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Διπλωματική Εργασία

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Title: A longitudinal study of BMI fluctuation during the use of CPAP in OSAS patients

Abstract

Obstructive Sleep Apnea Syndrome (OSAS) is linked to obesity. Continuous positive airway pressure (CPAP) treatment is thought to facilitate weight loss. The aim of this study is to investigate body mass index (BMI) fluctuation among OSAS patients who are on CPAP and to explore whether the addition of diet to regular CPAP usage will alter the results of weight loss.

A total of 291 patients on CPAP were examined. Twenty two of the above patients followed a diet for at least 3 months and were compared to 24 matched patients.

BMI change in one year was significantly correlated to apnea-hpopnea index (AHI), desaturation index (DI), min$SatO_2$% and mean$SatO_2$% and was greater in patients with daytime sleepiness, nocturia and bad mood. Only mean$SatO_2$% was related significantly to BMI change after adjustment. BMI and %fat decreased significantly in the 22 patients who followed a diet and not in the 24, who were only on CPAP. The improvement of $satO_2$ and AHI was greater in the group with the diet. BMI change could not be predicted from the available parameters.

BMI decrease in OSAS patients is greater in more severe cases and it is achieved by diet additionally to CPAP therapy.

Introduction

Obstructive Sleep Apnea Syndrome (OSAS) is a the most common form of apnea. Intermittent upper-airway closure during sleep causes apnea - hypopnea episodes during which oxygen desaturation is observed, followed by an increased ventilatory effort and arousal from sleep. Sleep is disrupted repetitively. Sleep fragmentation causes chronic sleep deprivation, that is accompanied by snoring, daytime sleepiness, fatigue, irritability, change of personality.[1,2]

Unfortunately the effect of OSAS is not limited to the above symptoms. Patients with sleep apnea have increased risk of diurnal hypertension, nocturnal dysrhythmias, pulmonary hypertension, right and left ventricular failure, myocardial infarction and stroke. Retrospective studies have shown that sleep apnea is associated with morbidity and mortality due to cardiovascular and cerebrovascular causes.[3, 4]

The syndrome is diagnosed by clinical history and polysomnography. The most commonly used index to define the severity of OSAS is apnea-hypopnea index (AHI), which is calculated as the number of obstructive events per hour of sleep and is obtained by nocturnal cardiorespiratory monitoring.[5] OSAS is defined by and AHI > 15 or an AHI > 5 with daytime and nighttime symptoms. The apnea severity is classified as mild (AHI 5 to 15), moderate (AHI 15.01 to 30) or severe (AHI > 30.1).[6]

OSAS is strongly linked to obesity. Data on the natural history of sleep-disordered breathing from the Wisconsin Sleep Cohort suggest that factors important in progression of disease include baseline obesity, older age and the presence of snoring.[7] Longitudinal Data from the same cohort show that among patients with mild OSAS at baseline, a 10% increase in body weight leads to 6-fold risk of developing moderate of severe OSAS.[8]

Obesity may narrow the upper airway, making it more easily collapsible and resulting in the block of airflow.[9] Central obesity is often indicated as the biggest determinant of OSAS. Obese individuals present high serum leptin levels, an hormone that regulates energy intake and expenditure[10] and improves respiratory control during sleep.[11] High serum leptin levels suggest a resistance to this hormone, which in turn may increase the likelihood of OSA in obese individuals.[12]

Continuous positive airway pressure (CPAP) therapy is recognized as the gold standard treatment of OSAS. It is an effective and commonly used treatment that provides maintenance of upper airway patency by increasing the upper airway pressure above a “critical” value (pressure below which the airway collapse).[13] Effective treatment of apnea may facilitate weight loss in some patients. Restriction of daytime sleepiness and fatigue may increase the motivation to lose weight.[14]

The aim of this study is to investigate body mass index (BMI) fluctuation among OSAS patients who are on CPAP therapy and whether their BMI change could be related to demographic, clinical and respiratory characteristics. Secondarily, it is to examine whether the addition of diet to regular CPAP usage will alter the results of weight loss in those patients.

