Response of Blood Parameters to CPAP Treatment in Patients with Obstructive Sleep Apnea

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ABSTRACT

Introduction: Many studies have evaluated the relationship between the NLR and PLR in patients with obstructive sleep apnea (OSA), and have shown that they are related to inflammation. We evaluated whether 3 months of continuous positive airway pressure (CPAP) treatment in patients with moderate to severe OSA without any comorbidities would affect the NLR and PLR values.

Methods: Full blood count parameters were evaluated before and after 3 months of CPAP treatment in patients with a diagnosis of moderate to severe OSA without any comorbidities.

Results: Twenty-nine patients (18 [62.1%] males) were enrolled. The mean body mass index (BMI) was 34.85±5.75 kg/m², the apnea-

hypopnea index score was 49.85±27.42, and CPAP was 9.34±1.77. No significant change in BMI was observed after the third month of treatment. Although the Epworth Sleepiness Scale (ESS) score decreased significantly (p=0.000), no changes were observed in the NLR, PLR, or C-reactive protein level (p>0.05). Mean platelet volume and red blood cell distribution width changed significantly after treatment (p=0.01; p<0.001).

Conclusions: The NLR and PLR did not change after CPAP treatment in patients with moderate to severe OSA without any comorbidities.

Key words: Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, positive airway pressure, obstructive sleep apnea

Cite this article as: Özdemir C, Sökücü S, Aydın Ş, Önür ST, Kara K. Response of Blood Parameters to CPAP Treatment in Patients with Obstructive Sleep Apnea. Arch Neuropsychiatry 2019;56:182-185.

INTRODUCTION

Many different proinflammatory cytokines have been studied in patients with obstructive sleep apnea (OSA). The neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are recently described systemic inflammation indicators. These parameters can be determined by a simple complete blood count (CBC) analysis of peripheral blood. The NLR and PLR increase in different types of systemic inflammation-related diseases, which helps predict the prognosis of the disease processes, particularly for some cancers (1-3).

The relationship of these parameters with disease severity has been described in patients with obstructive sleep apnea syndrome (OSAS) (4-7). However, no study has evaluated changes in the NLR or PLR after continuous positive airway pressure (CPAP) treatment. The aim of our study was to determine how the NLR and PLR can be used as a clinical tool to assess the treatment response in patients indicated for CPAP without any comorbidities.

METHODS

Our hospital ethics committee approved this study (2015/35/3675), and informed consent was obtained from all subjects.

All patients who underwent overnight polysomnography (PSG) testing, and provided blood samples between January 2015 and December 2015, were recruited for the preliminary evaluation. In total, 220 patients treated with CPAP were screened and 50 patients who fulfilled the inclusion criteria were enrolled. All 50 patients were re-evaluated at the 3-month visit and blood samples were taken from the patients who complied with treatment. Exclusion criteria were diabetes mellitus, dyslipidemia, cardiovascular disease or hypertension, any known malignancy, thyroid dysfunction, chronic hepatic disease, renal failure, or any infectious disease within the past month. Hypercholesterolemia was defined as having a previous diagnosis for hypercholesterolemia, lipid-lowering medication use or a serum total cholesterol >240 mg/dL and low density lipoprotein (LDL) cholesterol >160 mg/dL. The presence of hypertension (HT) was defined as; having a previous HT diagnosis, antihypertensive medication use or a blood pressure >140/90 mmHg. The people who received oral antidiabetic drugs or insulin therapy, and those diagnosed

with DM according to the American Diabetes Association guide were considered as DM patients.

Demographic variables, such as age, sex, neck circumference, waist circumference, hip circumference, body mass index (BMI), total sleep time, sleep efficiency, apnea-hypopnea index (AHI) score, average saturation, oxygen desaturation index (ODI), time spent with arterial oxygen saturation <90% (min), and CPAP treatment status were documented.

Blood serum variables, such as the white blood cell (WBC) count, hemoglobin (Hb) level, red cell distribution width (RDW), mean platelet volume (MPV), C-reactive protein (CRP) concentration, and neutrophil, lymphocyte, and platelet counts were all recorded before and 3 months after treatment. The NLR was calculated as the ratio of neutrophil count to lymphocyte count and the PLR was calculated as the ratio of platelet count to lymphocyte count.

