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Mean platelet volume in retinal vein occlusion

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Abstract. – OBJECTIVE: The exact pathogenic mechanism underlying the thrombotic tendency in retinal vein occlusion (RVO) is still not fully established. We investigated relationship between platelet indices including mean platelet volume (MPV) and platelet count in RVO patients compared to control group.

PATIENTS AND METHODS: Forty six patients (19 female, 27 male) diagnosed as RVO were included in the study. Forty-six subjects (26 female, 20 male) served as controls. Patients were evaluated by careful biomicroscopic examination using a fundus contact lens and fluorescein angiography. Blood samples for total blood count with MPV were obtained after overnight fasting from the antecubital vein.

RESULTS: The mean platelet volume was 8.11 ± 1.15 fl in RVO group. It was 8.68 ± 0.98 fl in controls. When compared, the mean MPV was significantly lower in RVO patients ($p < 0.05$). The mean platelet volume was also significantly lower in branch retinal vein occlusion group in comparison to controls (7.92 ± 1.19 fl. versus 8.68 ± 0.98 fl.) ($p < 0.05$).

CONCLUSIONS: MPV was significantly lower in patients with RVO than control group. MPV does not seem to be a potentially useful biomarker for prediction of RVO.

Key Words:
Mean platelet volume, Retinal vein occlusion.

Introduction

Retinal vein occlusion (RVO) is the second most common retinal vascular disorder and is a significant cause of visual loss. Depending on the area of retinal venous drainage effectively occluded it is mainly classified as either central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO). Presentation of RVO in general is with variable painless visual loss with any combination of fundal findings consisting of retinal vascular tortuosity, retinal hemorrhages, cotton wool spots, optic disc swelling and macular edema[1,2].

The pathophysiological mechanism of RVO is not fully established. The pathogenesis of RVO seems to be multifactorial and may be due to a combination of Virchow's triad: compression of the vein at the arteriovenous crossing, degenerative changes of the vessel wall and abnormal hematological factors. Thrombosis and thrombolysis are involved in every RVO; therefore, an understanding of these biochemical pathways is also important. Paradoxically, predisposition to thrombosis, thrombophilia, has the least impact of the three components of Virchow's triad from a public health perspective (abnormalities of the vessel wall have the most). Nevertheless, thrombophilia plays a role in a few RVOs and familiarity with genetic and acquired maladies of coagulation and fibrinolysis has a role in clinical care of some patients[3-6].

Platelet volume is a marker of platelet function and activation. It is readily measured as mean platelet volume (MPV) by clinical haematology analysers using sodium citrate as the anticoagulant. MPV is increased in certain vascular risk factor states, including hypertension, hypercholesterolaemia and diabetes mellitus[7,8]. Leoncini et al[9] reported increased platelet response to thrombin in RVO patients. They suggested that platelet hyperaggregability inducing thrombus formation might be an important factor in the onset and/or development of RVO. Studies performed by Watson et al[10] Priluck[11] and Houtsmuller et al[12] supported these findings. Increased MPV values with lower platelet counts in hypertensive BRVO patients has been shown in a recent study by Onder et al[13].

MPV is a simple and cost-effective tool that should be used and explored extensively, for predicting the possibility of impending acute events like retinal vein occlusion. This study was aimed to investigate relationship between platelet indices including mean platelet volume and platelet count in CRVO and BRVO patients compared to control group.

Patients and Methods

This study was conducted at the Outpatient Clinic of Department of Ophthalmology of Kırıkkale University Hospital. The research was

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reviewed and approved by Institutional Review Board and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from each subject after an explanation of the study protocol.

Forty-six patients were included in this study. Central retinal vein occlusion was diagnosed on the basis of the presence of retinal hemorrhages combined with retinal vein dilatation in four retinal quadrants. Patients with venous dilation and tortuosity with flame-shaped and dot-blot hemorrhages in a wedge-shaped region were diagnosed as BRVO. We randomly selected 46 healthy subjects matched for age, gender for control group. Exclusion criteria for entry into the study were use of any medication affecting platelet function, diabetes mellitus and alcohol consumption.

All participants underwent full ophthalmologic examination including best corrected visual acuity, pupillary reactions, intraocular pressure measurement, biomicroscopic and funduscopic examination at the beginning of the study. RVO patients were evaluated by careful biomicroscopic examination using a fundus contact lens. Fundus findings were confirmed by standardized fundus color photography. Fluorescein angiography was performed with a Topcon TRC-50 EX fundus camera (Tokyo Optical Co Ltd., Tokjo, Japan).

