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Comparison of erythrocyte distribution width, mean platelet volume and platelet distribution width in patients with obstructive sleep apnea syndrome

Obstrüktif uyku apne sendromlu hastalarda eritrosit dağılım genişliği, ortalama trombosit hacmi ve trombosit dağılım aralığı karşılaştırılması

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Abstract

Aim: Reliable markers are needed to evaluate the response of chronic inflammation in obstructive sleep apnea syndrome (OSAS) to positive airway pressure (PAP) treatment. In this study, we aimed to investigate the long-term effects of PAP treatment on hemogram parameters and its relationship with inflammation and severity of disease in OSAS patients.

Methods: Based on polysomnography (PSG) results, 61 (35.1%) participants and 113 OSAS patients (64.9%) were included in the control and study groups, respectively. Among these patients, 31.6% had moderate and 33.3% had severe OSAS. MPV, PDW, RDW, hemoglobin, hemotocrit, platelet values were evaluated and compared between the groups at six and twelve-month intervals in this prospective cohort study.

Results: All participants (n=174) were males aged between 33-62 years. Hemoglobin, hematocrit and MPV values of the study group were significantly higher at the baseline (P=0.008, P=0.007, P=0.004, respectively) and had decreased significantly by the 6th and 12th months in both groups P=0.004, P=0.003, P=0.004, respectively).

Conclusion: All participants were chosen from males to exclude hormonal effects on hemogram parameters, which also turned out to be a limitation of this study. Our study showed a correlation between MPV, RDW, PDW, hemoglobin and hematocrit values and OSAS severity. MPV, RDW, hemoglobin, hematocrit and platelet may be considered inexpensive biomarkers easily obtained from blood tests which make it useful in determining the severity of OSAS and prioritizing patients for PAP therapy.

Keywords: Obstructive sleep apnea syndrome, Red cell distribution width, Mean platelet volume, Platelet distribution width

Öz

Amaç: Obstrüktif uyku apne sendromunda (OUAS) intermitant hipoksiye bağlı gelişen kronik inflamasyonun PAP tedavisine yanıtını değerlendirmede kullanılacak güvenilir belirteçlere ihtiyaç vardır. Bu çalışmada, pozitif havayolu basıncı tedavisinin uzun dönem sonuçlarının hemogram parametreleri üzerine etkisini ve OUAS'lı hastalarda inflamasyon ve hastalığın ciddiyeti ile ilişkisini araştırmayı amaçladık.

Yöntemler: Çalışma prospektif kohort tipi çalışma olarak planlandı. Polisomnografi (PSG) sonuçlarına göre OUAS saptanmayan 61 katılımcı (%35.1) kontrol grubu olarak alındı. OUAS saptanan 113 hasta (%64,9) çalışma grubu olarak alındı. Çalışma grubunun (%31,6)'sı orta OUAS, 58'i (%33,3) şiddetli OUAS idi. Hastaların MPV, PDW, RDW, hemoglobin, hemotokrit, trombosit değerleri değerlendirildi ve altı ve on iki ay arayla karşılaştırıldı.

Bulgular: Yaşları 33 ile 62 arasında değişen, toplam 174 hasta çalışmaya alındı. Başlangıçta hemoglobin, hematokrit ve MPV değerleri çalışma grubunda kontrol grubuna göre anlamlı derecede yüksek (sırasıyla P=0,008, P=0,007, P=0,004), her iki grupta da 6 ve 12 aydaki düşüşler istatistiksel olarak anlamlıydı (sırasıyla P=0,004, P=0,003, P=0,004).

Sonuç: Tüm katılımcıların erkek olması hemogram parametrelerine hormonal etkilerin dışlanması nedeni ile idi. Ancak çalışmaya sadece erkek katılımcıların dahil edilmesi aynı zamanda bu çalışmanın limitasyonu olabilir. Çalışmamız MPV, RDW, PDW ve hemoglobin, hematokrit değerleri ve OUAS şiddeti arasında bir ilişki olduğunu göstermiştir. MPV, RDW, hemoglobin, hematokrit, trombosit, PAP tedavisini değerlendirmeyi bekleyen OUAS hastalarını önceliklendirmede faydalı kılan basit, ucuz bir kan biyobelirteçine dönüşebilir.

