

Sleep Extension Improves Glycemic Control in Type 2 Diabetes with Obstructive Sleep Apnea

Chih-Shan Huang, MD^{1,2}, Yong-Ning Tan, MS³, Tsui-San Chang, MSc^{1,2,4}, Chien-Ming Yang, PhD^{3,5} and Jia-Ying Sung, MD, PhD^{1,2,4,6*}

¹Department of Neurology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan.

²Taipei Neuroscience Institute, Taipei Medical University, Taipei, Taiwan.

³Department of Psychology, National Chengchi University, Taipei, Taiwan.

⁴Department of Neurology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan.

⁵The Research Center of Mind, Brain, & Learning, National Chengchi University, Taipei, Taiwan.

⁶Department of Nursing, Chang Gung University of Science and Technology, Linkou, Taiwan.

*Correspondence:

Jia-Ying Sung, No. 111, Sec. 3, Xinglong Rd., Wenshan Dist., Taipei City 11696, Taiwan, Tel: +886-2-29307930 ext. 6940; Fax: +886-2-29302447.

Received: 14 September 2021; **Accepted:** 10 October 2021

Citation: Huang CS, Tan YN, Chang TS, et al. Sleep Extension Improves Glycemic Control in Type 2 Diabetes with Obstructive Sleep Apnea. *Int J Psychiatr Res* 2021; 4(5): 1-6.

ABSTRACT

Background: The purpose of this study was to investigate whether sleep extension lowers blood glucose in patients with type 2 diabetes and chronic sleep restriction, and the moderating role of sleep apnea on the effect of sleep extension.

Methods: This study enrolled 19 adults with type 2 diabetes and a sleep duration of less than 7 hours per night, of whom 16 (84.2 %) had obstructive sleep apnea. They were instructed to sleep at their usual time for 3 weeks as baseline, and then to increase their time in bed by 1 more hour per night for 3 weeks. Their sleep duration was recorded using actigraphy monitoring and sleep logs. Their fasting plasma glucose, glycated albumin, and glycated hemoglobin were measured before and after sleep extension.

Results: Nine of the 19 (47.4 %) participants had a decrease in glycated albumin after sleep extension, and these participants had a significantly higher apnea-hypopnea index (AHI; $p < 0.001$). The participants with an AHI ≥ 30 times per hour were older ($p = 0.04$), had a shorter baseline total sleep time measured by actigraphy ($p = 0.04$), and had a more significant decrease in glycated albumin after sleep extension ($p = 0.01$). The AHI level was significantly correlated with the extent of decrease in glycated albumin after sleep extension ($r = 0.72$, $p = 0.001$).

Conclusion: The current study showed the potential of 3-week sleep extension in decreasing blood glucose in patients with diabetes comorbid with severe obstructive sleep apnea and sleep deprivation.

Keywords

Glycated albumin, Obstructive sleep apnea, Sleep extension, Type 2 diabetes.

Introduction

The quality and quantity of sleep have been reported to affect the metabolism of blood glucose in humans and significantly predict the risk of developing type 2 diabetes mellitus (DM) [1].

Population studies have observed a U-shaped relationship between sleep duration and the risk of type 2 DM, in which individuals who self-report a habitual sleep duration of less than 7 hours or more than 8 hours are at an increased risk [2,3].

A sleep duration of less than 7 hours per night is regarded as being "short sleep" [4], although this is quite common nowadays for people living in modern societies. This chronic restriction of sleep may increase the risk of obesity and diabetes via multiple pathways, including harming glucose regulation parameters, dysregulation of the neuroendocrine control of appetite leading to excessive food intake, and decreased energy expenditure [4,5]. Recurrent partial sleep restriction has been shown to lead to marked alterations in glucose metabolism, including decreased glucose tolerance, decreased insulin sensitivity, and increased insulin resistance [5,6]. The neuroendocrine regulation of appetite has also been shown to be affected by decreased levels of the anorexigenic hormone leptin and increased levels of the orexigenic factor ghrelin [5,7]. Importantly, these neuroendocrine abnormalities have been correlated with increased hunger and appetite, especially for calorie-dense foods with high carbohydrate content, which may further lead to overeating and weight gain [7].

