Effect of Continuous Positive Airway Pressure Therapy on Glycemic Excursions and Insulin Sensitivity in Patients with Obstructive Sleep Apnea-hypopnea Syndrome and Type 2 Diabetes

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Abstract

Background: For patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) and type 2 diabetes mellitus (T2DM), the night sleep interruption and intermittent hypoxia due to apnea or hypopnea may induce glycemic excursions and reduce insulin sensitivity. This study aimed to investigate the effect of continuous positive airway pressure (CPAP) therapy in patients with OSAHS and T2DM.

Methods: Continuous glucose monitoring system (CGMS) was used in 40 patients with T2DM and newly diagnosed OSAHS. The measurements were repeated after 30 days of CPAP treatment. Subsequently, insulin sensitivity and glycohemoglobin (HbA1c) were measured and compared to the pretreatment data.

Results: After CPAP therapy, the CGMS indicators showed that the 24-h mean blood glucose (MBG) and the night time MBG were significantly reduced ($P < 0.05$ and $P = 0.03$, respectively). The mean ambulatory glucose excursions (MAGEs) and the mean of daily differences were also significantly reduced ($P < 0.05$ and $P = 0.002$, respectively) compared to pretreatment levels. During the night, MAGE also significantly decreased ($P = 0.049$). The differences between the highest and lowest levels of blood glucose over 24 h and during the night were significantly lower than prior to CPAP treatment ($P < 0.05$ and $P = 0.024$, respectively). The 24 h and night time durations of high blood glucose (>7.8 mmol/L and > 11.1 mmol/L) decreased ($P < 0.05$ and $P < 0.05$, respectively) after the treatment. In addition, HbA1c levels were also lower than those before treatment ($P < 0.05$), and the homeostasis model assessment index of insulin resistance was also significantly lower than before CPAP treatment ($P = 0.034$).

Conclusions: CPAP therapy may have a beneficial effect on improving not only blood glucose but also upon insulin sensitivity in T2DM patients with OSAHS. This suggests that CPAP may be an effective treatment for T2DM in addition to intensive diabetes management.

Key words: Continuous Glucose Monitoring System; Continuous Positive Airway Pressure; Obstructive Sleep Apnea-hypopnea Syndrome; Type 2 Diabetes Mellitus

INTRODUCTION

It is estimated that the prevalence of obstructive sleep apnea-hypopnea syndrome (OSAHS) among adults ranges from 2% to 4%, with a higher prevalence among men. With an increasing understanding of factors causing type 2 diabetes mellitus (T2DM) and influencing its control, numerous studies have demonstrated that sleep disordered breathing (SDB), especially OSAHS, and T2DM are frequently comorbid conditions. The Sleep Heart Health Study¹ in 2003 reported that patients with diabetes had a higher prevalence of sleep disorders. On the other hand, several studies based on outpatient and the general population indicate that the prevalence of OSAHS in patients with T2DM...

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ranges from 18% to as high as 36%;[2,3] while the prevalence of T2DM in patients with OSAHS is even higher.[3,4] Recent studies have revealed the association of SDB with glycemic excursions and insulin resistance (IR). For patients with OSAHS and T2DM, the night sleep interruption and intermittent hypoxia due to apnea or hypopnea may induce glycemic excursions and reduce insulin sensitivity. Therefore, this study was designed to observe the effect of continuous positive airway pressure (CPAP) treatment on glycemic excursions and insulin sensitivity in patients with OSAHS and T2DM. Furthermore, we investigated the therapeutic effect on the stabilization of blood glucose and elevation of insulin sensitivity.

**Methods**

**Subjects**
Consecutive subjects with type 2 diabetes admitted to the Ministry of Health, Beijing Hospital from July 2008 to November 2009. Forty-three patients who were newly diagnosed with OSAHS and did not have CPAP treatment or any other surgical interventions were recruited. They were instructed to maintain a constant diet, lifestyle, and anti-diabetic regimen for 3 months, and then started the CPAP therapy. All of the patients satisfied the 2003 Diagnostic Criteria of T2DM by American Diabetes Association. Exclusion criteria were an inability to follow instructions: The existence of sinusitis, nasal polyps, nasal septum deviation, hypertrophy of tongue or tonsil, lymphoid hyperplasia at the base of the tongue or any other respiratory anatomical stenosis; hypothyroidism, acromegaly, adrenal cortical hyperplasia or any other endocrine diseases; taking drugs which affect insulin sensitivity, such as steroids, and application of biguanides, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers within 4 weeks before enrollment. The study was approved by the Ethics Commission of the Institutional Review Board of the Beijing Hospital, and all the patients gave written informed consent to participate.

