimesterde anemi tedavisi için oral demir III hidroksi polmaltoz kullanan hastalardan oluşuyordu. Kan sayımı parametrelerinin tedavi etkileri. gruplar arasında karşılaştırıldı.

Bulgular: Demografik ve bazal özellikler her iki grupta da benzerdi. Tedavi öncesi ortalama hemoglobin düzeyleri intravenöz tedavi grubunda 9.03±0.47 g / L, oral tedavi grubunda 8.82±0.39 g / L idi. Tedaviden 30 gün sonra, ortalama hemoglobin düzeyleri intravenöz tedavi grubunda 10.7±0.55 g / L, oral tedavi grubunda 10.9±0.58 g / L idi. Doğum öncesi ortalama hemoglobin düzeyleri intravenöz tedavi grubunda 11.38±0.56 g / L, oral tedavi grubunda 11.35±0.47 g / L idi. Gruplar arasında hemoglobin düzeyleri açısından tedaviden önce, tedaviden 30 gün sonra ve doğumdan önce anlamlı fark yoktu (sırasıyla p = 0.355, p = 0.513 ve p = 0.975). Ortalama korpüsküler hakim (MCV), ortalama korpüsküler hemoglobin (MCH) ve ortalama korpüsküler hemoglobin konsantrasyonu (MCHC) seviyeleri, tedaviden önce, tedaviden 30 gün sonra ve doğumdan önce gruplar arasında istatistiksel olarak farklı değildi.

Sonuçlar: İntravenöz demir sukroz uygulaması, üçüncü trimesterde demir eksikliği anemili gebelerin tedavisinde kan transfüzyonuna bir alternatiftir.

Anahtar kelimeler: Demir sukroz, Demir eksikliği anemisi, Üçüncü trimester gebelik

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Introduction

Iron deficiency anemia is the most common nutritional disorder worldwide and it is the most common form of anemia. Approximately 40% of all pregnancies are complicated by anemia, which causes increased perinatal morbidity and mortality, as well as low birth weight and preterm labor [1-3].

The increased requirement for iron in pregnancy can further aggravate the anemia if untreated. Recently, a range of oral, intramuscular, and intravenous iron formulations have been applied for the treatment of anemia [4]. Oral iron preparations are the first choice as they are efficacious, safe, and low cost. However, orally administered iron is poorly tolerated and associated with various gastrointestinal side effects (nausea, vomiting, abdominal pain, constipation, and diarrhea). Iron gluconate and iron dextran preparations are traditionally used for intravenous iron therapy, but their application is limited by high rates of side effects. Iron sucrose is the most recently developed intravenous iron preparation; it is increasingly used owing to its efficacy, safety, and good side-effect profile, making it one of the first options in patients who cannot tolerate oral iron preparations [4-6].

In the present study, the efficacy of intravenous iron sucrose and oral iron hydroxy polymaltose was compared for the treatment of women with iron deficiency anemia in third-trimester pregnancies.

Materials and methods

The present study was conducted at Sivas Şarkışla Government Hospital in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Cumhuriyet University (approval no:2018-1/13).

The study included pregnant women between the ages of 18 and 35, between 30 and 34 gestational weeks, with a single gestation, with iron deficiency anemia. The study was composed of two groups. The first group (IV group) consisted of patients who could not tolerate oral iron therapy and were treated with intravenous iron sucrose (Venofer, Abdi İbrahim İlaç Sanayi, Turkey). The second group (Oral group) was composed of patients who used oral iron III hydroxy polymaltose (Ferrum Hausmann Fort, Abdi İbrahim İlaç Sanayi, Turkey) for at least 4weeks. Anemia was defined as having a hemoglobin level of 70–110 g/L and patients known to have hemoglobinopathy, a history of allergic reactions, or systemic disease were excluded from the study.

For oral iron therapy, the patients were administered two100-mg elemental iron III hydroxy polymaltose tablets per day. The dose of intravenous iron sucrose used in this study was calculated as kg (target Hb-present Hb) × 0.24 + 500mg. The dose was diluted to 200mg and given on consecutive days to not exceed 600mg per week [5-8].

