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Original Article

In the Absence of Co-Morbidities Mean Platelet Volume is not A Severity Indicator in OSAS

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ABSTRACT

Objective: *To evaluate the relationship of mean platelet volume and OSAS severity, in OSAS patients without any vascular risk factors and co-morbidites.* ***Method:*** *The patients files and polysomnographies of OSAS patients who admitted to sleep laboratory between January 1st 2011 and April 1st 2012 have been retrospectively evaluated. Inclusion criteria are to have no vascular risk factors and no co-morbidities, to be a non-smoker, to be older than 18 years of age and not be taking any medications. Patients have been grouped as severe and non-severe OSAS according to their apne- hypopne indices. Mean platelet volume (MPV) of patients in the two groups have been compared.* ***Results:*** *Among 81 patients who met the inclusion criteria, 39.6% of the patients had severe OSAS while 60.4% had non-severe OSAS. MPV in the severe group was 9.05+0.89 (fL), while it was 9.00+0.82 (fL) in the non-severe group. The difference of MPV between two groups was not significant (p:0.800).* ***Conclusion:*** *Controversially with the former studies which declared higher MPV in severe OSAS, our study concludes that when all other risk factors are excluded MPV is not an indicator of severity in OSAS.*

Key words: *OSAS, mean platelet volume, vascular risk factors*

Ortalama Trombosit Hacmi Ek Hastalık Yokluğunda OSAS'ın Ağırlık Derecesi için Gösterge Değildir

ÖZET

Amaç: *Herhangi bir vasküler risk faktörü ve ko-morbiditesi olmayan OSAS hastalarının ortalama trombosit hacmi ve OSAS şiddeti arasındaki ilişkiyi değerlendirmek.* ***Yöntem:*** *1 Ocak 2011 ve 1 Nisan 2012 tarihleri arasında uyku laboratuvarına başvuran OSAS hastalarının hasta dosyaları ve polisomnografileri retrospektif olarak incelendi. Çalışmaya dahil edilme kriterleri 18 yaşından büyük olmak ve herhangi bir ilaç kullanmamak, hiçbir vasküler risk faktörü, hiçbir ko-morbiditesi olmamak ve sigara içicisi olmamaktır.* ***Bulgular:*** *Hastalar apne- hipopne endekslerine göre ağır ve ağır olmayan OSAS olarak gruplandırılmıştır. İki gruptaki hastaların ortalama trombosit hacmi (MPV) karşılaştırılmıştır. Dahil edilme kriterlerine uyan 81 hasta içinde; 60.4% hasta ağır olmayan OSAS'a sahipken, hastaların % 39.6'sında ağır OSAS vardı. Ağır olmayan grupta MPV 9.00 + 0.82 (fL) iken ağır OSAS grubunda MPV, 9.05 + 0.89 (fL) idi. İki grup arasında MPV farkı anlamlı değildi (p: 0.800).* ***Sonuç:*** *Ağır OSAS'ta MPV'nin daha yüksek olduğunu savunan önceki çalışmaların aksine bizim çalışmamız diğer tüm risk faktörleri dışlandığında MPV'nin OSAS şiddeti için bir gösterge olmadığı sonucuna varmaktadır.*

Anahtar kelimeler: *OSAS, ortalama trombosit hacmi, vaskuler risk faktörleri*

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a highly prevalent disorder which affects approximately 5% of adult population (1,2). Young et al. released that, 1 of every 5 adults had at least mild OSAS and 1 of 15 had at least moderate OSAS (2). Patients with OSAS may frequently be burdened with multiple co-morbidities including obesity, hypertension, insulin resistance and dyslipidemia (3).

The first approach to explain the mechanism of OSAS was the mechanical theory. Clinical evidence pointed to the upper airway obstruction among most of the OSAS patients, occuring either in the nasopharynx or the oropharynx (4). Afterwards local and systemic inflammatory theories were generated. A chronic low-grade systemic inflammation characterized by increased serum concentrations of cytokines and chemokines was suggested to be present in OSAS patients (5,6). Some recent studies have found MPV which is an indicator of enhanced platelet function and an inflammatory marker (7), to be higher in severe OSAS patients concluding on enhanced platelet functions and aggregability in OSAS (8,9).

MPV is an indicator of platelet activation but it is not specific for any diseases. Increased MPV has been reported in patients with vascular risk factors such as hypercholesterolemia, diabetes mellitus, hypertension, ischemic stroke, myocardial infarction and smoking (10-12). Some recent studies have shown increased MPV in subclinical hypothyroidism (13) and major depression, as well (14).