Methods

A limited sleep study with the Embletta portable device (Medcare, Iceland) was performed to all subjects under attendance in the sleep laboratory. The device consists of a finger pulse oximeter for recording saturation of oxygen ($SatO_2$) and the pulse rate, thermistors for flow detection from nose and mouth, a nasal pressure detector for flow limitation, two piezoelectric belts for recording thoracic and abdominal movements, a neck vibration sensor for snore detection, sensors for leg movement activity, a built-in position sensor and actigraph. Automatic data analysis was manually checked and corrected every 2 minutes by a trained nurse taking into account the time of sleep latency and the awakenings of each patient. The diagnostic accuracy of the device used has been validated by Dingli et al.[10]

For CPAP titration an autoCPAP device (AutoSet T, ResMed, Sydney, Australia) was used simultaneously with oximetry under attendance in the sleep laboratory.

Patients who were diagnosed with OSAS at the sleep laboratory of Agios Pavlos Hospital of Thessaloniki and underwent CPAP therapy for at least one hour daily for at least 3 months were included in the study. Minimum level of AHI to diagnose OSAS was 5. Desaturation index was defined as episodes of $SatO_2$ reduction by >4% from the baseline per hour of sleep.

Patients were questioned about possible symptoms as daytime sleepiness, bad mood, depression, headaches, nycturia, sexual incompetence, fatigue. Clinical history of arterial hypertension and hypelidemia was reported. Smoking and drinking habits were reported as well. Body mass index (BMI) was calculated as weight in kg per square of height in m^2.

A total of 291 patients fulfilled the inclusion criteria and were included in the study.

In a second part of the study 22 of the above pool of patients, who consented to follow a weight loosing diet, were compared to another 24 OSAS patients on CPAP therapy, who continued with their eating habits. BMI, %fat, $satO_2$ and AHI were assessed at the beginning and at follow up visit. Differences between the two groups in BMI change, %fat change, $satO_2$ change and AHI change from baseline to follow up visit were explored.

The study was approved by the ethical committee of Aristotle University of Thessaloniki. A priori informed consent was obtained from all patients.

Analyses were conducted using IBM SPSS Statistics Version 22 (SPSS Inc., Chicago, IL). Spearman's rho was the correlation coefficient of choice since deviations from normal distribution was observed in numerous variables in the dataset by using the Kolmogorov Smirnov test. The Mann-Whitney and the t test were used to compare the means of scale variables between independent groups. The Wilcoxon signed-rank test and the paired t test were used to compare means of the same scale variable in two different time points, at the beginning of therapy and on follow up. Bonferroni correction was used for multiple testing. Univariate analysis of variance and linear regression analysis were performed in order to create a predictive model adjusted for confounding factors. Scale variables are presented as mean ± standard deviation (sd) and nominal variables are presented as frequency (percentage of total).

Results

Patients' characteristics are listed on table 1.

Table 1. General characteristics of patients

No	291
males	222 (76.3%)
age (years)	53 ± 11
BMI (Kg/m^2)	35.7 ± 7
current smokers	107 (36.8%)
current drinkers	112 (38.5%)
years of education	10.5 ± 4
arterial hypertension	150 (51.5%)
hyperlipidemia	86 (29.6%)

Variables are presented as mean ± sd or frequency (percentage)

Abbreviations: BMI body mass index

The results of the sleep study are listed in table 2.

Table 2. Sleep results of 291 OSAS patients	
min $SatO_2$%	66.8 ± 12.6
mean $SatO_2$%	90.6 ± 4.4
AHI	56.3 ± 24.8
DI	48.7 ± 25.8
Abbreviations: min $SatO_2$% lowest oxygen saturation, mean $SatO_2$% mean oxygen saturation, AHI apnea-hypopnea index, DI desaturation index, data presented as mean ± sd	

Patients were questioned about daytime and nighttime symptoms related to OSAS (table 3).

