J Surg Med. 2020;4(4):259-262.
DOI: 10.28982/josam.650854

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN=2602-2079

The effect of iron carboxymaltose treatment on quality of life in women with iron deficiency

Demir eksikliği olan kadınlarda demir karboksimaltoz tedavisinin hayat kalitesine etkisi

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Ethics Committee Approval: The study was approved by the Ethics and Research Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital (REF: 2016/04/10). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Bu çalışma Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Etik ve Araştırma Komitesi (REF: 2016/04/10) tarafından onaylanmıştır. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 4/20/2020
Yayın Tarihi: 20.04.2020

Abstract

Aim: Iron deficiency is the most common cause of anemia in over the world and affects 20% of women, even in developed countries. In this study, our aim is to calculate the change in the quality of life of patients treated with parenteral ferric carboxymaltose.

Methods: In this retrospective cohort study, quality of life scores were evaluated before and after 6 weeks of treatment using the Short Form 36 scale. Fifty patients receiving parenteral ferric carboxymaltose treatment in Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Department of Gynecology and Obstetrics were included.

Results: Pretreatment ad posttreatment hemoglobin values were 8.22 g/dl and 12.02 g/dl, respectively. Pretreatment physical role functioning score was 34.7 (39) and it was calculated as 54.2 (39.8) after the treatment (P=0.006). There were no significant differences between pre- and post-treatment emotional strength, (P=0.330), energy vitality, (P=0.210), mental health (P=0.910) scores and sub-dimensions. Minor side effects were observed in 3 patients.

Conclusion: Parenteral ferric carboxymaltose therapy significantly improves quality of life, especially physical role strength. Iron deficiency should be replaced effectively.

Keywords: Iron, Anemia, Quality of life, Gynecology

Öz

Amaç: Demir eksikliği anemisi; en sık tespit edilen anemi nedeni olup, gelişmiş ülkelerde bile kadınların %20'sini etkilemektedir. Bu çalışmada parenteral ferrik karboksimaltoz tedavisinin hastaların yaşam kalitesine olan etkisi değerlendirilmiştir.

Yöntemler: Bu retrospektif kohort çalışma SBÜ Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniği'nde yapılmıştır. Parenteral ferrik karboksimaltoz tedavisi verilen 50 hastada, tedavi öncesi ve sonrası 6. hafta arasında yaşam kalitesi açısından değişim; Kısa Form 36 ölçeği kullanılarak değerlendirilmiştir.

Bulgular: Tedavi öncesi hemoglobin düzeyi 8,22 gr/dl iken tedavi sonrası 6. Haftada 12,02 gr/dl düzeyine yükselmiştir. Tedavi öncesi 34,7 (39) olan fiziksel rol güçlüğü, tedavi sonrasında 54,2 (39,8)'e yükselmiştir (P=0,006). Emosyonel rol güçlüğü, (P=0,330), enerji canlılık (P=0,210) ve ruh sağlığı (P=0,910) alt boyutlarında anlamlı farklılık olmadığı saptanmıştır. 3 hastada minör yan etki gözlenmiştir.

Sonuç: Parenteral demir karboksimaltoz tedavisi özellikle fiziksel rol güçlüğü kategorisinde olmak üzere yaşam kalitesini belirgin şekilde artırmıştır. Bu yüzden demir eksikliği etkili bir şekilde replase edilmelidir.

Anahtar kelimeler: Demir, Anemi, Yaşam kalitesi, Jinekoloji

How to cite/Atıf için: Helvacıoğlu Ç, Ekin M. The effect of iron carboxymaltose treatment on quality of life in women with iron deficiency. J Surg Med. 2020;4(4):259-262.

Introduction

When negative iron balance occurs in the body (due to chronic blood loss, increased need for iron, absorption deficiency), hemoglobin (Hb) synthesis is maintained by the mobilization of iron from the stores, and if the iron stores do not provide the iron necessary for Hb synthesis, iron deficiency anemia (IDA) develops [1].

It is known that more than 30% of the patients in developed countries who are admitted to the hospital have anemia and this rate is higher in developing countries [2]. In the world and in Turkey, the most common factor that may cause anemia is iron deficiency. In developed countries, 3% of adult men, 20% of women and 50% of pregnant women have iron deficiency [3,4].

The prevalence of etiologic factors in IDA varies according to age groups. The most prominent factors are type of feeding in 0-2-year-old children, menstrual loss in fertile women and gastrointestinal system disorders in elderly people. Nutritional disorders and parasitic diseases gain importance in the etiology especially in developing countries [5].

The actual control of IDA has two stages: Treatment of the underlying disease and correcting iron deficiency. The aim of treatment is to gradually increase the iron levels and Hb to normal values [6].

The most common treatment method in IDA is oral iron replacement therapy [7]. The main advantage of oral replacement is that it is an inexpensive method. However, it has some disadvantages such as the need for long-term use, adverse effects on gastrointestinal system (GIS) and difficulties in patient compliance. We observed that the oral iron therapy is not used optimally in majority of our patients. Intravenous (IV) iron replacement is a relatively expensive form of treatment, and less patient compliance problems and lack of adverse effects on GIS make it a better treatment option.

