Effect of Continuous Positive Airway Pressure Treatment on Mean Platelet Volume and Platelet Distribution Width in Patients with Sleep Apnea Syndrome

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Abstract

Objective: Obstructive sleep apnea (OSA) syndrome is a common disorder that can cause hypercoagulation. Mean platelet volume (MPV) and platelet distribution width (PDW) are associated with hypercoagulability. This study aimed to investigate whether MPV and PDW values change in patients with OSA who were treated with continuous positive airway pressure (CPAP) device.

Methods: A total of 43 adult patients with OSA who were treated with CPAP were included in this retrospective study. Patients who underwent CPAP treatment for <5 days/week and <4 h/day were excluded. Blood parameters, including MPV and PDW, were recorded before CPAP treatment and at the third month of CPAP treatment. All patients underwent polysomnographic evaluation with full night polysomnography and in the second night CPAP titration was performed together with full night polysomnography and MPV and PDW values were statistically compared before and after CPAP treatment.

Results: Apnea hypopnea index was significantly reduced, whereas oxygen saturation was significantly increased at CPAP titration night ($p<0.001$). The third month of CPAP treatment resulted in significantly low PDW ($p=0.004$) values, but MPV values did not change.

Conclusion: PDW value at the third month of CPAP treatment revealed a significant improvement compared with the values before treatment; moreover, no change was observed in MPV values. It was concluded that in patients with OSA who were treated with CPAP, activation of platelets may result in recovery.

Keywords: CPAP treatment, obstructive sleep apnea, platelet activation, platelets mean platelet volume

INTRODUCTION

Obstructive sleep apnea (OSA) syndrome is a disease that is characterized by recurring episodes of complete or partial interruption of breathing during sleep, which last at least 10 seconds. The incidence is 4% in middle-aged men and approximately 2% in middle-aged women (1). Because of respiratory oxygen desaturation that occurs during sleep, increased sympathetic activity and peripheral vasoconstriction develop (2). OSA is associated with an increased risk of cardiovascular morbidity and mortality (3). Previous studies have demonstrated an association between OSA and arterial and venous thromboembolism (4). The actual mechanism of this hypercoagulability is not completely understood.

Platelets have an important role in coronary artery disease (CAD). Mean platelet volume (MPV) and platelet distribution width (PDW) are indirect methods that reveal the morphological parameters of platelets. Previously performed studies have demonstrated that an increase in MPV value is an indicator of platelet activation (5, 6). Similarly, an increase in PDW values is also a marker that reveals platelet activity, and it may be a better MPV predictor (7).

Continuous positive airway pressure (CPAP) is the gold standard for OSA (8). Mortality in patients disusing CPAP is higher than those using (9). Previous studies have demonstrated that disease

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severity and hypoxia are correlated with MPV and PDW in OSA (10). Another study demonstrated that PDW values were increased but MPV values were not changed in severe OSA (11).

Although previous studies have indicated a positive effect of CPAP treatment on MPV values, to the best of our knowledge, there are very few studies reporting the changes in PDW values (12). This study aimed to determine whether a change in MPV and PDW values would be detected in patients with OSA who underwent CPAP treatment.

METHODS

This retrospective study was conducted in the Pulmonary Diseases and Otolaryngology Departments of Adana Numune Training and Research Hospital. Because of the retrospective design of this study, informed written consents were not obtained from the subjects. The study protocol was approved by the institutional ethics committee.

Patients

We included 43 adult patients who underwent CPAP treatment for OSA syndrome in our clinic between January 1 and December 31, 2013. During the time interval, 650 polysomnography (PSG) were performed. As a result of PSG, either patients with severe OSA having apnea hypopnea index (AHI) of >30/h or those having AHI between 5 and 30 were provided CPAP devices. Moreover, if a patient with OSA had AHI between 5 and 30, daytime sleepiness, hypertension, cerebrovascular disease, and CAD were evaluated. According to the indication, 236 patients for whom PSG was performed were provided a CPAP device. Because 98 patients who were provided a CPAP device used it for <4 h/day and <5 days/week, they were not included in the study. Ninety-five patients who did not come in the proper measurement time (earlier or later than 3 months) were excluded and the study was completed with the remaining 43 patients. Besides demographic data, such as age and gender, blood count parameters of MPV, PDW, platelet count, and white blood cell counts were recorded before treatment and at the third month of CPAP treatment. Each patient in the study used the CPAP device for at least 4 h/day and at least 5 days/week. We note that polysomnographic data collected first night polysomnography and CPAP titration night. Blood samples were analyzed within 20 min after collection using an automated hematology analyzer Sysmex XT 1800i (Roche Diagnostic, Shanghai, China) that is based on an optical system. For hematological analysis, blood samples were collected using ethylenediaminetetraacetic acid (EDTA)-coated tubes.

Patients using any drugs, such as acetyl salicylic acid, clopidogrel, dipiradamol, heparin, aminophylline, verapamil, nonsteroidal anti-inflammatory drugs, corticosteroids, furosemide, and antibiotics, and alcohol, which may affect the platelet function, and patients with diagnosed hematological diseases were excluded.

