Platelet indices in obstructive sleep apnea: the role of mean platelet volume, platelet distribution widht and plateletcrit

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SUMMARY

Platelet indices in obstructive sleep apnea: the role of mean platelet volume, platelet distribution widht and plateletcrit

Introduction: *Because studies report controversial findings of mean platelet volume (MPV) and platelet distribution width (PDW), we aimed to investigate platelet indices in patients with obstructive sleep apnea (OSA).*

Materials and Methods: *One hundred seventy three patients with OSA and 43 control subjects included in analyses. Patients with an apnea-hypopnea index (AHI) ≥ 5 were considered to have OSA and an AHI < 5 were considered as control. Platelet indices (MPV, PDW, plateletcrit) were obtained from routine analysis of blood samples using an automated blood cell counter.*

Results: *Among platelet indices, only PDW was higher in patients with OSA, especially in severe OSA when compared to control group (16.80 ± 0.56 vs. 16.21 ± 1.51, p= 0.015 and 16.82 ± 0.06 vs.16.21 ± 1.51, p= 0.014, respectively). Correlation analysis showed a significant but a weak correlation between the PDW and AHI (r= 0.161, p= 0.018) and the PDW and the desaturation index (r= 0.171, p= 0.016). The ROC curve analysis showed that the optimal cut-off value, distinguishing patients with OSA from those in control group, for PDW was 16.62 (sensitivity 57.8%, specificity 58.1%, AUROC 0.60, p= 0.042). After the exclusion of patients with comorbid diseases (cardiovascular diseases, diabetes mellitus and chronic inflammatory diseases), we also found weak but a significant correlation between PDW and AHI (r= 0.179, p= 0.040).*

Conclusion: *In conclusion, among the platelet indices, only PDW was found to be higher in patients with OSA, especially in severe OSA. PDW was also correlated with apnea-hypopnea index and oxygen desaturation index.*

Key words: *Obstructive sleep apnea, apnea-hypopnea index, mean platelet volume, platelet distribution width, plateletcrit*

ÖZET

Obstrüktif uyku apnesinde trombosit indisleri: Ortalama trombosit hacmi, trombosit dağılım genişliği ve plateletcritin yeri

Giriş: *Ortalama trombosit hacmi "mean platelet volume (MPV)" ve trombosit dağılım genişliği "platelet distribution with (PDW)" yönünden obstrüktif uyku apnesi (OSA) olan olgularda çelişkili sonuçlar bildirilmesi nedeniyle, bu çalışmada OSA olgularında trombosit indislerinin araştırılması amaçlandı.*

Materyal ve Metod: *Çalışmaya 173 OSA ve 43 kontrol olgu dahil edildi. Apne-hipopne indeksi (AHİ) ≥ 5 olan olgular OSA hastası, AHİ < 5 olan olgular ise kontrol olarak değerlendirildi. Trombosit indisleri olan MPV, PDW ve plateletcrit değerleri, rutin tam kan sayımı raporlarından (otomatik kan sayımı cihazı ile) elde edildi.*

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Bulgular: *Trombosit indisleri arasında sadece PDW, kontrol grubuna göre OSA olgularında, özellikle ağır OSA olgularında yüksek bulundu (sırasıyla 16.21 ± 1.51'e karşın 16.80 ± 0.56, p= 0.015 ve 16.21 ± 1.51'e karşın 16.82 ± 0.06, p= 0.014). Korelasyon analizinde de PDW ile AHİ arasında (r= 0.161, p= 0.018) ve yine PDW ile desaturasyon indeksi arasında (r= 0.171, p= 0.016) anlamlı ama zayıf bir ilişki bulundu. ROC analizinde OSA'yı kontrol grubundan ayıran optimal PDW cut-off değeri olarak 16.62 (sensitivite %57.8, spesifite %58.1, AUROC 0.60, p= 0.042) bulundu. Komorbid hastalığı olan (kardiyovasküler hastalık, diabetes mellitus ve kronik inflamatuvar hastalıklar) olgular dışlandığında, PDW ve AHİ arasındaki anlamlı ilişkinin (r= 0.179, p= 0.040) korunduğu saptandı.*

Sonuç: *Trombosit indisleri arasında sadece PDW'nun OSA olgularında, özellikle ağır olgularda yüksek olduğunu ve yine PDW ile AHİ ve desaturasyon indeksi arasında anlamlı korelasyon olduğunu ortaya koymuştur.*

Anahtar kelimeler: *Obstrüktif uyku apnesi, apne-hipopne indeksi, ortalama trombosit hacmi, trombosit dağılım genişliği, plateletcrit*

INTRODUCTION

Platelet volume indices are known as biomarkers of platelet activation and are reported to be associated with systemic inflammatory responses (1-3). During routine complete blood count analyze, mean platelet volume (MPV) and platelet distribution width (PDW) are the most commonly measured platelet indices. In earlier studies, MPV and PDW were found to be significantly higher in patients with severe obstructive sleep apnea (OSA) when compared to control subjects (4-9). MPV was also reported to be correlated with disease severity and inflammation in patients with obstructive sleep apnea and therefore, it could be used as a marker to predict cardiovascular diseases in patients with OSA (6-8). Moreover continuous positive airway pressure treatment (CPAP) reported to cause a significant decrease in the MPV and PDW values in patients with OSA (10-12). On contrary, some other studies reported no relationship between MPV and OSA, and between PDW and OSA (13-18). Because there are controversies among studies, we aimed to investigate platelet indices in our patients with OSA.

