Original Article

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Quick Response Code:

Website: ***

DOI: 10.4103/ejop.ejop_11_18

Relationship between hematological examination, glucose, HbA_{1c} level, and disease stages in patients with obstructive sleep apnea syndrome

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Abstract:

OBJECTIVE: Obstructive sleep apnea syndrome (OSAS) is an episodic disease that is characterized by intermittent partial interruption of breathing during sleep, which results in low oxygen levels in organs and tissues. The characteristic symptoms of OSAS include snoring, apnea or hypopnea, and excessive daytime sleepiness. Our aim is to determine the early diagnosis of diabetes and to initiate treatments for OSAS patients according to the results of polysomnography (PSG) in the sleep polyclinic based on fasting blood glucose and HbA1c levels in patients with known OSAS without diabetes.

MATERIALS AND METHODS: Patients who applied to the sleep polyclinic of the Pamukkale University and were diagnosed with OSAS using PSG were included in the study.

RESULTS: A total of 44 patients with OSAS and a control group consisting of 47 people meeting these criteria were included. Compared with the control group, the patient groups showed significantly higher Hb values ($P < 0.05$) and lower mean corpuscular volume ($P < 0.05$). Significant negative correlations were found between glucose levels and mean O_2 saturation values in patients with severe OSAS (apnea–hypopnea index > 30) ($r = -0.583$, $P = 0.02$).

CONCLUSION: In conclusion, even though significant differences were not found in the glucose and HbA1c levels of patients with OSAS, glucose metabolism was deteriorated when saturation was decreased in severe OSAS. Therefore, glucose levels should be observed frequently, particularly in severe cases of OSAS or in patients with hypoxia, regardless of the stage. More attention should also be paid to the development of diabetes.

Keywords:

Diabetes mellitus, glucose, hypoxia, obstructive sleep apnea syndrome

Introduction

Obstructive sleep apnea syndrome (OSAS) is an episodic disease that is characterized by intermittent partial interruption of breathing during sleep, which results in low oxygen levels in organs and tissues.[1] The characteristic symptoms of OSAS include snoring, apnea or hypopnea, and excessive daytime sleepiness.[2] OSAS occurs in approximately 3%–7% of males and 2%–5% of females in the general population and is a significant cause of mortality and morbidity.[3] OSAS is diagnosed and classified according to the apnea–hypopnea index (AHI) in polysomnography (PSG). AHI >5 indicates OSAS, with AHI of 5–15 indicating mild, 15–30 indicating moderate, and over 30 indicating severe OSAS.[4]

Changes in oxygen saturation and frequent awakening episodes in OSAS can also

Received: 10.04.2017
Accepted: 01.07.2017

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How to cite this article: Ugurlu E, Can I, Ertürk MS, Akbudak IH, Dursunoglu N, Ozkurt S. Relationship between hematological examination, glucose, HbA_{1c} level, and disease stages in patients with obstructive sleep apnea syndrome. Eurasian J Pulmonol 2018;20:33-36.

damage respiratory, cardiac, metabolic, and cognitive functions.[5] High hypoxemia and elevated AHI cause dysfunction of the pancreatic beta cells.[6] In previous studies, fasting blood sugar and HbA_{1c} elevation were detected in patients with OSAS. However, the number of studies comparing the hematological parameters and glucose, HbA1c values with OSAS stages is limited. Fasting blood sugar and HbA_{1c} elevation cause atherosclerosis and can lead to cardiovascular diseases.[7]

Our aim is to determine the early diagnosis of diabetes and to initiate treatments for OSAS patients according to the results of PSG in the sleep polyclinic based on fasting blood sugar and HbA_{1c} levels in patients with known OSAS without diabetes. We also compare fasting blood sugar and HbA_{1c} levels according to the OSAS stages and to detect whether the stages are linked with diabetes mellitus. We also aimed to study whether there is a relationship between OSAS disease and other blood parameters.