Anahtar kelimeler: Obstrüktif uyku apne sendromu, Eritrosit dağılım genişliği, Ortalama trombosit hacmi, Trombosit dağılım aralığı

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Introduction

Obstructive sleep apnea syndrome (OSAS), which is the most common respiratory sleep disorder, is characterized by recurrent collapse of the upper airway during sleep, nocturnal hypoxemia, and sleep interruption [1]. OSAS progresses with inflammation and airway remodeling and is associated with systemic inflammation [2]. Systemic inflammation is also strongly related with various metabolic and cardiovascular diseases such as peripheral vascular disease, coronary artery disease, hypertension, heart failure, cardiac arrhythmias, and diabetes mellitus [2,3]. Red cell distribution width (RDW), platelet activation and inflammation are connected with OSAS pathogenesis. There are studies indicating that erythrocyte distribution width and platelet activation increase in cardiovascular events. Mean platelet volume (MPV) and Platelet distribution width (PDW) are indicators of platelet activation [3,4].

OSAS increases the risk of cardiovascular and metabolic diseases independent of weight [4]. Recently, the autonomic nervous system changes caused by recurrent respiratory events and arousals, systemic inflammatory changes caused by hypoxia attacks and sleep deprivation were researched and different results were obtained [5].

Inflammation is a reaction caused by harmful agents in the tissue. In OSAS, asphyxia, increased intrathoracic negative pressure, hypoxia-reoxygenation, ischemia-reperfusion, hypercapnia, acidosis, apnea, and arousal-induced autonomic nervous system activation are effective in the development of local and systemic inflammation [6]. Endothelial damage, increased inflammatory mediators, increased sympathetic activity and hypoxemia are the leading factors in the development of cardiovascular events frequently seen in OSAS [7]. The formation of hypoxia-induced free radicals is associated with subsequent oxidative stress and hypercapnia, which causes endothelial function loss by local, neural reflex mechanisms, paving the way for atherosclerosis. In patients with apnea, oxidative stress causes subclinical atherosclerosis without any cardiovascular disease, which may increase cardiovascular morbidity [8]. If treatment is begun after the detection of OSAS, it becomes less challenging to control a series of systemic and vascular diseases with severe morbidity such as hypertension, arrhythmia, and atherosclerosis [10,11]. Inflammation plays a key role in endothelial dysfunction and atherosclerotic vascular disease. Platelets are related to inflammation, thrombosis and atherogenesis [9,10] in the following way: Active platelets stimulate leukocyte activation by forming aggregates through physical interaction with leukocytes. These platelet-leukocyte complexes are considered as markers in platelet activating conditions such as stable coronary artery disease, unstable atherosclerosis, and vascular disease [11].

To better understand the pathophysiology of OSAS, recent studies have been conducted to evaluate the course of hematological parameters, especially MPV, PDW and RDW. However, the relationship between these parameters and severity of OSAS remains controversial. The aim of this study was to evaluate the relationship between hematological parameters, disease severity and response to PAP treatment in OSAS.

Materials and methods

Patients who were diagnosed with moderate and severe OSAS by polysomnography (PSG) between January 2017 and December 2018 in Izmir Eşrefpaşa Municipality Hospital sleep laboratory and treated with PAP were included in this prospective cohort study. Patients with other sleep disorders, anemia, polycythemia and other hematological diseases, any malignities, chronic liver-kidney disease, heart failure, ischemic heart disease, peripheral vascular disease, those receiving anticoagulant medications, patients with CRP>10 and female patients were excluded from the study. Only males were included in this study to exclude the variability of hormonal effects on hemogram parameters. According to studies, 17-beta estradiol inhibits erythropoietin synthesis caused by hypoxia in the kidneys and testosterone has a stimulating effect on erythropoiesis, the mechanism of which is unknown [12]. Individuals with normal PSG results and no known diseases were included in the control group.

