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Original Article

Efficacy of continuous positive airway pressure for obstructive sleep apnea in overweight patients with type 2 diabetes mellitus

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Abstract: Although the association between obstructive sleep apnea (OSA) and type 2 diabetes mellitus (T2DM) is well-established, the impact of continuous positive airway pressure (CPAP) therapy on glycemic control or metabolic profiles in T2DM patients with OSA is unclear. The objective of this study was to investigate metabolism-related parameters and diabetes treatment satisfaction following CPAP therapy for OSA in overweight patients with T2DM or impaired glycemic tolerance. This retrospective study included 16 overweight patients treated with CPAP for OSA by comparison of laboratory and anthropometric data between baseline (3 months before initiation of CPAP treatment) and at 3- and 6-months post-treatment, and by psychometric scores of DM treatment satisfaction using the Diabetes Treatment Satisfaction Questionnaire (DTSQ). Significant reductions in body weight and waist circumference were observed after initiating CPAP therapy (both $P<0.001$). Mean glycosylated hemoglobin (HbA1c) level measured at 3 months after CPAP therapy was lower than the baseline assessment, and the mean HbA1c level at 6 months post-treatment was lower than that at 3 months post-treatment (both $P<0.05$). In addition, fasting and postprandial plasma glucose levels decreased significantly at 3 months after CPAP therapy, remaining stable at 6 months ($P\leq0.009$). Furthermore, significant decreases in fasting insulin level ($P=0.037$), postprandial insulin level ($P<0.001$), and triglyceride level ($P=0.002$) were observed following CPAP. Finally, satisfaction with diabetes treatment improved significantly following initiation of CPAP therapy ($P<0.001$). CPAP for OSA improved anthropomorphic measures as well as glycemic control, insulin sensitivity and diabetes treatment satisfaction in overweight patients with T2DM or abnormal glucose metabolism.

Keywords: Continuous positive airway pressure, obstructive sleep apnea, overweight, type 2 diabetes mellitus

Introduction

Obstructive sleep apnea (OSA) is characterized by repeated episodes of complete (apnea) or partial (hypoapnea) upper airway blockage during sleep that can interrupt sleep and result in intermittent hypoxia [1]. Obesity is a risk factor for developing OSA due to upper airway narrowing and reduced lung volume as a result of soft tissue enlargement [2]. Thus, the prevalence of OSA has increased in recent decades due to the epidemic of obesity. Approximately 50%-60% of obese patients or those with metabolic syndrome have OSA [3, 4]. Furthermore, analysis of obese patients with type 2 diabetes mellitus (T2DM) revealed that 86% had OSA [5], and it is reported that 15%-30% of individuals with OSA have T2DM [6].

Cross-sectional, observational, and population-based studies have shown a consistent link between OSA and insulin resistance (IR), glucose intolerance and T2DM [7-10]. In addition, analysis of 475 patients with suspected OSA revealed that concomitant OSA and metabolic syndrome (MS) frequency was 70.52% in those who were obese [11]. Furthermore, OSA is an independent risk factor for T2DM [6]. Studies in animals [12] and healthy volunteers [13] have also shown that acute intermittent hypoxia can induce IR, and chronic intermittent hypoxia altered fasting hyperglycemia and induced glucose intolerance and IR in obese mice [14, 15].

Table 1. Baseline characteristics of overweight patients treated with CPAP for OSA (n=16)

	Variable*
Age (y)	49.5 ± 6.7
Sex (male)	8 (50%)
BMI (kg/m^2)	28.4 ± 1.9
Type 2 diabetes	13 (81.3%)
Impaired glucose tolerance	3 (18.8%)
Treatment	
Oral agents	14 (87.5%)
Lifestyle intervention	2 (12.5%)
Duration of OSA (y)	3.8 ± 2.2

Abbreviations: CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea; SD, standard deviation. *Values represent either n (%) or mean ± SD.

