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Original Investigation

New platelet indices as inflammatory parameters for patients with rheumatoid arthritis

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Abstract

Objective: To test new platelet indices for patients with rheumatoid arthritis (RA) as new acute phase reactants.

Material and Methods: In total, 120 patients with RA and 40 patients in the control group were analyzed. A DAS 28 score over 2.6 was accepted as active disease, and a DAS 28 score lower than 2.6 was accepted as under remission. Platelet distribution width, plateletcrit, and mean platelet volume were analyzed for three groups: patients with active RA, patients under remission, and the control group.

Results: There were 72 patients with active disease and 48 patients under remission. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), mean platelet volume (MPV), plateletcrit (PTC), and platelet distribution width (PDW) scores were all statistically different among groups. In our data, PTC was found to be a positive acute phase reactant and others were negative acute phase reactants for patients with RA.

Conclusion: These new indices are cheap, widely available, and useful parameters for routine clinical rheumatology practice.

Key words: Mean platelet volume, plateletcrit, platelet distribution width

Introduction

For patients with rheumatoid arthritis (RA), there are some biochemical parameters showing the intensity of inflammation. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) concentration are the most frequently used parameters (1, 2).

Recent studies revealed the association between platelet indices [plateletcrit (PCT), platelet distribution width (PDW), and mean platelet volume (MPV)] with inflammation (3). White blood cell count, age, and sex are other factors affecting platelet indices other than inflammation (3). These indices are known to be associated with mortality and acute phase reactants for infectious diseases (4, 5).

Santimone I. et al. found out the relation between inflammation and platelet indices in 2011, and afterwards, the relation between these parameters and inflammatory diseases, such as pulmonary tuberculosis and inflammatory bowel disease, were searched (3, 6-8). Milovanocic et al. (8) have shown the relation between platelet volume and disease activity in rheumatoid arthritis but not PTC and PDW (9). Furthermore, Kisacik et al. (7) have also reported MPV as an inflammatory marker for ankylosing spondylitis. To the current knowledge, plateletcrit increases during active inflammation, while MPV and PDW decrease (3). This also means that with inflammation, the number of platelets increases, but they become more monotypic and also smaller. These are cheap and widely available tests; therefore, clinicians may wonder about their role in inflammatory arthritis and especially for patients with rheumatoid arthritis. As clinicians, we have to order CBC for white blood cell count, hemoglobin level, and also for platelet count. These three new platelet indices are automatically reported during this routine test and have no extra costs.

Herein, we retrospectively analyzed the association between these new platelet indices and the intensity of inflammation for patients with RA and also tried to find out the normal ranges for these parameters for clinical use.

Material and Methods

One hundred twenty patients with RA and 40 healthy patients were enrolled in this retrospective study, and informed consent was taken from all. We evaluated all patients with RA in our clinic but had to exclude some for the following reasons.

In total, 21 patients with active infection or with other diseases that may affect the platelet indices or patients taking medication affecting platelet values (statins, anticoagulants, etc.) were excluded. Patients with

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Table 1. Median ESR and CRP scores according to disease activity and gender

			Sex	
DAS 28	ESR	CRP	Male	Female
Group-1 >2.6	46 (6-89)	18.65 (1-250)	28	44
Group-2 < 2.6	17.5 (1-44)	4.63(1-19)	11	37
Control group	19 (3-47)	3.42 (1-8,7)	12	28
Total	28 (1-89)	6.7 (1-250)	51	109
p	<0.05	<0.05	0.176	

ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; DAS: disease activity score

Table 2. Mean platelet indices among groups

DAS 28	PCT	PDW	MPV
Group 1 mean	0.2712	16.5557	8.2386
St. Dev	0.07641	0.67236	0.93488
Group 2 mean	0.2181	16.8880	8.7240
St. Dev	0.04636	0.66075	1.20755
Control group	0.2123	16.5950	9.1950
	0.02651	0.42181	1.12522
p	<0.05	<0.05	<0.05

PCT: plateletcrit; PDW: platelet distribution width; MPV; mean platelet volume

Table 3. The intervals of platelet indices among the groups (95% confidence interval)

Parameters	PCT	PDW	MPV
Group 1	0.25-0.29	16.39-16.71	8.01-8.46
Group 2	0.20-0.23	16.70-17.08	8.38-9.07
Total	0.23-0.25	16.57-16.77	8.47-8.81

PCT: plateletcrit; PDW: platelet distribution width; MPV: mean platelet volume

no known disease were included as a control group if they had no factor affecting the platelet indices and other acute phase reactants.