Table 3. Daytime and nighttime symptoms of 291 OSAS patients	
daytime sleepiness	271 (93.1%)
dizziness	196 (67.5%)
headache	128 (44%)
nocturia	212 (72.9%)
sexual imcompetence	74 (25.4%)
fatigue	252 (86.6%)
bad mood	206 (70.8%)
boredom	179 (61.5%)
depression	97 (33.3%)
Data presented as frequencies (percentage of total)	

Patients were on CPAP therapy for 1.8 ± 1.5 (0.25 - 7.5) years. The mean daily use was 4.9 ± 1.9 hours (figure 1). BMI after one year of follow up was 35.1 ± 6 Kg/m^2, significantly lower than BMI at baseline ($p<0.001$) (figure 2).

BMI change in one year was positively correlated to AHI ($r=0.15$, $p=0.009$) and DI ($r=0.129$, $p=0.034$) and negatively correlated to min$SatO_2$% ($r=-0.21$, $p<0.001$) and mean$SatO_2$% ($r=-0.28$, $p<0.001$). BMI change was also weakly correlated to hours of CPAP use per day, but with a lower level of significance ($r=0.085$, $p=0.152$). Age, years of education and years on CPAP use were not significantly correlated to BMI change ($p>0.2$).

When studied separately, BMI change in one year differ significantly in patients with daytime sleepiness ($p=0.035$), nocturia ($p=0.034$) and bad mood ($p=0.021$), (figures 3, 4,

5). BMI change was not different across groups formed by sex and presence of smoking, drinking, hypertension, hyperlipidemia, dizziness, headache, sexual incompetence, fatigue, boredom, depression ($p>0.05$).

Linear regression analysis including all the parameters that were significantly related to BMI change (AHI, DI, min$SatO_2$, mean$SatO_2$, hours of CPAP use per day, daytime sleepiness, nocturia, bad mood) did not produce any predictive model. The only variable that remained significantly related to BMI change after adjustment was mean $SatO_2$ (figure 6).

