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Original Article

Comparison of platelet count and mean platelet volume values before and after treatment in rheumatoid arthritis and ankylosing spondylitis patients receiving tumor necrosis factor alpha inhibitor therapy

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Abstract

Aim: In our study, we planned to reveal the change of the mean platelet volume (MPV) with anti-TNF treatment given in patients with Rheumatoid-Arthritis (RA) and Ankylosing-Spondylitis (AS) and to evaluate the clinical importance of MPV in the follow-up of these diseases.

Materials and Methods: Patients who applied to our hospital's between 2011 and 2013 were included in the study. 40 patients participated in the study. The average ages of the patients were 43.8±9.9 years (range:25-68 years). All patients were examined retrospectively, Hemoglobin (Hb), Hematocrit (Hct), Platelet count, Mean Red-Blood-Cell Volume (MCV), MPV, Erythrocyte-Sedimentation-Rate (ESR), C-Reactive Protein (CRP) before anti-TNF treatment were recorded. Then, the same values were checked six months after the treatment. Averages of the Hb, Hct, MCV, PLT, MPV, CRP, ESH parameters of patients before and after treatment were compared with each other.

Results: When the values before and after the treatment were compared, there was a significant decrease in ESR (p:0.002). There was also a statistically significant increase in Hb and Hct values after treatment (p:0.002, p:0.039, respectively). A significant decrease was observed in mean platelet count and MPV values after treatment (p:0.001). Although there was an increase in the MCV value, it was not statistically significant. Likewise, there was a decrease in CRP value but it was not statistically significant.

Conclusion: In this study, it was concluded that the MPV value and platelet count could be inexpensive biomarkers in the follow-up of RA and AS. However, more controlled prospective studies are needed in this regard.

Keywords: Mean Platelet Volume; anti-TNF; rheumatoid arthritis; ankylosing spondylitis

INTRODUCTION

Rheumatoid arthritis (RA) is an inflammatory rheumatological disease with an unknown etiology, showing systemic findings, and especially chronically affecting small joints symmetrically and progressing with deformities and showing extraarticular involvement. Extra-articular involvement occurs in 40% of patients. It is believed to be more common in active disease (1). Treatment of RA has changed significantly over the past decade. The start of treatment very early in the disease, the use of a combination of disease-modifying drugs (DMARD) and the emergence of tumor necrosis factor-alpha (TNF-α) inhibitors made it possible to control synovitis and improve quality of life in most patients with RA.

Ankylosing Spondylitis (AS), is the prototype of seronegative spondyloarthropathies. It is a systemic, chronic and inflammatory rheumatic disease that affects the spine and sacroiliac joints in particular, starting at a young age, with uncertain etiology (2). As with RA, the use of new biological agents in treatment has also reduced patients' complaints and improved quality of life in AS. Most biological agents have been developed against TNF-α. TNF-α is the main cytokine secreted by macrophages and causing a septic shock picture caused by gram negative bacteria (3). Infliximab (INF), adalimumab (ADA), etanercept (ETA) and golimumab are TNF-α blockers used in the treatment of AS and RA (4-9). Despite the improvement of symptoms and functional status in patients with RA and AS with the use of these

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agents, a complete treatment of these diseases is still not possible (10-12).

Chronic inflammatory diseases are often accompanied by hematological complications such as anemia, leukocytosis, lymphopenia, thrombocytosis. There are many potential causes of hematological complications detected in these patients. Inflammatory cytokines, especially interleukin-1 (IL-1), tumor necrosis factor (TNF) and interferons (α-INF, β-INF, γ-INF) play an important role in the development of hematological complications. TNF-α and IL-6, among these proinflammatory cytokines, have been shown to play a role in the pathogenesis of AS and RA (13,14). Although inflammatory events have been previously known to cause thrombocytosis, the relationship between inflammation and mean platelet volume (MPV) is unclear. Therefore, in our study, we aimed to investigate the change in platelet count and MPV with treatment, in patients diagnosed with RA and AS receiving anti-TNF-α treatment.

MATERIALS and METHODS

Study Design

Patients who were under follow-up and treatment with RA and AS in our hospital's Internal Diseases, Rheumatology and Physical Therapy and Rehabilitation outpatient clinic between 2011-2013 were included in this study. The files of the patients were analyzed retrospectively. Patients diagnosed with AS according to the modified New York diagnostic criteria and patients diagnosed as RA according to the ACR / EULAR criteria, aged between 18-65 years, undergoing anti-TNF treatment and volunteering for the study were included in the study (15,16). Patients with AS or RA who have not received anti-TNF treatment, those with liver kidney disease, those with acute coronary syndrome, those with myeloproliferative disease, those with systemic diseases such as sepsis, disseminated intravascular coagulation, pneumonia, those with lung disease such as chronic obstructive pulmonary disease, asthma, those with cerebrovascular diseases, any patients with malignancies, those who took medications such as oral anticoagulants, anti-aggregants, and oral contraceptives that could affect platelet count and function and the coagulation system, were excluded from the study.

Laboratory Tests Analysis

In all patients, hemogram examinations were taken from the antecubital vein into tubes containing K3EDTA, and the tests were performed with Cell-Dyn 3700 automated hematology analyzer. OTH reference range was taken as 7.4–10.4 fL. OTH was automatically calculated on the device. Hemoglobin (Hb), hematocrit (Hct), platelet count, MPV, Erythrocyte sedimentation rate (ESH), C-reactive Protein (CRP) values were recorded from the patient files. Then, the values were examined six months after the treatment and compared with the values evaluated before the treatment.

