Original Article

Access this article online

Quick Response Code:

Website: www.ijhonline.org

DOI: 10.4103/ijh.ijh_7_22

Effect of parenteral iron treatment on platelet counts in women who do not have concomitant diseases

Recep Alanli, Murat Bulent Kucukay

Abstract:

BACKGROUND: Iron replacement may change platelet counts. Parenteral iron treatment has different effects on platelets count in some diseases. the aim of this study was to inspect the effect of parenteral ferric carboxymaltose treatment on platelet counts and other hemogram parameters in females who have no other diseases, but iron deficiency.

MATERIALS AND METHODS: This study was conducted in a university hospital located in Ankara, Turkey, between January 2020 and October 2021. A total of 239 female participants who were diagnosed with iron deficiency and who were given parenteral ferric carboxymaltose treatment were included in the study. Participants were divided into two groups according to the existence of anemia. Hemogram parameters, ferritin, and C-reactive protein levels before and 3 months after parenteral ferric carboxymaltose treatment were compared between these two groups.

RESULTS: Hemoglobin and ferritin levels were increased ($P < 0.001$) and platelet counts ($P < 0.001$) and mean platelet volumes (MPVs) ($P = 0.015$) were decreased after parenteral ferric carboxymaltose treatment. In both groups, hemoglobin levels were increased and platelet counts were decreased, but in the group with patients having anemia, changes in hemoglobin levels and platelet counts were more prominent after treatment ($P < 0.001$). When compared to initiation of treatment, there was a significant negative correlation after treatment regarding changes in hemoglobin levels and platelet counts ($r = -0.369$, $P < 0.001$).

CONCLUSION: Parenteral ferric carboxymaltose treatment resulted in a decrease in platelet counts and MPV values compared to initiation of treatment. Parenteral ferric carboxymaltose treatment resulted in decreases in platelet counts and independent from correction of anemia.

Keywords:

Ferric carboxymaltose, iron deficiency, platelet count

Introduction

Iron deficiency usually affects children, young females, and the elder population. Thirty percent of the world population have iron deficiency.[1] In general, oral iron treatment is the first choice of treatment for iron deficiency. In patients who cannot tolerate oral iron treatment, parenteral iron treatment is an effective alternative, that rapidly improves iron status of patients.[2,3]

Parenteral iron treatment is superior to oral iron treatment and recommended in heart failure, chronic kidney disease (CKD), patients undergoing hemodialysis treatment, inflammatory bowel diseases, pregnancy, and to increase hemoglobin levels in patients who will have surgery.[4-7]

Platelets produce pro-inflammatory cytokines.[8] In acute and chronic inflammation, malignancy, blood loss and iron deficiency, and platelets counts may be increased.[9] Increased platelet counts are associated with increased risk for

Department of Internal Diseases, Faculty of Medicine, Lokman Hekim University, Ankara Hospital, Ankara, Turkey

Address for correspondence:
Dr. Recep Alanli, Lokman Hekim University Ankara SUAM, Polatli 2 Cad, Idil Sokak No: 44, Sincan 06930, Ankara, Turkey.
E-mail: recepalanli@gmail.com

Submission: 16-02-2022
Accepted: 30-03-2022
Published: 09-06-2022

How to cite this article: Alanli R, Kucukay MB. Effect of parenteral iron treatment on platelet counts in women who do not have concomitant diseases. Iraqi J Hematol 2022;11:56-9.

thromboembolic events.[10] Iron replacement may change platelet counts. Parenteral iron treatment resulted in a decrease in platelet counts in diseases such as CKD, inflammatory bowel diseases, and acquired platelet function defects.[2,11,12] However, in patients who do not have chronic diseases, the effect of parenteral iron treatment on platelet counts was not elucidated. In addition, the information about the effect of parenteral iron replacement treatment on platelet counts, in patients who have iron deficiency without anemia, is not sufficient.

The aim of this presented study is to inspect the effect of parenteral iron treatment on platelet counts and other complete blood count parameters in patients who do not have chronic diseases other than iron deficiency.

Materials and Methods

This single-center, retrospective interventional study was conducted in internal medicine outpatient clinics of a tertiary university hospital located in the capital city of Turkey, between January 2020 and October 2021. This study, approved by the local Ethics Committee of the Institute, was conducted in concordance with the Declaration of Helsinki and good clinical practice directives. Informed written consents were obtained from all of the patients who participated in the study.

Inclusion criteria

Patients who applied to outpatient clinics with various complaints and whose serum ferritin levels were below 67.42 pmol/L were enrolled in the study. Since iron deficiency is more frequent in the female population, this study was conducted on the female population who do not have chronic diseases other than iron deficiency.

Exclusion criteria

Patients who have diseases other than iron deficiency, anemia due to other reasons than iron deficiency, who are allergic to iron treatment, who are pregnant, and patients under 18 were excluded from the study.