The apparent association of OSA and T2DM suggests that OSA treatment, which primarily consists of continuous positive airway pressure (CPAP) therapy, may improve glycemic control or metabolic profiles in T2DM patients with OSA [16]. However, results of studies analyzing the effects of CPAP on glycemic dysregulation have been inconsistent [17-19]. In a systematic review of 22 studies examining the impact of CPAP for OSA in T2DM patients, improvements in HbA1c, postprandial and nocturnal glucose, and insulin sensitivity were observed following CPAP therapy, with greater improvement after its long-term use [19]. In contrast, another recent systematic review and meta-analysis that included six randomized, controlled studies or prospective observational studies showed that CPAP had no impact on HbA1c or body mass index (BMI) but did improve insulin sensitivity [18].

This retrospective, observational small-scale study aimed to ascertain whether OSA treatment by CPAP improves glycemic control and diabetes treatment satisfaction in overweight OSA patients with T2DM or impaired glucose tolerance. The results showed that several diabetic markers and anthropometric parameters were all improved significantly after CPAP treatment. In addition, satisfaction with diabetes treatment as measured by the Diabetes Treatment Satisfaction Questionnaire (DTSQ) improved significantly following initiation of CPAP therapy.

Material and methods

Study design and patients

This retrospective study included 16 overweight patients (eight males and eight females) with OSA who had a complete medical record and were treated from January 2013 to November 2014. Thirteen patients were diagnosed with T2DM and three with impaired glucose tolerance using the World Health Organization (WHO) criteria [20]. Anthropometric and laboratory data of candidate patients who had received CPAP treatment were retrieved from medical charts. The therapeutic protocol for T2DM or impaired glucose tolerance remained unchanged. This study was approved by the Institutional Review Board of the Guangdong General Hospital. Due to the retrospective nature of this study, informed consent was waived.

OSA diagnosis and treatment

OSA was diagnosed by real-time monitoring of sleep using standard 12-channel polysomnography (PSG) and mobile monitoring and using the definitions of the American Academy of Sleep Medicine (AASM) Manual for Scoring of Sleep and Associated Events. For each patient, CPAP was performed for >4 h daily for >5 times weekly. PSG was also used to confirm a diagnosis of OSA. In addition, OSA duration was determined by medical record review.

Laboratory analyses

Blood samples were collected from each participant, and metabolism-related parameters were measured before initiation of CPAP (baseline) as well as at 3 and 6 months following treatment initiation. The following parameters were assessed using the manufacturers' protocols: glycosylated hemoglobin (cation-exchange high-performance liquid chromatography; BioRad, Hercules, CA, USA), cholesterol (colorimetry; Beckmann Coulter, Brea, CA, USA), blood glucose (Beckmann Coulter), and insulin (electrochemiluminescence; Roche Diagnostics, Rotkreuz, Switzerland).

Analysis of treatment satisfaction

The DTSQ was employed to evaluate patients' quality of life before and after initiation of CPAP,

Table 2. Effects of CPAP therapy on the clinical characteristics of overweight patients with OSA (n=16)

Parameters	Pre-CPAP	Post-CPAP		
		3 months	6 months	*P*-value
Weight (kg)	78.4 ± 10.0	75.4 ± 9.7*	73.7 ± 8.6*,†	<0.001[a]
Waist circumference (cm)	89.9 ± 9.6	86.4 ± 8.5*	84.0 ± 7.3*,†	<0.001[a]
Systolic blood pressure (mmHg)	137.0 ± 7.7		136.9 ± 6.5	0.841[b]
Diastolic blood pressure (mmHg)	86.0 ± 6.8		85.7 ± 6.1	0.715[b]
DTSQ score	23.7 ± 1.6		28.1 ± 2.4	<0.001[b]

Abbreviations: CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea; DTSQ, diabetes treatment satisfaction questionnaire. [a]Analyzed using repeated-measures analysis of variance. Pair-wise comparisons between any two time points were performed with Bonferroni correction. [b]Analyzed using a paired t-test. *P<0.05, compared with the baseline measurement. †P<0.05, compared with measurements at 3 months after CPAP treatment.

as described previously [21, 22]. The DTSQ measures eight items that are scored on a scale of 0-6.