The demographic and clinical characteristics of each participant, i.e., age, weight, height, smoking, and medical history, were recorded. All participants were followed-up at night by a trained sleep technician in our sleep center with a PSG device, obtaining a PSG record of at least 6 hours. PSG was performed in accordance with the American Academy of Sleep Diseases Classification criteria [1]. Based on PSG results, apnea hypopnea index (AHI) <5 was considered normal and AHI ≥5 was classified as OSAS. Then the OSAS group was divided into three groups according to the degree of disease. Those with AHI scores of 5-15 were classified as mild OSAS, 15-30 as moderate OSAS and AHI score >30 as severe OSAS. Patients with mild OSAS were excluded because they were not indicated to receive PAP treatment.

Blood was collected into hemogram tubes for routine complete blood counts. Hemogram parameters were measured with an automated hematology analyzer (Abbott Cell-Dyn 3700 Hematology Analyzer, Abbott Diagnostics, USA). All test results were recorded. Baseline MPV, PDW, RDW, hemoglobin, hematocrit, platelet values of the three groups were recorded and compared.

One hundred thirteen patients with moderate and severe OSAS underwent PSG for the second time and positive airway pressure (PAP) titration was performed. MPV, PDW, RDW, hemoglobin, hematocrit, platelet counts were obtained in the 6^{th} and 12^{th} months when 113 moderate and severe OSAS patients receiving PAP treatment were invited for follow-up visits. Patients under PAP treatment were evaluated for compliance based on PAP software data. They were considered compliant with more than 4 hours of use per night for at least 4 days a week [13].

Statistical analysis

IBM SPSS Statistics v22 (SPSS IBM, Turkey) were used. Demographic definitions of individuals were presented as Frequency (n) and Percent (%). Kolmogorov-Smirnov test was performed to determine the normality of the data, which showed that not all variables were normally distributed ($P<0.05$). For non-normal distribution, non-parametric tests were used to evaluate the differences between the groups. Chi-Square test was used to determine whether obstructive sleep apnea syndrome

(OSAS) severity differed with demographic characteristics such as age and smoking status. Kruskal-Wallis test was used to compare the initial hemogram results of patients with moderate and severe OSAS. Friedman test was performed to evaluate hemogram values at baseline, 6th and 12th months moderate and severe OSAS patients. Spearman's Rho Correlation Coefficient was utilized to evaluate the relationship between red cell distribution width, apnea-hypopnea index, minimum oxygen saturation, average oxygen saturation and mean desaturation index.

Results

The study was conducted on 174 male patients aged between 33 to 62 years. 61 participants (35.1%) constituted the control group. 55 patients (31.6%) with moderate OSAS and 58 patiens (33.3%) with severe OSAS were included in the study group. The mean age of all patients was 44.6 (6.5) years. Mean apnea-hypopnea index (AHI) of patients with moderate and severe OSAS and all OSAS patients combined were 21.00, 50.90 and 35.4, respectively. The mean body mass index (BMI) of the cases was 31.4 (3.5). 74 (42.5%) patients had never smoked, 70 (40.2%) were smoking and 30 (17.3%) were ex-smokers.

There was no statistically significant difference with respect to age and smoking rates between moderate, severe OSAS and non-OSAS (P=0.076) participants. There was a significant difference between the BMI rates (P<0.001). However, no statistically significant BMI change was observed in the moderate and severe OSAS groups after PAP treatment (P=0.741). Demographic and clinical characteristics of moderate and severe OSAS and control groups are shown in Table 1.

