Abstract. – BACKGROUND AND OBJECTIVES: The relationship of the mean platelet volume (MPV) and C-reactive protein (CRP) values with mortality in patients with ischemic stroke is not clear. Besides, the correlation between CRP and MPV in patients with ischemic stroke has not been adequately studied yet. In the present study, our aim is to investigate the interrelationship of the CRP and MPV parameters together with their influence on mortality in patients with acute ischemic stroke.

PATIENTS AND METHODS: Sixty-three patients with acute ischemic stroke have been enrolled in the study. The stroke patients were divided into 2 groups as those who died within the first 10 days and those who survived. The MPV and CRP in both groups have been compared. Also, the MPV obtained from the ischemic stroke patients were compared with the MPV of the healthy volunteers.

RESULTS: A statistically significant difference ($p = 0.027$) was observed between the MPV of the stroke patients (8.6±1.95 fl) and the control group (7.93±0.82 fl). The MPV (9.24±1.98 fl) and CRP (10.8±7.0 mg/l) of those ischemic stroke patients who died were statistically significantly higher ($p < 0.05$) than the MPV (8.09±1.75 fl) and CRP (3.2±3.5 mg/l) of the patients who survived. There was also a positive correlation between the MPV and CRP of the ischemic stroke patients ($r = 0.31, p = 0.029$).

CONCLUSIONS: The fact that there is a relationship between the MPV and CRP in ischemic stroke patients and that the CRP and MPV are higher in the ischemic stroke patients who died in comparison to those who survived may be an indication of the roles these markers play in the mortality of stroke patients.

Key Words: Stroke, Mean platelet volume, C-reactive protein, Mortality.

Introduction

The mean platelet volume (MPV), a parameter of platelet function, is an important marker of platelet-related activities like platelet aggregation, thromboxane A2 generation, and platelet factor 4 and thromboglobulin secretion. High MPV-levels have been defined as a risk factor for myocardial infarction in patients with coronary heart disease. Also in patients with risk factors for stroke, like diabetes mellitus or hypercholesterolemia, the MPV values were found to be higher than the control groups. Although a relationship between the MPV values and the severity and prognosis of the ischemic stroke has been observed in some reports, other studies did not reveal such an interrelation. In atherosclerotic vascular disease, the C-reactive protein (CRP) levels in the systemic circulation are increased due to the underlying chronic inflammation. Although this increase in CRP has been pointed out as an important prognostic marker in stroke, it has also been claimed that CRP does not shed a light on the prognosis in cerebrovascular disease. Therefore, the relationship between inflammation and thrombosis still continues to be complicated: While the inflammation contributes to thrombogenesis, the thrombosis in return increases inflammation. It has already been specified that the CRP has prothrombotic properties and increases platelet activity. On the other hand, the CRP and platelet activation were suggested as two strong risk factors influencing the severity and incidence of cardiovascular disease. However, the relationship between CRP and MPV, of which the latter is a marker of platelet activation, has not been adequately studied in patients with ischemic stroke.

In the present study, our aim is to investigate the interrelationship of the CRP and MPV parameters together with their influence on mortality in patients with acute ischemic stroke.

Patients and Methods

For the purposes of this study, the clinical data, complete blood count (CBC) test results, CRP values and erythrocyte sedimentation rates (ESR) of 72 patients admitted with the diagnosis of acute ischemic stroke to the Dicle University School of Medicine, Neurology Department between January 2010 and November 2011 have been studied in a retrospective
manner following the obtainment of the approval of the local Ethics Committee. The age and sex data of the patients together with any history involving hypertension, diabetes mellitus, previous strokes as well as their cigarette and alcohol consumption have been recorded. The aetiological factors have been classified as atherothrombotic, cardioembolic, lacunar and cryptogenic according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. Forty-six healthy individuals in matching age and sex groups and with no history of strokes or any present haematological or infectious conditions have also been enrolled as the control group. The enrolled patients were chosen from among those who were not on any thrombolytic treatments or did not receive any anticoagulant therapy before the event. The patients who presented with high fever or in which infection developed within the first five days following the stroke, those with renal or hepatic insufficiency and the patients who had undergone a surgical procedure or had myocardial infarction within the last 3 weeks were excluded. The remaining sixty-three patients with ischemic stroke were divided into two groups as those who died in the first 10 days and those who survived. The venous count blood cells (CBC), CRP and erythrocyte sedimentation rate (ESR) values of these patients obtained from the blood collected in EDTA tubes within the first 24 hours as of their post-stroke hospital admission were recorded. The CRP, MPV and ESR values as well as the leukocyte and platelet counts were compared between the groups. Also, the MPV values of the ischemic stroke patients were compared to the values of the control group.

