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Research article

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Evaluation of the relationship between polysomnography parameters, physical examination findings and oxidative stress parameters in patients with obstructive sleep apnea syndrome

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Necmettin Erbakan University, Ethic Committee of Meram, Number: 2013/32
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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Abstract

Background/Aim: Oxidative stress status in obstructive sleep apnea syndrome (OSAS) is well discussed in the literature. Oxidative stress levels increase, and antioxidant system activity decreases in OSAS patients. However, the change in oxidative stress status in positional (pOSAS) and non-positional (npOSAS) OSAS has not been adequately examined. The aim of this study was to compare OSAS patients' polysomnographic (PSG) parameters and oxidative stress capacities with the structural and functional properties of the upper respiratory tract.

Methods: This study was designed as prospective case-control study and patients were divided into three groups as control, pOSAS and npOSAS according to their PSG findings. Ear nose throat examinations including rhinomanometry test and oxidative stress blood parameter tests were conducted to all patients. Variables among the groups were compared.

Results: All PSG parameters were significantly worse in the OSAS groups than the control group (P<0.05). The mean AHIs of the pOSAS and npOSAS groups were 21.7 (16.5), and 31.2 (21.9), respectively. AHI, desaturation number and minimal SpO_2 values of the pOSAS group were significantly lower compared to the npOSAS group (P=0.043, P=0.017 and P=0.006, respectively). TNF α was significantly lower and adiponectin was significantly higher in the pOSAS group compared to the npOSAS group (P=0.001, P<0.001 respectively). The two groups were similar in terms of rhinomanometry results (P=0.888).

Conclusion: The lack of difference between pOSAS and npOSAS patients in terms of rhinomanometry results may indicate that the nose may not play a decisive role in the differentiation of these groups. Only OSAS severity may not be a determinant factor in oxidative stress balance in patients with pOSAS and np OSAS.

Keywords: Obstructive sleep apnea, Oxidative stress, Rhinomanometry

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Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of apnea during sleep and is one of the most common health problems in the community [1]. Changes in sleep position can affect the occurrence and severity of obstructive sleep apnea. Apnea frequency and duration are affected by body position in approximately 56% to 75% of OSAS patients [2]. For the first time, Cartwright [3] defined positional OSAS (pOSAS) as a 50% or more difference in the hourly apnea index between the supine position and lateral lying positions. Depending on the differences in the diagnostic criteria, it has been reported that 53 to 77.4 % of all OSAS patients may be pOSAS [4].

Changes in blood saturation during sleep in OSAS patients may cause the oxidant-antioxidant balance to deteriorate in favor of oxidant molecules due to recurrent hypoxic periods. Chronic OSAS can result in mitochondrial dysfunction caused by tissue hypoxia, increased regulatory hormones, and altered adipocytokine patterns [5, 6]. Diseases with serious morbidity and mortality risk such as hypertension, diabetes mellitus and obesity have an increasing association with OSAS [1, 7]. It can be said that the relationship between OSAS and metabolic disorders is complex. The reason for this complex relationship is that obesity can be both the cause and effect and a confounding factor in OSAS [5]. In this study, we investigated the polysomnography (PSG) and some biochemical parameters to examine both the role of oxidative stress mechanisms and obesity in OSAS. Therefore, we tried to reveal the distribution of these parameters in OSAS subgroups and their relationship with PSG data, after dividing OSAS patients into pOSAS and non-positional OSAS (npOSAS) groups according to the PSG parameters.

Materials and methods

Patients who visited our hospital's sleep outpatient clinic with complaints of snoring and wanted to participate in our study voluntarily were included in this study. According to the PSG results, the patients were divided into three categories [3]. Those with an apnea-hypopnea index (AHI) <5 were included in the control group. Patients with AHI ≥5 in PSG were considered OSAS patients, who were divided into two groups according to PSG data. If the AHI values of the patients on supine position were 2 times or more than the AHI values on lateral position, the patients were considered to have pOSAS, and if the supine AHI values were less than 2 times the AHI values measured on lateral positions, they were considered to have npOSAS.

First, the body mass index (BMI)(kg/m^2) of the patients was calculated by measuring the height and weight. Neck circumference measurement was recorded from the cricothyroid membrane. Epworth Sleepiness Scale was used to determine the daytime sleepiness status of the patients. After ear nose throat examinations of the patients, anterior rhinomanometry test was performed and 3 tubes of venous blood were obtained in the morning and stored at -80°C.