The comparison of baseline Hb, Htc, PLT, MPV, PDW and RDW values yielded a statistically significant difference among all three groups (P<0.05). Initial hemogram values and multiple comparison tests of the patients are shown in tables 2 and 3. The hematological parameters of moderate OSAS patients under treatment are shown in Tables 4 and 5. Baseline, 6th and 12th month-RDW values of moderate OSAS patients remained similar (P=0.473). All other hemogram values were significantly different in at least two measurements. The hemogram values of severe OSAS patients under treatment are shown in Tables 6 and 7.

In severe OSAS patients, the only statistically non-significant overall change from baseline until the 6th and 12th months occurred in PDW values (P=0.101). All other hemogram values differed significantly. In addition, the multivariate analysis revealed that RDW values between baseline and at the 6th month were similar (P=0.971), and all other changes were significant.

Table 1: Comparison of demographic and clinical characteristics of the groups

	OSAS None (n=65)	Moderate OSAS (n= 55)	Severe OSAS (n=58)	*P*-value
Age	45.6 (7.6)	44.5 (1.4)	43.7 (5.3)	0.076
BMI	29.2 (2.5)	31.8 (1.7)	33.8 (3.1)	<0.001
Cigarette				
Never smoked	29 (16.7%)	22 (29.7%)	23 (13.2%)	0.240
Ex smoker	11 (6.3%)	11 (36.7%)	8 (4.6)	
Smoker	21 (12.1%)	22 (31.4%)	27 (15.5%)	

OSAS: Obstructive Sleep Apnea Syndrome, BMI: Body mass index

Table 2: Kruskal Wallis test results for initial hemogram values

Variant	OSAS Classification	n	Mean Average (SD)	Median	Test Value	*P*-value
Hemoglobin	Control group	61	12.16 (1.282)	12.20	110.426	0.008*
	Moderate OSAS	55	16.03 (1.305)	16.10		
	Severe OSAS	58	16.75 (1.508)	16.80		
Hematocrit	Control group	61	36.36 (5.614)	37.10	104.374	0.007*
	Moderate OSAS	55	47.54 (6.953)	47.20		
	Severe OSAS	58	136.65(663.303)	50.75		
Platelet	Control group	61			62.704	0.004*
	Moderate OSAS	55				
	Severe OSAS	58				
MPV	Control group	61	8.31 (1.134)	8.20		
	Moderate OSAS	55	11.65 (1.272)	11.30	109.714	0.007*
	Severe OSAS	58	12.78 (1.647)	12.55		
PDW	Control group	61	13.94 (2.231)	13.20		
	Moderate OSAS	55	17.61 (3.317)	16.50	53.694	0.008*
	Severe OSAS	58	15.12 (9.157)	13.15		
RDW	Control group	61	13.24 (1.285)	13.20		
	Moderate OSAS	55	14.17 (1.626)	13.50	11.006	0.004*
	Severe OSAS	58	13.77 (1.626)	14.20		

Kruskal Wallis Test, *: Statistically significant (P<0.05), SD: Standard Deviation, MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 3: Multiple comparison test results for initial hemogram values

Variant	Multiple groups	Test Value (SD)	*P*-value
Hemoglobin	Control-Mod. OSAS	-73.381 (9.360)	0.007*
	Control-Svr. OSAS	-91.431 (9.231)	0.005*
	Mod.OSAS-Svr. OSAS	-18.050 (9.474)	0.170
Hematocrit	Control-Mod. OSAS	-75.048 (9.364)	0.004*
	Control-Svr. OSAS	-86.777 (9.236)	0.006*
	Mod.OSAS-Svr. OSAS	-11.729 9.479)	0.648
Platelet	Control-Mod. OSAS	-64.187 (9.352)	0.003*
	Control-Svr. OSAS	1.506 (9.224)	0.99
	Mod.OSAS-Svr. OSAS	65.693 (9.466)	0.002*
MPV	Control-Mod. OSAS	-68.462 (9.357)	0.004*
	Control-Svr. OSAS	-93.120 (9.226)	0.006*
	Mod.OSAS-Svr. OSAS	-24.658 (9.471)	0.028*
PDW	Control-Mod. OSAS	-57.283 (9.351)	0.003*
	Control-Svr. OSAS	5.361 (9.223)	0.97
	Mod.OSAS-Svr. OSAS	62.645 (9.465)	0.001*
RDW	Control-Mod. OSAS	-30.704 (9.334)	0.007*
	Control-Svr. OSAS	-18.023 (9.326)	0.151
	Mod.OSAS-Svr. OSAS	12.681 (9.447)	0.539