Statistical analysis

Data were presented as mean and standard deviation (SD) for continuous variables or as number and percentage for categorical variables. Paired t-tests were used to examine differences in blood pressure, insulin levels, triglyceride levels and diabetes treatment satisfaction before, three and six months after CPAP therapy initiation. For variables measured at three time points (i.e., weight, waist and glucose levels), repeated-measures analysis of variance (rANOVA) was performed to examine whether significant changes occurred across time points. If the sphericity assumption was violated, *P*-values were corrected using the Greenhouse-Geisser method. Multiple comparisons with Bonferroni correction were then made to test differences between any two time points. All statistical analyses were carried out using IBM SPSS statistical software version 22 for Windows (IBM, New York, NY, USA). A two-tailed *P*-value less than 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 16 overweight patients (BMI of 28.4 kg/m^2) diagnosed with OSA were recruited; their mean age was 49.5 y (SD=6.7 y, range=37-60 y; **Table 1**). The average duration of OSA was 3.8 ± 2.2 y (range=1-8 y). Most patients had T2DM (81.3%) and were treated with oral agents (87.5%).

Effects of CPAP on the clinical and biochemical characteristics of overweight OSA patients

As shown in **Table 2**, patients' body weight and waist circumference decreased significantly after treatment with CPAP (both P<0.001). Satisfaction with diabetes treatment improved significantly following initiation of CPAP therapy (P<0.001). CPAP therapy did not alter blood pressure levels (P=0.841 for systolic blood pressure and P=0.715 for diastolic blood pressure).

HbA1c values decreased across follow-up measurements (P<0.001; **Figure 1A**). Specifically, multiple comparison analysis also showed that the mean HbA1c level measured 3 months after CPAP therapy was lower than the baseline assessment (7.0% ± 0.6% vs. 7.4% ± 0.6%), and the mean HbA1c level at 6 months post-treatment was lower than that at 3 months post-treatment (6.7% ± 0.5% vs. 7.0% ± 0.6%). Furthermore, fasting plasma glucose levels decreased significantly 3 months after CPAP therapy (6.7 ± 0.5 mmol/L vs. 7.0 ± 0.5 mmol/L), remaining stable thereafter at 6 months; similar reductions were observed for postprandial plasma glucose (8.5 ± 1.0 mmol/L vs. 9.0 ± 1.2 mmol/L) (**Figure 1C**). Moreover, significant decreases were found in fasting insulin levels (P=0.037), postprandial insulin levels (P<0.001; **Figure 1D**), and triglyceride levels (P=0.002; **Figure 1B**).

Discussion

Although links between OSA and T2DM have been observed consistently [7-10], the effects of CPAP therapy on the metabolic profiles of T2DM patients with OSA are inconsistent [17-19]. In the present retrospective study, significant reductions in body weight and waist circumference, as well as improvements in glycemic control, insulin sensitivity and triglyceride levels, were observed 3 months after initiation of CPAP therapy and were maintained at 6 months. In addition, satisfaction with diabetes treatment improved significantly following initi-