Short sleep not only increases the risk of developing type 2 DM [1,8-13], but has also been associated with poor glycemic control in diabetic patients [14]. Fasting blood glucose and glycated hemoglobin (A1C) show a U-shaped trend corresponding to sleep duration, with a sleep duration of 7 hours per night having the lowest A1C [14]. Therefore, increasing sleep duration may have beneficial effects on reducing blood glucose for short sleepers. In healthy non-obese young adults, Leproult and colleagues found that extending sleep by increasing the time in bed by 1 hour per day for 6 weeks resulted in improvements in fasting insulin sensitivity [15]. However, it was not known whether the same effects existed in diabetic patients.

In addition to self-imposed sleep restriction, comorbid sleep disorders can also affect sleep in DM patients. In particular, obstructive sleep apnea (OSA) shares common risk factors with DM, such as obesity. Up to 40 % of OSA patients have DM [16], and about 23 % of DM patients have OSA [17]. The pathophysiological link between OSA and DM is still unclear, however sleep fragmentation and intermittent hypoxia may be important mechanisms [18]. Sleep fragmentation has been shown to enhance sympathetic activity and reduce insulin sensitivity, causing hyperglycemia [19], and hypoxia has been shown to induce insulin resistance [20] and also trigger the release of sympathetic hormones such as epinephrine, norepinephrine, and cortisol [21-23]. Epinephrine has been shown to stimulate gluconeogenesis in the liver, and inhibit glucose utilization in muscle, thereby increasing blood glucose. Hypoxia can provoke oxidative stress, causing dysregulation of the hypothalamic-pituitary-adrenal axis and inflammatory responses [24]. The elevation of pro-inflammatory biomarkers, such as tumor necrosis factor- α , interleukin-6, high-sensitivity C-reactive protein, fibrinogen, and uric acid, may result in insulin resistance and impede the utilization of glucose [25,26].

Reutrakul and Van Carter proposed a mechanism to explain how sleep deprivation, sleep fragmentation, OSA, and hypoxia contribute to hyperglycemia and DM [27]. Taken together, OSA appears to be an essential factor that contributes to the dysregulation of blood glucose metabolism in DM. Therefore, gaining sufficient sleep may be particularly beneficial for DM patients comorbid with OSA with regards to blood glucose regulation.

The purpose of this study was to investigate whether extending sleep duration could improve glycemic control in DM patients with a short habitual sleep duration, in order to examine the potential of using sleep extension as a strategy to improve glycemic control in diabetic adults with chronic sleep restriction. The moderating role of OSA on the effect of sleep extension was also investigated.

Methods

Study Participants

This study was approved by the Taipei Medical University Joint Institutional Review Board (approval number N201602031). Written informed consent was provided by all participants. From June 2016 to November 2018, 24 patients with type 2 diabetes and a sleep duration of less than 7 hours per night were recruited from a university hospital and enrolled in this study. The inclusion criteria were: 1) adults aged 20 years or older; 2) a diagnosis of type 2 diabetes; 3) having a habitual sleep duration of less than 7 hours; 4) non-shift-workers; 5) not being pregnant; 6) not using steroids, insulin, or sleep-promoting medications; and 7) not having medical and/or psychiatric disorders, such as liver or kidney dysfunction, cardiovascular, thyroid, or any psychiatric diseases. At the time of recruitment, they received blood examinations to check their blood glucose levels and to make sure their renal function (blood urea nitrogen, BUN; and creatinine), liver function (serum glutamic oxaloacetic transaminase, SGOT; and serum glutamic pyruvic transaminase, SGPT) and thyroid function (free T4; and thyroid-stimulating hormone, TSH) were normal. They also received an overnight polysomnography study to evaluate sleep disorders.

Sleep Extension and Assessment of Sleep Parameters

The participants were requested to sleep according to their usual sleep schedule for 3 weeks. They were then instructed to extend their sleep by increasing the time in bed by 1 more hour per day for 3 weeks. Their sleep durations were recorded in daily sleep logs (subjectively) and with actigraphy monitoring (objectively).

(1) Daily Sleep Logs:

After getting up every day, the participants were asked to recall the previous night's sleep and record their sleep schedule, as well as their sleep onset latency (SOL), the total period of wakefulness occurring after sleep onset (WASO), and the time they got up. The total sleep time recorded in the sleep logs (logTST) was calculated by subtracting the total period of WASO from the time they fell asleep to the time they got up.