Blood samples for total blood count with MPV were obtained between 8:00 and 9:00 a.m. after overnight fasting from the antecubital vein in an upright position. Venous blood (1.8 ml) was taken and mixed with 0.2 ml of 3.8% sodium citrate solution (9:1) in order to perform a total blood count and MPV measurement. Measurements were completed within 1 hour.

Statistical Analysis

Statistical analysis was done by SSPS statistical software (SPSS for windows 10.0, Inc., Chicago, IL, USA). We compared the groups using Student's *t* test. Data were expressed as mean ± standard deviation (x±SD). Statistical significance was defined at a level of 5% ($p < 0.05$).

Results

Forty six patients (19 female, 27 male) with RVO with a mean age of 61.26 years ± 12.72 were included in this study. In RVO group, there were 28 (60.86%) BRVO and 18 (39.13%) CRVO patients. Control group had 46 (26 female, 20 male) subjects with a mean age of 62.6 years ± 9.87. There was no statistically significant difference in sex and age between groups ($p < 0.05$).

Nine (19.56%) controls had hypertension, one had inflammatory bowel disease and 15 (32.60%) smoked. Twenty eight (60.86%) patients in RVO group had hypertension and 15 (32.60%) smoked.

The mean MPV was 8.11 ± 1.15 fl in RVO group. It was 8.68 ± 0.98 fl in control group. When compared, the mean MPV was significantly lower in RVO patients ($p < 0.05$). Platelet count of RVO group was higher than controls (243.06 ± 59.70 versus 250.86 ± 54.67 ($p > 0.05$).

There was no significant difference in MPV between BRVO and CRVO groups (7.92 ± 1.19 fl versus 8.42 ± 1.06 fl) ($p > 0.05$). The mean MPV was significantly lower in BRVO group in comparison to controls (7.92 ± 1.19 fl versus 8.68 ± 0.98 fl) ($p < 0.05$). Platelet counts were 264.25 ± 55.79 in BRVO patients and 230.05 ± 47.06 in CRVO group. Platelet count revealed a significant difference between these two groups ($p < 0.05$) (Figures 1, 2).

Table I lists the demographic and clinical features in the study groups.

Discussion

Retinal vein occlusion is a common cause of vision loss in older population and the second most common retinal vascular disease after diabetic retinopathy. The pathogenesis of RVO is believed to follow the principles of Virchow's triad for thrombogenesis, involving vessel damage,

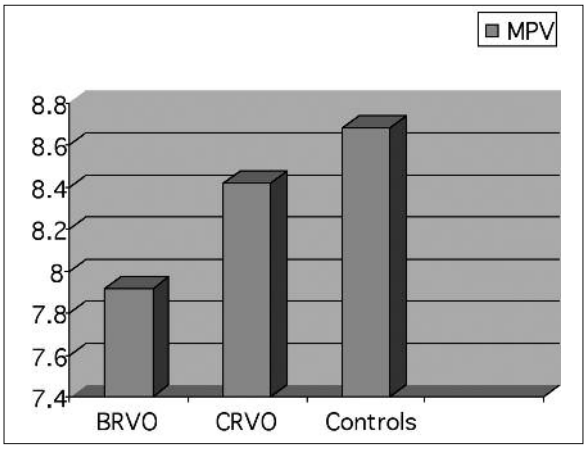

Figure 1. Mean MPV values in RVO patients and controls.

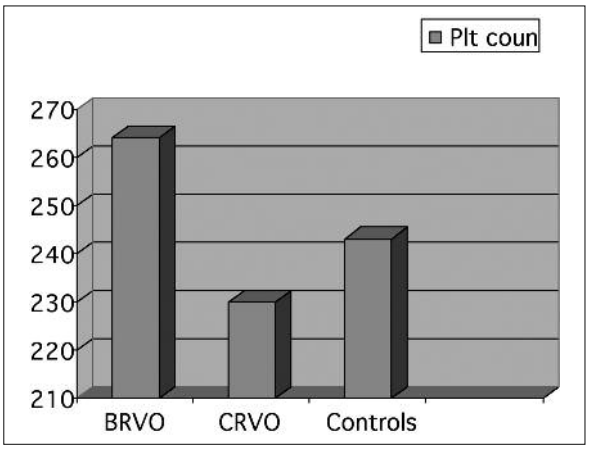

Figure 2. Mean platelet count in RVO patients and controls.

stasis and hypercoagulability. Several risk factors such as age, smoking, hypertension, diabetes mellitus, hyperlipidemia, glaucoma were attributed in the etiology of RVO[1-6].