Statistical Analysis

The results have been calculated as mean ± standard deviation (SD). The statistical analysis was carried out using the SPSS 11.5 software (SPSS Inc., Chicago, IL, USA). The comparison of the MPV values of the ischemic stroke patients and the control group was made through the Student’s t-test. The MPV and CRP levels of the ischemic patients who died or survived were also compared using the Student’s t-test. The relationship between the MPV and CRP values were further evaluated by means of the Pearson’s correlation analysis. An inter-group difference of \( p < 0.05 \) is statistically significant.

Results

The group of stroke patients consisted of 32 females and 31 males, while the healthy controls comprised 24 females and 22 males \((p > 0.05)\). The mean ages of the stroke patients \((64.0±15.3)\) and the controls \((60.4±7.9)\) were similar \((p > 0.05)\). A statistically significant difference \((p = 0.027)\) was observed between the MPV values of the stroke patients \((8.6±1.95 \text{ fl})\) and the MPV values of the control group \((7.93±0.82 \text{ fl})\). The comparison of the MPV values, platelet count, CRP levels, ESR and leukocyte counts is presented in Table I. The MPV \((9.24±1.98 \text{ fl})\) and CRP \((10.8±7.0 \text{ mg/l})\) values of the ischemic stroke patients who died were statistically significantly higher \((p < 0.05)\) than the MPV \((8.09±1.75 \text{ fl})\) and CRP \((3.2±3.5 \text{ mg/l})\) values of those who survived. There was a positive correlation between the MPV and CRP values of the ischemic stroke patients \((r = 0.31, p = 0.029)\). No statistically significant difference \((p > 0.05)\) was detected between the MPV values of the subgroups of ischemic stroke patients evaluated according to the TOAST classification. The platelet counts of the ischemic stroke patients who died \((246.3±73.6 \times 10^3/\text{mL})\) were statistically significantly lower \((p = 0.026)\) than the platelet counts of those who survived \((342.8±162.3 \times 10^3/\text{mL})\). There was no statistically significant difference \((p > 0.05)\) between the leukocyte and ESR values of those ischemic stroke patients who died and those who survived.

