

# The effect of continuous positive airway pressure on dyslipidemia in patients with obstructive sleep apnea

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**Background** Obstructive sleep apnea (OSA) is a prevalent disease associated with increased risk of cardiovascular mortality. However, the exact causal relationship is not clear. One of the proposed mechanisms is dyslipidemia.

**Aim** To study the effect of continuous positive airway pressure (CPAP) on dyslipidemia in patients with OSA.

**Patients and methods** Forty obese patients with OSA were recruited. All patients were subjected to history taking, physical examination, and polysomnography. Fasting blood sugar, liver function, kidney function, and lipid profile were measured after fasting for 14 h. Apnea/hypopnea index and BMI were calculated. The patients then received CPAP treatment during night for 3 months. Polysomnography and laboratory parameters were remeasured after 1 and 3 months of treatment.

**Results** The natural correlation between body weight and lipid profile is lost. Apnea/hypopnea index and high-density lipoprotein improved significantly after 1 month and more significantly after 3 months. Triglycerides were lowered after 1

month without more improvement after 3 months. Low-density lipoprotein-cholesterol and total-C did not change after 1 month with significant reduction after 3 months.

**Conclusion** Treatment with CPAP improves lipid profile in patients with OSA.

*Egypt J Bronchol* 2019 13:120–124

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*Egyptian Journal of Bronchology* 2019 13:120–124

**Keywords:** continuous positive airway pressure, dyslipidemia, obstructive sleep apnea

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**Received** 29 July 2018 **Accepted** 31 October 2018

## Introduction

Obstructive sleep apnea (OSA) syndrome is a condition characterized by complete or partial interruption of respiration during sleep leading to awakening from sleep, bouts of hypoxia, and hemodynamic changes [1].

The global prevalence of OSA is estimated at one billion people in 2018 [2]. Thirty percent of adult Egyptians have OSA [3]. The association between OSA and cardiovascular disease (CVD) is very strong [4]; 61.9% of patients with cerebrovascular disease have OSA [5]. There are several mechanisms that may lead to the development of CVD in patients with OSA. These mechanisms include and are not limited to intermittent hypoxia, hypercapnia, sleep disruption, and intrathoracic pressure oscillations [6].

Dyslipidemia as evidenced by low high-density lipoprotein-cholesterol (HDL-C), hypertriglyceridemia, high low-density lipoprotein-cholesterol (LDL-C), and high total-C is a major CVD risk factor [7]. The causative relationship between OSA and dyslipidemia is yet to be established. However, there is cumulative evidence that OSA is independently associated with dyslipidemia via the production of stearoyl-coenzyme A desaturase-1 and reactive oxygen species, peroxidation of lipids, and sympathetic system derangement [8]. So, there is a

conjecture that dyslipidemia is a nontraditional risk factor increasing the incidence of CVD in patients with OSA [9].

Continuous positive airway pressure (CPAP) is the main line of treatment of OSA with documented improvement of respiratory function. Moreover, it may improve the CVD outcome in those patients [10]. However, the mechanism of this improvement is not clear. Improvement of dyslipidemia may be among the factors that could improve the CVD outcome in this population. The effect of CPAP on dyslipidemia is not established and gave conflicting data [11,12].

## Aim

To study the effect of CPAP on dyslipidemia in patients with OSA.

## Patients and methods

The present study is a prospective, interventional trial carried out on 40 obese patients diagnosed as OSA

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[apnea/hypopnea index (AHI>15)] [13] referred to the Sleep Laboratory Unit in Chest Department at Menoufia University Hospital. Ethics committee approval was obtained before the beginning of the study.

All patients referred to our center over the year 2017 and diagnosed with OSA were included in the study. The patients were excluded if they were diabetic or hypertensive or receiving any treatment affecting the lipid profile. After taking an informed written consent, the following data were obtained from every patient:

- (1) Personal history included (age, sex, and smoking).
- (2) Clinical examination findings with special attention to body weight (kg), height (cm), BMI, and neck circumference (cm).
- (3) Epworth Sleepiness Scale: The Epworth Sleepiness Scale final score was categorized into less than 11 (low risk for sleepiness) and more than or equal to 11 (high risk for sleepiness).
- (4) Routine laboratory investigations included (fasting blood sugar, triglycerides, total-C, LDL-C, and HDL-C).