*: Statistically significant (P<0.05) MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width, Mod: Moderate, Svr: Severe

Table 4: Friedman test results for hemogram values in moderate OSAS patient group

Variable	Time	Mean	*P*-value
Hemoglobin	Baseline	16.03	0.004*
	6th month	13.70	
	12th month	12.85	
Hematocrit	Baseline	47.54	0.003*
	6th month	42.14	
	12th month	39.09	
Platelet	Baseline	339818	0.005*
	6th month	279090	
	12th month	228818	
MPV	Baseline	11.65	0.004*
	6th month	7.39	
	12th month	6.54	
PDW	Baseline	17.61	0.006*
	6th month	16.41	
	12th month	16.07	
RDW	Baseline	14.17	0.473
	6th month	14.33	
	12th month	14.21	

*: Statistically significant (P<0.05), MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 5: Multiple comparison test results for hemogram values in the moderate OSAS group

Variable	Multiple groups	Test Value	*P*-value
Hemoglobin	Baseline- 6th month	1.018	0.008*
	Baseline- 12th month	1.982	0.007*
	6th month-12th month	0.964	0.005*
Hematocrit	Baseline-6th month	1.000	0.006*
	Baseline-12th month	1.945	0.007*
	6th month-12th month	0.945	0.005*
Platelet	Baseline-6th month	0.909	0.008*
	Baseline-12th month	1.764	0.004*
	6th month-12th month	0.855	0.003*
MPV	Baseline-6th month	0.964	0.007*
	Baseline-12th month	1.982	0.004*
	6th month-12th month	1.018	0.008*
PDW	Baseline-6th month	0.473	0.040*
	Baseline-12th month	0.727	0.005*
	6th month-12th month	0.255	0.546

*: Statistically significant (P<0.05) MPV: Mean platelet volume, PDW: Platelet distribution width.

Table 6: Friedman test results for hemogram values in severe OSAS patients

Variable	Time	Mean (SD)	Test Value	*P*-value
Hemoglobin	Baseline	16.75 (2.95)	102.448	0.004*
	6th month	13.61 (1.98)		
	12th month	12.71 (1.07)		
Hematocrit	Baseline	49.58 (2.95)	100.652	0.006*
	6th month	42.97 (1.96)		
	12th month	39.58 (1.09)		
Platelet	Baseline	248224 (1.34)	48.517	0.007*
	6th month	283965 (2.02)		
	12th month	312120 (2.64)		
MPV	Baseline	12.78 (2.97)	110.103	
	6th month	7.62 (2.02)		0.008*
	12th month	6.21 (1.02)		
PDW	Baseline	15.12 (1.81)	4.586	
	6th month	14.54 (2.21)		0.101
	12th month	13.99 (1.98)		
RDW	Baseline	13.77 (2.28)	15.799	
	6th month	13.35 (2.13)		0.009*
	12th month	13.09 (1.59)		

*: Statistically significant (P<0.05), MN Mean: Mean of Row Numbers, MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 7: Multiple comparison test results for hemogram values in severe OSAS patient group

Variant	Multiple groups	Test value	*P*-value
Hemoglobin	Baseline-6th month	0.914	0.008*
	Baseline-12th month	1.879	0.007*
	6th month-12th month	0.966	0.009*
Hematocrit	Baseline-6th month	0.862	0.008*
	Baseline-12th month	1.853	0.007*
	6th month-12th month	0.991	0.009*
Platelet	Baseline-6th month	-0.672	0.005*
	Baseline-12th month	-1.293	0.004*
	6th month-12th month	-0.621	0.007*
MPV	Baseline-6th month	1.000	0.06*
	Baseline-12th month	1.948	0.005*
	6th month-12th month	0.948	0.008*
RDW	Baseline-6th month	0.155	0.971
	Baseline-12th month	0.698	0.007*
	6th month-12th month	0.543	0.009*