MATERIALS and METHODS

Subjects and Study Design

After the approval by the Ethics Committee of Karadeniz Technical University School of Medicine, all adult patients (> 18 years) scheduled for an overnight polysomnography between March 2012-September 2013 and who signed an informed consent were evaluated to participate in this study. Patients' information including demographic characteristics, co-morbid diseases and blood tests etc. were collected for each patient using a standard questionnaire, which was completed by face to face interviews and hospital records. Subjects who have central apnea, acute infectious/inflammatory diseases,

malignancy, hematologic diseases, and chronic renal or hepatic diseases were excluded. Cardiovascular disease was identified when the patients had heart failure, coronary artery disease, stroke, or arrhythmia.

Polysomnography and OSA Diagnosis

The diagnosis of OSA was based on attended full night polysomnography. All polysomnographic variables were recorded on a computer system (ALICE Sleepware, Philips Respironics, Inc, Murrysville, PA, USA), including electroencephalography (F3M2, F4M1, C3M2, C4M1, O1M2, O2M1), bilateral electro-oculography, submental electromyography, thoracic and abdominal movements (by inductive plethysmography), oxyhemoglobin saturation (using a pulse oximeter), oronasal airflow (recorded by thermistors and nasal canulla), electrocardiography, snoring microphone, and video monitoring using an infrared video camera. OSA was diagnosed and classified according to the International Classification of Sleep Disorders (19). Patients with an apnea-hypopnea index (AHI) ≥ 5 were considered to have OSA and patients with an AHI < 5 were considered as control.

Platelet indices (MPV, PDW, plateletcrit) were obtained from routine analysis of blood samples [in ethylenediaminetetraacetic acid (EDTA) tubes] using an automated blood cell counter (Beckman Coulter LH-750, Hematology Analyzer).

Statistical Analysis

The Kolmogorov-Smirnov test was used to test for a normal distribution of continuous variables. Data characterized by a normal distribution were expressed as mean ± standard deviation. Student's t-test was used for the comparison of data because data were distributed normally. Discrete variables were compared using the Chi-square test. Diagnostic

accuracies of platelet indices for identifying OSA were assessed using the area under the receiver operating characteristic (ROC) curve and area under curve (AUC). The Pearson test was used to assess the correlation between variables. Data were analyzed using SPSS statistical software (version 13.01, serial number 9069728, SPSS Inc., Chicago) and p< 0.05 was considered to be significant.

RESULTS

During the study period, a total of 216 subjects (173 patients with OSA and 43 controls) that met the selection criteria were included in the analysis. Patients were classified as mild, moderate and severe OSA in 40 (%23.1), 45 (%26.0) and 88 (%50.9) patients respectively. Control group was younger and had lower body mass index (BMI) than the patients with OSA. On contrary, OSA group had higher AHI and oxygen desaturation indexes and comorbid disease, hypertension, than the controls (Table 1).

Platelet indices were not different between control group and the patients with OSA except for PDW (Table 1). PDW was also higher in patients with severe OSA when compared to control group (16.82 ± 0.06 vs. 16.21 ± 1.51, p= 0.014), however there were no significant differences in mild and moderate

OSA. Correlation analysis showed a significant but a weak correlation between the PDW and AHI (r= 0.161, p= 0.018). Similarly, there was a significant correlation between the PDW and the oxygen desaturation index (r= 0.171, p= 0.016). The ROC curve analysis was performed to assess PDW in distinguishing patients with OSA from those in control group. The optimal cut-off value for PDW was 16.62 (sensitivity 57.8%, specificity 58.1%, AUC 0.60, p= 0.042).

After the exclusion of patients with comorbid diseases [cardiovascular diseases, diabetes mellitus and chronic inflammatory diseases (COPD, asthma, collagen vascular diseases etc.)], the remaining 101 patients and 31 controls were re-evaluated and we found a weak, but significant correlation between PDW and AHI (r= 0.179, p= 0.040). PDW was also higher in OSA patients, but p value was not statistically significant (Table 2).