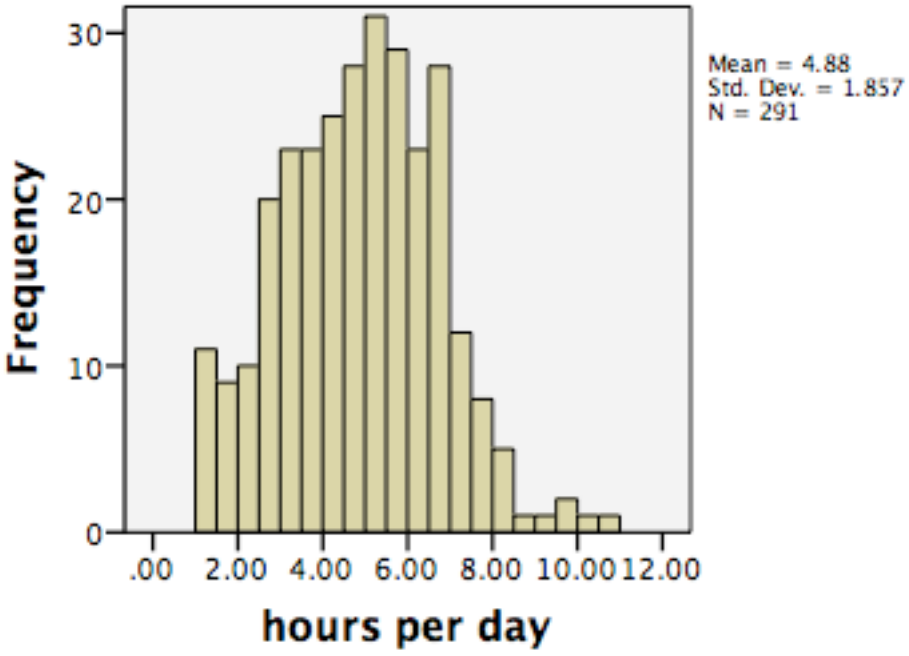

Figure 1. Distribution of hours on CPAP therapy per day

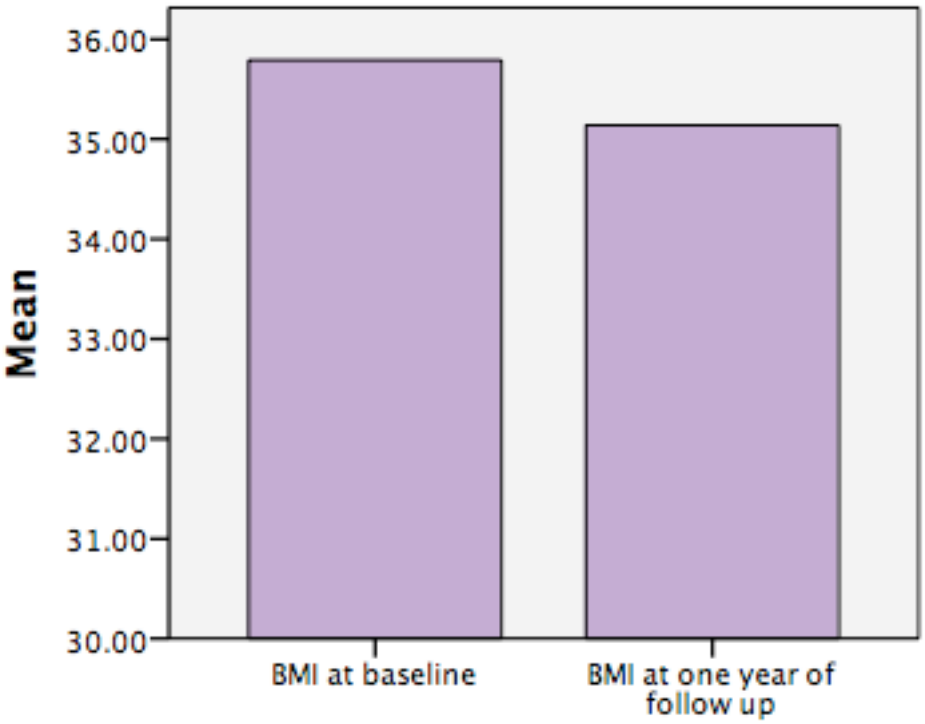

Figure 2. BMI change of 291 OSAS patients in one year of follow up

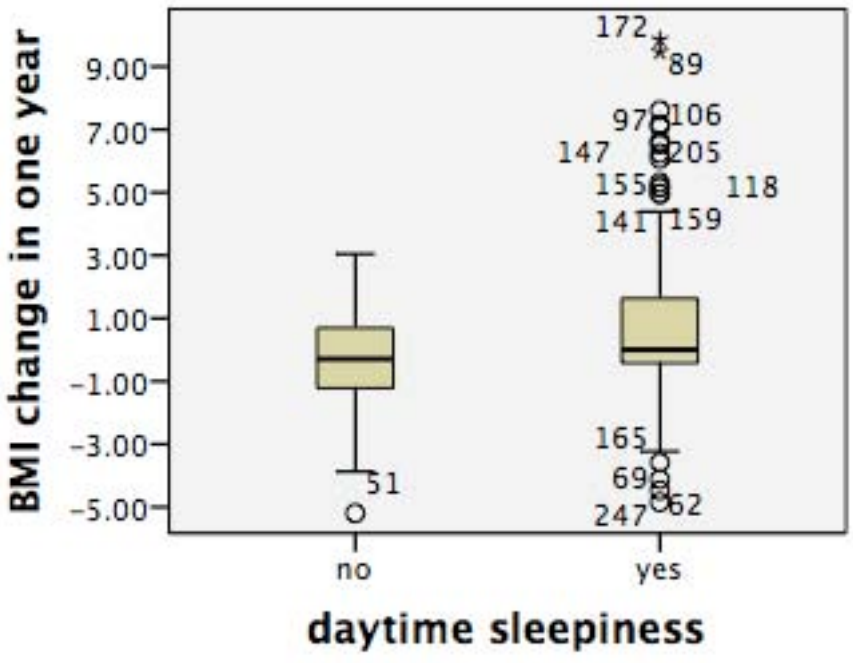

Figure3. BMI change in patients with daytime sleepiness or not

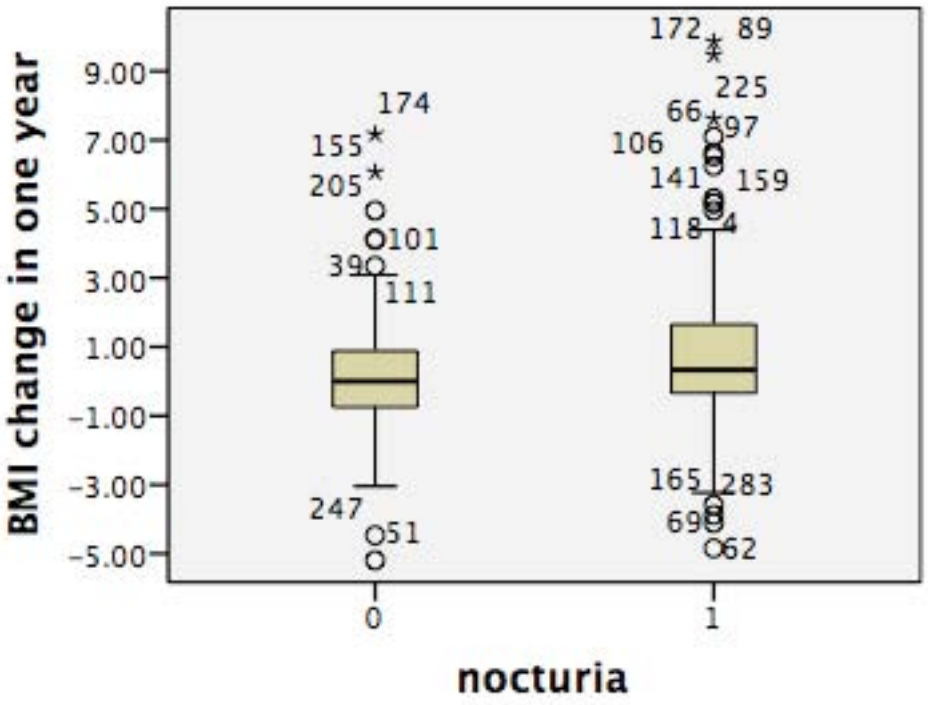

Figure 4. BMI change in patients with nocturia or not

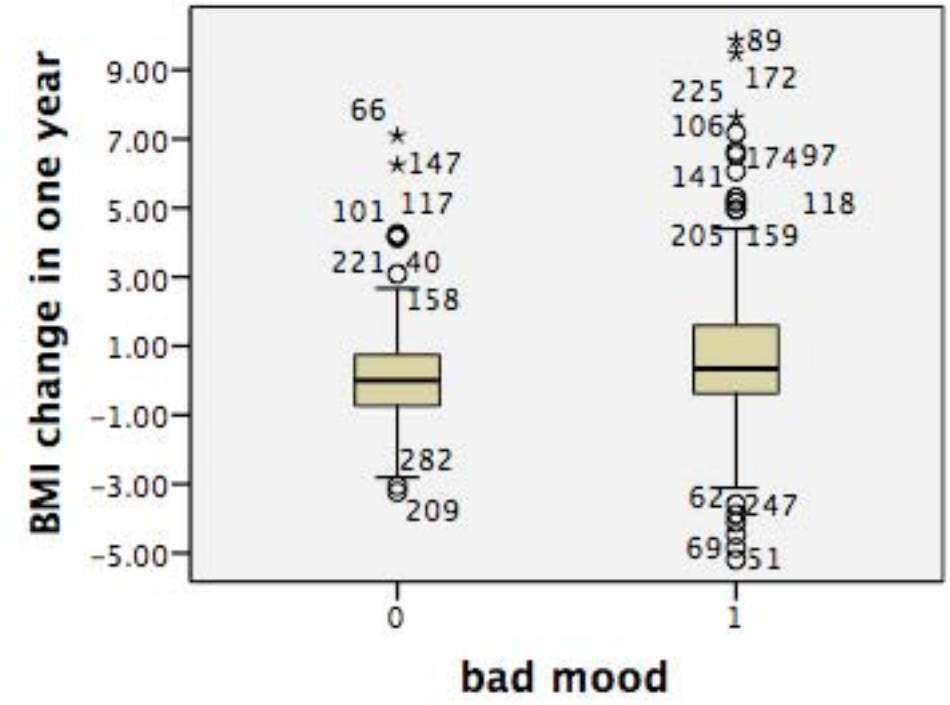

Figure 5. BMI change in patients with bad mood or not

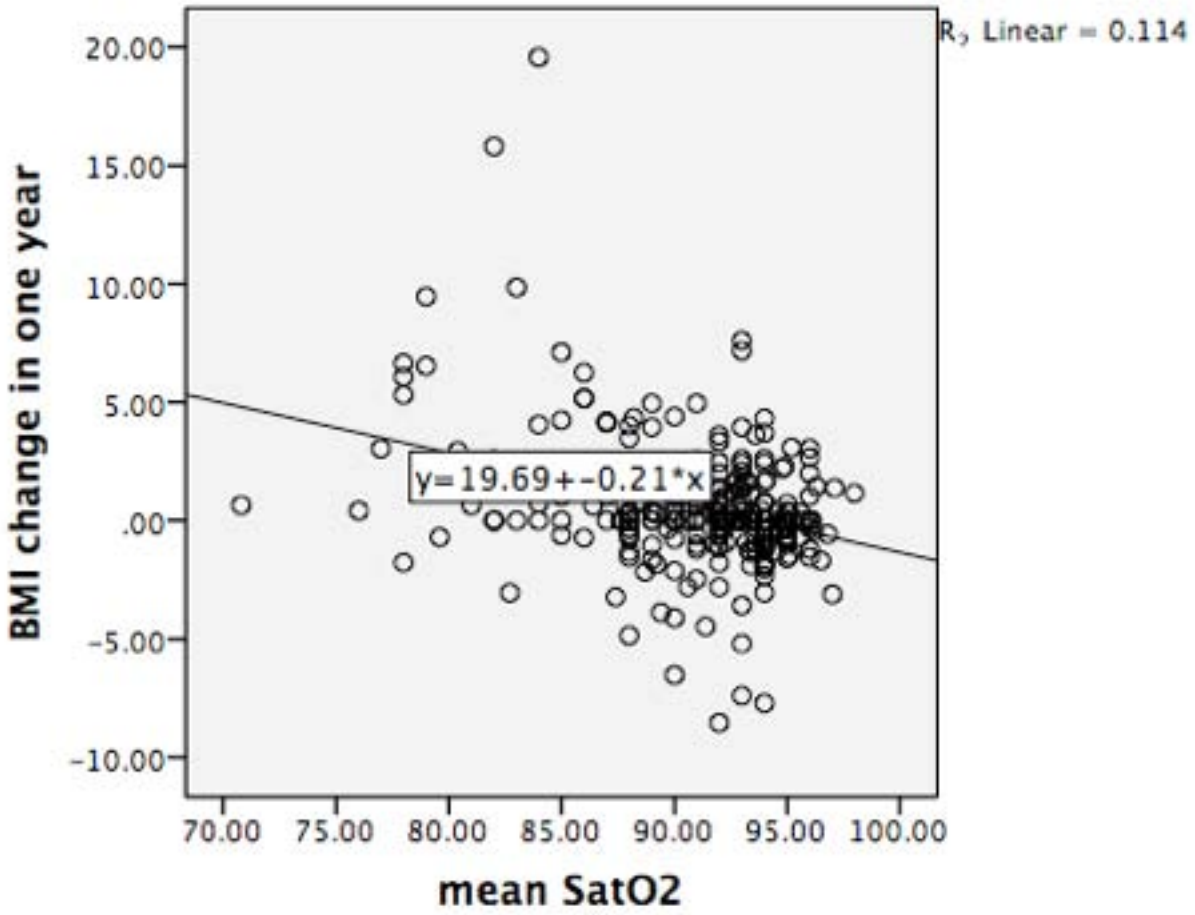

Figure 6. Linear regression of BMI change depending on mean SatO2

Weight losing diet was followed by 22 OSAS patients on CPAP therapy. These patients were compared to 24 OSAS patients with similar characteristics at baseline (table 4).