Demographic characteristics such as maternal age, gravida body mass index (BMI), gestational age at initiation of treatment, and gestational age at delivery were recorded. The mean mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) levels were measured before the treatment, 30 days after treatment, and before delivery, and the groups were compared.

Statistical analysis

The Shapiro–Wilk test was used to test the normality of the data. Levene's test was used to test the variance homogeneity. Values are expressed as mean±standard deviation (SD), median (25–75th percentile), or n (%). Parametric comparisons were made using a t-test or a z-test, and nonparametric comparisons were made using the Mann–Whitney U test. All comparisons were made using PASW Statistics ver. 18 (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered statistically significant.

Results

Of the 140 pregnant women enrolled in the study, 100 received oral treatment (oral group) and 40 received intravenous treatment (IV group). Their demographic and obstetric characteristics were compared and the details are presented in Table 1. Maternal age (p=0.537), gravida (p=0.753), BMI (p=0.944), gestational age at initiation of treatment (p=0.740), and gestational age at delivery (p=0.870) were similar in both groups.

Maternal blood count values were compared and are shown in Table 2. The mean hemoglobin levels before treatment were 9.03±0.47 g/L in the IV group and 8.82±0.39 g/L in the oral group. 30 days after treatment, the mean Hb levels were 10.7±0.55 g/L in the IV group and 10.9±0.58 g/L in the oral group. Before delivery, the mean Hb levels were 11.38±0.56 g/L in the IV group and 11.35±0.47 g/L in the oral group. There was no significant difference in Hb levels between groups before treatment, 30 days after treatment, and before delivery (p=0.355, p=0.513, and p=0.975), respectively). The mean MCV, MCH, and MCHC levels were not statistically different between groups before treatment, 30 days after treatment, and before delivery, as illustrated in Table 2.

Table 1: Comparison of maternal characteristics between groups

	IV group (n=40)	Oral group (n=100)	p
Maternal age (years)	25.44±5.49	25.78±2.82	0.537
Gravida	2.09±1.01	2.10±1.04	0.753
BMI (kg/m^2)	26.90 (26.20–27.75)	27.05 (26.10–27.95)	0.944
Gestational age at initiation of treatment (weeks)	32.4±1.4	32.6±1.3	0.740
Gestational age at delivery (weeks)	39.3±0.7	39.4±0.4	0.870

Values are expressed as mean±standard deviation (SD)

Table 2: Comparison of maternal blood count values between groups

	IV group (n=40)	Oral group (n=100)	p
Hb (g/L) Before treatment	9.03±0.47	8.82±0.39	0.355
After treatment 30 days	10.7±0.55	10.9±0.58	0.513
Before delivery	11.38±0.56	11.35±0.47	0.975
MCV Before treatment	85.35±1.91	85.73±1.70	0.342
After treatment 30 days	88.23±1.86	88.62±1.64	0.410
Before delivery	90.23±3.34	91.38±2.42	0.110
MCH Before treatment	25.73±1.11	25.70±1.01	0.611
After treatment 30 days	28.33±0.93	28.49±0.97	0.986
Before delivery	29.02±1.00	29.00±1.04	0.721
MCHC Before treatment	30.70±0.87	30.57±0.83	0.391
After treatment 30 days	32.29±1.63	32.73±0.84	0.349
Before delivery	32.96±1.77	33.19±1.18	0.735

Values are expressed as mean±standard deviation (SD), median (25–75th percentile), or n (%), Hb: hemoglobin, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration

Discussion

In routine clinical practice, all clinicians encounter anemic pregnant women who cannot tolerate oral iron or who do not benefit from oral treatment. It is well documented that the babies of mothers with moderate to severe anemia have significantly lower levels of serum ferritin in their cord blood, indicating that they have insufficient iron stores [9]. Moreover, increased levels of preterm births, stillbirths, babies that are small for their gestational age, and mortality have been observed in babies born to anemic mothers [10]. It was recently reported from a study of 130 women with severe anemia that 69.2% of the mothers experienced preterm deliveries and 24.6% of babies born had lower birth weights than would be expected [11]. The goal of this study was to compare the efficacy of intravenous iron sucrose and oral iron hydroxy polymaltose in third-trimester pregnancies with iron deficiency anemia.