Short Form 36 (SF-36) has been developed and presented to use by Rand Corporation to assess the quality of life [8]. SF-36 is a multi-purpose, short health survey form consisting of 36 questions. It has been successfully adapted to general population in many countries, particularly in the United States of America. SF-36 has been translated into Turkish by Bilir Kaya et al. [9] and its reliability and validity have been assessed in patients with rheumatoid arthritis.

The aim of this study was to determine the effects of IV ferric carboxymaltose treatment on quality of life in female patients presenting with anemia symptoms and diagnosed with iron deficiency anemia.

Materials and methods

This retrospective cohort study included 50 women treated with IV ferric carboxymaltose for iron deficiency anemia in Bakirkoy Dr. Sadi Konuk Hospital, Department of Gynecology and Obstetrics. Iron deficiency anemia of the patients was due to gynecological conditions and the patients with chronic kidney disease or gastrointestinal disorders were excluded from the study.

Ferric carboxymaltose (Ferinject®) is a novel non-dextran-containing complex of iron that allows for administration of a large replenishment dose (≤1.000 mg of iron) over a short infusion period (15 minutes). Patients those require higher doses were not included in the study.

Ethics committee approval was obtained from the Ethics and Research Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital (REF: 2016/04/10). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments. After obtaining oral and written informed consent from the patients who accepted to join the study, patients were asked to complete the SF-36 questionnaire before and at 6 weeks after the treatment. Nine patients were excluded from the study as they did not attend follow-ups.

Statistical analysis

Statistical analysis was performed using SPSS 23 package program (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: USA). The normal distribution of the data was evaluated by Shapiro-Wilk test. Mean standard deviation and median values were given for descriptive statistics. T test and Wilcoxon signed-rank tests were used to compare normally and non-normally distributed data, respectively. Cronbach Alpha coefficient was calculated for internal consistency of data set. The lowest reliability level was accepted as 0.50. G*Power 3.1.9.2 was used to calculate the power of the tests.

Results

This study included 41 volunteers who completed the baseline SF-36 questionnaire. The mean age of the patients was 43.8 (4.9) years, mean height was 1.61 (0.5) (cm), mean weight was 71.4 (9.2) kg and body mass index (BMI) was 27.6 (3.5) kg/m^2 (Table 1).

Before treatment physical role functioning score was 34.7 (39) and after treatment it increased to 54.2 (39.8) (P=0.006). The median value of physical role difficulty was higher after treatment (Table 2) Post-hoc power, which was statistically significant, was 91% for this variable.

Physical functions score was 58.1 (24.3) before and 64.6 (23.1) after treatment (P=0.059). The pre- and posttreatment pain scores were 46.6 (29.8) and 51.7 (23.89), respectively (P=0.33). General health score increased to 40.6 (20.2) from 38.7 (19.6) after treatment (P=0.49) (Table 2). Improvement in these subscales were numerical, but not statistically significant.

Emotional role functions score was 52.4 (43.2) before treatment, decreasing to 45.1 (44.4) after treatment (P=0.33). Energy and vitality scores were 40.2 (18.8) before and 43.7 (19.9) after treatment (P=0.21). Pre- and post-treatment mental health scores were 56.9 (17.3) and 56.6 (20.5), respectively (P=0.91). The treatment did not significantly affect these quality of life subcategories (Table 3).

While the mean hemoglobin level of the participants was 8.29 gr/dl before the treatment, it increased to 12.2 gr/dl at 6^{th} week following treatment (Table 4). According to these data, there was a 3.8 g/dl difference between pre-treatment and post-treatment hemoglobin levels.

We observed minor side-effects in three participants which were temporary felling of sickness in one patient and

rashes around the infusion site in two patients. There were no major side-effects requiring hospitalization and additional treatments.

Table 1: Descriptive statistics for the mean age, weight, height, and BMI of the study group

(n=41)	Mean (SD)
Age (years)	43.8 (4.9)
Height (m)	1.61 (0.05)
Weight (Kg)	71.4 (9.2)
BMI	27.6 (3.5)

SD: Standard deviation, BMI: Body mass index

Table 2: The comparison between the levels of physical functions, physical role difficulty, pain, general health quality of life before and after treatment

	Before treatment Mean (SD)	After treatment Mean (SD)	*P*-value
Physical functions	58.1 (24.3)	64.6 (23.1)	0.059
Physical role functioning	34.7 (39)	54.2 (39.8)	0.006
Pain	46.6 (29.8)	51.7 (23.8)	0.330
General health	38.7 (19.6)	40.6 (20.2)	0.490

SD: Standard deviation, Wilcoxon Signed Ranks Test

Table 3: The comparison between the levels of emotional role difficulty, energy and vitality, and mental health quality of life before and after treatment

