

Mean platelet volume in patients with retinal artery occlusion

Volume médio de plaquetas em pacientes com oclusão da artéria da retina

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ABSTRACT

Purpose: The aim of this study was to investigate the mean platelet volume (MPV) of patients with retinal artery occlusion (RAO).

Methods: Thirty-seven patients diagnosed with RAO and 32 control subjects were included in this retrospective study. Retinal artery occlusion was diagnosed on the basis of clinical examination and fundus fluorescein angiography. All participants underwent complete ocular examination, and MPV, hematocrit, hemoglobin, and platelet counts were recorded. RAO patient data were compared with those of the control subjects.

Results: Patients with RAO had significantly higher MPV values (7.96 ± 1.2 fL) compared with control subjects (7.33 ± 0.7 fL, $p < 0.001$). No significant difference was found with regard to platelet count between the RAO group and the control group ($262 \pm 70.1 \times 10^9/L$ and $251 \pm 56.6 \times 10^9/L$, respectively, $p = 0.50$). MPV was an independent predictor of RAO [odds ratio (OR) = 0.50; 95% confidence interval (CI) = 0.28-0.89; $p = 0.019$].

Conclusions: Our results demonstrated that MPV values were significantly higher in patients with RAO, suggesting that larger platelets may contribute to the pathogenesis of the RAOs.

Keywords: Mean platelet volume; Blood platelets; Retinal artery occlusion; Retinal diseases; Retinal vessels

RESUMO

Objetivo: O objetivo deste estudo foi investigar o volume plaquetário médio (MPV) de pacientes com oclusão da artéria da retina (RAO).

Métodos: Trinta e sete pacientes com diagnóstico de RAO e 32 indivíduos do grupo controle foram incluídos neste estudo retrospectivo. A oclusão da artéria da retina foi diagnosticada com base em exame clínico e angiografias de fluoresceína. Todos os participantes foram submetidos ao exame ocular completo. MPV, hematócrito, hemoglobina e contagem de plaquetas dos participantes foram registrados. Os dados dos pacientes com RAO foi comparado com os de sujeitos do grupo controle.

Resultados: Pacientes com RAO apresentaram valores significativamente mais elevados MPV ($7,96 \pm 1,2$ fL) em comparação aos indivíduos do grupo controle ($7,33 \pm 0,7$ fL) ($p < 0,001$). Nenhuma diferença significativa foi encontrada no número de plaquetas entre os grupos RAO e controle ($262 \pm 70,1 \times 10^9/L$ and $251 \pm 56,6 \times 10^9/L$, respectivamente, $p = 0,50$). MPV foi um preditor independente de RAO (odds ratio (OR) = 0,50; intervalo de confiança de 95% (IC) = 0,28-0,89; $p = 0,019$).

Conclusões: Os resultados demonstraram que os valores de MPV foram significativamente maiores nos pacientes com RAO, sugerindo que plaquetas maiores podem contribuir na patogênese da RAO.

Descritores: Volume plaquetário médio; Plaquetas; Oclusão da artéria retiniana; Doenças retinianas; Vasos retinianos

INTRODUCTION

Retinal arterial occlusion (RAO) is a rare cause of irreversible and profound vision loss, particularly in patients over the age of 60 years of age, despite the existence of various treatment modalities^(1,2). RAOs are classified according to the anatomic region of the occlusion as central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and cilioretinal artery occlusion (CLRAO)⁽³⁾.

CRAO was first described by von Graefes in 1859⁽⁴⁾. Patients with CRAO present with sudden, painless, severe visual loss. BRAO causes sudden segmental visual loss associated with visual field damage⁽⁵⁾. The incidence of CRAO has been estimated to be approximately 0.85 in 100,000 per year⁽⁶⁾. CRAO constitutes 57% of acute RAOs, whereas BRAO and CLRAO constitute 38% and 5% of acute RAOs, respectively⁽⁷⁾. CRAO by virtue of its pathogenesis shares important risk factors with other vascular diseases such as ischemic heart disease and cerebrovascular disease⁽⁸⁾. The majority of RAOs are either thrombotic or embolic in nature⁽⁶⁾. Arterial occlusions in the eye are almost always due to micro-embolism and the major source of micro-emboli is plaque(s), which may be present with or without significant stenosis of the carotid artery. Therefore, absence of significant stenosis of the carotid artery does not necessarily rule out the carotid artery as the source of micro-embolism⁽⁹⁾. The most frequent retinal emboli are

represented by cholesterol emboli (74.0%), platelet fibrin emboli (15.5%), and calcific emboli (10.5%)⁽¹⁰⁾.