(2) Actigraphy Monitoring:

In this study, a Mini Mitter ActiWatch (Mini Mitter Company, Inc., USA) with Actiware software version 5.0 was used to assess the quantity of sleep. During the study period, the participants were asked to wear the actigraphy device on the non-dominant wrist all day, except when they were taking a bath/shower. The total sleep time estimated by the actigraphy watch (wTST) was calculated as the total sleep duration minus the total period of WASO.

Blood Glucose Measurement

The participants' blood glucose levels were measured once after 3 weeks of regular sleep, and then once again after 3 weeks of sleep extension. In addition to fasting plasma glucose and A1C (which reflects the average blood glucose in the previous 2-3 months), glycated albumin (GA) was measured as a marker of average blood glucose, specifically within the recent 2-3 weeks [28,29], in order to reflect instant blood glucose changes after short-term sleep extension for 3 weeks. For the diagnosis of prediabetes and diabetes, the established cut-off points for fasting plasma glucose are 100 mg/dL (5.55 mmol/L) and 126 mg/dL (6.99 mmol/L), and for A1C are 5.7 % (39 mmol/mol) and 6.5 % (48 mmol/mol). For GA, the corresponding cut-off points were defined as 14.5 % (264 mmol/mol) and 16.5 % (299 mmol/mol), respectively, as suggested by Hsu et al for Taiwanese populations [30]. After blood glucose measurements, the average total sleep times were collected from the daily sleep logs and actigraphy devices. Five participants with missing sleep duration data were excluded, and the remaining 19 participants completed the study. Figure 1 shows the study flow chart.

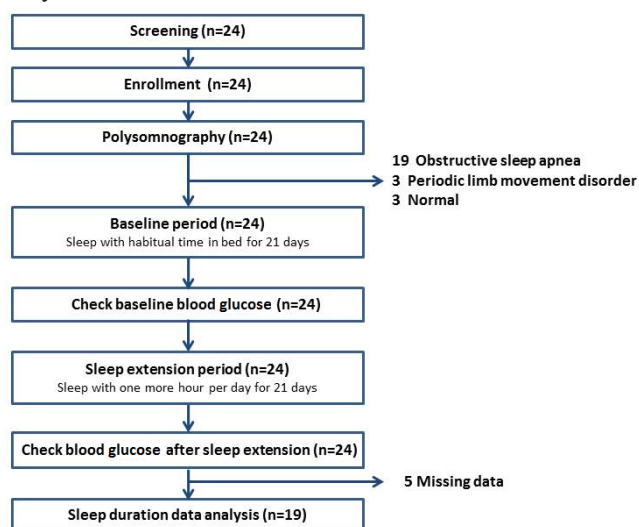


Figure 1: Flow chart of the study.

Statistical Analysis

Means and standard deviations (SD) were calculated for all continuous variables. The t-test and analysis of variance were used to compare differences between baseline and after sleep extension. The chi-square test was used to compare nominal variables, and Pearson correlation coefficients were used to assess correlations between the sleep and blood sugar variables. An alpha level of 0.05 was used for statistical significance. All statistical analyses

were performed using IBM SPSS Statistics version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Participants' Characteristics

Of the 19 participants, 12 (63.2 %) were male and seven were female (36.8 %), with an average age of 58.9 ± 9.6 (range, 41-79) years. All of them had type 2 diabetes and were using oral hypoglycemic agents. Eight (42.1 %) had $A1C \leq 6.4$ % (46 mmol/mol) and 11 (57.9 %) had $A1C \geq 6.5$ % (48 mmol/mol). All of them had normal levels of BUN, creatinine, SGOT, SGPT, free T4, and TSH. The polysomnography study revealed that 16 of the participants (84.2 %) had OSA, of whom two (12.5 %) had mild OSA (apnea-hypopnea index, AHI = 5-15 times per hour), five (31.3 %) had moderate OSA (AHI = 15-30 times per hour), and nine (56.3 %) had severe OSA (AHI ≥ 30 times per hour). Table 1 shows the characteristics of the participants.

Table 1: Characteristics of the study participants.