Polysomnography

All participants underwent PSG using the Compumedics E series (Compumedics E and somte series, Melbourne, Victoria, Australia). PSG recordings included electroencephalography, electrooculography, submental electromyography, oxygen saturation by an oximeter finger probe, respiratory movements via chest and abdominal belts, airflow, electrocardiography, and leg movements via both tibial anterolateral electrodes. Sleep stages and respiratory parameters were scored according to the standard criteria of the American Academy of Sleep Medicine (AASM). On the basis of the AASM guidelines, respiratory event was scored as an apnea if there was a decrease in the peak signal excursion by ≥90% of baseline and duration of the ≥90% drop in sensor signal was ≥10 s and at least 90% of the event's duration met the amplitude reduction criteria for apnea (recommended criteria). Respiratory event was scored as hypopnea if the following conditions occurs: 1) the peak signal excursions drop by ≥30% of pre-event baseline, 2) the duration of the ≥30% drop in signal excursion is ≥10 seconds, 3) there is a ≥4% oxygen desaturation from pre-event baseline. AHI was calculated on the basis of the following formula: total number of obstructive apnea+hypopnea/total sleep time (h). Sleep stage scoring was performed by a certified registered PSG technologist using a software (Profusion PSG 3) in 30-s epochs, according to AASM criteria (13).

CPAP titration studies were performed by a trained sleep technologist during laboratory PSG using the Somnoset (Weinmann, Hamburg, Germany). CPAP titration was performed according to the AASM guidelines (14).

Statistical Analysis

For statistical analyses, the values were expressed as mean ± standard deviation whenever appropriate. The normality of distributions was tested using the Kolmogorov–Smirnov test. Normally distributed variables were compared using a paired Sample t-test, whereas non-normally distributed variables were compared using a Wilcoxon signed-rank test.

A p value of <0.05 was considered statistically significant.

RESULTS

The mean patient age was 49.3±11.8 years. Of all patients, 56.1% (n=25) were male and 41.9% (n=18) were female. While MPV and PDW values before CPAP treatment were 10.58±1.28 fL and 13.53±2.27 fL, respectively, MPV and PDW values at the third month of CPAP treatment were determined to be 10.58±0.89 fL and 12.73±1.75 fL, respectively. Results of blood parameters were compared before CPAP treatment and at the third month of CPAP treatment. The comparison revealed that PDW values were significantly decreased at the third month of CPAP treatment (p=0.004). However, no significant changes (p>0.05) were observed in the remaining the parameters (Table 1).

Results of comparison of polysomnographic parameters before CPAP treatment and CPAP titration night demonstrated that significant improvement was observed in all parameters. Mean AHI value was dramatically reduced from 56.2 to 6.97 in CPAP titration night (p<0.001). Mean oxygen saturation index changed from 75 to 86 (p<0.001). Furthermore, mean duration of <90% oxygen saturation changed from 76.2 to 2.6 min (p<0.001). The other parameters are presented in Table 2.

DISCUSSION

Our study clearly revealed that with CPAP treatment, PDW values were significantly reduced but MPV values did not change. The re-

Table 1. Comparison of blood parameters before and at the third month of CPAP treatment

	Before CPAP treatment (n=43) Mean ± SD	At third month of CPAP treatment (n=43) Mean ± SD	p
MPV (fL)	10.58±1.28	10.58±0.89	0.967
PDW (fL)	13.53±2.27	12.73±1.75	0.004
Hb (g/dL)	14.3±1.9	14.2±2	0.263
Plt ($\times 10^3$/μL)	269±58	272±78	0.748
WBC ($\times 10^3$/μL)	8.35±2.10	8.86±2.68	0.122

CPAP: Continuous positive airway pressure; Hb: hemoglobin; MPV: mean platelet volume; PDW: platelet distribution width; Plt: platelet; SD: standard deviation; WBC: white blood cell

Table 2. Presentation and comparison between before CPAP treatment and CPAP titration night polysomnographic parameters

	First night polysomnography (n=43)	CPAP titration night (n=43)	p
AHI (mean±SD)	56.2±27.1	6.97±7.65	<0.001
Oxygen saturation (min–max)	75 (46–89)	86 (68–93)	<0.001
Apnea episodes (mean±SD)	155.8±149.3	5.8±12.6	<0.001
Apnea index (min–max)	22.4 (0.2–109.9)	0.3 (0–15.4)	<0.001
AHI in REM sleep (mean±SD)	8.81±6.50	14.69±8.36	<0.001
AHI in non-REM sleep (min-max)	58 (4.6–117.9)	3.4 (0–32.6)	<0.001
Duration of <90 oxygen saturation (min–max)	76.2 (0.40–311.8)	2.6 (0–261.9)	<0.001
REM latency (mean±SD)	83.14±1.69	65.59±1.25	0.004

AHI: Apnea hypopnea index; CPAP: continuous positive airway pressure; REM: rapid eye movement at sleep stage; SD: standard deviation

duced PDW values demonstrated that CPAP treatment improved platelet function in patients with OSA.