Platelets have an important role in the pathogenesis of thrombo-occlusive disease. Mean platelet volume (MPV) is an indicator of platelet size and has been known to be a marker of platelet activity. Large platelets are more reactive than small platelets and produce more thromboxane A₂, express more glycoprotein Ib and glycoprotein IIb/IIIa receptors, and aggregate more easily^(11,12).

In the present study, we aimed to investigate the platelet activity in the development of RAO through MPV. To the best of our knowledge, we are the first to report MPV in patients with RAO.

METHODS

The study protocol was approved by the local ethic committee, and the study was performed in accordance with the Declaration of Helsinki. The patients who were diagnosed with RAO (i.e., CRAO, BRAO, or CLRAO) between January 2011 and December 2014 were reviewed retrospectively. All subjects underwent a full ocular examination, including measurement of visual acuity and intraocular pressure (IOP), slit lamp biomicroscopic anterior segment, and fundus examination. We also performed fundus fluorescein angiography (FFA) and optic coherence tomography in all patients.

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Age, gender, ocular pathology, systemic disease, and complete blood count (CBC) parameters [i.e., MPV, hemoglobin (hb), hematocrit (htc), and platelet count] were recorded. The diagnosis was based on the sudden visual loss accompanied by one or more of the following signs as observed by slit-lamp biomicroscopy with a 90-diopter lens: (1) reduced and thinned retinal artery flow; (2) fragmentation of the blood column in retinal arterioles; (3) retinal opacification combined with absent or poor residual retinal blood flow; and (4) the presence of a cherry-red spot (for CRAO). FFA revealed diminished blood flow in the retinal arteries. These findings were compared with the fellow unaffected eye. Patients with any systemic disease other than hypertension (HT) and diabetes mellitus (DM) were excluded from the study. Patients with anemia (htc <38.0%), any cardiovascular disease, such as heart valve disease treated with anticoagulant, congestive heart failure, chronic renal failure, stroke, history of smoking, and history of alcohol consumption were excluded; patients with glaucoma and with a history of any ocular surgery or trauma, and giant cell arteritis were also excluded. Age- and gender-matched subjects in the control group were recruited from an outpatient clinic of the same ophthalmology department.

Blood samples were taken at the time of RAO diagnosis. CBC samples drawn into vacutainer tubes containing 0.04 mL of 7.5% K3 salt of EDTA were analyzed within an hour after sampling with a commercially available analyzer (CELL-DYN 3700, Abbott Diagnostics, Abbott Park, IL, USA). MPV, platelet count, hb, and htc were recorded. Normal MPV values ranged between 7.0 and 10.4 fL.

STATISTICAL ANALYSIS

All values are given as means \pm SD. For statistical analysis, the SPSS statistical software package version 18.0 for Windows (SPSS, Chicago, IL) was used. The *Kolmogorov-Smirnov* test was applied to test the distribution pattern of each data. Student's *t*-test was used for normally distributed data in the group comparisons. *P* value <0.05 was considered statistically significant. Univariate logistic regression analysis was used to assess associations among MPV, htc and hb levels, HT, DM, age, and gender with RAO.

RESULTS

Of the 45 patients with RAO that were consecutively examined, 37 patients were eligible for the study. The control group consisted of 32 subjects, and the mean age of the RAO group and the control group was 55.4 ± 18.9 and 57.7 ± 13.1 years, respectively. The male-to-female ratio was 17:20 in the RAO group and 18:14 in the control group. There were no statistical difference in age and sex between the groups ($p=0.41$ and $p=0.22$, respectively) (Table 1). There was no

difference between the control and the RAO groups with respect to the presence of HT and DM.

Mean platelet volume was significantly higher in patients with RAO than in the control group (7.96 ± 1.2 fL vs. 7.33 ± 0.7 fL, $p<0.001$). In contrast, the mean platelet count was higher in the control group compared with the RAO group, although not statistically significant ($p=0.50$). Logistic regression analysis showed that MPV was an independent predictor of RAO [odds ratio (OR)=0.50; 95% confidence interval (CI)=0.28-0.89; $p=0.019$].

DISCUSSION

The present study showed increased levels of MPV in patients with RAO. To the best of our knowledge, this is the first study that shows the relationship between high MPV values and RAO.

Several mechanisms such as thrombosis, embolization, vasculitis, and vasospasm are attributed to RAO⁽¹³⁾. Thrombosis resulting from atherosclerotic plaques is the major cause of CRAO⁽¹⁴⁾. Rupture of an atherosclerotic plaque triggers platelet aggregation and consequently thrombus formation. It is likely that most CRAOs are due to a thrombosis at the level of the lamina cribrosa⁽¹⁵⁾. Emboli may be seen in up to 20% of patients with CRAO and up to 68% of those with BRAO⁽¹⁶⁾. These emboli are believed to typically arise from ulcerated atherosclerotic plaques or thrombi within internal or carotid arteries, or from cardiac valves.