Polysomnographic evaluation

Standard polysomnography was performed with the digital polysomnographic system (Somnoscreen plus, Somnomedics GmbH, Germany) all night in the sleep laboratory. Four-channel (C1A2, C2A1, O1A2, O2A1) electroencephalography (EEG), 2-channel (right and left) electrooculography (EOG), submental electromyelography (EMG) electrodes were placed on the patients for sleep assessment. Air flow in the mouth and nose were recorded by placing an oro-nasal flow meter and thermistor in the nose for respiratory monitoring, thorax and abdominal movements were recorded by placing a thoraco-abdominal effort sensor. In addition, hemoglobin oxygen saturation and heart rate were monitored by pulse oximetry. Leg movements were recorded with the EMG sensor placed on the anterior tibialis muscle. Sleep stages and respiratory events were scored manually according to AASM scoring criteria.

Anterior rhinomanometry test

Rhinomanometry measurements were made with the Rhino 30 (Lenzkirch / Germany) device after the patient rested in a sitting position for 20 minutes in a quiet environment. Nasal resistance measurements were performed with the active anterior technique in accordance with the International Rhinomanometry Standardization Committee. After the right and left nasal cavity measurements were made separately, the total nasal resistance was obtained. The measurements were evaluated at 150 Pascal, as recommended by the standardization committee.

Evaluation of blood parameters

Blood samples obtained from the patients and control groups into straight tubes were centrifuged in a Hettich centrifuge device at 4000 rpm for 10 minutes, and the serums were separated. Separated serum samples were stored at -80 ° C until the end of the study. Total Antioxidant Status (TAS), Malondialdehyde (MDA), Leptin, Adiponectin and Tumor Necrosis Factor alpha (TNFα) parameters were investigated.

TAS was calculated according to absorbance concentration calibration graphs using Bio-rad Microplate absorbance reader xMark (Bio-rad Laboratories, California, United States) system (Rel Assay Diagnostics, Gaziantep, Turkey). MDA levels were measured using the thiobarbituric acid reactivity method. MDA, a product of fatty acid peroxidation, reacts with thiobarbituric acid in a hot and acidic environment, the absorbance of the reacting colored complex was calculated in micromol/L using the Bio-rad Microplate absorbance reader xMark (Bio-rad Laboratories, California, United States) system at 532 nm. Leptin (Boster, California, United States), Adiponectin (Assaypro, Missouri, United States), and TNF α (Boster, California, United States) levels were calculated with ELISA kits according to absorbance concentration calibration graphs using Biotek (Biotek, Vermont, United States) ELX 50 microplate washer and ELX 800 absorbance reader system.

Statistical analysis

Continuous variables were expressed as mean (SD), and categorical data, as numbers and percentages. In the intergroup analysis of continuous variables, normality analyses were performed using the Kolmogorov-Smirnov goodness of fit test. The One-way Anova test (Post hoc: LSD) was used for comparisons of the data in three groups and above, since the data were suitable for normal distribution. Comparison of categorical data was made using the chi-square test. Analyses were

performed with IBM SPSS version 22. (IBM Corporation, Amonk, NY, USA). Statistical significance level was P <0.05.

Sample size

Based on the case-control study conducted by Ursavas et al. [8] whose purpose was to investigate the relationship between plasma adiponectin, leptin, ghrelin, resistin levels and OSAS, at an alpha error (p value) of 0.05 and 1-beta error (Power) of 0.80, 15 individuals per group would be sufficient for testing the absence hypothesis. G Power Statistics Program version 3.1.9.4 (Universität Düsseldorf, Germany) was used for the analysis [9].

Results

In this study in which 71 patients were included, there were 25 patients in the control group, 24 patients in the pOSAS group and 22 patients in the npOSAS group. Demographic and physical examination data of the patients are shown in Table 1. The BMI, neck circumference and rhinomanometry values of the control group were significantly lower than the OSAS groups (P=0.001, P=0.001 and P<0.001, respectively). In addition, the control group consisted of younger patients than the OSAS group. There was no significant difference between pOSAS and npOSAS groups in terms of examination physical findings except for Epworth scale scores (P>0.05). PSG was sufficient in terms of sleep efficiency in all three groups (> 70%). All PSG parameters were significantly better in the control group than both OSAS groups (P<0.05). AHI, desaturation number and minimal SpO2 values of pOSAS group were significantly lower than npOSAS group (P=0.043, P=0.017 and P=0.006, respectively) (Table 2).