Study design

Demographic characteristics, neutrophil, lymphocyte, platelet, and eosinophil counts, mean platelet volume (MPV), C-reactive protein (CRP), hemoglobin, and ferritin levels of the participants were recorded before parenteral iron treatment. Patients who were treated with parenteral ferric carboxymaltose (Vifor Pharma Management Ltd. Glattbrugg, Switzerland) for iron deficiency were distributed into two Groups according to hemoglobin levels; patients who had iron deficiency anemia (hemoglobin levels below 125 g/L) constituted Group 1 and patients who had iron deficiency only (hemoglobin levels above 125 g/L) constituted Group 2. Patients whose hemoglobin levels were below and above 100 g/L, received 1500 mg and 1000 mg of parenteral ferric carboxymaltose, respectively. Parenteral intravenous ferric carboxymaltose infusions were delivered in 250 ml isotonic sodium chloride solution in 15 min. Obtained blood samples for complete blood count, ferritin, and CRP tests 3 months after parenteral ferric carboxymaltose treatment were recorded. Test results, before and after treatment were compared between groups.

Complete blood counts were analyzed with Sysmex XN-1000 analyzer (USA), ferritin levels were analyzed with Roche Hitachi Cobas 601 analyzer (Switzerland), and CRP levels were analyzed with Roche Hitachi Cobas 501 analyzer (Switzerland).

Statistical analysis

IBM SPSS 15 (SPSS Inc., Chicago, IL, USA) statistical analysis computer software program was used in data analysis. Normality of data distribution in continuous variables was tested with Kolmogorov–Smirnov test. Paired *t*-test was used to evaluate data obtained before and after treatment. Independent samples *t*-test was used to compare data between groups. Correlations among parameters were analyzed with Pearson correlation test. A P 0.05 was considered statistically significant.

Results

Hemoglobin and ferritin levels were increased and platelet counts and MPV were decreased after parenteral ferric carboxymaltose treatment. Compared to initiation of treatment, neutrophil, lymphocyte, eosinophil counts and CRP levels were similar in both the groups. Blood parameters of participants before and after treatment are shown in Table 1.

The mean age of participating 239 females was 35.59 ± 8.23 years. In both groups, hemoglobin levels were increased and platelet counts were decreased, but in the group with patients having anemia (Group 1), changes

Table 1: Blood parameters of all participants before and after treatment

	Before treatment	After treatment	*P**
Hemoglobin (g/L)	120.8±17.7	133.1±12.3	<0.001
Platelet counts (×10^9/L)	297.27±81.98	264.04±64.33	<0.001
MPV (fL)	10.32±0.94	10.23±0.91	0.015
Neutrophil counts (×10^9/L)	4.2±1.53	4.35±1.63	0.222
Lymphocyte counts (×10^9/L)	2.22±0.67	2.17±0.73	0.195
Eosinophil counts (×10^9/L)	0.14±0.11	0.14±0.12	0.466
CRP (nmol/L)	27.14±35.98	29.32±40.38	0.481
Ferritin (pmol/L)	40.63±47.03	359.66±284.43	<0.001

*Paired *t*-test. CRP=C-reactive protein, MPV=Mean platelet volume

in hemoglobin levels and platelet counts were more prominent after treatment. Demographic characteristics and changes in blood parameters of participants before and after treatment are shown in Table 2.

In the iron deficiency group (Group 2), blood parameters before and after treatment were compared. Interestingly, such as the group having anemia, hemoglobin, and ferritin levels were also increased after treatment in the iron deficiency group. Blood parameters of participants who do not have anemia before and after treatment are shown in Table 3.

When compared to initiation of treatment, there was a significant negative correlation after treatment, between changes in hemoglobin levels and platelet counts [Figure 1].

Discussion

According to the results of the present study, hemoglobin and ferritin levels were increased and platelet counts and MPV values were decreased after parenteral ferric carboxymaltose treatment. In both groups, platelet counts were decreased, but in the anemia group decrease in platelet counts was more prominent.