*: Statistically significant, MPV: Mean platelet volume, PDW: Platelet distribution width

The hemogram values of moderate and severe OSAS patients under treatment are presented in Tables 8 and 9. There was no statistically significant difference in platelet and PDW values between baseline and post-treatment hemogram results in patients with moderate and severe OSAS (P=0.334, P=0.089, respectively). All other hemogram values (Hb, Htc, MPV, RDW) were statistically different between at least two measurements. In the multiple comparison test analysis performed to compare the variables at baseline and 6th month of PAP therapy between moderate and severe OSAS groups, the only non-significant result was detected in RDW values (P=0.994). All other hemogram values were significantly different between baseline, 6th and 12th month measurements.

Table 10 presents the analysis performed to determine the correlation between RDW, apnea hypopnea index (AHI) of moderate and severe OSAS patients under treatment, minimum oxygen saturation, average oxygen saturation and ODI (Oxygen desaturation index). A positive and statistically significant correlation was found between baseline and 6th month RDW values, and 6th month and 12th month RDW values (Rho = 0.427, P<0.01). A negative statistically significant correlation of 15.5% was found to exist between 12th month RDW and ODI (Rho=-0.155, P<0.05). AHI was seen to negatively correlate with minimum O_2 saturation and mean O_2 saturation, and strongly positively correlate with ODI by 94.7%. Finally, mean O_2 saturation was found to significantly negatively correlate with ODI (Rho=-0.539, P<0.01).

Table 8: Friedman test results for hemogram values in moderate and severe OSAS patient groups

Variable	Time	Mean (SD)	Test Value	*P*-value
Hemoglobin	Baseline	16.40 (2.96)	211.218	0.008*
	6th month	13.65 (2.00)		
	12th month	12.78 (1.04)		
Hematocrit	Baseline	48.54 (2.96)	204.520	0.007*
	6th month	42.97 (1.99)		
	12th month	39.58 (1.06)		
Platelet	Baseline	248224 (2.09)	2.195	0.334
	6th month	283965 (2.02)		
	12th month	312120 (1.89)		
MPV	Baseline	12.78 (2.98)	218.071	
	6th month	7.62 (2.02)		0.006*
	12th month	6.21 (1.02)		
PDW	Baseline	15.12 (2.10)	4.832	
	6th month	14.54 (2.07)		0.089
	12th month	13.99 (1.87)		
RDW	Baseline	13.77 (2.10)	8.783	
	6th month	13.35 (2.13)		0.012*
	12th month	13.09		

*: Statistically significant (P<0.05), MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 9: Multiple comparison test results for hemogram values in moderate and severe OSAS patient groups

Variable	Multiple groups	Test value	*P*-value
Hemoglobin	Baseline-6th month	0.965	0.008*
	Baseline-12th month	1.929	0.006*
	6th month-12th month	0.965	0.009*
Hematocrit	Baseline-6th month	0.969	0.007*
	Baseline-12th month	1.898	0.005*
	6th month-12th month	0.929	0.009*
MPV	Baseline-6th month	0.982	0.008*
	Baseline-12th month	1.965	0.006*
	6th month-12th month	0.982	0.009*
RDW	Baseline-6th month	-0.031	0.994
	Baseline-12th month	0.323	0.046*
	6th month-12th month	0.354	0.023*

*: Statistically significant (P<0.05), MPV: Mean platelet volume, RDW: Erythrocyte distribution width

Table 10: Correlation analysis results to determine the correlation between the variants