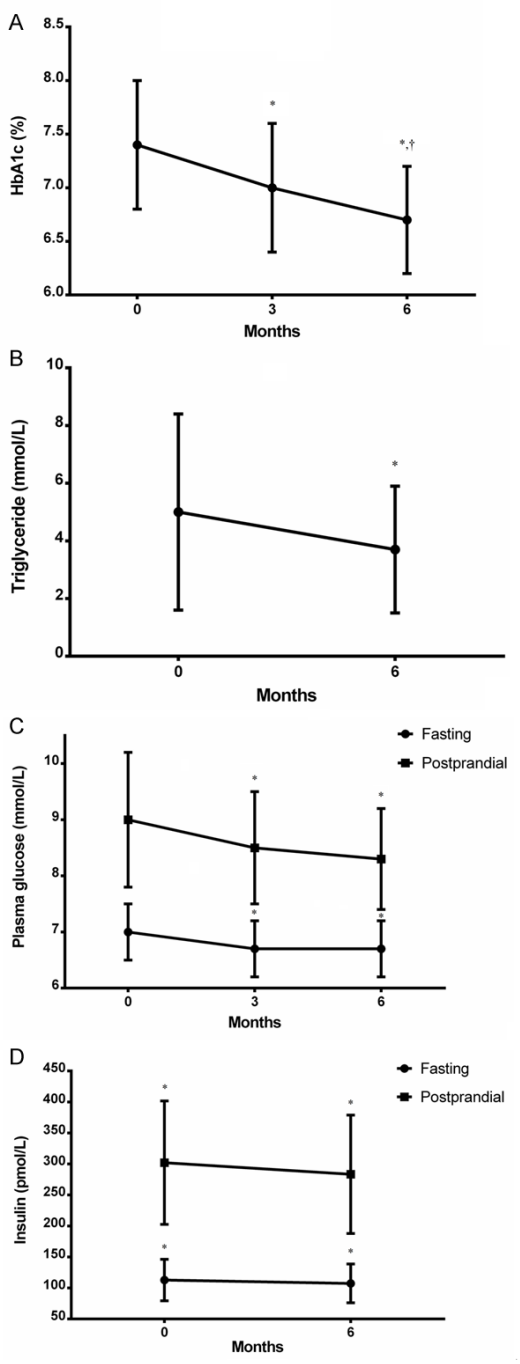

Figure 1. Changes in biochemical measures for overweight patients with OSA before and after CPAP therapy (n=16). Abbreviations: CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea. HbA1c and triglyceride were analyzed by paired t-test. Plasma glucose and insulin were analyzed by repeated-measures analysis of variance; pair-wise comparisons between any two time points were performed with Bonferroni correction. $^{*}P<0.05$, compared with the baseline measurement. $^{\dagger}P<0.05$, compared with measurements at 3 months after CPAP treatment.

ation of CPAP therapy. To our knowledge, this is the first study to examine the effects of CPAP therapy on diabetes treatment satisfaction.

With the exception of blood pressure, which was not affected, the improved metabolic parameters observed in the present study are consistent with previous reports [23, 24]. Specifically, in patients with metabolic syndrome, CPAP therapy for >4 h/night for 8 weeks improved blood pressure, triglyceride levels and glucose levels to a greater extent than in those using CPAP for <4 h/night [23]. In a randomized, double-blind, crossover study, Sharma et al. [24] observed decreases in blood pressure as well as cholesterol, triglyceride, and Hba1c levels with CPAP therapy. However, other studies did not observe an improvement in glucose metabolism with CPAP treatment in obese patients with [25] and without [26] T2DM, which may be due to lower compliance (use of an average of 3.9 h/night vs. >4 h/night in the present study). Thus, further studies are required to examine the extent to which CPAP duration impacts metabolic parameters.

Previous studies have shown that CPAP therapy reduces OSA-associated IR and diabetic inflammation, which may reduce pancreatic β cell damage [16]. Furthermore, reduced metabolic hormone levels, including adiponectin and leptin, were observed after 3 months of CPAP in obese individuals [27]. As observed previously with the application of CPAP and left ventricular remodeling in patients with abdominal obesity [28], the metabolic improvements observed in the present study may be due at least in part to the accompanying reductions in weight and waist circumference following CPAP therapy, which continued to improve at 6 months post-treatment. Similarly, Sharma et al. [24] reported that BMI and visceral adiposity were reduced after CPAP. However, not all studies noted such changes in anthropomorphic indices [29, 30], and a recent meta-analysis of randomized trials showed that CPAP may actually increase BMI and body weight [31]. These inconsistencies may be due to differences in the duration and frequency of the CPAP therapy as well as CPAP compliance, which may be different for obese and non-obese individuals [32]. Because the patients in the present study only received CPAP and were not participating in a diet or exercise program simultane-

ously, their weight loss appears to be a consequence of the CPAP therapy and parallel to the improvement of other parameters, including blood glucose. However, further analyses are required to fully elucidate the effects of CPAP on body weight and BMI.

Although it is known that obesity is a risk factor for developing OSA [2], and that OSA is highly prevalent in obese patients with T2DM (up to 86%) [5], the relationship between OSA and the occurrence of metabolic syndrome is not well-characterized. OSA may increase the risk of developing T2DM [33]; thus, it is possible that OSA and T2DM coexist due to shared risk factors, including obesity [34]. Additionally, studies showing altered glucose metabolism in non-diabetic individuals with OSA independent of obesity [7, 35, 36] suggest that OSA and T2DM may be linked by an underlying metabolic disorder. Analysis of patients with suspected OSA revealed that those with metabolic syndrome had significantly lower levels of nesfatin-1, a neuropeptide that regulates food ingestion as well as paradoxical sleep [37]. Because the level of nocturnal hypoxia is related to IR [38], OSA-associated hypoxia may induce concomitant metabolic dysfunction [39]. This is consistent with the results of our study as well as those of another study involving 31 nondiabetic obese adolescents in whom hypercapnia was associated with carotid narrowing [40].