The platelets have a key role in the pathogenesis of thrombo-embolic disorders. Since larger platelets store and release larger amounts of serotonin, β -thromboglobulin, and thromboxane A_2 , they are more reactive and prone to aggregation^(12,17). MPV is an indicator of the size and activity of platelets. Increased values of MPV have been shown to be a risk factor for deep venous thrombosis, acute myocardial infarction, stroke, and acute ischemic cerebrovascular events⁽¹⁸⁻²¹⁾. Bath and Butterworth reported that platelet hyperactivity results in an increase in MPV⁽²²⁾. In our study, the MPV values were significantly higher compared with the control group, suggesting that large platelets may contribute to the pathogenesis of RAO. Logistic regression analysis revealed that MPV is an independent predictor of RAO. The presence of high MPV in these patients may have increased their risk of developing RAO.

Platelets have an important role in the initiation of atherosclerotic lesions and subsequent complications⁽²³⁾. Their role in carotid atherosclerosis has been demonstrated in previous studies. P-selectin stored in the secretory granules of the platelets is crucial for the growth and maturation of atherosclerosis plaques, including the presence of smooth muscle cells and calcification⁽²⁴⁾. Burger and Wagner suggested that platelets and their P-selectin also actively promote advanced development of atherosclerotic lesions.

Heidrich et al. reported that platelet aggregation test (PAT III) values were elevated in all patients with acute RAO⁽²⁵⁾. Therefore, high platelet aggregation can be one cause of long-term retinal capillary occlusion in patients with RAOs. Paterson et al. studied the role of platelets in retinal circulation and suggested that platelet aggregates cause vessel occlusion either by embolization or by localized thrombosis of the arterial or venous branch of retinal vessels^(25,26). Moreover, BRAO has been observed following platelet transfusion in humans⁽²⁷⁾. Finally, in an experimental study, RAO was developed by infusing aggregated platelets⁽²⁸⁾. These studies suggest a role for platelets in the development of retinal artery occlusions.

Serotonin, a vasoconstrictor amine, is released by platelet aggregation on atherosclerotic plaques in the carotid artery. It was demonstrated in an experimental model that serotonin can cause transient or complete occlusion or impaired blood flow in the central retinal artery by producing a transient spasm in atherosclerotic monkeys; this may contribute to the development of RAO⁽²⁹⁾.

MPV has been studied in a few ocular vascular disorders. Our team reported an increase in MPV in patients with retinal vein occlusion (RVO) and ocular Behçet's disease^(30,31). Ateş et al. found a significant

Table 1. Demographic and clinical features of RAO patients and control individuals

	RAO	Control	P value
Age	55.4 \pm 18.9	57.7 \pm 13.1	0.410
Gender (M/F)	17/20	18/14	0.220
HT	6/37	4/32	
HT and DM	2/37	2/32	
Hb (g/dL)	13.7 \pm 1.7	14.2 \pm 1.2	0.180
Hct (%)	41.2 \pm 4	41.9 \pm 3.8	0.470
Plt ($10^3/\mu$ L)	262.2 \pm 70.1	251.7 \pm 56.6	0.500
MPV (fL)	7.96 \pm 1.2	7.33 \pm 0.7	<0.001
IOP (mmHg)	14.6 \pm 2.9	13.9 \pm 2	0.100
VA (Snellen)	0.18 \pm 0.3	0.75 \pm 0.3	<0.001

RAO= retinal artery occlusion; HT= hypertension; DM= diabetes mellitus; Hb= hemoglobin; Hct= hematocrit; Plt= platelet count; MPV= mean platelet volume; VA= visual acuity; IOP= intraocular pressure.

increase in MPV in patients with diabetic retinopathy⁽³²⁾. In addition, the role of platelets in RVO was also studied by Leoncini et al.⁽³³⁾, who reported an increased platelet response to thrombin in patients with RVO. Moreover, they suggested that platelet hyperaggregability inducing thrombus formation is an important factor in the onset and/or development of RVO.

Our study has some limitations: it was a retrospective analysis with a relatively small number of patients, which is inherent to investigations of rare diseases. With the lack of data on body mass index and lipid profiles, thrombin time, prothrombin time, and INR and no carotid artery Doppler ultrasound performed on patients, the results merely demonstrate the hematologic status at the acute stage of RAO within 48 hours. Thus, these results may not reflect the status of the patients over longer periods.

In conclusion, the present study demonstrated that MPV values were significantly higher in patients with RAO than in controls. Despite the retrospective design of our study, we suggest that MPV may be used as a predictive tool for identifying the risk of developing RAO. Further studies are needed to confirm the predictive value of MPV in RAO risk assessment.

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