Regarding the vast spectrum of diseases that may increase MPV, we believe that it is important to exclude any co-morbidities to be able to meticulously evaluate the relationship of platelet activation with OSAS. To our knowledge, no previous study, excluding all co-morbidities and vascular risk factors which may confuse the origin of enhanced platelet activation has been performed in OSAS yet. In this study we aimed to investigate the mean platelet volume (MPV) in OSAS patients in the absence of all other probable causes of increased MPV.

MATERIAL AND METHODS

This study was performed in Department of Respiratory Diseases, Istanbul, Turkey. All patient admissions to our sleep disorders unit between January 1st, 2011 and April 1st, 2012 have been retrospectively scanned. The patients who have been evaluated with the same two physicians (1 neurologist and 1 respiratory diseases specialist) have been collected. The inclusion criteria for patients were to be older than 18 years of age, to be diagnosed as OSAS by polysomnography (PSG) in our sleep unit, to have no history of any other illnesses (hypertension, hyperlipidemia, diabetes, mycocardial infarction, stroke, respiratory diseases, depression, tyhroid diseases etc.) or operations, to be a non-smoker and not to be taking any medications including anti-platelet or anti-coagulant agents.

Polysomnography

All patients have been monitored with a nocturnal PSG which was performed with multichannel monitoring that includes neurophysiological variables (electroencephalography, electrooculography, chin electromyography) and cardiorespiratory variables (chest wall motion, abdominal motion, arterial oxygen saturation and electrocardiography) (Grass-Telefactor Cephalo, An Astro-med Inc. Product Group, 2005, USA). Oronasal airflow was measured by a thermistor. The oxyhemoglobin saturation was monitored with a finger pulse oxymeter with a sampling rate of 1 Hz. The body position was measured by a position sensor attached to the anterior chest wall. The sleep records were analyzed manually according to the criteria of Rechtshaffen and Kales using a 30-second epoch (15). The patient files which were filled in during the first visit before PSG were restropectively evaluated for each patient. Age, sex, history of snorring, daytime sleepiness and apnea complaints were questioned. Epworth Sleepiness Scale (ESS) (16), Body Mass Index (BMI), sleep efficiency and supine and non-supine AHI results were checked. Apnea was defined as an episode of >10 sec with a reduction of oronasal airflow of >90% and hypopnea as a reduction in oral/nasal airflow lasting >10 sec, accompanied with arousal or by a drop of >3% of SpO2. The hourly number of episodes of apnea and hypopnea in sleep was defined as apnea-hypopnea index (AHI). Based on the severity of OSAS, patients were divided into two groups according to their AHI values: non-severe (AHI:5-30) and severe (AHI> 30). Complete blood count (CBC) records were checked from patient files. MPV and platelet counts were retreived.

Statistical Analysis

Statistical analysis was performed with NCSS 2007& PASS. For group comparisons of normally distributed parameters Student t-test, for group comparisons of non-normally distiributed parameters Mann Whitney U and

Table 1. Comparison of questioned items in two groups.

	Severe(n:32)	Non-severe(n:49)	p value
Age (mean)	41.59±7.68	46.00±8.98	0.025*
BMI(kg/m²) (mean)	33.10±6.28	30.55±5.31	0.053
Platelet count(10^9/L)(mean)	262.63± 43.89	260.76 ± 54.04	0.871
Snorring (%)	100	100	
Apnea (%)	96.9	89.8	0.395
Daytime Sleepiness (%)	96.9	77.6	0.023*
ESS (mean)	11.88±6.28	9.76±4.06	0.086
Sleep Efficiency (mean)	86.67±10.21	85.34±10.35	0.573

± Standard Deviation, * statistical significance: p<0.05

Kruskal Wallis tests were used. Fisher's Exact Test, Yates Continuity Correction and Chi-square Test were used for the comparison of qualitative data and Pearson test was used for correlation analysis. Statistical significance was set at p< 0.05.