Characteristics	(n=19)
Age, years	58.9 ± 9.6
Female, n (%)	7 (36.8)
Body mass index, kg/m ²	26.2 ± 4.3
Obstructive sleep apnea, n (%)	16 (84.2)
Total sleep time (actigraphy), minutes	
Baseline	266.1 ± 48.7
After extended sleep	276.6 ± 49.0
Total sleep time (log), minutes	
Baseline	392.1 ± 51.2
After extended sleep	415.2 ± 40.1
Fasting glucose, mg/dL (mmol/L)	
Baseline	125.2 ± 22.8 (6.95 \pm 1.27)
After extended sleep	122.8 ± 26.4 (6.82 \pm 1.47)
Glycated albumin, % (mmol/mol)	
Baseline	15.6 ± 2.1 (283 \pm 45)
After extended sleep	15.7 ± 2.0 (285 \pm 43)
Glycated hemoglobin, % (mmol/mol)	
Baseline	6.7 ± 0.7 (50 \pm 7)
After extended sleep	6.7 ± 0.7 (50 \pm 7)

Data are summarized as count (percentage) or mean \pm SD.

Sleep Parameters

According to the sleep logs, the mean logTST before (logTST_B) and after (logTST_E) sleep extension were 392.1 ± 51.2 minutes and 415.2 ± 40.1 minutes, respectively ($t = -2.05$; $p = 0.06$). According to actigraphy monitoring, the mean wTST before (wTST_B) and after (wTST_E) sleep extension were 266.1 ± 48.7 minutes and 276.6 ± 49.0 minutes, respectively ($t = -1.93$; $p = 0.07$). Although the participants were instructed to extend their sleep duration for 1 hour per day, the average sleep duration measured both by sleep logs and actigraphy showed only a marginal extension. According to the sleep logs, four participants (21.1 %) extended their sleep duration by at least 1 hour, four (21.1 %) increased their sleep duration by 30-60 minutes, and eight (42.1 %) failed to extend their sleep duration by more than 10 minutes. According to actigraphy monitoring, only one participant (5.3 %) extended their sleep duration by at least 1 hour, three (15.8 %) increased their sleep duration by 30-60 minutes, and nine (47.4%) failed to extend their sleep durations by more than 10 minutes.

Comparison of the Blood Glucose Levels before and after Sleep Extension

The fasting plasma glucose levels before and after sleep extension were 125.2 ± 22.8 mg/dL (6.95 ± 1.27 mmol/L) and 122.8 ± 26.4 mg/dL (6.82 ± 1.47 mmol/L) ($t = 0.74$; $p = 0.47$), respectively, and the GA levels before and after sleep extension were 15.6 ± 2.1 % (283 ± 45 mmol/mol) and 15.7 ± 2.0 % (285 ± 43 mmol/mol) ($t = -0.28$; $p = 0.78$), respectively. The A1C levels before and after sleep extension were 6.7 ± 0.7 % (50 ± 7 mmol/mol) and 6.7 ± 0.7 % (50 ± 7 mmol/mol) ($t = 0.73$; $p = 0.47$), respectively. When all of the participants were included in the analyses, none of the blood glucose measures showed a significant decrease after sleep extension.

Pearson correlation coefficients were used to analyze the associations between the extent of sleep extension estimated by the actigraphy watch (Δ wTST; calculated as wTST_E - wTST_B) and the reduction in blood glucose. The results showed no significant correlations between Δ wTST and the reduction in any of the glucose indices: Δ fasting glucose ($p = 0.479$, $r = -0.013$), Δ GA ($p = 0.262$, $r = -0.156$), and Δ A1C ($p = 0.276$, $r = -0.145$).

Demographic data and sleep measures were compared between the participants who had an increase and decrease in GA after sleep extension (Table 2). Those with decreased GA were marginally older ($p = 0.06$) and had a significantly higher AHI ($p < 0.001$). Demographic data and sleep measures were also compared between the participants with and without severe OSA (Table 3). Those with an AHI ≥ 30 times per hour (severe OSA) were older ($p = 0.04$), had a shorter baseline total sleep time measured by actigraphy ($p = 0.04$), and had a more significant decrease in GA after sleep extension ($p = 0.01$). As shown in Figure 2, the AHI level was significantly correlated with the extent of the decrease in GA after sleep extension ($r = 0.719$, $p = 0.001$).

Table 2: Comparison of the participants with an increase and decrease in glycated albumin after sleep extension.