Ethics Statement

All participants provided written consent for participation in the study. Approval for conducting this study was obtained from the Local Ethical Committee. All procedures were in accordance with the ethical standards of the committee on human experimentation of our institution and with the Declaration of Helsinki.

Data Analysis

The results of our study were analyzed with the program "The Statistical Package for the Social Sciences 24.0 (SPSS Armonk, NY: IBM Corp.)". Data that received continuous values were given as mean (± standard deviation), and categorical data were given as frequency and percentage (n,%). Student t-test was used as a parametric test and Mann Whitney U test was used as a non-parametric test to compare the averages before and after treatment. A p value <0.05 was considered statistically significant.

RESULTS

A total of 40 patients, 14 (35%) females, 26 (65%) males, were included in the study, 7 (17.5%) of the patients were diagnosed with RA and 33 (82.5%) were diagnosed with AS. The average age was calculated as 43.3 ± 9.9 years. When the relationship between treatment and the change of inflammatory parameters was examined, a statistically significant decrease in ESR values was observed after treatment compared to pre-treatment values. Although there was a decrease in CRP values after treatment, the difference was not statistically significant (Table 1).

In the analysis performed for the change of laboratory values after anti-TNF treatment, there were statistically significant changes in Hb, Hct, Plt and MPV measurements after anti-TNF treatment. There was a significant increase in Hb and Hct values after treatment (p <0.05). In addition, it was observed that there was a significant decrease in Plt and MPV values after treatment (p <0.05). However, after the treatment, there was an increase in MCV values of the patients but it was not statistically significant (p>0.05) (Table 2).

Table 1. Comparison of inflammatory parameters before and after treatment

	BEFORE TREATMENT	AFTER TREATMENT	p
CRP(mg/dL)	3.18±5.9	1.4±2.04	0.071
ESR (mm/hr)	26.3±21.51	14.45±14.62	0.002*

*p<0.05 **p<0.01

Table 2. Comparison of biochemical parameters before and after treatment			
	BEFORE TREATMENT	AFTER TREATMENT	*p*
HB (g/dL)	13.44±1.6	14.03±1.4	0.002*
HCT (%)	40.7±4.4	41.8±3.9	0.039*
MCV (fL)	83.7±5.94	85.28±5.7	0.079
PLT (10^3/ mm^3)	295000±72943	253000±73264	0.001**
OTH(fl)	8.95±1.5	8.2±1.1	0.001**
*p<0.05 **p<0.01			

DISCUSSION

Ankylosing Spondylitis is a systemic, chronic and inflammatory rheumatic disease that affects the spine and sacroiliac joints, can show extraarticular clinical findings, and its etiology is uncertain. It is the prototype of seronegative spondyloarthropathies (17). Rheumatoid arthritis, on the other hand, is a systemic, chronic and inflammatory rheumatic disease in the seropositive arthritis group that involves mostly small joints, and its etiology, similar to AS, is not definitively determined(18).

In studies conducted, increased mean platelet volume has been accepted as an independent risk factor in coronary artery diseases and cerebrovascular diseases (19). Although MPV and platelet counts are thought to be under independent hormonal control, the mechanisms controlling platelet production are difficult to understand and uncertain. It is accepted that the platelet volume and count is determined in thrombopoiesis, and as with ischemic heart disease, these findings suggest that primary changes are at the bone marrow (megakaryocyte) level. Also, an increase in megakaryocyte size and DNA content coincides with an increase in MPV. This direct relationship suggests the possibility that megakaryocyte activation may result in an increase in MPV as a proinflammatory feature (19,20). In recent studies, cytokines such as interleukin-3 or interleukin-6 have been reported to affect megakaryocyte DNA content and lead to the production of more reactive, larger platelets (21-23).

There are few studies evaluating MPV in AS and RA. Kısacık et al found significantly lower MPVs of patients with RA and AS compared to other groups in their study comparing basal MPVs of patients with RA and AS with osteoarthrosis and healthy group (24). They also found that patients with active RA and AS had an increase in their MPV values with treatment (24). However, in the study of Yazıcı et al. in 68 AS patients, they reported that MPV values were higher than healthy controls and that MPV decreased with 6 months of treatment (anti-TNF or conventional treatment) (25). The results of our study were similar to those of Yazıcı et al. when the values before and after the treatment were compared, a significant decrease in ESR was detected with treatment. There was also a statistically significant increase in Hb and Hct values after treatment. A significant decrease was observed in the mean platelet count and MPV values after treatment.

With this study, it can be concluded that MPV may be an inexpensive and simple marker that can be clinically useful in disease activation, but it does not indicate activation of the disease for certain. Reasons for the contradictory results in studies can be considered as the retrospective design of some studies, low number of cases, short time to evaluate treatment results, and the use of different materials such as citrated tube or EDTA tube to look at MPV. In addition, it can be said that the age, sex, co-morbidity and treatment of the patients are important factors.

Our study has some limitations and strengths. The design of our study being retrospective and the small number of cases are obvious limitations. The strength of our study is investigating the effectiveness of Anti-TNF treatment excluding all factors affecting MPV, platelet count and inflammatory markers.

CONCLUSION

In conclusion, we showed that MPV and platelet counts decreased significantly after treatment in patients with Ankylosing Spondylitis and Rheumatoid Arthritis. They can be considered as an easy, inexpensive and usable biomarker in the follow-up of chronic inflammatory diseases. However, we think that it will not make much sense to use them alone because of the lack of complete laboratory standardization and multiple factors affecting them. In order to clarify this issue, prospective, multi center studies with a broader participation are needed.

Conflict of interest : The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The approval of Human Ethics Committee of Haydarpasa Numune Education and Reserach Hospital (Decision number: 2012-79) was obtained.

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