Table 4. Baseline characteristics of two groups of patients: CPAP therapy or CPAP therapy + diet

	CPAP	CPAP + diet	p
Number	24	22	NS
age	50.9 ± 10	50.8 ± 10	NS
BMI	41.1 ± 7	39.3 ± 7	NS
%fat	42.1 ± 9	40.1 ± 9	NS
$satO_2$	91.3 ± 6	83.9 ± 17	NS
AHI	55.3 ± 21	65.4 ± 30	NS

Abbreviations: CPAP continuous positive airway pressure, NS not significant (p>0.05)

During the 209 ± 93 days of follow up on CPAP therapy with or without diet, $satO_2$ and AHI were improved as expected in both groups. However, BMI and %fat decreased significantly only in the group under diet (tables 5 & 6) (figure 7).

Table 5. Changes of parameters from baseline to follow up for group on CPAP therapy

	Baseline	Follow up visit	p
BMI	41.63 ± 8	41.83 ± 8	NS
%fat	42.13 ± 9	42.35 ± 10	NS
$satO_2$	91.46 ± 6	95.5 ± 2	1
AHI	56.08 ± 21	40.54 ± 21	0,001

Abbreviations: BMI body mass index, $satO_2$ oxygen saturation, AHI apnea hypopnea index, NS not significant (p>0.05)

Table 6. Changes of parameters from baseline to follow up for group on CPAP therapy and diet

	Baseline	Follow up visit	p
BMI	39.27 ± 7	38.18 ± 7	0,036
%fat	40.73 ± 9	39.18 ± 10	0,043
$satO_2$	83.9 ± 17	94.29 ± 5	0,002
AHI	65.36 ± 30	39.91 ± 24	0,001

Abbreviations: BMI body mass index, $satO_2$ oxygen saturation, AHI apnea hypopnea index, NS not significant (p>0.05)

The changes of all the above parameters from baseline to follow up (absolute differences of values) were compared between the two groups. Apart from the change in %fat, which was not different between groups, the decrease of BMI, the decrease of AHI and the increase of $satO_2$ were greater in the diet group (table 7).

Table 7. Absolute changes of parameters from baseline to follow up between groups: CPAP therapy or CPAP therapy + diet

	CPAP	CPAP + diet	p
BMI difference	0.21 ± 2	-1.09 ± 2	0,051
%fat difference	0 ± 3	-1.55 ± 3	NS
$satO_2$ difference	4.13 ± 5	14.36 ± 23	0,049
AHI difference	-15.5 ± 16	-25.36 ± 17	0,046

Abbreviations: BMI body mass index, $satO_2$ oxygen saturation, AHI apnea hypopnea index, NS not significant (p>0.05)

Univariate analysis of variance was performed in order to investigate whether BMI difference could be explained by age, BMI at baseline, period of follow up, addition of diet in the management with CPAP therapy. Moreover, AHI and $satO_2$ at baseline, which denote disease severity, and AHI and $satO_2$ changes which denote the benefit from CPAP therapy. After adjustment for all these parameters, none could predict BMI difference with significance.