**General data**
The data of all subjects including age, gender, height, and weight were recorded in detail. The height of the patients was measured barefoot standing before and after the experiment, and the weight was measured by emptying the bladder, fasting, and single underwear. Body mass index (BMI, kg/m²) = weight/height².

**Polysonmography monitoring**
The patients were subjected to nocturnal sleep polysonmography monitoring for at least 7 h at the sleep center with an Alice 4 Polysonmography Device that simultaneously recorded the following: (1) Oronasal airflow, (2) snoring, (3) percutaneous oxygen saturation (mean SaO₂ and minimum SaO₂), and (4) chest and abdominal breathing movements. These measurements were recorded and automatically calculated by a computer. Apnea was scored when cessation of airflow for 10 s or longer was observed, while hypopnea was defined as 50% or greater reduction of air flow from the normal range accompanied by a 4% or greater decline of SaO₂. An apnea or hypopnea event occurs when a paradoxical thoracoabdominal motion is defined as obstructive.

According to international standards,[5] the average number of apnea and hypopnea events during at least 7 h of sleep was defined as the apnea-hypopnea index (AHI). Patients with an AHI ≥5 and mainly obstructive apnea were diagnosed with OSAHS.

**Continuous glucose monitoring system**
Interstitial glucose levels were monitored using the continuous glucose monitoring system (CGMS; San Meditech Co. Ltd., China) for up to 72 h. The measurement principle is as follows: (1) The glucose-sensing probe is a glucose oxidase platinum electrode that contains a layer of semi-permeable membrane; (2) the sensing probe is implanted subcutaneously; (3) the interstitial glucose penetrates through the semi-permeable membrane and reacts with glucose oxidase in a redox reaction; (4) electrical signals proportional to the glucose concentration are generated; (5) the signals are transferred through the cables and converted to blood glucose values by a glucose recorder, downloaded to a computer by an information extractor, and finally analyzed by software. In this study, electrical signals were recorded every 11 s, and the average 3-m signals were saved, providing 480 glucose level readings per day, and 1440 data points for 3 consecutive days. Meanwhile, finger blood glucose levels were monitored at seven time points each day, including before breakfast, 2 h after breakfast, before lunch, 2 h after lunch, before supper, 2 h after supper, and at bedtime.

According to the CGMS results of a day before and after therapy, the following parameters were calculated: (1) Mean blood glucose (MBG) level (MBG¹): The average value and standard deviation (SD) of the 480 data points recorded during the 24-h of CGMS. (2) Mean ambulatory glucose excursions (MAGE¹): Ambulatory glucose excursions (AGE¹) that were calculated as the absolute distance from the summit to the valley. When AGE¹ was greater than the SD of MBG¹, an effective glucose excursion was counted, and the average number of all effective glucose excursions (NGE¹) was then recorded. (3) Absolute mean of daily differences (MODDs): The mean absolute deviation of matched values between two consecutive 24-h periods of CGMS monitoring. (4) The difference between the highest and lowest level of blood glucose (BGₘₐₓ): Calculated as the difference between the highest and lowest blood glucose values during 24 h of continuous glucose monitoring. (5) Tₘₐₓ >7.8 mmol/L and Tₘₐₓ >11.1 mmol/L: Recorded as the proportion of time that the blood glucose value was >7.8 mmol/L and 11.1 mmol/L, respectively. (6) Tₘₐₓ ≤3.9 mmol/L: Recorded as the proportion of time that the blood glucose value was <3.9 mmol/L. (7) MBG level at night: The average value and SD of the 120 data points recorded from midnight to 6:00 a.m of CGMS (8) MAGEs
at night (MAGE²): AGEs at night (AGE²) were calculated as the absolute distance from the summit to the valley from midnight to 6:00 a.m. When AGE² was greater than the SD of MBG², an effective glucose excursion was counted, and the average and NGE² were then recorded. (9) The difference between the highest and lowest level of blood glucose at night (BGₜₐₓ): Calculated as the difference between the highest and lowest blood glucose values from midnight to 6:00 a.m. (10) postprandial blood glucose (PBG) (PBGₖ): The blood glucose after breakfast; PBGₖ: The blood glucose after lunch; PBGₖ: The blood glucose after supper): Calculated as the average glucose levels of the interstitial fluid glucose from 120 m to 135 m after meals.