Discussion

The mean platelet volume is related to platelet activation and it has been suggested as a marker of haemostasis\(^1\). Larger platelets are more densely granulated and they are metabolically more active than smaller ones. Increases in MPV levels lead to increased secretions of the prothrombotic agents thromboxane A\(_2\), serotonin, \(\beta\)-thromboglobulin, the procoagulant surface protein P-selectin and glycoprotein-IIIa\(^,16,17\). It has already been demonstrated that larger platelets constitute a risk factor for myocardial infarction and death\(^18\). The relationship between MPV and the outcome of ischemic stroke is controversial in the literature. Guldiken et al\(^8\) compared the MPV levels and platelet counts of 102 acute ischemic stroke patients with a group of healthy controls and did not detect any statistically significant difference. Ntaios et al\(^7\) have also claimed that no relationship exists between the MPV values in the early phase of acute ischemic stroke, and the severity and prognosis of the stroke. In our study, we have found higher MPV values in the acute ischemic stroke patients in comparison to the control group. Besides, the MPV levels of the patients who died in the first 10 days were statistically significantly higher than the patients.
who survived. However, we did not observe any significant difference in the MPV levels between the subgroups classified according to the TOAST criteria. The increases in the MPV levels were also found to correlate with the severity of the ischemic stroke in other investigations conducted in parallel to our\textsuperscript{5,6}. These variances between the studies may stem from the differences in the number of the patient groups and the different criteria used in the classification of the subgroups. The MPV levels and the platelet count are inversely correlated: as the MPV increases, the platelet count decreases and, thus, the total platelet volume stays more or less constant\textsuperscript{19}. In our study, we have observed that the platelet count in the patients who died was statistically significantly lower than the patients who survived. In their report conducted on 384 acute ischemic stroke patients, Mayda et al\textsuperscript{6} suggested that higher MPV levels are a predictor of the prognosis independently from other risk factors; and that MPV, as a marker of increased platelet reactivity, becomes apparent before the ischemic stroke and contributes to the development of the disease. Since in our work the MPV values we obtained indicate the levels during the first 24 hours following the patients’ admittance to the hospital and since the platelets have a lifespan of 8 to 10 days, these findings may point to a disorder in platelet function present before the occurrence of the stroke. Also, as the size of the platelets is determined during the progenitor cell phase and as they later enter the circulation with this size unchanged, increased MPV levels and prothrombotic conditions before the ischemic stroke may reflect a proinflammatory environment\textsuperscript{5}. The increase detected in MPV in the ischemic stroke patients compared to the controls, and the higher MPV levels in the patients who died compared to those who survived in our study might indicate the role MPV plays in the pathogenesis and mortality in stroke.

Research is continuing on the role of the inflammatory elements accompanying the ischemia and the tissue damage caused by the inflammation in ischemic stroke. It is thought that the CRP activates the classical complement pathway and, thus, increases tissue damage through the end products of the complement system\textsuperscript{20}. Following a stroke, the plasma CRP levels may increase rapidly and may stay stable up to 28 days\textsuperscript{21}. Higher CRP levels have been demonstrated in stroke patients in several researches\textsuperscript{11,22}. Purfoy et al\textsuperscript{23} suggested that the higher CRP levels observed in patients who experienced transient ischemic attacks may be used as markers in order to predict the more severe ischemic events that may occur in the future. Several Authors\textsuperscript{24,25} have even suggested that CRP plays a direct role in the pathogenesis of atherosclerosis. Folsam et al\textsuperscript{26} claimed after a study they conducted on a large group of patients that higher levels of CRP are a strong predictor of thrombotic events rather than the severity of atherosclerosis. There is also a report\textsuperscript{14} stating that administering CRP to a person increases coagulation and fibrinolysis in the blood. It has been claimed\textsuperscript{27} that the CRP may cause thrombus formation by triggering platelet adhesion to the surface of the endothelial cells over the P-selectin stored in platelets. Also in our study, the CRP levels during the first 24 hours were statistically significantly higher in the patients who died compared to those who survived. However, we have not detected any significant difference between the leukocyte and ESR values.

Conclusions

These results support the view that the increase in CRP does not depend on an infectious origin and that CRP is a strong predictor of thrombotic events. A research conducted measuring the monocyte-platelet aggregates, which are a marker of platelet activation, demonstrated the relationship between CRP and platelet activation. Thus, the connection between thrombosis and inflammation has been suggested to be mediated through the high CRP levels\textsuperscript{15}. The connection we observed between the
MPV and CRP levels in the stroke patients supports the view that CRP increases platelet activation.

The fact that in our paper both the CRP and the MPV levels were found higher in the patients who died, compared to the patients who survived points out that these predictors may light the way in the follow-up and prognosis of stroke patients. Also, the correlation observed between MPV and CRP may indicate that the increase in CRP and MPV levels plays a role in the mortality of stroke patients. However, since our study was conducted on a limited number of patients, there is a need for further investigations on larger groups of patients in order to support these results.

Conflict of Interest

None to declared.

References