Table 2: Demographic characteristics and changes in blood parameters of participants before and after treatment

	Have anemia (*n*=127)	Do not have anemia (*n*=112)	*P**
Age (years)	37.17±7.53	33.79±8.65	0.001
Change in hemoglobin levels (g/L)	17.96±14.4	5.87±7.09	<0.001
Change in platelet counts (×10^9/L)	−43.87±54	−21.16±33.88	<0.001
Change in MPV (fL)	−0.13±0.62	−0.05±0.53	0.313
Change in neutrophil counts (×10^9/L)	0.13±1.77	0.12±1.48	0.969
Change in lymphocyte counts (×10^9/L)	−0.03±0.65	−0.06±0.53	0.749
Change in eosinophil counts (×10^9/L)	−0.01±0.1	0.01±0.09	0.869
Change in CRP levels (nmol/L)	4.49±43.2	1.14±36.28	0.485
Change in ferritin levels (pmol/L)	299.31±298.65	340.94±233.22	0.182

*Student's *t*-test. CRP=C-reactive protein, MPV=Mean platelet volume

Table 3: Blood parameters before and after iron treatment of participants who do not have anemia

	Before treatment	After treatment	*P**
Hemoglobin (g/L)	134.9±7.9	140.8±8.6	<0.001
Platelet counts (×10^9/L)	278.01±63.75	256.85±60	<0.001
MPV (fL)	10.29±0.92	10.23±0.83	0.291
Neutrophil counts (×10^9/L)	4.20±1.44	4.33±1.69	0.376
Lymphocyte counts (×10^9/L)	2.32±0.66	2.25±0.79	0.208
Eosinophil counts (×10^9/L)	0.14±0.09	0.13±0.11	0.457
CRP (nmol/L)	21.93±31.88	22.08±31.71	0.971
Ferritin (pmol/L)	55.03±55.96	395.97±239.91	<0.001

*Paired *t*-test. CRP=C-reactive protein, MPV=Mean platelet volume

The effect of parenteral iron treatment on platelet counts in various chronic diseases was researched previously. In patients with inflammatory bowel diseases, parenteral ferric carboxymaltose treatment resulted in significant decrease in platelet counts compared to the placebo group.[13] In CKD patients, platelet counts were decreased after parenteral ferric carboxymaltose treatment.[14] There are few studies inspecting the effect of parenteral iron treatment in patients who do not have chronic diseases. In a study, it was reported that oral iron replacement decreased platelet counts in blood donors who do not have concomitant diseases.[15] In all these aforementioned studies, anemia was present in the study populations. It is not clear that the decrease in platelet counts is whether due to parenteral iron treatment itself or due to the correction of anemia and suppression of hematopoiesis. The presented study reports a decrease in platelet counts after parenteral iron replacement treatment both in patients having iron deficiency alone and patients having anemia. Under the light of this finding, it was concluded that parenteral iron replacement treatment itself, resulted in decreased platelet counts.

Previously, it was reported that iron replacement affected megakaryocytes but had no effect on platelet lifespan.[12] A study revealed that megakaryocytes were larger and were producing more platelets in iron deficiency in rats.[16] The size of megakaryocytes was reported to be larger in patients with iron deficiency, and more platelets were produced from those megakaryocytes.[13] Iron has no effect on cytokines that affect thrombopoiesis, such as thrombopoietin, interleukin (IL)-3, IL-6, and IL-11; instead, iron directly affects megakaryocytes and decreases platelet counts.[13] With iron replacement treatment, platelet counts decrease but platelet counts do not drop below physiologic normal levels; thus, it was stated that iron had regulatory effect on platelets.[12]

In a study, it was shown that after parenteral iron treatment, there were no changes in inflammatory markers such as CRP, and it was reported that there was no association between decrease in platelet counts and inflammation.[12] The presented study has concordant results with these mentioned studies and there was no significant change in CRP level. Regarding this finding, it was thought that parenteral ferric carboxymaltose did not suppress inflammation, but directly affected megakaryocytes and decreased platelet counts.

With increased MPV values, platelets are reported to be more prone to aggregation and more thrombogenic.[17] In a study, pregnant women had a significant decrease in

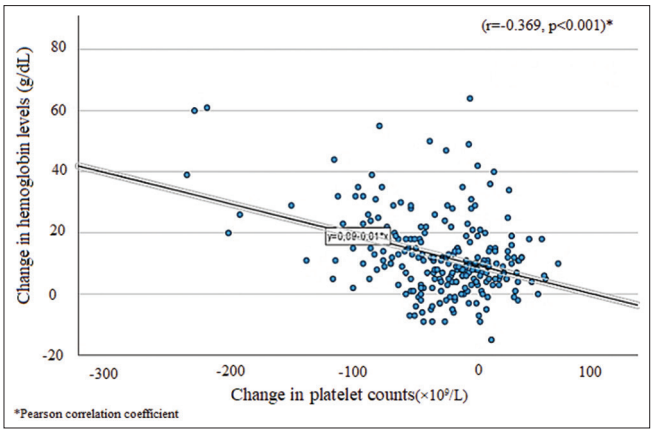

Figure 1: Correlation between changes in hemoglobin levels and changes in platelet counts

MPV values after oral iron treatment.[18] This presented study, consistently, reports a decrease in MPV values after parenteral iron treatment. This finding reminds the probability that parenteral iron treatment may decrease the risk for thrombogenic events.