	Increase (n=10)	Decrease (n=9)	p value
Female (%)	5 (50.0)	2 (22.2)	0.21
Age, years	55.0 ± 8.1	63.3 ± 9.7	0.06
Body mass index, kg/m ²	27.2 ± 4.1	25.1 ± 4.4	0.29
Apnea-hypopnea index, times/hour	15.3 ± 10.1	45.8 ± 19.1	<0.001
Baseline total sleep time, minutes*	268.7 ± 48.2	263.1 ± 52.0	0.81
Increase in total sleep time, minutes*	13.0 ± 20.7	7.8 ± 28.0	0.65
Baseline glycated hemoglobin, % (mmol/mol)	6.5 ± 0.5 (48 ± 5)	7.0 ± 1.1 (53 ± 12)	0.15

Data are summarized as count (percentage) or mean \pm SD. *Total sleep time was recorded using actigraphy.

Table 3: Comparison of the participants with and without severe obstructive sleep apnea.

	AHI < 30 (n=10)	AHI ≥ 30 (n=9)	P value
Female (%)	5 (50.0)	2 (28.6)	0.21
Age, years	54.7 ± 6.9	63.7 ± 10.3	0.04
Body mass index, kg/m ²	26.7 ± 4.1	25.7 ± 4.7	0.62
Baseline glycated hemoglobin, % (mmol/mol)	6.7 ± 0.4 (50 ± 4)	6.8 ± 1.2 (51 ± 13)	0.68

Decrease in glycated albumin, % (mmol/mol)	-0.5 ± 0.5 (-1 ± 16.3)	0.4 ± 0.9 (15 ± 23)	0.01
Baseline total sleep time (actigraphy), minutes	287.6 ± 35.7	242.1 ± 51.6	0.04
Increase in total sleep time (actigraphy), minutes	14.3 ± 26.2	6.3 ± 21.7	0.48
Baseline total sleep time (log), minutes	385.9 ± 47.4	399.0 ± 57.2	0.59
Increase in total sleep time (log), minutes	25.9 ± 53.7	20.0 ± 46.8	0.8

Data are summarized as count (percentage) or mean \pm SD. AHI = Apnea-hypopnea index.

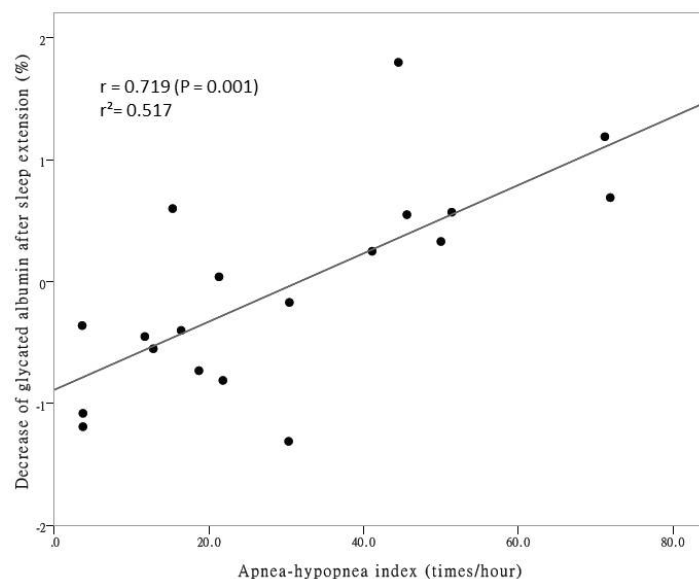


Figure 2: Correlation between the apnea-hypopnea index level and the extent of decrease in glycated albumin after sleep extension.

Discussion

To the best of our knowledge, this is the first study to demonstrate a potential reduction in blood glucose levels in Taiwanese adults with type 2 DM comorbid with severe OSA after extending their daily sleep duration over a short period of 3 weeks. In addition to fasting glucose and A1C, GA was chosen as a more suitable parameter to reflect a temporary blood glucose change after 3 weeks of sleep intervention. Although the results showed that the overall blood glucose level changes after the sleep intervention were not significantly improved, OSA had a moderating effect on the influence of sleep extension on blood glucose reduction.

At enrollment, the participants received overnight polysomnography, which showed that a high percentage (84.2%, 16/19) of the participants had OSA, and that nine of these 16 participants (56.3%) had severe OSA (AHI ≥ 30 times per hour).