**Blood biochemical examination**

Subjects fasted overnight for 10 h, and blood samples were drawn at 6:00 a.m. from the median cubital vein to measure fasting blood glucose (FBG), glycohemoglobin (HbA1c), and fasting insulin (FINS). FBG levels were measured in a local clinical biochemical laboratory using an Imx Analyzer Biochemical Analyzer (Abbott Inc., USA) with intra-batch and inter-batch coefficients of variation (CVs) <5%. HbA1c levels were tested by HPLC with intra-batch and inter-batch CVs <3%. FINS levels were tested by radioimmunooassay. IR was evaluated by the homeostasis model assessment of IR (HOMA-IR) index with the following formula: FINS (in mIU/L) × FBG (in mmol/L)/22.5.

**Intervention**

After the completion of baseline CGMS monitoring, 43 subjects were treated with a CPAP automatic single-level ventilator (ResMed Inc., USA). The CPAP treatment were adjusted according to the situation of patients who using ventilator after 1-3 days for trying. The CPAP treatment lasted 4 h per night for at least 4 weeks. All the subjects were instructed to maintain a constant lifestyle and antidiabetic regimen.

**Statistical analysis**

The normal distribution test was conducted in the variables, and the abnormal distribution test was applied to analyze the data after logarithm transition or nonparametric-test (the rank sum test). The normal distribution parameters are represented as mean ± standard deviation (SD) while abnormal distribution parameters are represented as medians and quartiles. All statistics were analyzed with SPSS 11.5 (SPSS Inc., USA). Comparisons of pre- and post-treatment values were performed by paired t-tests, with a P < 0.05 being statistically significant.

**Results**

Three patients quit from the study because they could not tolerate the CPAP therapy. The average age of the other 40 subjects was 54.8 ± 9.8 years, 28 males and 12 females, their mean BMI was 29.80 ± 3.50 kg/m², and AHI was 30.65 ± 18.56. The mean mechanical ventilation time was 57.03 ± 24.85 d, with an average daily ventilation time of 5.57 ± 1.19 h/d. The average continuous glucose monitoring time was 70.61 ± 9.19 h. There was a good correlation between the subcutaneous interstitial glucose concentration and reference fingertip blood glucose. While the mean absolute difference was 3.15%, the correlation coefficient was 0.937.

**Biomedical parameters**

We found that the BMIs of the patients did not significantly change after at least 30 days of CPAP treatment. However, HbA1c and FBG were significantly reduced compared with pretreatment levels (P < 0.05). Furthermore, HOMA-IR was also significantly reduced (P = 0.034) [Table 1].

**Continuous glucose monitoring**

MBG values were significantly reduced after at least 30 days of CPAP treatment. Moreover, the indicators that reflect the stabilization of blood glucose, such as SD, MAGE, MODD, and BGₜₐₓ, were significantly reduced compared with pretreatment values (P < 0.05). Furthermore, the time percentage of hyperglycemia and PBG was significantly decreased (P < 0.05). In our study, however, the NGE and time percentage of hypoglycemia did not significantly change after treatment with CPAP (P > 0.05) [Table 2].

**Discussion**

T2DM is characterized as IR and dysfunction of pancreatic β-cells. Studies have shown that IR is a common phenomenon in OSAHS patients by using either the HOMA index or the hyperinsulinemic-euglycemic clamp test. Previous studies have suggested that SDB due to OSAHS and IR are independent factors, while obesity might link them. Recent findings suggest that glycemic excursions due to IR may be directly worsened by the physiological stress caused by intermittent hypoxia and sleep disruption.