These 40 healthy patients, who were not on any medication and had no known diseases, were chosen from the check-up clinic. The clinical activity of the disease was tested by physical examination, CRP, and ESR levels, and DAS28 was calculated. All complete blood count (CBC) analyses were performed in the hematology laboratory in our hospital. Two milliliters of blood in standardized tubes containing 0.04 ml of 7.5% K3 salt of ethylene-diamine-tetra-acetic acid (EDTA) was used for analysis. Our CBC analysis was performed with the same analyzer with the use of a Cell-Dyn 3700 SL analyzer (Abbott Diagnostics, Chicago, IL, USA). Hematological parameters, which consisted of MPV range 7.4-10.4 fL, PDW range 15.6-18.2 fL, and PCT range 0.155%-0.320%, were analyzed by standard methods. Also, blood samples for ESR into tubes with 3.2% sodium citrate and CRP into 10-mL serum tubes were analyzed. These parameters were determined with automatic devices, and the ESR range was accepted as 0-20 mm/hour, and CRP was accepted as 0-8 mg/dL. Patients with DAS28 scores under 2.6 were accepted to be under remission, and others were accepted to have active diseases. All data were analyzed retrospectively, and CRP and ESR levels were taken from the electronic database of the hospital. Similarly, the platelet indices were also taken from the same database. The 22-parameter CBC has been used routinely for years in our hospital, and therefore, we could easily reach these data.

This retrospective study was approved by the Bülent Ecevit University ethics committee.

Statistical analysis

The SPSS (Statistical Package for Social Sciences Inc., Chicago, IL, USA) for Windows 18.0 program was used for the statistical analysis. All data were recorded in an SPSS database and were verified by a second independent researcher. The variables were analyzed with visual (histograms, probability plots) and analytical methods to determine whether or not they were normally distributed. Data are presented as mean±SD for normally distributed variables (age, PCT, PDW, MPV) and as median±IQR for skewed distributed continuous variables (ESR, CRP). Categorical variables are shown as frequencies. ANOVA test was used for normally distributed variables, and Kruskal-Wallis test was used for ESR and CRP variables to compare active and remission phases in patients with RA.

Results

In total, 120 patients (39 males and 81 females) were enrolled in this study. The mean age for female patients at the time of analysis was 53.6 (+/- 13.36) years and 55.8 (+/- 13.22) for male patients. The patients were grouped as Group 1 with active disease and Group 2 under remission. There were 48 (40%) patients in Group 2 and 72 (60%) patients in Group 1. There was no relation between disease activity and sex ($p>0.05$) (Table 1). Also, there were no statistical differences between the ages among Groups 1 and 2 and the control group (54.8, 53.8, and 54.0). The median values of ESR and CRP among patients in each group are shown in Table 1. The new platelet indices were also analyzed among the groups, and as can be seen in Table 2, there were statistically significant differences between the two groups for all three parameters. The plateletcrit values seemed to be higher during active disease, but both MPV and PDW were lower during active inflammation. Although the differences were not so big, their statistical evaluation revealed significant results ($p<0.05$).

On the other hand, the 95% confidence interval for each parameter was calculated for Groups 1 and 2 for clinical practice (Table 3). In our data, the normal ranges for PTC were 0.20-0.23, 16.70-17.08 for PDW, and 8.38-9.07 for MPV. These ranges need further evaluation before clinical use and may differ from population to population.

In our data, PTC was found to be a positive acute phase reactant and MPV and PDW were negative acute phase reactants in patients with active RA.

Discussion

Herein, we presented 120 patients with rheumatoid arthritis and tried to analyze the relation between disease activity and the new platelet indices.

To our knowledge, the new platelet indices have been searched as inflammatory markers in rheumatoid arthritis before (6-8). All of these manuscripts report that mean platelet volume is a useful inflammatory marker for patients

with rheumatoid arthritis. On the other hand, platelet distribution width and plateletcrit as acute phase reactants in patients with RA were not studied. As these new platelet indices are now widely available and are also cheap, clinicians should wonder about their importance.

In our retrospective trial, we analyzed 120 patients with RA and compared their results with 40 healthy patients. As was expected, these new indices were valuable parameters for active disease.

These new parameters were analyzed to estimate the coronary artery risk for patients with different diseases and also for the inflammatory response for various infections (9-12). As we know that inflammation is the fundamental of RA, these indices should be routinely used in clinical practice. On the other hand, in clinical practice, there are no adequate data or normal ranges for clinicians to support their routine usage. Therefore, we analyzed the intervals of these data for patients with RA.

One of the main problems in routine clinical practice is to set objective criteria for clinicians to decide a better treatment strategy. Acute phase reactants, physical examination, and radiologic evaluations are all included during this period, and these new platelet indices may help clinicians in making better decisions (13, 14).

On the other hand, the relation between these indices and radiologic progression is another point that should be studied. Clinicians still argue about the adequacy of the present criteria defining remission. Some authors insist on adding new clinical and laboratory parameters, such as imaging, fatigue, and the impact of the involvement of joints other than the 28 counted in the ACR/EULAR criteria. These new indices may also have a role in this strategy.

Another important point for laboratory parameters is their cost. In our country, a CBC test costs only 1 euro, while CRP costs 1.5 euros. A 22-parameter CBC yields the white blood cell count, hemoglobin level, thrombocyte count, PTC, MPV, and also PDW, meaning that 6 important parameters only cost 1 euro, but CRP on its own costs 1.5 euros. The cost of ESR is 0.6 euros. These costs may change from country to country, but the cost-effectiveness of these new parameters is valid worldwide.

These new platelets are cheap, widely available, and useful acute phase reactants for patients with RA. As it is the first study for this purpose, new trials should be done to support these results.

Ethics Committee Approval: Ethicsc ommitte eapproval was received for this study from the ethics committee of Bülent Ecevit University.

Informed Consent: Informed consent was obtained from patient who participated in this study.

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