	Before treatment Mean (SD)	After treatment Mean (SD)	*P*-value
Emotional role functioning	52.4 (43.2)	45.1 (44.4)	0.330
Energy and vitality	40.2 (18.8)	43.7 (19.9)	0.210
Mental health	56.9 (17.3)	56.6 (20.5)	0.910

SD: Standard deviation, Wilcoxon Signed Ranks Test, Dependent Sample T Test

Table 4: Before and after treatment hemoglobin levels

	Before treatment Mean (SD)	After treatment Mean (SD)	*P*-value
Hemoglobin levels (gr/dl)	8.2 (1)	12.02(1.2)	0.001

SD: Standard deviation, Dependent Sample T Test

Discussion

Iron is a quite crucial element in oxygen transport. It is found in the structure of hemoglobin in the erythrocytes, myoglobulin, and skeletal muscles, and plays important roles in oxygen diffusion and oxygen storage. In addition, it functions in oxidative reactions in the mitochondria and respiratory chain [10].

The most common cause of anemia in patients who were admitted to the gynecology outpatient clinic is iron deficiency. Iron deficiency anemia is a major health problem in both developed and developing countries. The most common cause of iron deficiency in adult patients is iron loss. According to a study by Davas et al. [11], 74.1% of pregnant women in Turkey have IDA. It is known that when menstrual losses cannot be met by iron intake in women of reproductive age, iron deficiency anemia can easily develop [12].

Viethen et al. [13] have shown that parenteral ferric carboxymaltose balances iron levels in the body and improves the quality of life and physical capacity in patients with pulmonary arterial hypertension and IDA. They have reported that the treatment is well tolerated, and they have not observed any major side-effects.

In an effective oral iron treatment, the increase in hemoglobin concentration levels should be 2 gr/dl in 3-4 weeks [14]. Regular use, good tolerability and low side-effects are prerequisites for an efficient oral iron treatment. We observed that the majority of patients do not regularly adhere to oral iron therapy in our clinic.

We showed that the hemoglobin levels have increased from 8.22 gr/dl to 12.02 gr/dl at 6 weeks after treatment. Khalafallah et al. [15] have reported an increase in hemoglobin levels similar to the results of our study. In the same study, it has been shown that ferric carboxymaltose increases hemoglobin levels in a shorter time compared to oral iron preparations. Unlike oral iron replacement, the most important advantage of parenteral iron therapy is that it does not require long-term patient compliance.

Parenteral iron therapy has the risk of anaphylaxis. Moore et al. [16] have performed a meta-analysis and have shown that the risk of anaphylaxis is quite low in ferric carboxymaltose molecule. Nevertheless, the parenteral carboxymaltose treatment is generally well-tolerated by the patients. We experienced minor side-effects in three participants. One patient had a temporary feeling of sickness and two patients suffered from rashes around the infusion site.

We assessed the effect of ferric carboxymaltose on quality of life by using SF-36 scale. According to our data, there was significant difference in physical role difficulty levels in patients who were treated with ferric carboxymaltose. Emotional role difficulty, energy/vitality and mental health subcategories did not reveal any significant differences. The treatment has not made a difference in these quality of life subcategories.

The improvement in physical role functions may be due to the significant role of iron in oxygen transport. Even though the hemoglobin levels increased after treatment, we did not find any significant relationship between emotional role difficulty, mental health, pain and general health levels. The treatment did not improve the mental quality of life of the patients. The underlying reasons may be the patient psychology, ongoing abnormal uterine bleeding, and other causes.

Previous studies have demonstrated that ferric carboxymaltose has a low risk of immunogenicity and a lower incidence of adverse events compared to oral iron or parenteral iron sucrose [17]. Ferric carboxymaltose has a lower pH and osmolarity than the other parenteral iron molecules which may lead to the increased safety of administration as well as a shorter duration of administration [18]. Ferric carboxymaltose does not require multiple doses so it can affect hemoglobin levels faster. This provides an advantage in especially its preoperative use [19].

We think that completing the SF-36 at the 6th week after treatment may be early in terms of showing the effect of the treatment on quality of life. Having said that, as anemia becomes chronic, treatment may not have improved the quality of life sufficiently due to adaptations in the body. We suggest that ferric carboxymaltose treatment can have more significant effects on quality of life in newly developed anemia cases.

Limitations

The most important limitations of our study were that it was a single-center study and the number of participants was low. In addition, six weeks for assessing the improvements in quality of life can be considered a brief period. Another limitation of our study was that the transferrin, ferritin, iron and serum iron binding capacity values were not compared. Future long-term studies may benefit from these parameters.

Conclusion

IDA is common in patients admitted to gynecology and obstetrics clinics. Iron deficiency must be effectively replaced, and the underlying reasons must be removed. Oral iron treatment requires regular use and patient compliance. Parenteral ferric carboxymaltose treatment improves hemoglobin levels in a brief time. Ferric carboxymaltose treatment positively improves

quality of life in suitable patients and it is a safe preparation in terms of side-effects.

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