Table 1: HbA1c, FBG, FINS, and HOMA-IR and its comparison pre- and post-treatment

| Characteristics | n  | Pretreatment | Posttreatment | P     |
|-----------------|----|--------------|---------------|-------|
| BMI (kg/m²)     | 40 | 29.80 ± 3.50 | 29.72 ± 3.55  | 0.191 |
| HbA1c (%)       | 40 | 8.70 (7.40, 10.40) | 6.95 (6.38, 7.52) | <0.001 |
| FBG (mmol/L)    | 40 | 9.35 ± 2.89  | 6.68 ± 1.19   | <0.001 |
| AHI (mean±SD)   | 40 | 30.66 ± 2.79 | 3.95 ± 0.35   | <0.001 |
| SBP (mmHg)      | 40 | 129.53 ± 3.75 | 129.19 ± 3.77 | 0.83  |
| DBP (mmHg)      | 40 | 86.51 ± 7.44 | 86.16 ± 7.78  | 0.83  |
| TC (mmol/L)     | 40 | 6.07 ± 2.31 | 4.82 ± 1.09   | 0.219 |
| TG (mmol/L)     | 40 | 2.64 ± 0.23 | 2.26 ± 1.43   | 0.307 |
| LDL-C (mmol/L)  | 40 | 3.28 ± 1.10 | 2.64 ± 0.68   | 0.001 |
| FINS (µU/ml)    | 40 | 8.06 (5.19, 13.70) | 8.30 (5.09, 11.30) | 0.442 |
| HOMA-IR         | 40 | 3.57 (1.95, 5.08) | 2.48 (1.38, 3.90) | 0.013 |

BMI: Body mass index; HbA1c: Glycated hemoglobin; FBG: Fasting blood glucose; HOMA-IR: Homeostasis model assessment insulin resistance; AHI: Apnea-hypopnea index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; TG: Triglyceride; FINS: Fasting insulin; LDL-C: Low density lipoprotein-cholesterol.
might be an independent risk factor for blood glucose disturbances among patients with diabetes.\textsuperscript{10}

The principle of CPAP treatment for OSAHS is to enforce positive airway pressure throughout the entire exhalation and inhalation process during spontaneous breathing, which prevents airway contraction, increases pulmonary functional residual capacity, improves pulmonary compliance, reduces breathing consumption, and lessens the severity of airway resistance. Moreover, upper airway muscle function is enhanced through the afferent inputs and feedbacks from the chest wall and vagus nerve, which keeps the upper respiratory tract open. Researchers have studied whether CPAP therapy for OSAHS improves glucose and lipid metabolism, but the limitation in the number of subjects and controls in most of those studies may have been insufficient to demonstrate an effect of CPAP therapy in obese or nonobese patients. Our study demonstrated that there was a decrease in HOMA-IR that insulin sensitivity improved and that FPG levels significantly decreased after at least 30 days of CPAP treatment. These findings were consistent with the report from Pamidi et al.\textsuperscript{11} and Iftikhar et al.\textsuperscript{12} In contrast, another recent randomized controlled trial\textsuperscript{13} reported that CPAP did not improve HbA1c levels. Generally, CPAP therapy takes effect only after treatment of 4 h or more per night, implying that the benefit of treatment would not be obvious when patients receive a shorter treatment time.\textsuperscript{14}

The previous results show that changes in HbA1c may be related to changes in sleep quality and sleep fragmentation.\textsuperscript{15} Whether CPAP therapy is beneficial to reduce the HbA1c levels in patients with T2DM is still controversial. Shpirer et al.\textsuperscript{16} found that HbA1c levels were significantly reduced after 3–5 months of CPAP treatment in 30 patients with OSAHS in diabetes and prediabetes. While a recent systematic review suggested that CPAP therapy dose not lower the HbA1c level in patients with OSAHS and T2DM.\textsuperscript{17} In our study, CPAP can effectively reduce the HbA1c level of the patients ($P < 0.001$).