Materials and Methods

Study population

Ethical approval was obtained from the University Ethical Board on Human Experiments (approval number 60116787-020/54962). All participants gave their written informed consent to the study. The patients, who had been diagnosed with OSAS by PSG after referring to the sleep clinic of the university with one or more complaints such as snoring, witnessed apnea, and excessive daytime sleepiness were taken to the study. Patients were not included in the study if they had a history of smoking, a previous diagnosis of diabetes, serious heart disease (congestive heart failure, valvular heart disease, etc.), other known lung disease (chronic obstructive pulmonary disease, asthma, interstitial lung disease, lung cancer, etc.), or other chronic diseases (hematological diseases, kidney, and liver diseases). These OSAS patients were divided into mild, moderate, and severe groups according to AHI. Healthy control group was composed of nonsmoker healthy persons who had no illnesses or no sleeping problems (apnea, snoring, excessive daytime sleepiness, insomnia, etc.), that came only for control purposes to the internal medicine clinic. Hemograms, fasting blood sugar, and HbA_{1c} levels were evaluated in both groups.

Polysomnography

The examination was made in a single, quiet, dark, heat-controlled room with Philips Respironics alice 6 LDxS sleeping devices. Electroencephalography, electro-oculography, chin electromyography, oral and nasal airflow measurements (nasal-oral "thermistor" and nasal cannulae) were performed. Thorax and abdominal movements were evaluated. Arterial oxygen saturation (with pulse oximeter) and ECG recordings were taken. All records were evaluated by a chest physician specializing in sleep. A hypopnea was defined as a 3% fall or wake in oxygen saturation with at least a 50% reduction in oral and nasal airflow for 10 s or more, while airflow stop for at least 10 s is defined as apnea. The rate obtained by dividing the sum of apnea and hypopnea counts seen in sleep by the hourly sleeping period is called the AHI.

Statistical analysis

Statistical analysis of the data was performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered to be statistically significant. All data are expressed as the mean ± standard deviation (SD). An independent-sample *t*-test was used to compare the parameters. Spearman's correlation coefficient was used to examine the correlation between continuous variables.

Before the study, assuming that the difference between the two groups will have a medium effect size (Effect size Cohen d = 0,5), it is calculated that when 100 participants (50 patients and 50 healthy control) were taken for the study 80% power can be obtained with 95% confidence.

When calculating for correlations, it is assumed that a moderate correlation would be obtained (Effect size $|\rho| = 0{,}4$), It was calculated that for the study group, 44 participants would be able to obtain 80% power with 95% confidence.

In our study, 44 patients and 47 healthy controls were taken. As a result of the power analysis performed by our own results, it is estimated that the power we have obtained is 99% with 95% confidence.

Results

A total of 44 patients with OSAS and a control group consisting of 47 people meeting these criteria were included. Table 1 shows the demographic characteristics and laboratory findings of the patients and control group. Compared with the control group, the patient groups showed significantly higher Hb values ($P < 0.05$) and lower mean corpuscular volume (MCV) ($P < 0.05$). Significant negative correlations were found between glucose levels and mean O_2 saturation values in patients with severe OSAS (AHI >30) ($r = -0.583$, $P = 0.02$) [Figure 1].

Discussion

The hemoglobin levels in patients with OSAS were 14.76 ± 1.72, which was significantly higher than in the control group. Feliciano *et al*. found that

Table 1: Demographic characteristics and laboratory findings of obstructive sleep apnea syndrome and control group

	OSAS group (*n*=44)	Control group (*n*=47)	*P*
Age (year)	49.05±10.77	44.98±13.38	0.11
Gender (male/female)	31/13	27/20	0.19
Hb (g/dL)	14.76±1.72	14.13±1.45	0.017
Glucose (mg/dL)	100.65±11.81	102.49±18.7	0.78
MCV (%)	86.29±7.37	89.57±5.6	0.043
RDW (%)	13.97±1.6	13.88±0.9	0.45
HbA_{1c} (%)	5.87±0.46	5.72±0.45	0.14
AHI	31±25.39		
Mean O_2 saturation	91.64±4.04		

