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The effect of positive airway pressure therapy on lipid profile

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Abstract:

CONTEXT: Obstructive sleep apnea syndrome (OSAS) emphasize the concurrence and interaction of disorders of lipid metabolism and components of metabolic syndrome (MS) such as insulin resistance.

AIMS: The aim of this study is to observe the effect of positive airway pressure (PAP) treatment on the lipid profile during 1-year follow-up of patients diagnosed with OSAS.

SETTINGS AND DESIGN: This was a single-center, retrospective, observational study.

MATERIALS AND METHODS: A total of 168 OSAS patients were diagnosed in our sleep laboratory and were recommended for PAP therapy. Among these patients, 64 patients who received effective PAP treatment for 1 year, and who did not have the comorbid disease, history of lipid-lowering treatment, or history of lifestyle change, dietary regulation or attempt to loose weight during the 1-year follow-up period were included in the study. Pretreatment measurement parameters including body weight, waist, neck and hip circumference, body mass index (BMI), blood lipid levels (total cholesterol [TC], triglyceride [TG], high-density lipoprotein [HDL], low-density lipoprotein [LDL]), and Epworth sleepiness scale (ESS) score were compared with the 3rd and 12th months parameters.

STATISTICAL ANALYSIS USED: SPSS version 16 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses.

RESULTS: The study included 64 (38 M, 26 F) patients (mean age of 53.1 years). The mean apnea-hypopnea index was 50.84 h. Although TC, HDL, LDL, and TG levels did improve with the PAP treatment (all $P < 0.05$), no significant decrease was observed with respect to the BMI, hip, neck, and waist circumference (all $P > 0.05$). There were statistically significant changes in sleep efficiency, oxygen desaturation index, and ESS score ($P < 0.05$).

CONCLUSIONS: The results show that effective PAP treatment has beneficial effects on the blood lipid profile, which enhances sleep efficiency and sleep quality in patients.

Keywords:

Body mass index, dyslipidemia, obstructive sleep apnea syndrome, positive airway pressure

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Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of upper airway obstruction that result in arousals, sleep fragmentation, nocturnal oxygen desaturation, and day-time sleepiness.[1] Metabolic syndrome (MS) develops as a result of insulin resistance, and its clinical picture involves Type 2 diabetes, obesity with particularly abdominal type, hypertension, dyslipidemia, hyperuricemia, and fibrinolysis defect. It is often the main cause of coronary heart disease and is implicated in premature atherosclerosis.[2] In numerous studies, the development of metabolic events in OSAS has been associated with hypoxia and an increased inflammatory state in the respiratory system and in the systemic circulation. Repetitive obstructive apnea and frequent sleep fragmentation are the main cause of cardiovascular and metabolic disturbances associated with

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OSAS. Animal and cell culture experiments show that intermittent exposure to hypoxia cause dyslipidemia, which often leads to insulin resistance, hypertension, and atherosclerosis.[3] Many studies on OSAS emphasize the concurrence and interaction of disorders of lipid metabolism and components of MS such as insulin resistance.[4-6] However, there are only a few reports as regards the effects of positive airway pressure (PAP) therapy on the lipid profile in the data and these studies yielded conflicting results.[7,8] Therefore, the objective of this study was to explore the effects of PAP therapy on the blood lipid profile during 1-year follow-up of patients diagnosed with OSAS.

Materials and Methods

Study design and participants

A total of 218 patients who had undergone a sleep study at our sleep laboratory between January 2015 and January 2016 based on the clinical suspicion that they may have OSAS were recruited to the study. Out of 168 OSAS cases diagnosed in sleep laboratory, of the 145 patients who started PAP therapy, 60 patients were excluded for comorbid disease or history of lipid-lowering treatment, or weight loss or lifestyle change attempts and 21 patients were excluded from the study due to PAP intolerance. A total of 64 cases who received effective PAP therapy and did not have any comorbid disease or history of lipid-lowering treatment, or weight loss or lifestyle change attempts were included in the study. As effective PAP treatment criteria, PAP administration at least 4 h a day and 5 days a week was sought,[9] and PAP time was confirmed by examining the device records in all cases.

Data collection

Clinical and demographical feature such as age, gender, and body mass index (BMI) were noted. All patients provided medical history, and a physical examination was performed. Waist, neck, hip circumference, and BMI were calculated. All patients provided blood samples for measurement of total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels. All patients were evaluated with Epworth sleepiness scale (ESS).[10] Anthropometric measurements were carried out following overnight fasting, whereas patients were dressed in indoor clothes and standing. Waist circumference was measured as the smallest circumference between the costal arch and anterior superior iliac spine. Neck circumference was measured at the level of the superior border of the cricothyroid membrane. Hip circumference was measured with a measuring tape positioned over the maximum circumference of the buttocks and symphysis pubis. BMI was calculated with the weight (kg)/height^2 (m) formula.[11]