DISCUSSION

Platelets are known to secrete many substances mediating coagulation, inflammation, thrombosis, and atherosclerosis (20). Platelet volume is a marker of platelet function and activation (21). Larger platelets have greater prothrombotic potential

Table 1. Demographic characteristics and platelet indices in patients with obstructive sleep apnea and in the control group

	Control (n= 43)	OSA (n= 173)	p
Age (years)	42.3 ± 10.5	53.9 ± 10.8	< 0.0001
Gender (M, %)	18 (41.9)	105 (60.7)	
Comorbidity (n, %)			
Hypertension	7 (16.3%)	96 (55.8%)	< 0.0001
CVD*	2 (4.7%)	22 (12.8%)	0.177
DM*	1 (2.3%)	23 (13.3%)	0.054
Pulmonary	10 (23.3%)	38 (22.0%)	0.855
Inflammatory diseases	1 (2.3%)	6 (3.5%)	1.000
Platelet indices (Mean ± SD)			
Platelet count (/ µL)	255348.8 ± 72000.3	252439.0 ± 57427.0	0.778
MPV* (fL)	8.54 ± 1.24	8.36 ± 1.00	0.310
Plateletcrit (%)	0.214 ± 0.049	0.207 ± 0.044	0.393
PDW* (fL)	16.21 ± 1.51	16.80 ± 0.56	0.015
Polysomnography			
Apnea-hypopnea index	1.5 ± 1.2	38.9 ± 28.2	< 0.0001
Oxygen desaturatrion index	3.3 ± 4.6	31.2 ± 28.2	< 0.0001
BMI (kg/m^2)	31.1 ± 6.3	34.3 ± 7.3	0.014
Epworth sleepiness scale	6.6 ± 4.0	7.5 ± 4.7	0.258

CVD: Cardiovascular disease, DM: Diabetes mellitus, MPV: Mean platelet volume, PDW: Platelet distribution with.

Table 2. Platelet indices in 101 patients with obstructive sleep apnea and 31 control subjects [After the exclusion of patients with comorbid diseases (cardiovascular diseases, diabetes mellitus and chronic inflammatory diseases)]

Platelet indices (Mean ± SD)	Control (n= 31)	OSA (n= 101)	P
Platelet count (/µL)	246225.8 ± 60826.9	248485.1 ± 53494.8	0.843
MPV (fL)	8.73 ± 1.32	8.33 ± 1.06	0.084
Plateletcrit (%)	0.210 ± 0.040	0.201 ± 0.040	0.295
PDW (fL)	16.20 ± 1.54	16.77 ± 0.58	0.055

MPV: Mean platelet volume, PDW: Platelet distribution width.

because they are metabolically and enzymatically more active (22). Mean platelet volume, an indicator of platelet activation, is known to have an important role in the pathophysiology of cardiovascular diseases (20-22). Because OSA patients have increased cardiovascular events, studies focused on the role of activated platelets in patients with OSA.

The first study investigating the relationship between mean platelet volume and OSA was performed by Varol et. al. and they showed that MPV was significantly higher in patients with severe OSA (4). The following studies confirmed this preliminary result and also reported that MPV was correlated with AHI and desaturation index (5-9). These studies were hypothesized that the alterations in MPV may be a confounding factor behind the increased cardiovascular events in OSA (4,6,7,23). One another platelet indices, PDW, was also reported to be higher in non-diabetic patients with severe OSA when compared to control group (5,9). Another study by Kurt et al. reported a meaningful correlation between PDW and AHI (17). Moreover in some studies, it was proposed that treatment with continuous positive airway pressure (CPAP) devices and surgical intervention significantly reduce MPV and PDW values in patients with severe OSA (10-12,24). On contrary, almost similar number of study reported no relationship between MPV and OSA, and between PDW and OSA (13-18).

In our study we investigated all platelet indices including MPV, PDW and plateletcrit and found that only PDW was higher in severe OSA when compared to control group. Other indices including MPV and plateletcrit were not different then the control. As mentioned above, there are several studies reporting no difference in MPV between patients with OSA and control (13-18). The studies reporting difference in MPV, found that MPV was higher only in patients

with severe OSA (but not milt-moderate OSA) than the control group (4-7,9). Again, except one study (18), PDW was found to be higher in patients with OSA when compared to control in some studies (5,9,14). Vagdatli et al. reported that PDW may a more specific marker of platelet activation, since it does not increase during simple platelet swelling (25). The plateletcrit is analogous to the hematocrit and reflects the mass of platelets. Because it is associated with the platelet count and MPV, we considered that it may be more valuable than MPV and PDW, however we could not demonstrate a relationship between plateletcrit and AHI and OSA. There is only one study reporting the role of plateletcrit in OSA and the findings in this study were in accordance to our results (18).

The controversies among studies might be due to sensitive structure of platelets because platelet volume increases significantly in a time-dependent manner (21). Blood sample collection time and their waiting periods in laboratories may be variable in different centers. On the other hand, despite some known factors (diabetes, cardiovascular diseases, inflammatory diseases, antiaggregant and, antihypertensive treatment, etc.) affecting platelet size were excluded in most studies, the standardization of some other factors that may be associated platelet volume (such as lifestyle modification, lipid lowering and diet therapies) might be difficult (26).

In conclusion, among the platelet indices, only PDW was found to be higher in patients with OSA, especially with severe OSA and it was also correlated with apnea-hypopnea index and oxygen desaturation index. This finding confirms that PDW might be a marker of OSAS severity, however we think large, prospective and well-standardized studies are needed to determine the value platelet indices in routine clinical practice.

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