A relationship between intermittent hypoxia and IR has been shown in both animals [12] and healthy volunteers [13]. Analysis of the effects of intermittent hypoxia have shown increased hepatic inflammation, oxidative stress, and steatosis as well as increased pancreatic β cell death and decreased glucose-induced insulin secretion [39]. In skeletal muscle, decreased glucose metabolism and GLUT4 translocation was observed with intermittent hypoxia [39]. In addition, impaired sympathetic nervous system activation that has been observed in patients with OSA can be induced with intermittent hypoxia [41, 42], which has the potential to impact lipid and glucose metabolism [39]. Given the beneficial effects of CPAP treatment on glycemic control and insulin sensitivity observed in the present study, we propose that OSA may cause secondary diabetes that develops independent of insulin-dependent, non-insulin-dependent, or gestational diabetes mellitus, and this underlying mechanism may be ameliorated by CPAP. However, further studies are necessary to explore this hypothesis.

The present study is limited by its retrospective nature. In addition, we did not examine the effects of sleep improvement with CPAP on the metabolic parameters assessed. Finally, the present study focused on overweight patients with OSA who also had T2DM or impaired glucose control; therefore, further studies are needed to determine the impact of CPAP therapy in otherwise healthy adults with OSA.

In conclusion, glycemic control and insulin sensitivity improved significantly after CPAP treatment. In addition, patients' satisfaction with diabetes treatment improved significantly following initiation of CPAP therapy.

Disclosure of conflict of interest

None.

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References

[1] American Academy of Sleep Medicine. Sleep-related breathing disorders in adults. Recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999; 22: 667-689.

[2] Drager LF, Togeiro SM, Polotsky VY and Lorenzi-Filho G. Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol 2013; 62: 569-576.

[3] Resta O, Foschino-Barbaro MP, Legari G, Talamo S, Bonfitto P, Palumbo A, Minenna A, Giorgino R and De Pergola G. Sleep-related breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. Int J Obes Relat Metab Disord 2001; 25: 669-675.

[4] Drager LF, Lopes HF, Maki-Nunes C, Trombetta IC, Toschi-Dias E, Alves MJ, Fraga RF, Jun JC, Negrão CE, Krieger EM, Polotsky VY and Loren-