Polysomnography evaluation

All patients underwent overnight polysomnography with 55 channel Alice 6 computerized system (Respironics; Philips, Illinois, USA). The channels used in the study were as follows: 6 channels for electroencephalogram, 2 channels for electrooculogram, 1 channel for nasal pressure sensor, 1 channel for thermistor, 1 channel for microphone, 1 channel for respiratory effort, 1 channel for abdominal effort, 2 channels for foot electromyogram (EMG), 1 channel for heart rate and oxymeter sensor, 2 channels for chin EMG, 4 channels for electrocardiogram, and 1 channel for body position. Respiratory and abdominal efforts were measuredusing an elastomeric plethysmography method. Polysomnography scores and definition of OSAS were based on the American Academy of sleep medicine criteria.[12] Apnea was defined as 90% or greater reduction of airflow as measured by thermistor, lasting for at least 10 s. In addition, the amplitude criteria had to be met for at least 90% of the duration. Two different criteria were used for hypopnea, and the presence of either one of them was accepted as hypopnea. The first criterion was a 30% or greater reduction of the nasal pressure signal compared to the baseline lasting for 10 s at least, simultaneously with 4% or greater desaturation. The second criterion was a 50% or greater reduction of the nasal pressure signal compared to the baseline lasting for 10 s at least, and simultaneously with a 3% or greater desaturation. In addition, in both criteria, the amplitude criterion had to be met for at least 90% of the duration. The total number of apnea and hypopnea episodes per hour was defined as the apnea-hypopnea index. All measurements and tests were repeated at the 3rd and 12th months of PAP therapy.

Statistical analysis

SPSS version 16 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. Data were expressed as mean ± standard deviation or percentage. Normal distribution was analyzed with the Kolmogorov–Smirnov test. The Chi-square test or Fisher's exact test was used for categorical variables between the groups where appropriate. One-way ANOVA analysis was used to determine whether there were any significant differences between the repeated measures. A value of $P = 0.05$ was set as the significance level.

Results

A total of 64 patients (38 M, 26 F) with a mean age of 53.10 years were included in the study. Baseline and after-treatment values of the lipid profile are summarized in Table 1. There was a significant decrease in the total cholesterol, LDL, and triglyceride levels in terms of the baseline-3rd month, 3rd month-12th month, and baseline-12th month evaluations (all $P < 0.005$). However,

HDL levels significantly improved only in the 12th month measurement compared with the baseline.

Repeated measures and variance analysis did not show a significant change in weight, waist circumference, or BMI between measurements at the time of diagnosis, 3rd and 12th months of treatment ($P > 0.05$) [Table 2].

Initial sleep efficiency, awake SpO_2, minimum SpO_2 were significantly lower, but Epworth scores means were significantly higher, compared to values at the 3rd and 12 months of treatment. There were significant differences when initial the percentage of total sleep time (TST%) with SpO_2 <90% and longest apnea duration means were compared to values at the 3rd and 12th months of treatment ($P < 0.05$). Accordingly, initial the percentage of TST% with SpO_2 <90% and longest apnea duration means were significantly higher compared to values at the 3rd and 12th months of treatment. Initial mean ESS score was significantly higher than that of the values at the 3rd and 12th months, and the mean ESS score at the 3rd month was significantly higher than that of the values at the 12th month of treatment [Table 3].

Table 1: Baseline and after-treatment values of total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides

Variables/mg/dL (mean±SD)	Baseline	3rd month	12th month	*P*
LDL	159.3±45.9	148.9±37.5	142.2±30.7	0.012
Total cholesterol	191.2±48.4	178.7±45.8	168.9±41.6	0.000
Triglyceride	242.3±91.9	234.1±65.5	227.5±65.1	0.027
HDL	43.1±11.3	43.1±11.3	48.6±7.7	0.000

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SD: Standard deviation

Table 2: Body mass index and measurement of the waist, hip, and neck circumference

Variables	Baseline	3rd month	12th month	*P*
BMI (kg/m²)	33.94±6.7	33.85±6.6	33.78±6.4	0.507
Waist circumference (cm)	125.0±20.3	125.0±20	124.5±20.1	0.300
Hip circumference (cm)	133.9±21.9	133.7±21.6	133.1±20.9	0.207
Neck circumference (cm)	52.7±7.1	52.5±6.9	52.1±6.6	0.369

BMI: Body mass index

Table 3: Investigation of the difference between time periods in terms of sleep efficiency, awake SpO_2, min SpO_2, the percentage of total sleep time with SpO_2 <90%, the longest apnea period and Epworth sleep value

Variables	Baseline	3rd month	12th month	*P*
Sleep efficiency (%)	82.92±8.1	86.89±5.8	88.28±4.2	0.000
Awake SpO_2 (%)	91.6±3.9	93.01±2.6	93.71±2.5	0.000
Minimum SpO_2 (%)	68.51±15.6	79.59±10.1	81.23±7.9	0.000
The percentage of total sleep time with SpO_2 <90% (min)	27.76±27.1	16.98±19.06	14.24±16.22	0.002
The longest apnea period(s)	33.30±10.4	25.09±7.3	23.83±6.8	0.000
Epworth sleep value	19.92±3.2	17.81±2.6	17.10±2.6	0.000

Discussion

In this study, we aimed to explore whether the continuous PAP treatment is effective on lipid profile and MS. We have three main findings in the light of our results. First, lipid profiles did improve with the PAP treatment. Second, no significant difference was observed with respect to the BMI, hip, neck, and waist circumferences. Third, there were statistically significant changes in sleep efficiency, oxygen desaturation index, and ESS scores.