The CBC values were measured in the study group 1 day after the PSG evaluation, and after 3 months of CPAP therapy when the patients attended follow-up. No intervention other than CPAP treatment was introduced at follow-up. Morning venous blood samples were drawn from participants after an overnight fast >8 h (07:00–08:00) and analyzed within 1 hour. The neutrophil, lymphocyte, and platelet counts were determined using an Abbott Cell-Dyne 3700 System (Abbott Diagnostics, Santa Clara, CA, USA); a differential count was included as part of the CBC count. Serum biochemical parameters were measured using a Beckman Coulter AU 2700 plus instrument (Olympus, Tokyo, Japan).

Overnight PSG was performed using an Embla A-10 data acquisition and analysis system (Medcare Flaga, Reykjavik, Iceland) in the attended setting at a sleep laboratory under baseline conditions. The following physiological parameters were monitored: brain electrical activity on electroencephalography (electrodes placed at C4-A1, C3-A2, O2-A1, and O1-A2); eye movements on electro-oculography; submental muscle activity on electromyography; ribcage and abdominal effort by respiratory inductive plethysmography (Xact-Trace; Medcare Flaga); body position by a calibrated sensor; snoring sounds by a piezoelectric sensor; oronasal flow by a nasal pressure cannula (Medcare Flaga); Hb oxygen saturation (SpO₂) by pulse oximetry (8000J; Nonin Medical, Plymouth, MN, USA) with the averaging time set at 3 s; and electrical activity of the heart by electrocardiography (lead II) sampled at 512 Hz. Sleep stages and arousals were scored according to standard criteria by a skilled pulmonary physician using the Somnologica Studio software package (Medcare Flaga). Apnea and hypopnea was defined by the American Academy of Sleep Medicine (ASSM) criteria.

Patients underwent a second night of PSG with CPAP for titration purposes. The optimal CPAP level was determined in the laboratory under supervision by a technician, and was defined as the lowest pressure at which the fewest respiratory events and arousals occurred with the highest sleep efficiency.

All patients with moderate to severe OSA were treated with fixed pressure nasal CPAP. Data from the CPAP machines were downloaded after 3 months to assess treatment adherence. The number of hours logged on the integrated time recorder was evaluated. Patients were considered CPAP compliant if they used CPAP ≥4 h/night for 5 days per week; all such patients were included in the study. Symptoms of snoring and daytime sleepiness were evaluated using the Epworth Sleepiness Scale (ESS).

Data were analyzed with SPSS for Windows software (SPSS Inc., Chicago, IL, USA). All variables were tested for normality of the distribution

using the Kolmogorov-Smirnov test. Continuous variables with normal distributions are expressed as means ± standard deviation. Continuous variables with non-normal distributions are summarized as medians (interquartile range). Categorical variables are expressed as numbers (percentages). The NLR and PLR were not normally distributed, so the Wilcoxon test was used to compare values before and after CPAP treatment. Correlations between continuous variables, and those between categorical variables, were evaluated by Pearson's and Spearman's correlation analyses, respectively. A p-value <0.05 was considered significant.

RESULTS

Of the 220 patients screened, 50 were re-evaluated after 3 months of treatment. Twenty-nine patients (18 males [62.1%]; mean age, 46±10.11 years) were treatment-compliant and were evaluated. Demographic variables of the patients and PSG findings for the first night evaluation are given in Table 1. The mean AHI score of the patients was 49.85±26.42. Mean CPAP ordered after the second night of the study was 9.34±1.78. The ESS score changed significantly after treatment (p=0.001). BMI was not different between the groups.

No significant difference was found in the WBC count, Hb level, neutrophil, lymphocyte, or platelet counts, CRP concentration, or NLR or PLR after treatment. However, RDW and MPV changed significantly after treatment (p=0.001 and p=0.010; Table 2).

CRP values before treatment were correlated with the NLR after treatment (p=0.035). No other correlations were observed between the CRP concentration, WBC count, NLR, or PLR before treatment. The NLR was correlated with the ODI and AHI (p=0.042 and p=0.032), whereas the PLR was correlated with minimum desaturation (p=0.041).

Table 1. Demographical properties of the patients and polysomnographic findings

Age	46±10.11	22–67
Sex	18 male (62.1%)	18 m/11f
BMI	34.85±5.75	25.22–49.02
Neck circumference	40.20±2.9	33–47
Waist circumference	107.62±10.91	87–132
Hip circumference	112.72±11.16	142–93
Total sleep time	365.82±72.7	195.5–463
Sleep efficiency (%)	84.76±8.10	70–95.9
AHI	49.85±26.42	15–120
Average saturation	89.41±5.71	68–96.2
Minimum O2 saturation	73.72±11.67	45–88
Desaturation index	38.1 (IQR: 29.35)	12.9–118.5
Time spent <90% (min)	74.1 (IQR: 85.75)	0.4–355.1
CPAP pressure	9.34±1.78	6–12

BMI, body mass index; AHI, apnea-hypopnea index; CPAP, continuous positive airway pressure.