	RDW at the 6th month	RDW at the 12th month	Minimum O_2 saturation	Apnea-hypopnea index	Mean O_2 saturation	ODI
RDW Baseline	0.458** (P<0.01)	0.138 0.069	0.1 0.191	-0.067 0.377	-0.108 0.156	0.098 0.200
RDW 6th month		0.427** (P<0.01)	-0.085 0.264	0.056 0.460	-0.043 0.569	-0.111 0.144
RDW 12th month			-0.123 0.105	0.021 0.783	0.184 0.015	-0.155 0.042
Apnea-hypopnea index				-0.684** (P<0.01)	-0.510** (P<0.01)	0.947** (P<0.01)
Minimum O_2 Saturation					0.526** (P<0.01)	-0.719** (P<0.01)
Mean O_2 Saturation						-0.539** (P<0.01)

**: Statistically significant (P<0.01) , RDW: Red cell distribution width, ODI: Oxygen desaturation index

Discussion

In this study, we aimed to investigate the relationship between severity and MPV, PDW, RDW, Hb, and platelet count. The secondary aim was to investigate the effects of inflammation in OSAS and its response to PAP treatment. MPV, PDW and RDW were considered as markers of inflammation.

New indices related to erythrocytes and platelet counts were investigated and their relationship with MPV, PDW and RDW gained importance [14]. Platelet size measured by MPV is the best-known platelet indice and a sign of platelet activity and aggregation. Another sign would be the platelet distribution width (PDW), which is obtained from direct flow cytometric measurements of platelet cell volume. RDW is a dimensional measure of variability of circulating erythrocytes. Impaired eryhtropoiesis and increased eryhtrocyte destruction lead to greater heterogeneity and subsequentially, higer RDW. These parameters are useful clinical markers of various cardiovascular and thrombotic diseases [15].

In our study, MPV, an indicator of platelet activation, was significantly higher in patients with both moderate and severe OSAS at baseline compared to the control group.

Decreases in MPV values at the 6th and 12th months compared to baseline values after PAP treatment were statistically significant in both groups and the decrease in MPV correlated with AHI and desaturation index.

In a previous study, a relationship was found between MPV and cardiovascular disease risk and prognosis [16]. PAP is known to reduce cardiovascular risks by reducing ambulatory blood pressure and arterial stiffness while increasing the sensitivity of arterial baroreflex [17]. In addition, PAP reduces systemic inflammation, airway obstruction and hypoxia, and decreases levels of OSAS-mediated inflammatory mediators [18]. Similar to our results, it was found that a 6-month-long PAP treatment significantly reduced MPV values in patients with severe OSAS [19,20]. Decreased MPV can be explained by reduced hypoxia and inflammation.

Günbatar at al. [21] investigated the relationship between OSAS and MPV values and found that MPV values were similar in OSAS and control groups. However, subjective tests were applied to control group patients and polysomnography (PSG) was not performed. One of the major differences of our study was that the control group was selected from patients with AHI <5 based on the results of PSG examination.

Increased inflammatory markers causing inflammation have been reported in OSAS patients [22]. This situation is one of the presumed links between OSAS and increased cardiovascular morbidity. Inflammation is strongly associated with pro-inflammatory cytokine production, ineffective erythropoiesis, tumor necrosis factor alpha, interleukin 6, which renders bone marrow erythroid progenitors susceptible to erythropoiesis, prevents erythrocyte maturation and promotes anisocytosis [23]. Other mechanisms responsible for increased thrombotic risk in OSAS patients, which should not be ignored, are obesity and concurrently reduced exercise capacity [24].

In our study, no statistically significant difference was found in the BMI values of patients before and after treatment. The fact that BMI values do not affect the results of the study is valuable. RDW is hypothesized to change in coronary artery diseases, in which erythropoiesis is disrupted due to chronic inflammation or increased due to erythropoietin production [25].

In our study, RDW values were significantly higher in patients with moderate OSAS compared to controls at baseline, but the decrease in RDW at 6th and 12th months of treatment was not significant. In the severe OSAS group, the initial RDW values were non-significantly higher than the control group and there was a significant decrease in RDW between the 6th and 12th months.