OSAS: Obstructive sleep apnea syndrome, AHI: Apnea–hypopnea index, MCV: Mean corpuscular volume, RDW: Red cell distribution width, Hb: Hemoglobin, HbA_{1c}: Glycated hemoglobin

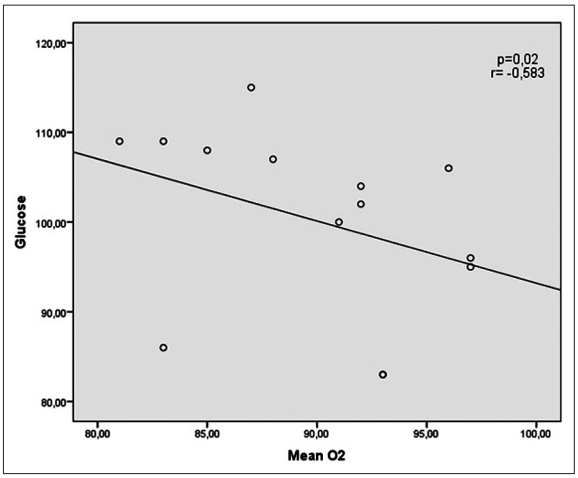

Figure 1: Negative correlations between glucose levels and mean O_2 saturation

hemoglobin levels were 15.3 ± 1.1 before treatment and 14.9 ± 1 ($P < 0.0001$) after treatment in a hematological parameter study on OSAS patients.[8] Hemoglobin levels were elevated in OSAS and significantly decreased with treatment.[8] Erythropoietin levels increase in hypoxic conditions, and there is a tendency for polycythemia to occur.[9,10]

The red cell distribution width (RDW) is a part of the hemogram that provides information about the size of circulating erythrocytes and is routinely observed.[11,12] This parameter is calculated by dividing the SD of the erythrocyte volume by the MCV.[13] In recent studies, RDW has provided essential information for determining the prognosis in acute myocardial infarction, cardiac diseases such as stable coronary artery disease and heart failure,[14-16] and noncardiac conditions such as stroke, pulmonary hypertension, and intensive care patients.[17-19] The increase in RDW is attributed to inflammation in these diseases.[17-19]

OSAS is also associated with hypoxia, increased oxidative stress, and consequently increased inflammation.[20] For this reason, an increase in RDW is expected in OSAS. However, studies on OSAS suggest that RDW increases[11,12] or similar.[21] RDW increased in our study, although not significantly. RDW negatively correlates with MCV,[11] which can explain the decrease in MCV. In addition, four of the patients in our study had severe anemia. Accordingly, MCV may be low.

There was no significant difference between glucose levels and HbA_{1c} levels between the OSAS group and control group. However, there was a negative correlation between mean O_2 saturation values and glucose levels in severe OSAS. OSAS and type 2 diabetes mellitus are common comorbidities.[22] There is evidence supporting an independent association between OSAS and impaired glucose metabolism.[23] In a study with 1599 patients by Priou *et al*., the proportion of patients with AHI <5 and HbA_{1c} >6% was 10.8%, while the proportion of patients with AHI ≥50 and HbA_{1c} >6% was 34.2%.[24] Similarly, in our study, there was a significant, independent association between decreases in saturation levels and HbA_{1c} >6%.[24] This disorder in OSAS and glucose metabolism is linked to intermittent hypoxia.[25]

The greatest limitation of our study is the limited number of cases. OSAS is associated with comorbid diseases such as heart failure, cardiovascular diseases, stroke, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and arrhythmia. Thus, the number of cases was reduced considerably since participants with any of these diseases and smokers were excluded from the study.

Conclusion

Even though significant differences were not found in the glucose and HbA_{1c} levels of patients with OSAS, glucose metabolism was deteriorated when saturation was decreased in severe OSAS. Therefore, glucose levels should be observed frequently, particularly in severe cases of OSAS or in patients with hypoxia, regardless of the stage. More attention should also be paid to the development of diabetes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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