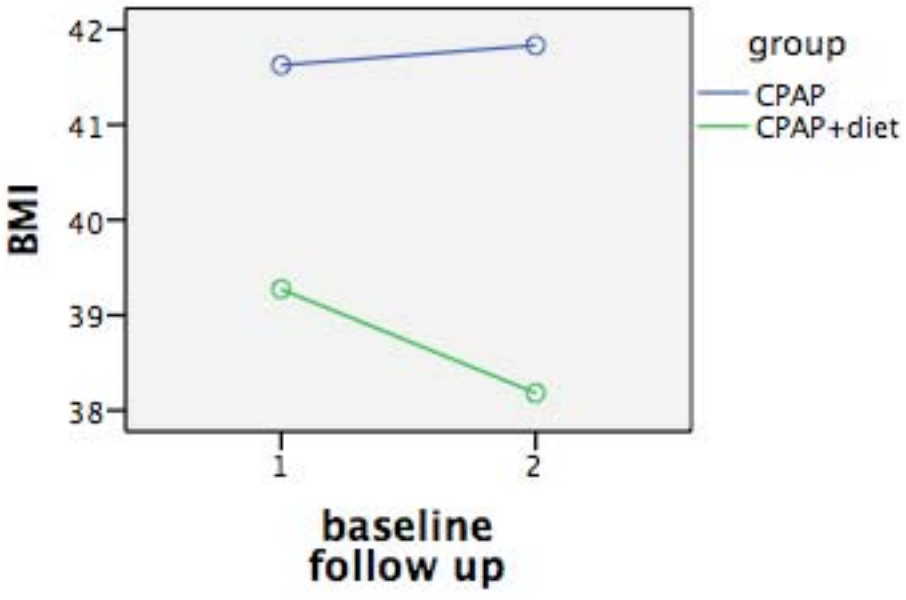

Figure 7. BMI change from baseline (1) to follow up visit (2) in the two groups: CPAP and CPAP+diet

Conclusion

This study examined the link between CPAP therapy and BMI change in OSAS patients. According to bibliography the improvement of sleep apnea by the application of CPAP therapy is expected to be accompanied by weight loss.

Simple correlations revealed that higher decreases of BMI were observed in more seriously ill patients. The disease severity was assessed by AHI, DI, min$SatO_2$ and mean$SatO_2$. Furthermore, patients suffering from daytime sleepiness, nocturne and bad mood were found to have greater decrease in their BMI. Other factors like smoking and drinking habits, hypertension and hyperlidemia did not influence significantly BMI change. However, after adjustment for all the parameters mentioned above, only mean$SatO_2$ remained significantly related to BMI change. The less mean$SatO_2$ at baseline the greater the decrease in BMI.

In the second part of the study it was shown that only CPAP therapy was not enough for weight loss in our patients. The addition of diet was necessary for BMI decrease. Moreover, the benefit from CPAP therapy shown by an improvement in $satO_2$ and AHI was significantly greater in the patients who followed a diet along with CPAP application. Unfortunately, analysis of our data did not conclude to a predictive model of BMI change in OSAS patients.

Limitations to this study include the small sample size and the high variance of CPAP use among our patients. A larger study with a minimum limit for CPAP usage set seems justified.

CPAP therapy may impact weight in ways not accounted for in the present study. A more complete work would include measurement of leptin levels and energy expenditure. Nevertheless, OSAS patients should should take an active role in weight loss plans in addition to their compliance to CPAP usage. The later improves daytime sleepiness but this benefit is abated if the patient does not increase activity levels and caloric expenditure beyond energy intake.

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