Table 1: Distribution of demographic data and physical examination findings according to the groups

Parameters	Control Mean (SD) (n=25)	pOSAS Mean (SD) (n=24)	npOSAS Mean (SD) (n=22)	*P*-value
Age (years)	37.7 (8.4[a])	45.0 (9.6)	46.4 (10.9)	0.006*
Female/Male	6/19	6/18	5/17	0.984**
BMI (kg/m2)	25.0 (2.33[a])	28.0 (6.68)	30.1 (3.08)	0.001*
Neck Circumference (cm)	37.4 (2.34[a])	39.6 (3.99)	41.3 (3.25)	0.001*
Epworth Scale	4.7 (2.26[a])	6.8 (3.82[a])	9.5 (5.4[a])	0.001*
Rhinomanometry (Pascal)	0.30 (0.11[a])	0.61 (0.09)	0.60 (0.24)	<0.001*

* One-way ANOVA Test (Post hoc: [a] LSD), ** Chi-square Test

Table 2: Distribution of polysomnography parameters according to the groups

Parameters	Control Mean (SD) (n=25)	pOSAS Mean (SD) (n=24)	npOSAS Mean (SD) (n=22)	*P*-value
Total Sleep Time (Second)	331 (29.1[a])	300 (58.0)	288 (82.3)	0.045*
Sleep Efficiency (%)	75.1 (8.0)	74.5 (10.8)	74.9 (13.9)	0.982*
AHI	2.4 (0.9[a])	21.7 (16.5[a])	31.2 (21.9[a])	<0.001*
Desaturation Number	1.2 (0.9[a])	16.6 (16.2[a])	26.3 (17.0[a])	<0.001*
Minimal SpO_2	89.3 (1.4[a])	82.5 (5.5[a])	78.2 (6.6[a])	<0.001*
Average SpO_2	94.0 (1.5[a])	90.7 (2.3)	90.1 (2.2)	<0.001*
SpO_2 <90(%)	0.6 (0.6[a])	26.3 (31.1)	37.1 (28.8)	<0.001*

* One-way ANOVA Test (Post hoc: [a] LSD)

There was no significant difference between the OSAS groups in terms of TAS levels, while the TAS levels of the control group were significantly higher than the pOSAS group (P=0.006). While there was no significant difference between OSAS groups in terms of MDA, MDA levels of the control group were significantly lower than OSAS groups (P=0.058, P<0.001 respectively). TNF α was significantly higher in npOSAS group than the pOSAS and control groups (P<0.001). There was no significant difference in terms of TNF-α between pOSAS and control groups (P=0.319). Adiponectin levels were significantly lower in npOSAS group than pOSAS and control groups (P<0.001). There was no significant difference between OSAS groups in terms of leptin levels (P=0.390). However, the leptin levels of the control group were significantly lower than the OSAS groups (P<0.001) (Table 3).

Table 3: Distribution of blood parameters according to the groups

Parameters	Control Mean (SD) (n=25)	pOSAS Mean (SD) (n=24)	npOSAS Mean (SD) (n=22)	*P*-value
TAS	0.55 (0.33[a])	0.29 (0.18[a])	0.42 (0.17)	0.006*
MDA (TBARS)	7.15 (1.93[a])	13.94 (5.92)	17.07 (7.39)	<0.001*
TNF α	5.12 (2.01)	6.35 (3.06)	10.55 (6.69[a])	<0.001*
Adiponectin	6.03 (1.85)	6.24 (1.25)	3.56 (1.09[a])	<0.001*
Leptin	7.43 (3.87[a])	16.80 (7.08)	15.21 (7.30)	<0.001*

* One-way ANOVA Test (Post hoc: [a] LSD)

A negative correlation was found between AHI and TAS (r=-0.249, P=0.036), BMI and adiponectin (r=-0.345, P=0.003), TAS and MDA (r=-0.236, P=0.048) and leptin and TAS (r=-0.278, P=0.019), while a positive correlation was detected between AHI and MDA (r=0.439, P=0.00), BMI and TNF α (r=0.371, P=0.001) and leptin (r=0.379, P=0.001).