In the current literature, some reports showed an association between altered haemorheological variables and the occurrence of RVO, whereas other studies did not confirm these observations[14-20]. Trope et al[18] demonstrated several abnormalities in RVO which suggest possible involvement of blood viscosity and haemostasis. They reported that increased blood viscosity, platelet activation, and activation of blood coagulation may exist in RVO patients. All these findings put a special stress on the importance of platelets, which are essential counterparts of coagulation cascade. From a pathophysiological point of view, we may expect that an increase in platelet size and activity may result from enhanced production of thrombin during coagulation.

Mean platelet volume was studied in a limited number of ocular vascular diseases. Ate et al[21] reported significant increase in MPV in patients with diabetic retinopathy. They found a correlation between the severity of diabetic retinopathy and MPV values. Coban et al[22] suggested a relationship between hypertensive retinopathy and platelet activation Ricart et al[23] found that MPV was not related with posterior uveitis in Behçet's disease. In a recent study, Onder et al[13] have shown higher MPV values with lower platelet counts in hypertensive BRVO patients.

In this study, we found lower MPV values in the RVO group than in controls, although the percentage of hypertensive patients were higher in the RVO group. Among the RVO patients, BRVO patients had the lowest MPV levels in comparison to CRVO patients and controls. Platelet counts were higher in RVO patients than controls. BRVO group had significantly higher platelet counts than CRVO group.

The central retinal artery and central retinal vein lie side by side in the center of the optic nerve enclosed by a common fibrous tissue envelope. With aging, thickening and sclerotic change in this fibrous tissue envelope and in the central retinal artery results in narrowing of the lumen and causes stagnant flow and hemodynamic changes in the central retinal vein. According to Virchow's triad, blood flow stasis promotes thrombosis. A similar mechanism most probably works in BRVO because invariably the site of occlusion in it is at the arteriovenous crossing. Thus, pathogenetically, the primary factor in the development of CRVO and BRVO seems to be the change in the adjacent arteries, and not systemic hematologic abnormalities. This is different from other systemic venous occlusive disorders where hematologic abnormalities may play the primary role. Thus, pathogenetically there seems to be a fundamental difference between retinal vein occlusion and other systemic venous occlusive disorders.

Hayreh et al[24] reported that the negative findings about the association between hematologic abnormalities and development of RVO outweighed the positive findings. The Authors concluded that there is no definite evidence of a cause-and-effect relationship between the various hematologic abnormalities and the development

Table II. The demographic and clinical features of study groups.

	RVO group	Control group	*p* value
Number of patients	46	46	> 0.05
Age (years)	61.26 ± 12.72	62.6 ±.9.87	> 0.05
Gender (female/male)	19/27	26/20	> 0.05
Plt (K/µl)	250.86 ±.54.67	243.06 ±.59.70	> 0.05
MPV (fl)	8.11 ±.1.15	8.68 ±.0.98	< 0.05

of.RVO in the vast majority of the patients. Ingerslev[25] stated that most well-known hematologic risk factors for general venous thrombosis occur sporadically only in RVO and it seems that these have no major importance in the pathophysiology of RVO. He suggested that there is no particular reason for a complete haemostasiological investigation in RVO patients. A population-based study of an Italian genetic isolate revealed that MPV is not a risk factor for venous thrombosis[26]. Our findings do not also support the current data that increased MPV could contribute to the development of thrombosis in RVO patients.

The argument for treating CRVO patients with anticoagulants is that hematologic abnormalities may be responsible for their development and that treatment of those abnormalities with anticoagulants may have protective or beneficial effect in such patients. In his small series of CRVO cases treated with anticoagulants, Sedney[27] found that the clinical course was disappointing with visual deterioration in 92% and no change in 8%. Koizumi et al[28] concluded that the independent predictors for CRVO were glaucoma, aspirin use, and warfarin use in a study of 144 patients with CRVO. Hayreh et al[29] have reported that antiplatelet therapy was associated with a worse visual outcome and no apparent benefit in these patients.

Conclusions

We did not find increased MPV values in patients with RVO compared to controls. Therefore, our results do not support the observation that MPV may be a potentially useful biomarker for prediction of RVO. Further studies are needed to clarify that platelets may have a causal role or not in the pathogenesis of retinal vein occlusion.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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