There is no consensus in the literature about the RDW expression in OSAS. Some authors have shown that RDW values are higher in OSAS patients than controls [25,26], while other studies have reported that the RDW values of OSAS patients, indiviuals with simple snoring and control group were similar. Similar to our study, there are studies reporting that patients with OSAS have higher RDW values than controls, but there is no correlation between OSAS severity and RDW [26]. In our study, RDW was significantly increased regardless of the severity of OSAS, but it was associated with OSAS severity after PAP treatment and there was a more significant decrease in RDW value in the second six-month period. The precise mechanism of these results is unclear; however, this may be related to the presence of chronic inflammation In fact, chronic inflammation increases RDW by increasing the deformability of the red blood cell membrane and changes erythropoiesis [27]. In this sense, the strongest correlation of 94.7% existed between AHI and ODI values. Finally, there is a statistically significant negative relationship between the average O_2 saturation and ODI.

In our study, PDW values were significantly higher in patients with moderate OSAS compared to controls at baseline and a significant decrease in PDW was observed when the baseline and 6th month and baseline and 12th month measurements of treatment were compared. In the severe OSAS group, the initial PDW values were non-significantly higher than the control group, and there was no statistically significant difference between the 6th and 12th month measurement values. Our results regarding the tendency of MPV and PDW to increase with OSAS severity can be explained by increased platelet activation [28]. MPV is the best known of platelet parameters, whereas PDW is less documented and derived from direct flow cytometric measurements of platelet cell volume. Interestingly, there is no data and acceptance to show cut-off values for MPV and PDW and to diagnose increased platelet activation in patients with OSAS.

Bülbül and collegues [29] suggested that the optimal PDW value that differentiates non-apneic controls from patients with OSAS is 16.62. However, a consensus is yet to be reached. Due to the quantitative nature of PDW in the assessment of platelet size and volume, its use remains limited [28,29].

Initially, Hb and Htc values were significantly higher in patients with moderate and severe OSAS compared to the control group, and the decrease in values at 6 and 12 months after treatment was statistically significant. Platelet values were higher in both moderate and severe groups than that of the control group, but statistically significant only in the moderate group and the decreases at 6 and 12 months after PAP treatment were significant in both groups.

Chronic intermittent hypoxia with an increase in hematological parameters causes an increase in erythropoietin expression, which induces erythropoiesis [28].

Correction of respiratory events with PAP and associated hypoxia and inflammation may result in decreased RDW, hemoglobin, and hematocrit as in our study. These findings contradict the expected increase in RDW following a decrease in hemoglobin. Therefore, RDW may be affected by PAP regardless of hemoglobin levels due to the beneficial effects of PAP on hypoxia, which may reduce RDW.

Significant decrease in MPV, hemoglobin and hematocrit levels in both OSAS groups after PAP treatment in OSAS is consistent with similar studies [29,30]. In our study, there was no statistically significant difference between the baseline and post-treatment platelet and PDW values, in which patients with moderate and severe OSAS were evaluated together. This can be attributed to the decrease in mean values of platelets and PDW in the severe OSAS group. In all other hemogram values (Hb, Htc, MPV, RDW), a statistically significant difference was found between at least two

measurements when the control group and the medium-severe group were compared.

In the multiple comparison test analysis of the variables with statistically significant differences in the moderate-severe OSAS group, no statistically significant difference was found between the initial and 6th month-RDW values. All other hemogram values were statistically different between baseline, 6th and 12th month measurements. Our study demonstrated the importance of hematological assessment as a complementary tool for diagnosis and response to treatment in OSAS patients.

Limitations

The inclusion of only the male patients in the study is the limitation of our study. The findings of this study must be evaluated in light of this limitation.

Conclusion

RDW and PDW values can be used as indicators of OSAS severity. They are easy and inexpensive tools to assess OSAS patients initially and after PAP treatment in laboratories with long waiting lists.

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