RESULTS

During 15 months (from January 1st, 2011 to April 1st, 2012) 718 PSGs were evaluated by the same two physicians who performed this study. Excluding the patients with any co-morbidites and smokers, we had a group of 81 patients. Only the data of these 81 patients who met the inclusion criteria were included in the study. Considering AHI scores, patients were divided into two groups regarding their severity; non-severe OSAS and severe OSAS. Thirty-two patients (39.6%) were in the severe group while 49 patients (60.4%) were in the non-severe group. In the severe group, 30 patients were male (93.8%) and 2 patients were female (6.3%). In the non-severe group 39 patients were male (79.6%) and 10 patients were female (20.4%). The difference of two groups in gender was not significant (p:0.112). Mean age in the severe OSAS group was 41.59+7.68 while it was 46.00+8.98 in the non-severe OSAS group. The difference of ages was statistically significant (p:0.025). Non-severe OSAS patients were significantly older than severe OSAS patients. Mean BMI in severe OSAS was 33.10±6.28 (kg/m²), and mean BMI in non-severe OSAS was 30.55±5.31 (kg/m²). Difference between severe and non-severe patients was not significant (p:0.053). ESS scores was found to be 11.88±6.28 in severe OSAS while it was 9.76±4.06 in non-severe OSAS. The difference between two patient groups was not significant (p:0.086). Mean sleep efficiency was %86.67±10.21 in severe group while it was %85.34±10.35 in non-sever group. There was no difference between the two groups (p:0.573). History of daytime sleepiness was present in 31(96.9%) severe patients and in 38 (77.6%) non- severe patients. Non-severe OSAS patients reported significantly more frequent daytime sleepiness (p:0.023). No statistical significance have been found about history of snorring and apnea in two groups. The questioned items have been shown in Table 1. In severe OSAS patients mean AHI was 51.54±20.65. Mean supine AHI was 68.05±22.14 while non-supine AHI was 36.55±29.61. In non-severe OSAS patients mean AHI was 16.33±7.36. Mean supine AHI was 34.99±23.21 while non-supine AHI was 8.77±14.88. Overall AHI, supine and non-supine AHI were significantly higher in severe OSAS group (p:0.001, p:0.001, p:001). Mean platelet count in the severe OSAS group was found to be 262.63±43.89 (109/L) and it was 260.76±54.04 (109/L) in the non-severe group. The difference was not significant (p:0.871). In the severe group mean MPV was 9.05±0.89 (fL), while it was 9.00±0.82 (fL) in the non-severe group. The difference of MPV between severe and non-severe OSAS patients was not significant (p:0.800). With the correlation analysis MPV was found to be weakly correlated with AHI (p:0.046, r: 0.222).

DISCUSSION

Theories about the mechanism of OSAS gain growing attention in sleep medicine. The inflammatory processes are being blamed lately and hence studied frequently. Relationship of platelet activation markers, including MPV between OSAS has been evaluated several times, especially during the last decade. Despite controversial results, none of these studies were designed to strictly

exclude all co-morbidities and vascular risk factors. We designed our study based on this principle and found out that MPV did not differ between severe and non-severe OSAS patients.

OSAS is known to be associated with several cardiovascular, cerebrovascular, metabolic and psychiatric morbidities (17-19) which may be the consequences of multiple inflammatory processes activated by OSAS (20,21). OSAS activates multiple inflammatory processes that could increase platelet activation and it is suggested that the hypoxic stress of OSAS is potentially a proximal mediator of the systemic inflammation and platelet activation (22). Inreased levels of epinephrine and nonepinephrine caused by hypoxemia and repetetive arousals have been blamed for the mechanism of enhanced platelet activation in OSAS (23,24) which is one of the suggested potential causes for the increased incidence of cardiovascular events (25). Our study showed no significant difference in MPV between severe and non-severe patients in the whole group. Despite the weak statistical significance of correlation analysis, MPV difference between severe and non-severe OSAS patients was not significant. MPV was found to be higher in obesity (26). In our both patient groups mean BMI was >30 kg/m^2 and there was no significant difference between the two groups consistent with MPV.

The challenging results about MPV and OSAS relationship in previous studies probabaly arise from patient selection. Nena et al. partly dealed with this issue and designed a study with non-diabetic OSAS patients in which MPV was found to be higher in severe OSAS patients (8). But diabetes is definitely not the only reason which may increase MPV. In addition to former literature, later studies have shown that MPV is higher in metabolic syndrome (27,28) while several others have concluded that passive and active smoking activated platelet function (29-31). These studies emphasize the importance of excluding all co-morbidities and vascular risk factors for an accurate analysis of MPV and OSAS relationship.

Our study showed that when all co-morbidities and vascular risk factors were excluded, MPV was not related to OSAS severity. To be able make a strong association between a disease and a marker, it's mandatory to eliminate all other factors that may affect the results.

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