The main aim of anemia treatment in pregnancy is to restore hemoglobin to normal levels at the time of giving birth to avoid complications such as preterm births, stillbirths, babies that are small for their gestational age, and mortality, and to reduce the risk associated with blood transfusions. Various treatment options are available to increase hemoglobin levels, but the fastest and most reliable should be selected. Typically, oral administration of iron was believed to be a convenient, safe, and low-cost method of treatment. However, its efficacy is significantly hampered by gastrointestinal side effects, including nausea, vomiting, diarrhea, and constipation. In addition, oral administration of iron is associated with poor adsorption and a long time (months) is needed to replenish iron stores and restore hemoglobin levels [12]. Intravenous iron dextran can be used, but it leads to severe anaphylactic reactions, including sudden cardiovascular collapse, respiratory failure, and loss of life, in 0.1 to 2% of patients. Furthermore, adverse effects were reported by 30% of patients treated with iron dextran, including fever, arthritis, and urticarial [4]. Intramuscular administration of iron in the form of an iron–sorbitol citric acid complex has various side effects, including a metallic taste on the tongue, nausea, vomiting, and pain at the site of injection [13]. Other parenteral iron preparations are available in the form of ferric gluconate and ferric citrate, but they have been reported to cause severe and extended necrosis of the liver [14,15].

Our results showed that maternal serum Hb levels in pregnant women treated with IV iron sucrose and oral iron III hydroxy polymaltose were similar after 30 days and before delivery. There are now multiple reports in the literature on treatment of iron deficiency anemia in pregnancy using parenteral iron therapy, demonstrating similar or faster increases in hemoglobin levels and improved restoration of iron stores versus oral iron therapy, particularly for IV iron sucrose [4,16-21]. The positive outcomes with iron sucrose are attributed to it being a polynuclear iron complex that is analogous to ferritin, which is well tolerated and with a low level of antigenicity. It can be used for erythropoiesis within 5 min of infusion. Moreover, since it is stored in reticuloendothelial rather than parenchymal cells, it has a 68–97% utilization rate after 2–4 weeks [22]. When compared to iron dextran, the main advantage of iron sucrose is that no test dose is required before administration. There is a low level of adverse reactions to iron sucrose (0.002%) reported in the literature [23] and no adverse reactions or any other major side effects were observed during this study. However, the sample size in this study was not sufficient to statistically confirm the safety of iron sucrose.

Blood transfusions can be used to treat moderate and severe anemia in the third trimester of pregnancy. However, blood transfusion is associated with severe side effects, including, febrile and hemolytic reactions, infections anaphylactic shock, alloimmunization, and graft versus host disease [20]. In a meta-analysis of 75 clinical trials and 72 studies, treatment with IV iron preparations was associated with increased hemoglobin concentrations and it reduced the need for red blood cell transfusions (risk ratio: 0.74, 95% confidence interval: 0.62–0.88) [24]. Intravenous administration of iron sucrose may reduce the need for blood transfusions because it rapidly restores hemoglobin to normal levels. Therefore, IV iron sucrose can be considered as an alternative to oral iron treatment, thus reducing the need for blood transfusions, in the treatment of pregnant women with moderate iron deficiency anemia during the third trimester.

There are some limitations of our study. The small number of patients is the most important limitation of the study.

Conclusion

Intravenous administration of iron sucrose is a viable alternative to oral administration of iron III hydroxy polymaltose for the treatment of pregnant women with moderate iron deficiency anemia during the third trimester, which may help to reduce the need for risky blood transfusions.

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