Discussion

pOSAS constitutes an important part of OSAS. pOSAS patients tend to be younger than npOSAS patients, have lower BMI, and shorter neck and waist circumferences. They experience less respiratory anomalies during sleep, most pOSAS patients (70-80%) have mild or moderate OSAS [4,10]. In our study, there was no significant difference between the pOSAS and npOSAS groups in terms of demographic data and physical examination findings except for the Epworth scale scores. Rhinomanometry results were similar in both OSAS groups. There was a significant difference between OSAS groups in terms of some PSG parameters, and AHI, desaturation number and minimal SpO2 values of pOSAS group were significantly lower than npOSAS group. In other words, our pOSAS patients also consisted of mild and moderate OSAS patients.

Many studies have shown that oxidative stress levels increase, and antioxidant system activity decreases in OSAS patients [6, 11-13]. As we have already mentioned, OSAS can be seen with various clinical conditions that have a devastating effect on vascular reactivity such as hypertension, cardiovascular diseases, metabolic syndrome, and insulin resistance. This makes it difficult to evaluate the oxidant-antioxidant status because these disorders accompanying OSAS have the potential to reduce antioxidant capacity and increase oxidant load [6]. Cofta et al. [14] stated that the increase in OSAS severity correlated with the increase in total antioxidant status and thiobarbituric acid-reacting substances plasma levels, and these markers may play important roles in the classification of the metabolic properties of OSAS. In our study, there was no significant difference between pOSAS and npOSAS groups in terms of TAS and MDA levels. In addition, as expected, a positive correlation was found between AHI and MDA and a negative correlation was detected between AHI and TAS. While there was a significant difference between pOSAS and npOSAS groups in terms of some PSG parameters, the TAS and MDA levels of the two groups were similar, suggesting that these blood parameters may have been affected by metabolism factors other than OSAS. However, there was no correlation between BMI, neck circumference and these blood parameters.

OSAS is a chronic inflammatory disorder and can cause increased production of certain inflammatory mediators in

circulation, including TNF α. In OSAS patients, proinflammatory cytokine levels increase and the level of anti-inflammatory factors decreases, causing endothelial dysfunction [15, 16]. TNF-α regulates the immune system, induces inflammation and participates in the regulation of fat metabolism. TNF-α levels in the blood of OSAS patients are generally higher than those of healthy controls [17, 18]. In a meta-analysis, TNF-α levels in circulation were higher in OSAS patients than in the control group, and this difference was more evident with increased OSAS severity. The authors claimed that TNF-α could be a promising circulatory biomarker for OSAS development [15]. However, it is controversial whether the high circulating TNF-α levels in these patients are the cause or the result of OSAS. In this study, the TNF α value of the npOSAS group was significantly higher than the pOSAS and control groups. In addition, while there was no correlation between TNF α and AHI, a positive correlation was found between BMI and neck circumference. In this study, it can be said that TNF α levels are affected by physical examination findings rather than the severity of OSAS.

There is a strong relationship between OSAS, obesity and inflammation. Leptin and adiponectin are major adipocytokines indicating the clinical and metabolic effects of obesity. Serum leptin levels increase in response to the degree of obesity, insulin resistance and hypoxia, while adiponectin levels are inversely related to the degree of obesity and insulin resistance [5]. Leptin is a potent pro-inflammatory agent, while adiponectin reduces inflammatory cytokine production and activity [8]. There are publications reporting that leptin levels are increased in OSAS patients, as well as articles reporting otherwise [8, 19, 20]. However, the number of articles reporting paradoxical results in this area are not small. Mutairi et al. [5] reported that adiponectin levels decreased with OSAS severity, and leptin levels decreased paradoxically with increasing OSAS severity. Therefore, they stated that adiponectin may be an independent marker of disease severity in OSAS patients. In our study, there was no significant difference between OSAS groups in terms of leptin levels. While leptin was not correlated with AHI, it negatively correlated with TAS, and positively correlated with MDA. Adiponectin was significantly lower in the npOSAS group compared to the other two groups. In addition, as expected, there was a negative correlation between adiponectin and BMI.

Limitations

The main limitation of this study is the small number of patients. In addition, since it was a double-blind study, the patient groups became clear at the end of the study, which can explain why the patients in the control group consisted of younger patients.

Conclusion

The lack of a homogeneous correlation between AHI and other PSG and blood parameters indicates that these blood values may have been affected by more than one factor in this patient group. Also, the lack of difference between pOSAS and npOSAS patients in terms of rhinomanometry results may indicate that the nose may not play a decisive role in the differentiation of these groups. Other upper respiratory tract sections can also be examined in the determination of positional dependence of OSAS patients.

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