OSA is characterized by recurring complete or partial interruption of breathing during sleep, which can cause reduced oxygen saturation of up to 50% (15). OSA is a risk factor for cardiovascular disease (CVD) (3, 16). However, the relationship between OSA and CVD remains unclear (17). Chronic hypoxia can cause catecholamine-related platelet activation and an increase in MPV and PDW values (18, 19). PDW and MPV were reported to be markers, which were associated with cardiovascular and thrombotic events (17, 20).

CPAP treatment is the gold standard therapy in patients with OSA (8). An increased mortality rate has been reported in patients with OSA who did not undergo CPAP treatment (9). CPAP treatment improves upper airway obstruction and prevents repetitive hypoxia during sleep. Because repetitive hypoxia is improved via CPAP treatment, we consequently expect an improvement in platelet functions. Varol et al. (21) revealed decreased MPV values after 6 months of CPAP treatment. Similarly, adenosine diphosphate-induced platelet aggregability increased in patients with moderate to severe OSA compared with patients with mild or no OSA. In addition, platelet aggregability demonstrated improvements after 3 months of CPAP treatment (22).

Compared with MPV, Vagdatli et al. (7) reported PDW to be a better indicator of platelet functions. Although there are a number of studies related to MPV and OSA, only a few studies report regarding the change in PDW values after CPAP treatment (12). Sökücü et al. (12) reported in a comparison of 44 patients with severe OSA and control group that MPV values were found to be higher in the severe OSA group, whereas PDW values were similar. In contrast to our study, they reported decreased MPV values and increased PDW values after 6 months of CPAP treatment in their study. Both MPV and PDW are an indirect platelet function indicators. The results of both studies have shown that improvement in indirect platelet function's indicator although they showed it through decrease in MPV while we showed it through decrease in PDW Table 2 clearly shows the oxygen levels and AHI improvement with CPAP treatment at CPAP titration night. We think that is directly related between PDW and improvement of oxygenation. Several previous studies have demonstrated a direct correlation between AHI level and PDW values (10, 11). This improvement in PDW values with CPAP treatment is a quite reasonable result. However, regarding this issue very few publications could be found in the literature (12), and thus, we do not know the exact mechanisms.

EDTA or sodium citrate can be used as an anticoagulant in the tubes in which blood sample is collected for hematological analysis. The shape and ultrastructure of platelets vary depending on the medium temperature and the method used (23). Furthermore, platelets in the blood collected in EDTA-coated tubes take the shape of a sphere, whereas those in the blood collected in citrate-coated tubes take the shape of a discoid. Dastjerdi et al. (24) reported that the blood kept for <1 h does not cause a change in MPV values. When this period is prolonged, EDTA causes platelet swelling. MPV values can be measured through impedance or optic methods. When the impedance measurement is conducted using EDTA, MPV values increase over 24 h with a maximum value at the second hour. When an optic system is used, MPV values are decreased by 10% with EDTA within 2 h (23, 25). MPV values do not change over time when citrate is used as the anticoagulant. MPV values change by 3% within 3 h at 37°C temperature, whereas it increases by 20% at room temperature (23). Considering MPV measurements in previous studies have been conducted with

EDTA causing platelet swelling, Bath et al. (26) measured MPV values using sodium citrate. In that study, significant difference was found between patients with hypertension and healthy controls (26). In our study, there was no direct correlation between CPAP treatment and MPV values, suggesting that MPV values might be influenced by the abovementioned various laboratory methods.

The risk of cerebrovascular accidents and CVD is well known to increase with OSA (3). Likewise, the risk of venous thromboembolism (VTE) is also increased (4). This relationship between VTE and OSA is yet to be completely elucidated. Three primary pathogenetic mechanisms that facilitate VTE development have been described approximately 150 years ago and remain valid. This definition is known as the Virchow's triad and includes hypercoagulability, hemodynamic changes, and endothelial injury/dysfunction. Microvascular endothelial dysfunction occurs in patients with OSA and is resolved with proper treatment (27). This finding indicates the increased endothelial dysfunction with OSA existence. PDW is an indirect indicator of hypercoagulability, which is another component of Virchow's triad. In our study, an improvement in PDW values was observed with CPAP use. This improvement may be helpful in explaining OSA-related mortality, which is decreased with CPAP.

This study had several limitations. Although platelet count and MPV samples were supposed to be analyzed within 20 min, it was not possible to guarantee that those samples were analyzed within the specified time period because this is a retrospective study. The relatively small number of patients surveyed during the study period was another limitation. A prospective, controlled clinical setting with the participation of multiple institutions would clarify the association between MPV and the effects of CPAP on MPV.

CONCLUSION

As a result, OSA syndrome is an independent risk factor for increased CVD. To reduce CVD risk, CPAP treatment might be demonstrated using inexpensive and simple platelet activation markers such as PDW.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Adana Numune Training and Research Hospital.

Informed Consent: Because the retrospective design of this study, informed written consents were not obtained from the subjects.

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