AHI was estimated three times: at baseline, after 1 month, and after 3 months. Overnight polysomnography on room air was done using EMBLA S 4000 system (Biomed, Reykjavik, Iceland). It was conducted in the Sleep Laboratory Unit, Chest Department, Menoufia University Hospital over a whole night (at least 8 h sleep). Factors that affect sleep rhythm such as xanthines, hypnotics, and central nervous system stimulants were stopped at least one night before the session. ECG electrodes were fixed one below the clavicle in the mid-clavicular line and the second was fixed at the apex of the heart; the abdominal belt was fitted at the level of umbilicus; the thoracic belt was fitted at the level of the nipples; the body position sensor was fixed between the two belts; oronasal thermistor transducer was fitted in the nostrils to measure changes in inhalation and exhalation and the rate of breathing. Pulse oximeter was placed on a patient's finger to detect blood oxygen saturation levels and the sound probe was placed over the trachea or on the side of the neck.

Any breathing irregularities, mainly apneas and hypopneas, were recorded. Apnea means a complete or near-complete interruption of airflow for at least 10 s, while hypopnea means reduction of airflow more than or equal to 30% of pre-event baseline for at least 10 s associated with 3% oxygen desaturation from pre-event baseline and/or the event is associated with an

arousal [13]. However, it is acceptable for hypopnea to be associated with more than or equal to 4% oxygen desaturation from pre-event baseline.

Polysomnography was done on room air followed by follow-up after 1 and 3 months of CPAP treatment.

AHI is calculated by the number of apnea and hypopnea events divided by the number of hours of sleep [13,14].

Fasting blood sugar and cholesterol profile were measured after overnight fasting at baseline without CPAP. Reevaluation was done after 1 month and after 3 months of CPAP treatment during sleep.

#### Statistical analysis

The statistical analysis of data was done using the statistical package for the social sciences, version 22 (SPSS Inc., Chicago, Illinois, USA). The quantitative variables were described as mean±SD and range as appropriate. Qualitative variables were described as number or frequency. Paired *t* test was used to indicate collectively the presence of any significant difference between two groups for a normally distributed quantitative variable.  $\chi^2$  test was used to compare two groups as regards qualitative variables.

#### Results

The present study is a prospective interventional study on 62 patients (32 men and 30 women). All patients were instructed to use CPAP for 6–8 h per night with a pressure ranging from 8 to 12 cm H<sub>2</sub>O at least 5 days per week. Only 40 (22 men and 18 women) (64%) were compliant and fulfilled the criteria till the end of the study, while 22 (36%) patients dropped out.

The included patients were overweight or obese (BMI=36.01±4.25) and have OSA (AHI=44.00±11.96). The fasting blood sugar ranged from 78 to 99 mg/dl. Their basal lipid profiles were as follows: total-C=255.90±40.18 mg/dl, LDL-C=166.90±40.13 mg/dl, HDL-C=30.45±5.73 mg/dl, and triglycerides=292.75±64.99 mg/dl. Other baseline criteria are presented in Table 1.

All patients received CPAP as the main line of treatment and were reevaluated after 1 month. Paired sample *t* test showed significant improvement of AHI, significant reduction of triglycerides, and elevation of HDL-C. On the other hand, no significant changes were noticed as regards total-C and LDL-C (Table 3, Figs 1 and 2).

After 3 months of CPAP, there was a significant reduction of AHI, total-C, LDL-C, and triglycerides while HDL-C was elevated as compared with the baseline levels (Table 2, Fig. 1).

Comparison of lipid profile after 1 month and after 3 months of CPAP therapy showed a significant reduction of total-C and LDL-C, there was more significant elevation in HDL-C while there were no significant changes in triglyceride levels (Table 3, Figs 1 and 2).

**Table 1 Descriptive statistics of the studied group (N=40)**

	Minimum	Maximum	Mean	SD
Age (years)	38.00	70.00	56.45	8.941
Sex (male/female)	22/18			
Weight (kg)	70.00	140.00	96.20	19.975
Height (cm)	150.00	191.00	163.20	12.463
BMI (kg/m <sup>2</sup> )	27.00	42.00	36.01	4.251
Neck circumference (cm)	35.00	46.00	43.65	2.560
Apnea/hypopnea index	15.90	65.70	44.00	11.962
Fasting blood sugar (mg/dl)	78.00	99.00	93.65	5.999
AST (U/l)	20.00	42.00	31.70	6.814
ALT (U/l)	19.00	40.00	29.20	6.685
Creatinine (mg/dl)	0.70	1.20	0.91	0.146
Total-C (mg/dl)	200.00	320.00	255.90	40.176
LDL-C (mg/dl)	108.00	237.00	166.90	40.133
HDL-C (mg/dl)	21.00	39.00	30.45	5.725
Triglycerides (mg/dl)	150.00	380.00	292.75	64.999

