The Comparison of Platelet Counts between the before and after Treatments of Women with Iron Deficiency Anemia

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ABSTRACT

Objective: Iron deficiency is the most common etiological cause of anemia in premenopausal patients and characterized with hypochromic, microcytic erythrocytes. Iron deficiency anemia (IDA) has been reported to accompany the changes in both the count and the parameters of platelets (PLT). In our study, we evaluated possible PLT changes by complete blood count (CBC) and anemia tests conducted on women aged between 15 and 48 who were diagnosed with IDA before and after iron replacement treatment.

Methods: Ninety-six patients with the diagnosis of IDA were included in our study. Iron (Fe), total iron-binding capacity (TIBC), ferritin, hemoglobin (HGB), hematokrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell distribution volume (RDW) levels, and PLT counts of the patients before and after the treatment were compared. In this comparison, Wilcoxon test and for the relationship between the variables Pearson correlation analysis were used. A p value of <0.05 was considered to be statistically significant.

Results: Ferritin, Fe, HGB, HCT, MCV, and MCH levels after the treatment were found to be significantly increased (p=0.0001) and UIBC, TIBC, RDW, and PLT were significantly decreased (p=0.0001) when compared with those before the treatment. A negative correlation between PLT and HCT, MCV, and MCH (r=0.216, 0.236, 0.366; p=0.035, 0.021, 0.0001, respectively) and a positive correlation between PLT and RDW (r=0.35 and p=0.0001) was observed.

Conclusion: PLT counts of the patients after the treatment were found to be decreased. PLT counts that were increased but in the normal range could be because the hypochromic, microcytic erythrocytes were probably counted as PLT on automated blood count analyzers and/or because of increased erythropoietin (EPO) in IDA. *(JAREM 2015; 5: 94-6)*

Keywords: Anemia, iron deficiency, thrombocytosis

INTRODUCTION

Iron (Fe) deficiency anemia (IDA) is a common hematologic disorder and particularly affects children, young women, and the elderly. IDA, which is a major public health problem in developed and developing countries, is estimated to affect more than 30% of the world's population. Inadequate dietary intake, bleeding (menstrual cycle, injuries, and blood donors), pregnancy, childbirth, malabsorption, and parasite infestations can be considered to be the common causes of IDA among young women. IDA is characterized by low hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), Fe and transferrin saturation, low ferritin, and an increase in the total iron-binding capacity (TIBC) (1).

Platelets are small cell fragments derived from mature megakaryocytes. Their volumes are 7–11 femtoliters (fl) and their diameters are 1–3 µm. Approximately 100 billion platelets are produced daily in an adult. The primary role of platelets is to provide hemostasis by binding the von Willebrand factor and fibrinogen. In addition, they are the source of a number of pro-inflammatory and antimicrobial mediators. Neoplastic proliferative diseases or other secondary conditions, asplenia, malignancies, and blood loss/Fe deficiency can be considered to be among the reasons for an increased number of platelets (thrombocytosis) in circulation. A number of changes in platelet count (PLT) have been reported in IDA (2). It has been indicated in various studies that moderate IDA is seen to be accompanied by thrombocytosis (3, 4) and severe IDA (HGB <7 g/dL) by thrombocytopenia (5, 6).

MCV indicates the average volume of red cells and is used for the classification of anemia. The classes are named as follows: MCV<80 fl microcytosis (erythrocytes smaller than normal), 80–98 fl normocytosis (erythrocytes of normal size), and >98 fl macrocytosis (erythrocytes larger than normal). Erythrocyte sizes vary in IDA. If microcytic erythrocytes or erythrocyte particles are <36 fl, they cannot be detected as erythrocytes by complete blood count devices and counted as platelets (7).

In this study, we aimed to study possible changes in platelets by evaluating blood count parameters before and after the treatment of young women patients diagnosed with IDA.

METHODS

In an archive scan performed between 2011 and 2012 in the laboratory information system of Gaziosmanpaşa Taksim Training and Research Hospital, 96 women who were admitted to outpatient clinics and diagnosed with IDA were included. The mean age of the patients was 37 (15-48 years). Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of Gaziosmanpaşa Taksim Training and Research Hospital (04.03.2013 Resolution No. 16). In our laboratory, ABX Pentra DX 120 devices and compatible kits (Horiba Medical, USA) were used for blood counting. The values of HGB, HCT, MCV, mean corpuscular hemoglobin (MCH), red cell distribution width (RDW), PLT, Fe, TIBC, and ferritin were compared at the time of diagnosis and after treatment with oral Fe preparations. Tests for Fe and unsaturated Fe-binding capacity (UIBC) were performed photo-

This study was presented at the 13th National Clinical Biochemistry Congress of Turkish Clinical Biochemistry Association, 25-28 April 2013, İzmir, Turkey.