zi-Filho G. The impact of obstructive sleep apnea on metabolic and inflammatory markers in consecutive patients with metabolic syndrome. PLoS One 2010; 5: e12065.
[5] Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, Wadden TA, Kelley D, Wing RR, Pi-Sunyer FX, Reboussin D, Kuna ST; Sleep AHEAD Research Group of Look AHEAD Research Group, Sleep AHEAD Research Group. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care 2009; 32: 1017-1019.
[6] Pamidi S and Tasali E. Obstructive sleep apnea and type 2 diabetes: is there a link? Front Neurol 2012; 3: 126.
[7] Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R and Resnick HE. Sleep Heart Health Study Investigators. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. Am J Epidemiol 2004; 160: 521-530.
[8] Reichmuth KJ, Austin D, Skatrud JB and Young T. Association of sleep apnea and type II diabetes: a population-based study. Am J Respir Crit Care Med 2005; 172: 1590-1595.
[9] Botros N, Concato J, Mohsenin V, Selim B, Doctor K and Yaggi HK. Obstructive sleep apnea as a risk factor for type 2 diabetes. Am J Med 2009; 122: 1122-1127.
[10] Togeiro SM, Carneiro G, Ribeiro Filho FF, Zanella MT, Santos-Silva R, Taddei JA, Bittencourt LR and Tufik S. Consequences of obstructive sleep apnea on metabolic profile: a population-based survey. Obesity 2013; 21: 847-851.
[11] Dacal Quintas R, Tumbeiro Novoa M, Alves Pérez MT, Santalla Martínez ML, Acuña Fernández A and Marcos Velázquez P. Obstructive sleep apnea in normal weight patients: characteristics and comparison with overweight and obese patients. Arch Bronconeumol 2013; 49: 513-517.
[12] Liyori N, Alonso LC, Li J, Sanders MH, Garcia-Ocana A, O'Doherty RM, Polotsky VY and O'Donnell CP. Intermittent hypoxia causes insulin resistance in lean mice independent of autonomic activity. Am J Respir Crit Care Med 2007; 175: 851-857.
[13] Louis M and Punjabi NM. Effects of acute intermittent hypoxia on glucose metabolism in awake healthy volunteers. J Appl Physiol 2009; 106: 1538-1544.
[14] Drager LF, Li J, Reinke C, Bevans-Fonti S, Jun JC and Polotsky VY. Intermittent hypoxia exacerbates metabolic effects of diet-induced obesity. Obesity 2011; 19: 2167-2174.
[15] Polotsky VY, Li J, Punjabi NM, Rubin AE, Smith PL, Schwartz AR and O'Donnell CP. Intermittent hypoxia increases insulin resistance in genetically obese mice. J Physiol 2003; 552: 253-264.
[16] Zhong W, Tang YG, Zhao X, Go FY, Harper RM and Hui H. Treating obstructive sleep apnea with continuous positive airway pressure benefits type 2 diabetes management. Pancreas 2014; 43: 325-330.
[17] Seetho IW and Wilding JP. Sleep-disordered breathing, type 2 diabetes and the metabolic syndrome. Chron Respir Dis 2014; 11: 257-275.
[18] Feng Y, Zhang Z and Dong ZZ. Effects of continuous positive airway pressure therapy on glycaemic control, insulin sensitivity and body mass index in patients with obstructive sleep apnoea and type 2 diabetes: a systematic review and meta-analysis. NPJ Prim Care Respir Med 2015; 25: 15005.
[19] Gallegos L, Dharia T and Gadegbeku AB. Effect of continuous positive airway pressure on type 2 diabetes mellitus and glucose metabolism. Hosp Pract 2014; 42: 31-37.
[20] Alberti KG and Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998; 15: 539-553.
[21] Pouwer F, Snoek FJ, van der Ploeg HM, Heine RJ and Brand AN. A comparison of the standard and the computerized versions of the Well-being Questionnaire (WBQ) and the Diabetes Treatment Satisfaction Questionnaire (DTSQ). Qual Life Res 1998; 7: 33-38.
[22] Reaney M, Yu M, Lakshmanan M, Pechtner V and van Brunt K. Treatment satisfaction in people with type 2 diabetes mellitus treated with once-weekly dulaglutide: data from the AWARD-1 and AWARD-3 clinical trials. Diabetes Obes Metab 2015; 17: 896-903.
[23] Dorkova Z, Petrasova D, Molcanyiova A, Popovnakova M and Tkacova R. Effects of continuous positive airway pressure on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome. Chest 2008; 134: 686-692.
[24] Sharma SK, Agrawal S, Damodaran D, Sreenivas V, Kadhiravan T, Lakshmy R, Jagia P and Kumar A. CPAP for the metabolic syndrome in patients with obstructive sleep apnea. N Engl J Med 2011; 365: 2277-2286.
[25] West SD, Nicoll DJ, Wallace TM, Matthews DR and Stradling JR. Effect of CPAP on insulin resistance and HbA1c in men with obstructive sleep apnoea and type 2 diabetes. Thorax 2007; 62: 969-974.
[26] Coughlin SR, Mawdsley L, Mugarza JA, Wilding JP and Calverley PM. Cardiovascular and metabolic effects of CPAP in obese males with OSA. Eur Respir J 2007; 29: 720-727.
[27] Sánchez-de-la-Torre M, Mediano O, Barceló A, Piérola J, de la Peña M, Esquinas C, Miro A,

Durán-Cantolla J, Agustí AG, Capote F, Marin JM, Montserrat JM, García-Río F and Barbé F. The influence of obesity and obstructive sleep apnea on metabolic hormones. Sleep Breath 2012; 16: 649-656.