Current considerations of the functional impairments caused by the dysfunction of glycemic excursions and exacerbated IR due to OSAHS might include the following components: (1) Activation of the sympathetic nervous system: OSAHS patients have high sympathetic nervous activity whether they are asleep or awake, which induces IR by increasing glycogenolysis and triggering gluconeogenesis. The increased sympathetic activity is likely to be related to nocturnal hypoxia, and sympathetic activity may also be boosted by repeated awakening during obstructive sleep apnea. (2) Direct effects hypoxia: Hypoxia due to OSAHS may increase anaerobic glycolysis, resulting in pyruvate being partially reduced to lactic acid without oxidation and then converted to heparin in the liver. Intermittent hypoxia in the general population may decrease insulin sensitivity and increase IR and has a strong independent association with poorer glycemic control.\textsuperscript{18} (3) Hypothalamic-pituitary–adrenal (HPA) dysfunction: Hypoxia and sleep pattern disorders may lead to dysfunction of the HPA axis, abnormal elevation of glucocorticoid levels, and worsening of IR. (4) Systemic inflammatory response: Studies have shown that all OSAHS patients with or without obesity have elevated inflammatory markers (interleukin-6 [IL-6], IL-10, and tumor necrosis factor-$\alpha$).\textsuperscript{19} These inflammatory factors may affect glucose metabolism by inhibiting glucose uptake in fat and muscle and increasing the levels of hormones that counteract insulin. (5) Adipocytokines: Elevated leptin levels with decreased adiponectin levels occur in patients with OSAHS.\textsuperscript{20} In addition, the reduction of patients’ physical activities or increased sedentary behavior caused by fatigue

**Table 2: The change of continuous glucose monitoring pre- and post-CPAP treatment**

| Items                        | $n$ | Pretreatment | Posttreatment | $P$   |
|------------------------------|-----|--------------|---------------|------|
| MBG$^1$ (mmol/L, mean)       | 40  | 7.85 (6.80, 8.85) | 6.75 (5.92, 7.68) | <0.001 |
| SD$^1$ (mmol/L, mean)        | 40  | 1.84 (1.35, 2.52) | 1.12 (0.86, 1.46) | <0.001 |
| MAGE$^1$ (mmol/L, mean)      | 40  | 4.06 (2.98, 5.54) | 2.68 (1.97, 3.28) | <0.001 |
| NGE$^1$ (times/day, mean)    | 40  | 6.00 ± 1.91 | 6.68 ± 1.90 | 0.060 |
| MODD (mmol/L, mean)          | 40  | 1.76 (1.16, 2.87) | 1.29 (0.85, 1.81) | 0.001 |
| BG$^2_{h}$ (mmol/L)          | 40  | 8.46 ± 3.32 | 5.24 ± 1.76 | <0.001 |
| MBG$^3$ (mmol/L, mean)       | 40  | 6.35 (5.50, 7.60) | 6.00 (5.13, 6.55) | 0.030 |
| SD$^2$ (mmol/L)              | 40  | 0.73 ± 0.51 | 0.53 ± 0.38 | 0.012 |
| MAGE$^2$ (mmol/L, mean)      | 40  | 1.29 (1.05, 2.38) | 0.91 (0.59, 1.83) | 0.008 |
| NGE$^2$ (times/day, mean)    | 40  | 3.55 ± 1.75 | 3.83 ± 1.85 | 0.456 |
| BG$^2_n$ (mmol/L)            | 40  | 2.25 (1.52, 3.85) | 1.60 (1.13, 3.05) | 0.029 |
| T$_{bg} > 7.8$ (mmol/L, %)   | 40  | 37.5 (27.5, 75.3) | 19.25 (5.28, 42.43) | <0.001 |
| T$_{bg} > 11.1$ (mmol/L, %)  | 40  | 11.80 (0.00, 31.63) | 0.00 (0.00, 0.45) | <0.001 |
| T$_{bg} < 3.9$ (mmol/L, %)   | 40  | 0.00 (0.00, 0.60) | 0.00 (0.00, 0.00) | 0.522 |
| PBS$^1$ (mmol/L, mean)       | 40  | 9.77 ± 3.00 | 7.77 ± 2.08 | <0.001 |
| PBS$^2$ (mmol/L, mean)       | 40  | 9.82 ± 3.48 | 7.58 ± 1.87 | <0.001 |
| PBS$^3$ (mmol/L, mean)       | 40  | 9.93 ± 3.06 | 7.63 ± 1.48 | <0.001 |

MBG$^1$: Mean blood glucose level; MAGE$^1$: Mean ambulatory glucose excursions; MODD: Absolute means of daily differences; NGE$^1$: Numbers of glucose excursions; BG$^2$: The difference between the highest and lowest blood glucose values of 24 h of continuous glucose monitoring; MBG$^3$: MBG level at night; NGE$^2$: Numbers of glucose excursions at night; BG$^2_n$: The difference between the highest and lowest blood glucose values at night; T$_{bg}$ > 7.8 (mmol/L): The time span percentage when blood glucose value >7.8 mmol/L; T$_{bg}$ > 11.1 (mmol/L) refers to time span percentage when blood glucose value <3.9 mmol/L; PBS$^1$: Postprandial blood glucose (after breakfast); PBS$^2$: Postprandial blood glucose (after lunch); PBS$^3$: Postprandial blood glucose (after supper); SD: Standard deviation.
and somnolence due to OSAHS may also be a risk factor of diabetes.

