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Original Research Article

Insulin resistance and affecting factors in patients with obstructive sleep apnea syndrome

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ABSTRACT

Background: Metabolic syndrome and insulin resistance are common in patients with obstructive sleep apnea syndrome (OSAS) independently of obesity. This study aims to examine and evaluate the insulin resistance and the factors affecting the insulin resistance in patients with OSAS.
Methods: Patients admitted to the sleep disorders clinic of our hospital with snoring complaints and diagnosed with OSAS in the last 6 months were included to the study. Insulin resistance was calculated by the Homa-IR formula. >2.7 was considered insulin resistance.
Results: The mean Homa-IR value was 3.86±4.69 and 42 (49.4%) patients were found to have insulin resistance. Mean insulin resistance was 2.68±2.2 in normal weight patients, 2.30±1.41 in overweight patients, 3.96±1.83 in obese patients, and 8.61±12.13 in morbid obese patients. The mean apnea hypopnea index of the patients was 22.95±15.20; 30 (35.2%) were with mild, 26 (30.6%) were with moderate and 29 (34.1%) were with severe OSAS. Insulin resistance was 2.35±1.36 in patients with mild AHI; 3.09±1.30 in patients with moderate AHI, and 6.11±7.35 in severe cases. In our study, the most significant relationship was found to be between insulin resistance in OSAS patients with insulin resistance and BMI and AHI.
Conclusions: Insulin resistance is common in patients with OSAS independently of obesity. In our study, BMI and AHI were found to be the most important factors associated with insulin resistance in patients with OSAS.

Keywords: Insulin Resistance, Obstructive Sleep Apnea Syndrome, Obesity, Homa-IR

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a chronic condition characterized by recurrent narrowing of the upper respiratory tract during sleep.[1] The prevalence of OSAS in the general population is reported to be 2-4% on average, varying according to age, sex and societies in different studies. Being seen in all age groups including childhood, the most common age is 40-65. Major symptoms in OSAS are defined as snoring, probable apnea and daytime extreme sleepiness. Male sex, advanced age, obesity, anatomical anomalies, hypothyroidism, acromegaly, inheritance, alcohol, sedative drugs and deterioration in respiratory control during sleep are suggested as risk factors in OSAS.[1]

OSAS is a major cause of morbidity and mortality. OSAS may cause various complications such as systemic hypertension, cardiovascular disease, impaired stroke and glucose metabolism disorder.

Metabolic imbalances and insulin resistance develop as a result of intermittent hypoxia caused by apnea hypopnea

and sympathetic stimulation increase with subsequent re-oxygenation, oxidative stress, systemic inflammation accompanied by obesity.[2] In addition, increased levels of cortisol as a result of hypoxia and sympathetic system activation contribute to imbalances in glucose metabolism. Metabolic syndrome, cardiovascular diseases, and insulin resistance are frequently observed in patients with OSAS independently of obesity.[3] There is a clear relationship between apnea-hypopnea index (AHI) and oxygen saturation (SaO2) and insulin resistance. Metabolic effects are associated with oxygen desaturation, with an insulin resistance of about 20% in OSAS. The metabolic disorder is recovered 3 months after starting the use of CPAP. Type-2 diabetes mellitus (DM) is seen in 30% of patients with obstructive sleep apnea syndrome. OSAS is common in children with type-1 diabetes and in diabetic neuropathic adult patients. In addition, insulin resistance in OSAS is directly proportional to the severity of the disease. There is an independent relationship between OSAS and type-2 DM, and DM also suppresses basal ventilatory functions.

In this study, we aimed to investigate the frequency of insulin resistance and factors affecting insulin resistance in patients with OSAS.

METHODS

Patients admitted to the sleep disorders clinic of our hospital with snoring complaints in the last 6 months between January 2015 and January 2016 and diagnosed with OSAS with polysomnography were included to the study and studied prospectively. Demographic characteristics, anthropometric measures, and family histories of the patients were recorded. Patients between the ages of 18 and 75 who did not use positive airway pressure therapy for OSAS were included to the study after the written approval was obtained. Patients with congestive heart failure, chronic liver and kidney disease, cerebrovascular disease, diabetes mellitus (DM) history, hypothyroidism, hyperthyroidism, alcohol use, and steroid use were excluded.

Polysomnography (PSG) shots of all patients were performed with a GRASS (Comet, USA) polysomnography device between 22:00 and 7:00 in in the spontaneous sleep in the sleep laboratory under the supervision of a technician. Electroencephalography (EEG), electrooculography (EOG), electromyograms (EMG) and electrocardiography (ECG) of the patients were recorded. Thoracic and chest band were used for airflow nasal-oral cannula and respiratory effort. Patients' positions during sleep were recorded with the body position sensor. Audio and video recording was done with the video camera system all night. PSG records were scored according to the 2007 American Academy Sleep Medicine (AASM) criteria using the Twinpolisomnographic analysis program.

Fasting blood glucose and fasting insulin levels of the patients were determined in the morning after PS. Insulin resistance was calculated by the Homa-IR formula. >2.7 was considered insulin resistance. Patients were classified as mild OSAS (AHI: 5-15), moderate OSAS (AHI: 15-30), and severe OSAS (AHI:>30) according to Apnea Hypopnea Index (AHI).

BMI of patients was calculated. Patients were classified as underweight with BMI below 18.5, normal weight at 18.5-24.9, overweight at 25.0-29.9, obese at 30.0-39.9, morbid obese at over 40.0.

The data were analyzed by SPSS (statistical package for social sciences), version 19.0 for Windows (IBM/SPSS Inc. Chicago/IL, USA). Pearson Chi-square test was used to determine the relationship between qualitative variables. Significance was evaluated at $p<0.05$.