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

**Table 2 Pearson's correlation between BMI and basal lipid profile and apnea/hypopnea index**

	r	P value
Total-C (mg/dl)	-0.090	0.705
LDL-C (mg/dl)	-0.143	0.547
HDL-C (mg/dl)	-0.112	0.639
Triglycerides (mg/dl)	0.212	0.369
Apnea/hypopnea index	0.077	0.748

HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

**Table 3 Paired t test of the lipid profile before, 1, and 3 months after continuous positive airway pressure**

	Basal (mean±SD)	1 month (mean±SD)	3 months (mean±SD)	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
Total-C (mg/dl)	255.90±40.18	257.15±46.56	234.91±44.62	0.771	0.000	0.000
LDL-C (mg/dl)	166.90±40.13	165.60±44.71	142.52±45.09	0.781	0.000	0.000
HDL-C (mg/dl)	30.45±5.73	35.70±5.47	37.45±4.02	0.00	0.000	0.018
Triglycerides (mg/dl)	292.75±64.99	279.25±60.46	274.65±54.39	0.028	0.002	0.208
Apnea/hypopnea index	44.00±11.99	10.15±2.68	4.75±0.97	0.000	0.000	0.000

HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol. P<sub>1</sub>, comparison between the basal levels and after 1 month of therapy. P<sub>2</sub>, comparison between the basal levels and after 3 months of therapy. P<sub>3</sub>, comparison between the levels and after 1 month and levels after 3 months of therapy.

## Discussion

The present study is a prospective interventional study to show the effect of CPAP on dyslipidemia in patients with OSA. The natural correlation between body weight and all basal lipid profile parameters were lost in this study (Table 2). This reflects the effect of OSA on lipid profile [15,16]. The association between OSA and dyslipidemia is explained on the basis of excessive adipose tissue lipolysis during sleep leading to an increase in plasma-free fatty acids. This systemic lipotoxicity may be one of the causes of increased CVD risk in patients with OSA [17,18]. The activated lipolysis is thought to be through sympathetic and adrenocortical activation due to stress at night [19].

After 1 month of therapy with CPAP, and as expected, there was marked improvement of AHI. This was in agreement with other studies which confirmed the improvement of AHI with CPAP therapy [20–22]. Other studies failed to reach the same conclusion and the researchers explained the results by lack of adherence to therapy [23].

Triglycerides were lowered significantly very early after 1 month of CPAP therapy. This is in accordance with Drager *et al.* [24] who recently arrived at the same conclusion. This improvement is through reinstatement of lipolysis rate of triglyceride-rich lipoproteins and accelerating the removal of remnant particles. Of interest, these changes have been reversed again after stoppage of CPAP therapy [19]. In our study, there was no further improvement in the level of triglycerides after 3 months of CPAP therapy.

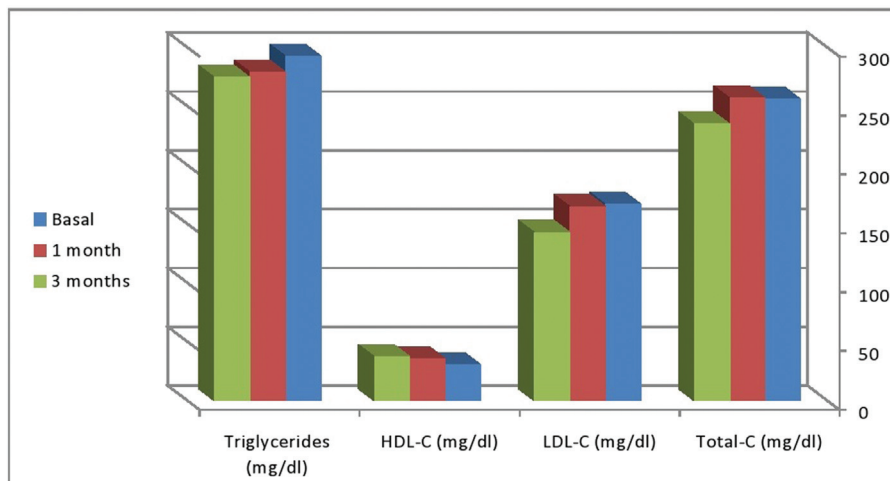
As regards HDL-C level, there was a significant increase in its level after 1 month which continued to rise significantly after 3 months of CPAP therapy. This finding is in agreement with Chin *et al.* [25] who found a significant increase in HDL-C after 8 months of CPAP therapy regardless of the changes in body weight. Borgel *et al.* [26] also demonstrated a significant increase in HDL-C ( $P < 0.013$ ) after 6 months of CPAP therapy in 127 patients with