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Received Date: 16.03.2015 **Accepted Date:** 16.04.2015

DOI: 10.5152/jarem.2015.712

metrically using a Roche Hitachi Modular P800 device and Roche kits (Mannheim, Germany), respectively, by TPTZ and nitroso-PSAP methods and by an electrochemiluminescence method using a Roche Hitachi Modular E170 autoanalyzer and a Roche kit (Mannheim, Germany). TIBC was calculated by adding the results for Fe and UIBC.

Statistical Analysis

Statistical analyses were performed with the Number Cruncher Statistical System 2007 (Utah, USA). The Wilcoxon test was used for the comparison of values before and after treatment, and Pearson correlation analysis was used to determine the relationships of variables with each other. The results were assessed at a significance level of $p<0.05$.

RESULTS

In comparison with values before treatment, a statistically significant increase ($p=0.0001$) in the values of ferritin, Fe, HGB, HCT, MCV, and MCH was observed after treatment and a statistically significant decrease ($p=0.0001$) in the values of UIBC, TIBC, RDW, and PLT (Table 1). When the values of PLT of the patients were compared with the values of HCT, MCV, and MCH, a negative correlation was observed ($r=0.216$, 0.236, and 0.366, respectively). A positive correlation ($r=0.35$) was found between the values of PLT and RDW (Table 2).

DISCUSSION

In IDA, changes in PLT and PLT parameters were reported. Apart from hyposplenia/asplenia, the mechanisms underlying the causes of secondary thrombocytosis and the clinical significance of secondary thrombocytosis have not yet been sufficiently clarified. An increase in megakaryopoiesis leads to an increased release of megakaryocytic growth factors such as thrombopoietin, interleukin (IL)-3, IL-6, and IL-11. Further investigation of these factors is needed for the elucidation of the mechanisms of the causes of secondary thrombocytosis (2).

Kullnigg-Dabsch et al. (2) studied the effects of treatments with oral iron sulfate (n=56) and intravenous iron sucrose/ferric carboxymaltose (n=252) that they administered to 308 patients with inflammatory bowel disease (IBD), concomitant anemia (chronic disease and IDA), and thrombocytosis on PLT. The mean PLT value of patients decreased significantly after oral and intravenous Fe therapy. Although the values of HGB, ferritin, and transferrin saturation recovered, the amount of C-reactive protein and number of leukocytes did not change. They stated that the inflammatory parameters were low and did not change during treatment with Fe and therefore the thrombocytosis that accompanied IBD might be a result of IDA rather than systemic inflammation. In addition to iron sucrose therapy, by giving placebo or erythropoietin (EPO) randomly to Crohn's disease patients (n=40) whom they included in the study, they wanted to investigate whether or not EPO had an effect on the decrease in PLT. PLT values decreased in the EPO and placebo groups at the same rate and speed, and the average percentage weekly changes in PLT were 3.7% and 4%, respectively ($p=0.703$). The weekly changes (decreases) in EPO were 5.5% and 14%, respectively ($p=0.021$), which was statistically significant. Based on these data, they stated that EPO during Fe therapy did not have any effect on the changes in PLT.

Düzgün et al. (8) found that the PLT values of 102 pediatric patients who had normal levels of serum vitamin B_{12} and folate and were diagnosed with IDA were higher than those of a healthy control group ($p<0.05$). They observed significantly high levels of neutrophil hypersegmentation in peripheral smears of anemic children with normal levels of vitamin B_{12} and folate in comparison with a control group ($p<0.05$).

Kadikoylu et al. (9) evaluated PLT parameters such as PLT, mean platelet volume (MPV), and platelet distribution width in 86 women patients who were diagnosed with IDA. They observed that

Table 1. Comparison of means of parameters before and after treatment

	X±SD		
	Before treatment	After treatment	p value
Ferritin (ng/mL)	7.15±9.81	28.77±35.76	0.0001
Iron (µg/dL)	23.2±21.78	77.88±46.93	0.0001
UIBC (µg/dL)	392.2±63.44	296.17±88.65	0.0001
TIBC (µg/dL)	415.45±59.67	374.05±60.91	0.0001
HGB (g/dL)	10.15±1.51	12.62±1.56	0.0001
HCT (%)	30.52±3.62	41.26±34.35	0.0001
MCV (μm^3)	70.98±8.1	84.91±6.01	0.0001
MCH (pg)	23.61±3.28	28.02±2.51	0.0001
RDW (%)	16.57±2.38	14.94±2.78	0.0001
PLT ($x10^9$/L)	300.77±71.66	265.55±65.11	0.0001

X±SD: mean±standard deviation
A value of $p<0.05$ is considered to be significant.
UIBC: unsaturated iron-binding capacity; TIBC: total iron-binding capacity; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; RDW: red cell distribution width; PLT: platelet count

Table 2. Comparison of the relationships between platelet counts and IDA parameters