[28] Grandi AM, Laurita E, Marchesi C, Maresca AM, Solbiati F, Bernasconi A, Marogna M, Salina C, Nicolini E, Guasti L, Colombo F and Venco A. OSA, metabolic syndrome and CPAP: effect on cardiac remodeling in subjects with abdominal obesity. Respir Med 2012; 106: 145-152.

[29] Hoyos CM, Killick R, Yee BJ, Phillips CL, Grunstein RR and Liu PY. Cardiometabolic changes after continuous positive airway pressure for obstructive sleep apnoea: a randomised sham-controlled study. Thorax 2012; 67: 1081-1089.

[30] Sivam S, Phillips CL, Trenell MI, Yee BJ, Liu PY, Wong KK and Grunstein RR. Effects of 8 weeks of continuous positive airway pressure on abdominal adiposity in obstructive sleep apnoea. Eur Respir J 2012; 40: 913-918.

[31] Drager LF, Brunoni AR, Jenner R, Lorenzi-Filho G, Benseñor IM and Lotufo PA. Effects of CPAP on body weight in patients with obstructive sleep apnoea: a meta-analysis of randomised trials. Thorax 2015; 70: 258-264.

[32] Kim H, Kim MS, Lee JE, Kim JW, Lee CH, Yoon IY and Rhee CS. Treatment outcomes and compliance according to obesity in patients with obstructive sleep apnea. Eur Arch Otorhinolaryngol 2013; 270: 2885-2890.

[33] Tasali E, Mokhlesi B and Van Cauter E. Obstructive sleep apnea and type 2 diabetes: interacting epidemics. Chest 2008; 133: 496-506.

[34] Vale J, Manuel P, Oliveira E, Oliveira AR, Silva E, Melo V, Sousa M, Alexandre JC, Gil I, Sanchez A, Nascimento E and Torres AS. Obstructive sleep apnea and diabetes mellitus. Rev Port Pneumol 2015; 21: 55-60.

[35] Seicean S, Kirchner HL, Gottlieb DJ, Punjabi NM, Resnick H, Sanders M, Budhiraja R, Singer M and Redline S. Sleep disordered breathing and impaired glucose metabolism in normal weight and overweight/obese individuals: the Sleep Heart Health Study. Diabetes Care 2008; 31: 1001-1006.

[36] Kent BD, Grote L, Bonsignore MR, Saaresranta T, Verbraecken J, Lévy P, Sliwinski P, Tkacova R, Kvamme JA, Fietze I, Hedner J, McNicholas WT; European Sleep Apnoea Database collaborators. Sleep apnoea severity independently predicts glycaemic health in nondiabetic subjects: the ESADA study. Eur Respir J 2014; 44: 130-139.

[37] Aksu O, Aydın B, Doguç DK, Ilhan I, Ozturk O, Altuntas A, Demirkan H, Koroglu BK and Tamer MN. The evaluation of Nesfatin-1 levels in patients with OSAS associated with metabolic syndrome. J Endocrinol Invest 2015; 38: 463-469.

[38] Borel AL, Monneret D, Tamisier R, Baguet JP, Faure P, Levy P, Halimi S and Pépin JL. The severity of nocturnal hypoxia but not abdominal adiposity is associated with insulin resistance in non-obese men with sleep apnea. PLoS One 2013; 8: e71000.

[39] Briançon-Marjollet A, Weiszenstein M, Henri M, Thomas A, Godin-Ribuot D and Polak J. The impact of sleep disorders on glucose metabolism: endocrine and molecular mechanisms. Diabetol Metab Syndr 2015; 7: 25.

[40] Koren D, Chirinos JA, Katz LE, Mohler ER, Gallagher PR, Mitchell GF and Marcus CL. Interrelationships between obesity, obstructive sleep apnea syndromeand cardiovascular risk in obese adolescents. Int J Obes (Lond) 2015; 39: 1086-1093.

[41] Carlson JT, Hedner J, Elam M, Ejnell H, Sellgren J and Wallin BG. Augmented resting sympathetic activity in awake patients with obstructive sleep apnea. Chest 1993; 103: 1763-1768.

[42] Somers VK, Dyken ME, Mark AL and Abboud FM. Sympathetic-nerve activity during sleep in normal subjects. N Engl J Med 1993; 328: 303-307.