RESULTS

General characteristics of the patients are summarized in Table 1. A total of 85 patients including 22 (25.8%) females were included in the study. The mean age of the patients was 47.30±11.41. The mean body mass index (BMI) of the patients was 33.07±5.60. 11 (0.12%) patients were normal weight, 25 (29%) were overweight, 39 (45%) were obese and 10 (11%) were morbid obese.

Table 1: General characteristics of the patients.

Characteristics	n=85
Age (years)	47.30±11.41
BMI (kg/m2)	33.07±5.60
Waist circumference (cm)	109.57±13.50
Gender (M/F)	63/22
AHI	22.95±15.20
Homa-IR	3.86±4.69
Fasting blood glucose (mg/dl)	92.98±11.89
Insulin (µU/ml)	15.29±8.89
DM history in the family	(n) 33

Mean Homa-IR value was 3.86±4.69 and 42 (49.4%) patients were found to have insulin resistance. Mean insulin resistance was 2.68±2.22 in normal weight patients, 2.30±1.41 in overweight patients, 3.96±1.83 in obese patients, and 8.61±12.13 in morbid obese patients. The mean apnea hypopnea index of the patients was 22.95±15.20; 30 (35.2%) patients were with mild, 26 (30.6%) were with moderate and 29 (34.1%) were with severe OSAS. Insulin resistance was 2.35±1.36 in patients with mild AHI; 3.09±1.30 in patients with moderate AHI; and 6.11±7.35 in severe cases. Factors affecting insulin resistance in patients are summarized in Table 2.

There was a positive correlation between BMI and AHI and Homa-IR in favor of Homa-IR. There was a significant difference in insulin resistance between the morbid obese group and other groups (normal weight, obese, overweight) in the comparison made within the

groups (p<0.05). While Homa-IR was 2.68±2.24 in normal weight patients, Homa-IR was 8.6±12.13 in morbid obese group.

Table 2: Comparison of the presence of insulin resistance and the other factors.

Factors	Insulin resistance	No insulin resistance	P
Age (years)	46.81±11.405	51.13±11.33	0.767
Gender (M/F)	36/12	27/10	0.990
AHI	25.77±15.16	22.17±13.50	0.001
Waist circumference	113.74±10.49	108.07±11.27	0.110
DM history in the family (n)	18	15	0.145
BMI (kg/m2)	34.52±4.98	30.4±3.86	0.009

Table 3: Homa-IR values compared to BMI and AHI.

		n	Homa-IR
BMI	Normal weight	11	2.68±2.24
	Overweight	25	2.30±1.41
	Obese	39	3.96±1.83
	Morbid obese	10	8.6±12.13
AHI	Mild	30	2.35±1.36
	Moderate	26	3.09±1.30
	Severe	29	6.11±7.38

There were significant differences in insulin resistance between the patients divided into three groups according to the AHI groups (p<0.05). In the comparison between groups, there was a significant difference in insulin resistance between the severe and mild, and severe and moderate AHI groups (p<0.05). While Homa-IR was 2.35±1.36 in mild group, Homa-IR was 6.11±7.38 in severe group. Homa-IR values compared to BMI and AHI are summarized in Table 3.

DISCUSSION

OSAS is a widespread disease with increasing worldwide prevalence. Obstructive sleep apnea syndrome is a syndrome that leads to mortality and morbidity.[4]

In some studies, it has been shown that there is a relationship between respiratory disorder during sleep and DM development. Meslier et al reported that they applied a 2 hour glucose tolerance test to the patients diagnosed with OSAS and without OSAS with Polysomnography (PSG).[5] They have found diabetes diagnosis rate as 30.1% in patients with OSAS and 13.9 in patients without OSAS. In a study conducted on Korean males who were not hypertensive, diabetic and obese, it was reported that although fasting blood glucose and insulin levels were not different, glucose and insulin levels were found to be significantly higher in patients with habitual snoring at the 1st and 2nd hours than those without habitual snoring in a 75 g oral glucose tolerance test.[6]

Diabetes mellitus was found in 5.4% of patients with habitual snoring and 2.41% of patients without habitual snoring as a result of a 10 year follow-up.[7] In our study, 42 of 85 patients with OSAS (49.4%) were found to have insulin resistance. In our study, we found that there is a positive correlation between BMI and AHI and Homa-IR in favor of Homa-IR.

In comparison according to BMI, there was a statistically significant difference in terms of insulin resistance among the morbid obese group and other groups (normal weight, obese, overweight) (p<0.05).

The groups were compared within themselves. There was a significant difference in terms of insulin resistance between severe and mild, and severe and moderate AHI groups (p<0.05). Obesity is a common risk factor for insulin resistance, diabetes and OSAS. Besides this, obesity, insulin resistance, and DM are shown in studies to pose a risk in OSAS.[8] Thus, it is difficult to distinguish whether insulin resistance and DM in patients with OSAS are associated with obesity or OSAS. Therefore, independent risk factors are studied using statistical models. In our study, it was observed that HT was affected by BMI and AHI, and both DM and CAD (coronary artery disease) were not affected by both of them. Presence of obesity in patients with OSAS may be a predisposing factor for the development of insulin resistance.

Insulin resistance is common in patients with OSAS independently of obesity. In our study, we found that the most important factor associated with insulin resistance in patients with OSAS was BMI and AHI.

As a result, according to our study, OSAS is a risk factor for insulin resistance. As the severity of BMI and AHI increases, the risk of insulin resistance increases. With this study, while struggling with obesity, we aimed to re-emphasize OSAS and insulin resistance association.

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Ethical approval: This study was approved by Recep Tayyip Erdoğan University, Non-Invasive Clinical Research Ethical Committee (40465587-18) in accordance with the ethical standards of the institution and the 1964 Helsinki declaration and its later amendments or comparable ethical standards

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