Daily glycemic excursions in patients with T2DM have the following characteristics: (1) high PBG levels, and (2) the blood glucose nadir appears at a period between 1:00 a.m. and 6:00 a.m. Nocturnal severe hypoxemia has a direct impact on the amplitude of glycemic excursions in patients with T2DM and OSAHS. The results of this study also demonstrate that the MAGE and MODD levels of the patients were significantly lower ($P < 0.05$ and $P = 0.002$), as was the hyperglycemia time percentage, after CPAP treatment. Dawson et al.\(^2\) found that CPAP treatment did not significantly improve PBG in patients with OSAHS and T2DM. They speculated that PBG was mostly affected by mealtime and food type, which could not be regulated by CPAP treatment. In contrast, the results of Babu et al.\(^2\) support the idea that CPAP treatment significantly improved PBG levels. In this study, all the interstitial PBG levels ($\text{PBG}_1$, $\text{PBG}_2$, and $\text{PBG}_3$) monitored by CGMS were significantly different when pre- and post-treatment levels were compared ($P < 0.05$ for each). Indicating that CPAP therapy may have a beneficial effect on improving not only blood glucose but also upon insulin sensitivity in T2DM patients with OSAHS, due to improved sleep quality and decreased IR.

This study also compared nocturnal glycemic excursions before and after CPAP treatment, showing significant differences in nocturnal MBG and glycemic excursions. Compared to pretreatment, the posttreatment MAGE, and $\text{BG}_{\text{natt}}$ levels significantly decreased ($P = 0.049$ and $P = 0.024$, respectively) during the time between midnight and 6:00 a.m. Pamidi et al.\(^3\) reached the same conclusion. In the latter study, the CPAP treatment efficacy for improving interstitial MBG and glycemic excursions in the treatment of patients with T2DM and OSAHS occurred at the beginning of CPAP application. In this study, the nocturnal MBG and glycemic excursions after CPAP treatment were significantly decreased, suggesting that CPAP treatment may have improved the intermittent night time hypoxia in OSAHS patients. Once the hypoxia state was corrected, the overall nocturnal MBG decreased compared to the pretreatment MBG levels, similar to the decrease in MAGE levels, which reflect the glycemic excursions.

In this study, only 3 of 43 subjects (7.0%) were excluded because of nonadherence to the CPAP therapy. The major limitation of our study was the lack of a control group. The study conducted by West et al.\(^4\) suggested that study results might be influenced if subjects modified their behaviors, including diet and exercise, because they knew they were being monitored. In this study group, BMI did not significantly decrease, which suggests that their diet and exercise did not substantially change, at least during the CPAP treatment period.

Our findings need to be confirmed by a larger study that randomly assigns subjects to sham-CPAP and effective-CPAP groups. CPAP treatment not only improves sleep quality in patients with T2DM but also significantly improves insulin sensitivity and reduces the Hba1c level in patients with OSAHS and T2DM. In addition to lifestyle intervention and drug treatment, CPAP treatment might be an effective treatment for T2DM patients, particularly in poorly controlled subjects on maximum therapeutic regimens.

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Conflicts of interest

There are no conflicts of interest.