Furthermore, these participants with severe OSA had a shorter baseline total sleep time as measured by actigraphy, but their baseline total sleep time recorded in sleep logs was similar to that of the participants with AHI < 30 times per hour. This is probably

because sleep-disordered breathing induces brief “movement arousals” during sleep, which would be interpreted as being “awake” in actigraphy but as “sleep” in subjective reports [31]. Thus, the participants with severe OSA may have had a shorter total sleep time when measured using actigraphy than in sleep logs.

More importantly, we found a significant decrease in GA after sleep extension in the participants with AHI ≥ 30 times per hour, and a linear correlation between the extent of GA reduction and the AHI level. This finding suggests that sleep extension for a short period of 3 weeks can reduce GA in patients with severe OSA, even if the total sleep time is not increased by 1 full hour per night. As such, severe OSA patients with DM may be advised to avoid self-imposed sleep deprivation in order to have better control over their blood glucose level. However, the long-term effect of sleep extension on blood glucose and the underlying mechanisms remains undetermined and warrant further studies.

Because OSA induces insulin resistance, continuous positive airway pressure (CPAP) treatment should improve blood glucose control in patients with DM and OSA. However, previous studies have reported controversial results about the effect of CPAP treatment on blood glucose control [32]. Some studies have found that CPAP can improve insulin sensitivity [33–38], whereas others have shown no significant therapeutic effect of CPAP on hyperglycemia or insulin resistance [39–41]. While these inconsistencies may be due to difference between the studies such as sample sizes and populations, other confounding factors such as sleep duration may also have contributed to the inconsistent results. This finding also indicates the importance of lifestyle factors in the treatment of DM.

There are several limitations to this study. First, only 19 participants were included, and only some successfully extended their total sleep time. The average sleep extension time was far less than 1 hour, with a mean sleep extension duration of 23.12 minutes as measured by sleep logs and 10.54 minutes as measured by actigraphy. The sleep extension in this study might not be sufficient to influence blood glucose. In addition, Tsai and colleagues (2012) reported worse blood glucose control in patients with DM who had worse sleep quality (Pittsburgh Sleep Quality Index ≥ 8) [42]. Thus, sleep quality, in addition to sleep duration, should probably be taken into consideration. Second, the present study did not control for other possible confounding variables, such as diet, exercise, medications, and the duration of diabetes. This may have caused negative findings in the overall effect of sleep extension. Future studies with a larger sample size, better control of the sleep extension procedure, and better control over confounding variables are warranted to further investigate this issue.

Conclusions

In conclusion, we did not find an overall beneficial effect of a 3-week sleep extension on glucose metabolism in DM patients with chronic sleep restriction. However, OSA was found to be a moderator for the effect. Sleep extension decreased the blood glucose marker, GA, in our type 2 DM patients with severe OSA.

Sleep extension may modify glucose metabolism by improving insulin sensitivity and by reducing insulin resistance. Although hypoglycemic agents with diet control are the mainstay of treatment for type 2 DM, sleep extension could be a complementary therapy, especially for patients with self-imposed sleep deprivation who are comorbid with severe OSA. These findings may have great clinical implication. However, due to the preliminary nature of the study, future studies are warranted to confirm our findings.

Acknowledgments

This manuscript has been edited by an experienced native English-speaking medical editor provided by ATS Medical Editing.

Funding statement

This study was financially supported by Taipei Municipal Wan-Fang Hospital, Taipei Medical University, Taipei, Taiwan (grant number 106-wf-eva-04).

References

1. Cappuccio FP, D’Elia L D, Strazzullo P, et al. Quantity and quality of sleep and incidence of type 2 diabetes: A systematic review and meta-analysis. *Diabetes Care*. 2010; 33: 414-420.
2. Chaput JP, Després JP, Bouchard C, et al. Sleep duration as a risk factor for the development of type 2 diabetes or impaired glucose tolerance: Analyses of the Quebec Family Study. *Sleep Med*. 2009;10: 919-924.
3. Shan Z, Ma H, Xie M, et al. Sleep duration and risk of type 2 diabetes: A meta-analysis of prospective studies. *Diabetes Care*. 2015; 38: 529-537.
4. Knutson KL, VanCauter E. Associations between sleep loss and increased risk of obesity and diabetes. *Ann N Y Acad Sci*. 2008; 1129: 287-304.
5. Spiegel IK, Knutson K, Leproult R, et al. Sleep loss: A novel risk factor for insulin resistance and Type 2 diabetes. *J Appl Physiol*. 2005; 99: 2008-2019.
6. Spiegel IK, Leproult R, VanCauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet*. 1999; 354:1435-1439.
7. Spiegel IK, Tasali E, Penev P, et al. Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. *Ann Intern Med*. 2004;141: 846-850.
8. Ayas NT, White DP, Al-Delaimy WK, et al. A Prospective Study of Self-Reported. *Diabetes Care*. 2003; 26: 380-384.
9. Mallon L, Broman JE, Hetta J. High incidence of diabetes in men with sleep complaints or short sleep duration: A 12-year follow-up study of a middle-aged population. *Diabetes Care*. 2005; 28: 2762-2767.
10. Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care*. 2006; 29: 657-661.
11. Gangwisch JE, Heymsfield SB, Boden-albala B, et al. Sleep duration as a risk factor for diabetes incidence in a large US sample. *Sleep*. 2007; 30: 1667-1673.