Table 2. Values of patients before and 3 months after CPAP treatment

Value	Before treatment	3 rd month of treatment	p
BMI	34.85±5.75	35.51±5.88	0.059
ESS	11.28±5.37	0.55±0.91	0.001
Hemoglobin	14.83±0.98	14.64±1.19	0.289
Neutrophil	4.42±1.49	4.69±1.33	0.163
Lymphocyte	2.89±0.69	3.06±0.91	0.127
Platelet	247.38±53.61	251.41±43.20	0.589
NLR	1.56±0.47	1.63±0.58	0.905
PLR	90.82±29.39	88.44±27.1	0.524
CRP	4.5±2.76	4.09±1.75	0.624
RDW	12.36±0.76	13.16±0.72	0.001
MPV	9.25±1.55	9.66±1.22	0.010

BMI: body mass index, ESS: Epworth sleep scale, NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, CRP: C reactive protein, RDW: red cell distribution width, MPV: mean platelet volume.

DISCUSSION

We evaluated CBC parameters in patients with OSA because it is an inexpensive, simple, and widely available method. However, we found no change in the NLR or PLR after 3 months of CPAP treatment in patients with OSA without any comorbidities.

Sleep-disturbed breathing is characterized by repetitive episodes of upper airway collapse, which causes low-level systemic inflammation (8). Although the exact mechanism underlying these health problems remain unclear, chronic inflammation has been implicated in their pathogenesis (9). It is unclear if the inflammation is the result or cause of these pathologies, but there seems to be a bidirectional relationship between them (10).

The association between OSA and CRP levels is inconsistent in the literature. Some studies have reported a relationship between OSAS severity and CRP level (11, 12), whereas others were unable to demonstrate any such relationship (4, 13). We did not find a change in the CRP level before versus after treatment.

The NLR and PLR of peripheral blood are markers of systemic inflammation (5). Evaluating the NLR in different types of diseases may predict the progression and prognosis of disease processes, particularly some types of cancers (3). As a variety of diseases, metabolic syndromes, and drugs can affect the NLR, we excluded patients with these comorbidities. In a recent study, the PLR decreased in patients with OSAS compared to a control group and was related with disease severity. In the same study, no significant correlation was detected between the AHI and NLR values, but nocturnal time spent with arterial oxygen saturation <90% increased as the NLR increased (6). Another study reported that the NLR was significantly higher in patients with cardiovascular disease than in those without. In that study, significant correlations were observed between the NLR and the AHI, mean SaO₂, and ODI (7).

Chronic intermittent hypoxia increases sympathetic activity and causes systemic inflammation. Some indicators of inflammation, such as CRP, tumor necrosis factor- α and interleukin-6, decrease with CPAP therapy (12). Although NLR data are controversial regarding any association with OSA, most studies show a relationship. We found no significant change in the NLR or PLR values after CPAP treatment, although the ESS changed significantly. This was explained by the exclusion of patients with comorbidities from the study. The pathogenesis of inflammation is not clearly understood but is thought to be responsible for the cardiovascular complications seen in patients with OSA (14).

A major limitation of this study was the number of patients included. Although we screened 220 patients, we only enrolled 50 without defined comorbidities, and only 29 of these were compliant with the CPAP treatment. Further studies comparing patients compliant with CPAP therapy to noncompliant patients, and including more patients, are needed.

CONCLUSION

The inflammatory markers PLR and NLR did not help predict the effect of CPAP treatment on systemic inflammation in patients with OSA. Systemic inflammation is an important mechanism underlying OSA and the effect of CPAP treatment on inflammation is important. These results indicate that the PLR and NLR cannot be used to follow-up CPAP treatment effects in clinical practice in patients with OSAS.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Yedikule Thorax Diseases and Surgery Training and Research Hospital.

Informed Consent: Informed consent was obtained from all subjects.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - ŞA, SNS; Design- ŞA, SNS, CÖ; Supervision- ŞA, CÖ Resource- ŞA, STÖ, NKP; Materials- ŞA; Data Collection and/or Processing - ŞA, STÖ, OA; Analysis and/or Interpretation - ŞA, NKP, OA; Literature Search- ŞA, OA, STÖ; Writing Manuscript - CÖ, ŞA; Critical Review - ŞA, CÖ, SNS.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: This study was not financially supported by any individual or organization.

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