Impacts of PAP treatment on lipid profile was previously reported in the data. The outcome of effective PAP therapy on the lipid profile has also been investigated in many studies and has produced contradicting results. Rebelo *et al*.[7] studied the effects of PAP treatment on lipid profile in 39 male patients. They concluded that long-term PAP treatment improves OSA but not change the levels of lipid profiles. On the other hand, Xu *et al*.[8] reported a meta-analysis of the controlled trials concerning the effects of PAP treatment on lipid profile in OSAS patients. They highlighted that although PAP treatment decreases the TC level, PAP treatment did not change TG, LDL, or HDL levels. Besides, TC levels did decrease more in younger and more obese patients, and in patients who used PAP for a longer period. Furthermore, it has been hypothesized that PAP therapy may prevent dyslipidemia by preventing intermittent hypoxia and sympathetic hyperactivity. In addition, increased day-time physical activity and calorie expenditure due to PAP therapy may have beneficial effects on dyslipidemia.[13] A study by Joyeux-Faure *et al*.[14] found that despite their lipid-lowering effects, statins did not have any effect on markers of inflammatory or autonomic activity. They stated that the lipid (HDL, LDL, TC, and TG) lowering effect was significant in studies showing reduced sympathetic activity with PAP therapy.[14] In another study, Kumor *et al*. found that PAP therapy resulted in reduced lipid concentrations in the OSAS alone, but did not have an effect in the case of OSAS with concurrent ischemic heart disease. They showed that 3 months of Continuous positive airway pressure (CPAP) therapy lowered TC and LDL levels but did not have an effect on serum homocysteine and leptin levels in OSAS patients without ischemic heart disease.[15] Several studies have noted that compliance with PAP therapy is an important factor regarding the effect on lipid metabolism, and the use of PAP for over 4 h a night could improve lipid profile. The beneficial effect of PAP therapy on the lipid

profile was found to be correlated with the duration of PAP therapy, and this was more pronounced as the study duration increased; this condition was attributed to the effects of various parameters other than PAP, including diet and exercise.[16-18] In our study; for all patients, the CPAP compliance is at an acceptable level according to device records and their feedbacks. Effective PAP therapy was observed to cause a significant reduction in TC and LDL levels, a significant increase in HDL level, and no effect on TG levels. It was concluded that PAP therapy had a positive contribution to the lipid profile because of the number of samples was lower, and sympathetic activities were relatively lower compared to the patients' age and BMI, and effective PAP therapy might have had a positive effect on lipid profiles.

Whether OSAS leads to obesity is still a controversial subject. However, concurrent obesity and OSAS results in increased frequency of complications. One related study has shown that OSAS risk was increased 6-fold under a weight gain >10% of the initial body weight, and 4-fold for every 6 kg/m^2 increase in BMI.[3] In addition, OSAS has been shown to be closely associated with visceral obesity and even more so compared to its association with BMI.[19] An effective PAP therapy may improve apnea scores, complaints, and some of the complications.[20] PAP therapy has been shown to eliminate obstructive apnea-hypopnea and snoring, reduce respiratory effort, normalize oxygen saturation during sleep, and improve patients life quality.[21] However, its effects on weight and BMI reduction are still controversial. In one study by Kajaste *et al*. (which included 31 obese male patients with OSAS), the subjects were enrolled in a 2-year weight reduction program and were randomized in two groups that did and did not receive PAP therapy. At the end of the study, they did not find a significant difference between the two groups.[22] Bamberga *et al*.[23] showed that PAP therapy did not have a statistically significant effect on body weight or routine physical activity level. In our study, we found a statistically significant effect for PAP therapy on sleep efficiency, oxygen saturation, and ESS score. However, it did not have any effect on weight reduction or BMI.

Limitations

We have a few important limitations for this study. First, the small sample size is relatively small. Lack of a control group is a limitation as well. Third, the exact data for the CPAP compliance is another limitation. However, the patients with inadequate compliance were excluded from the study.

Conclusions

OSAS is thought to play a role in the development of many important systemic disorders including hypertension, insulin resistance, cardiovascular diseases, and dyslipidemia. In light of the findings of various studies that have examined the cause and effect relationship between these and similar disorders, add-on therapies are gaining significance. Increasing the number of studies that examine the effect of PAP therapy (the most effective treatment in OSAS) on chronic systemic diseases that are thought to be associated with OSAS and are resistant to medical treatment. These studies show beneficial effects of PAP on these disorders, which is consistent with our positive effect on the lipid profile. Nevertheless, large-scale studies with long-term follow-up will be necessary to comprehensively investigate its effects.

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Conflicts of interest

There are no conflicts of interest.

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