References

1. Resnick HE, Redline S, Shahar E, Gilpin A, Newman A, Walter R, et al. Diabetes and sleep apnea: findings from the Sleep Heart Health Study. Diabetes Care 2003;26:702-9.
2. Einhorn D, Stewart DA, Erman MK, Gordon N, Philis-Tsimikas A, Casal E. Prevalence of sleep apnea in a population of adults with type 2 diabetes mellitus. Endocr Pract 2007;13:355-62.
3. West SD, Nicolij DJ, Strading JR. Prevalence of obstructive sleep apnoea in men with type 2 diabetes. Thorax 2006;61:945-50.
4. Sharafkhanene A, Richardson P, Hirshkowitz M. Sleep apnea in a high risk population: A study of Veterans Health Administration beneficiaries. Sleep Med 2004;5:345-50.
5. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: Update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 2012;8:597-619.
6. Gruber A, Horwood F, Sithole J, Ali NJ, Idris I. Obstructive sleep apnoea is independently associated with the metabolic syndrome but not insulin resistance state. Cardiovasc Diabetol 2006;5:22.
7. Schahin SP, Nechanitzky T, Dittel C, Fuchs FS, Hahn EG, Konturek PC, et al. Long-term improvement of insulin sensitivity during CPAP therapy in the obstructive sleep apnoea syndrome. Med Sci Monit 2008;14:CR117-21.
8. Louis M, Punjabi NM. Effects of acute intermittent hypoxia on glucose metabolism in awake healthy volunteers. J Appl Physiol (1985) 2009;106:1538-44.
9. Stamatakis KA, Punjabi NM. Effects of sleep fragmentation on glucose metabolism in normal subjects. Chest 2010;137:95-101.
10. Wang X, Bi Y, Zhang Q, Pan F. Obstructive sleep apnoea and the risk of type 2 diabetes: A meta-analysis of prospective cohort studies. Respirology 2013;18:140-6.
11. Pamidi S, Wroblewski K, Stepien M, Sharif-Sidi K, Kilkus J, Whitmore H, et al. Eight hours of nightly continuous positive airway pressure treatment of obstructive sleep apnea improves glucose metabolism in patients with prediabetes. A randomized controlled trial. Am J Respir Crit Care Med 2015;192:96-105.
12. Ifitkhar IH, Hoyos CM, Philips CL, Magalan UJ. Meta-analyses of the association of sleep apnea with insulin resistance, and the effects of CPAP on HOMA-IR, adiponectin, and visceral adipose fat. J Clin Sleep Med 2015;11:475-85.
13. Pamidi S, Wroblewski K, Stepien M, Sharif-Sidi K, Kilkus J, Whitmore H, Tasali E. Eight Hours of Nightly CPAP Treatment of Obstructive Sleep Apnea Improves Glucose Metabolism in Prediabetes: A Randomized Controlled Trial. Am J Respir Crit Care Med. 2015 Apr 21. [Epub ahead of print].
14. Dorkova Z, Petrasova D, Molcaniova A, Popovnakova M, Tkacova R. Effects of continuous positive airway pressure on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome. Chest 2008;134:686-92.
15. Knutson KL, Ryden AM, Mander BA, Van Cauter E. Role of sleep duration and quality in the risk and severity of type 2 diabetes mellitus. Arch Intern Med 2006;166:1768-74.
16. Shpirer I, Rapoport MJ, Stav D, Elizur A. Normal and elevated HbA1C levels correlate with severity of hypoxemia in patients with obstructive sleep apnea and decrease following CPAP treatment. Sleep Breath 2012;16:461-6.

17. Feng Y, Zhang Z, 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.

18. Torrella M, Castells I, Gimenez-Perez G, Recasens A, Miquel M, Simó O, et al. Intermittent hypoxia is an independent marker of poorer glycaemic control in patients with uncontrolled type 2 diabetes. Diabetes Metab 2015.[Epub ahead of print].

19. De Luca Canto G, Pachêco-Pereira C, Aydinoz S, Major PW, Flores-Mir C, Gozal D. Biomarkers associated with obstructive sleep apnea: A scoping review. Sleep Med Rev 2014;23C: 28-45.

20. Tatsumi K, Kasahara Y, Kurosu K, Tanabe N, Takiguchi Y, Kuriyama T. Sleep oxygen desaturation and circulating leptin in obstructive sleep apnea-hypopnea syndrome. Chest 2005;127:716-21.

21. Dawson A, Abel SL, Loving RT, Dailey G, Shadan FF, Cronin JW, et al. CPAP therapy of obstructive sleep apnea in type 2 diabetes improves glycemic control during sleep. J Clin Sleep Med 2008;4:538-42.

22. Babu AR, Herdegen J, Fogelfeld L, Shott S, Mazzone T. Type 2 diabetes, glycemic control, and continuous positive airway pressure in obstructive sleep apnea. Arch Intern Med 2005;165:447-52.

23. West SD, Nicoll DJ, Wallace TM, Matthews DR, Stradling JR. Effect of CPAP on insulin resistance and HbA1c in men with obstructive sleep apnoea and type 2 diabetes. Thorax 2007;62:969-74.