There are some limitations to this study. This study is a single-center study. It did not include male patients and for this reason, the results of this study may not be generalized to the whole population. In addition, only blood parameters 3 months after parenteral iron treatment were evaluated, thus it cannot be projected whether the effects of parenteral iron treatment lasted for longer duration or not.

Conclusion

This study revealed that parenteral ferric carboxymaltose treatment resulted in decreases in platelet counts and MPV values. Platelet counts were decreased after treatment, whether the patient had anemia or not. Parenteral ferric carboxymaltose treatment resulted in a significant decrease in platelet counts in the anemia group when compared with the iron deficiency group. It was shown that there was negative correlation between changes in platelet counts and changes in hemoglobin levels. It was concluded that there is a need for studies evaluating the clinical impacts of this decrease in platelet counts after parenteral iron treatment in the development of thromboembolic disorders.

Acknowledgments

Authors would like to thank Mr. Fatih ACİKGOZ for statistical advice.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Higgins T, Eckfeldt JH, Barton JC, Doumas BT. Hemoglobin, iron and bilirubin. In: Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics. 7th ed. St Louis: Elsevier; 2014.
2. Scaramellini N, Capecchi M, Artoni A, La Marca S, Cappellini MD, Motta I. Ferric carboxymaltose for sub-acute and chronic iron deficiency anemia in inherited platelet function defects. Intern Emerg Med 2021;16:505-7.
3. Cançado RD, Brasil SA, Noronha TG, Chiattone CS. Evaluation of the efficacy of intravenous iron III-hydroxide saccharate for treating adult patients with iron deficiency anemia. Rev Assoc Med Bras (1992) 2005;51:323-8.
4. Bonovas S, Fiorino G, Allocca M, Lytras T, Tsantes A, Peyrin-Biroulet L, *et al.* Intravenous versus oral iron for the treatment of anemia in inflammatory bowel disease: A systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) 2016;95:e2308.
5. Ponikowski P, Kirwan BA, Anker SD, McDonagh T, Dorobantu M, Drozdz J, *et al.* Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: A multicentre, double-blind, randomised, controlled trial. Lancet 2020;396:1895-904.
6. O'Lone EL, Hodson EM, Nistor I, Bolignano D, Webster AC, Craig JC. Parenteral versus oral iron therapy for adults and children with chronic kidney disease. Cochrane Database Syst Rev 2019;2:CD007857.
7. Radhika AG, Sharma AK, Perumal V, Sinha A, Sriganesh V, Kulshreshtha V, *et al.* Parenteral versus oral iron for treatment of iron deficiency anaemia during pregnancy and post-partum: A systematic review. J Obstet Gynaecol India 2019;69:13-24.
8. Cognasse F, Laradi S, Berthelot P, Bourlet T, Marotte H, Mismetti P, *et al.* Platelet inflammatory response to stress. Front Immunol 2019;10:1478.
9. Schafer AI. Thrombocytosis and thrombocythemia. Blood Rev 2001;15:159-66.
10. Koupenova M, Clancy L, Corkrey HA, Freedman JE. Circulating platelets as mediators of immunity, inflammation, and thrombosis. Circ Res 2018;122:337-51.
11. Yessayan L, Yee J, Zasuwa G, Frinak S, Besarab A. Iron repletion is associated with reduction in platelet counts in non-dialysis chronic kidney disease patients independent of erythropoiesis-stimulating agent use: A retrospective cohort study. BMC Nephrol 2014;15:119.
12. Kulnigg-Dabsch S, Evstatiev R, Dejaco C, Gasche C. Effect of iron therapy on platelet counts in patients with inflammatory bowel disease-associated anemia. PLoS One 2012;7:e34520.
13. Kulnigg-Dabsch S, Schmid W, Howaldt S, Stein J, Mickisch O, Waldhör T, *et al.* Iron deficiency generates secondary thrombocytosis and platelet activation in IBD: The randomized, controlled thromboVIT trial. Inflamm Bowel Dis 2013;19:1609-16.
14. Hazara AM, Bhandari S. Intravenous iron administration is associated with reduced platelet counts in patients with chronic kidney disease. J Clin Pharm Ther 2015;40:20-3.
15. Eder AF, Yau YY, West K. The effect of iron balance on platelet counts in blood donors. Transfusion 2017;57:304-12.
16. Choi SI, Simone JV. Platelet production in experimental iron deficiency anemia. Blood 1973;42:219-28.
17. Handtke S, Thiele T. Large and small platelets-(When) do they differ? J Thromb Haemost 2020;18:1256-67.
18. Aly SS, Fayed HM, Ahmed SS, Abdella AH, Tamam AA, Mohammed NA. Effects of oral iron (ferrous versus ferric) supplementation on oxidative stress and antioxidant status in pregnant women with iron deficiency: Controlled trial. Egypt J Haematol 2016;41:31-41.