OSA. On the other hand, Davies *et al.* [27] did not find any significant changes in HDL-C or other lipid parameters after 3 months of CPAP therapy in two groups of patients: snorers and OSA. Their results are inconvenient as they did paired sample *t* test only on 10 patients. Similarly, Lattimore *et al.* [28] showed a nonsignificant change in HDL-C after 3 months of CPAP therapy. Again, it was a small study on only 10 patients. As regards total-C and LDL-C, no changes happened after the first month of therapy. However, a significant reduction in both parameters had occurred after 3 months of therapy. This result matches with the results of Kumor *et al.* [29] who confirmed the reduction of both total-C and LDL-C after 3 months of CPAP therapy of 75 patients with OSA. Xu and colleagues in a meta-analysis on six randomized

control trials confirmed the reduction of the total-C but not triglycerides, HDL, or LDL-C. They underestimated the clinical importance of CPAP on lipid profile [12]. In general, meta-analysis trials gain its power from the large number of patients included in the study; however, it lacks the homogeneity of the patients included.

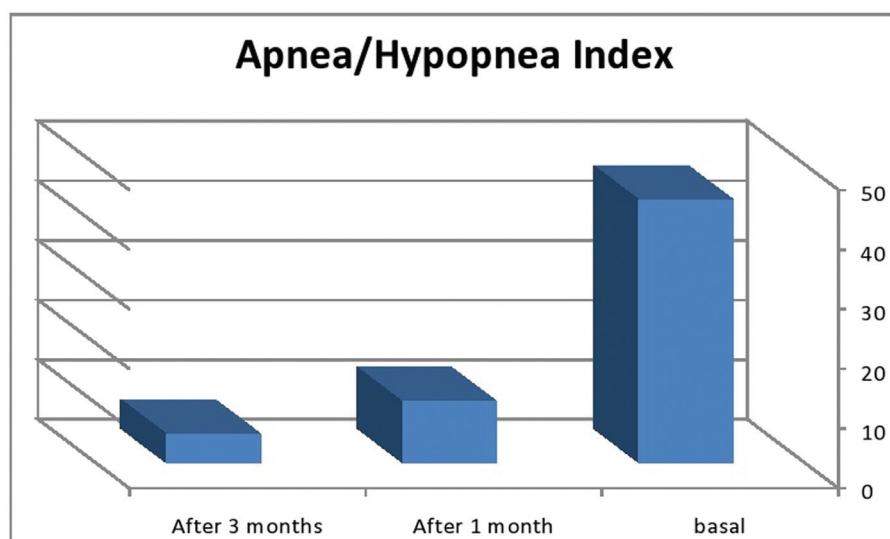
The beneficial effect of CPAP on lipid profile was confirmed again in a large meta-analysis study of six randomized control studies on 699 patients with OSA [30]. These conflicts in the literature are mainly due to the difference in sample size, duration of CPAP therapy, and adherence to therapy. Improvement of chronic intermittent hypoxia and sympathetic hyperactivity are the main mechanisms that correct

Figure 1



Comparison of basal lipid profile and after 1 and 3 months of CPAP therapy. CPAP, continuous positive airway pressure.

Figure 2



Comparison of basal apnea/hypopnea index after 1 and 3 months of CPAP therapy. CPAP, continuous positive airway pressure.

lipid profile after CPAP therapy. The use of lipid-lowering agents is still the main line of treatment of dyslipidemia in those patients.

## Conclusion

Treatment with CPAP improves lipid profile in patients with OSA. The early effect ensues on the triglycerides and HDL-C, followed by total-C and LDL-C.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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