		HCT	MCV	MCH	RDW	PLT
HCT	r		0.065	0.03	0.004	−0.216
	p		0.534	0.771	0.97	0.035
MCV	r	0.065		**0.776**	**−0.526**	−0.236
	p	0.534		**0.0001**	**0.0001**	0.021
MCH	r	0.03	**0.776**		**−0.51**	**-0.366**
	p	0.771	**0.0001**		**0.0001**	**0.0001**
RDW	r	0.004	**−0.526**	**0.51**		**0.35**
	p	0.97	**0.0001**	**0.0001**		**0.0001**
PLT	r	−0.216	0.236	**−0.366**	**0.35**	
	p	0.035	0.021	0.0001	**0.0001**	

p <0.05 significant.
HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; RDW: red cell distribution width; PLT: platelet count; IDA: iron deficiency anemia

PLT increased when serum Fe, Fe saturation, ferritin, and MPV fell. They found an inverse correlation between PLT and both MPV and Fe saturation. They stated that there was thrombocytosis in 27.9% and thrombocytopenia in 2.3% of the patients whom they included in the study. This situation is consistent with the studies that reported the association between moderate IDA and thrombocytosis and between severe IDA and thrombocytopenia. In our study, the average HGB level in patients before treatment was 10.4 g/dL and they had moderate IDA; the PLT value was within normal limits but significantly higher than that after treatment.

In our study, the PLT value of female patients diagnosed with IDA was significantly higher before treatment than that after treatment. However, the PLT that increased within normal limits as a consequence of IDA can also be explained by the effect of EPO. Akan et al. (3) examined the levels of serum thrombopoietin, EPO, leukemia inhibitory factor, IL-6, and IL-11 in blood samples that they obtained before Fe treatment, in the first and third months of treatment, and at the end of treatment in 15 female patients with IDA and thrombocytosis (PLT>) (450 x 10^9/1) and 16 female patients whose IDA and PLT were normal. They found a positive correlation between EPO and PLT in both groups; even though they thought that an increase in the level of EPO could increase the PLT, they stated that the increase in the EPO level had no effect on the PLT in the patient group with IDA and normal PLT. They observed no changes in other thrombopoietic cytokines in either group.

CONCLUSION

Iron deficiency anemia is the cause of reactive thrombocytosis. Although increases in moderate PLT values usually accompany IDA, these values may rarely exceed 1 million. The underlying mechanisms have not yet been fully elucidated. In our study, PLT values that increased within normal limits after treatment compared with before treatment can be explained by the fact that erythrocytes that were hypochromic and microcytic before treatment were counted as platelets by the blood count device. MCV and MCH, which are the parameters related to the size and shape of erythrocytes, increased significantly after treatment and RDW decreased significantly (p=0.0001). These data also support the statement that microcytes that can be counted as platelets accidentally by the device decrease in the complete blood count after treatment or turn into mature erythrocytes.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziosmanpaşa Taksim Training and Research Hospital.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - N.N.A., Z.S.; Design - Z.S., N.B.; Supervision - N.N.A., N.O.S.; Resources - N.B., N.A., A.K.; Materials - N.N.A., Z.S., N.B.; Data Collection and/or Processing - N.N.A., N.B., N.A.; Analysis and/or Interpretation - N.A., A.K., Z.S.; Literature Search - Z.S., N.O.S., N.A.; Writing Manuscript - N.N.A., A.K., N.O.S.; Critical Review - N.O.S., N.B., A.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Higgins T, Eckfeldt JH, Barton JC, Doumas BT. Hemoglobin, Iron and Bilirubin. Burtis CA, Bruns DE, editors. Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics. Seventh ed. St Louis: Elsevier; 2014. p.509-13.
2. 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. [CrossRef]
3. Akan H, Güven N, Aydogdu I, Arat M, Beksaç M, Dalva K. Thrombopoietic cytokines in patients with iron deficiency anemia with or without thrombocytosis. Acta Haematol 2000; 103: 152-6. [CrossRef]
4. Hiçsönmez G, Suzer K, Suloglu G, Donmez S. Platelet counts in children with iron deficiency anemia. Acta Haematol 1978; 60: 85-9. [CrossRef]
5. Ibrahim R, Khan A, Raza S, Kafeel M, Dabas R, Haynes E, et al. Triad of iron deficiency anemia, severe thrombocytopenia and menorrhagia- A case report and literature review. Clin Med Insights Case Rep 2012; 5: 23-7.
6. Beguin Y. Erythropoietin and platelet production. Haematologica 1999; 84: 541-7.
7. Gedikoğlu G, Ridolfi F. Otomatik Kan Sayımı Parametreleri ve Sonuçlarının Yorumlanması. 1. Baskı İstanbul: İstanbul Medikal Yayıncılık; 2005.
8. Düzgün S, Yildirmak Y, Cetinkaya F. Neutrophil hypersegmentation and thrombocytosis in children with iron deficiency anemia. Turk J Pediatr 2005; 47: 251-4.
9. Kadikoylu G, Yavasoglu I, Bolaman Z, Senturk T. Platelet parameters in women with iron deficiency anemia. J Natl Med Assoc 2006; 98: 398-402.