12. Beihl D A, Liese AD, Haffner SM. Sleep duration as a risk factor for incident type 2 diabetes in a multiethnic cohort. *Ann Epidemiol.* 2009; 19: 351-357.
13. Hayashino Y, Fukuhara S, Suzukamo Y, et al. Relation between sleep quality and quantity, quality of life, and risk of developing diabetes in healthy workers in Japan: The High-risk and Population Strategy for Occupational Health Promotion (HIPOP-OHP) Study. *BMC Public Health.* 2007;7:1-9.
14. Kim BK, Kim BS, An SY, et al. Sleep duration and glycemic control in patients with diabetes mellitus: Korea national health and nutrition examination survey 2007-2010. *J Korean Med Sci.* 2013; 28:1334-1339.
15. Leproult R, Deliens G, Gilson M, et al. Beneficial impact of sleep extension on fasting insulin sensitivity in adults with habitual sleep restriction. *Sleep.* 2015; 38:707-715.
16. Botros N, Concato J, Mohsenin V, et al. Obstructive Sleep Apnea as a Risk Factor for Type 2 Diabetes. *Am J Med.* 2009; 122:1122-1127.
17. West SD, Nicoll DJ, Stradling JR. Prevalence of obstructive sleep apnoea in men with type 2 diabetes. *Thorax.* 2006; 61: 945-950.
18. Nannapaneni S. Effect of obstructive sleep apnea on type 2 diabetes mellitus: A comprehensive literature review. *World J Diabetes.* 2013; 4:238 -244.
19. Stamatakis KA, Punjabi NM. Effects of sleep fragmentation on glucose metabolism in normal subjects. *Chest.* 2010; 137: 95-101.
20. Hermans MP, Ahn SA, Mahadeb YP, et al. Sleep apnoea syndrome and 10-year cardiovascular risk in females with type 2 diabetes: relationship with insulin secretion and insulin resistance. *Diabetes Metab Res Rev.* 2013; 29: 227-234.
21. Pamidi S, Wroblewski K, Broussard J, et al. Obstructive sleep apnea in young lean men: Impact on insulin sensitivity and secretion. *Diabetes Care.* 2012; 35: 2384-2389.
22. Iiyori N, Alonso L C, Li J, et al. Intermittent hypoxia causes insulin resistance in lean mice independent of autonomic activity. *Am J Respir Crit Care Med.* 2007;175: 851-857.
23. Oltmanns KM, Gehring H, Rudolf S, et al. Hypoxia causes glucose intolerance in humans. *Am J Respir Crit Care Med.* 2004; 169: 1231-1237.
24. Punjabi NM, Beamer BA. Alterations in glucose disposal in sleep-disordered breathing. *Am J Respir Crit Care Med.* 2009; 179: 235-240.
25. Ciftci TU, Kokturk O, Bukan N, et al. The relationship between serum cytokine levels with obesity and obstructive sleep apnea syndrome. *Cytokine.* 2004; 28: 87-91.
26. Yudkin JS, Stehouwer CDA, Emeis JJ, et al. Obesity, Insulin Resistance, and Endothelial Dysfunction. *Arterioscler Thromb Vasc Biol.* 1999;19: 972-978.
27. Reutrakul S, VanCauter E. Interactions between sleep, circadian function, and glucose metabolism: Implications for risk and severity of diabetes. *Ann N Y Acad Sci.* 2014; 1311: 151-173.
28. Furusyo N, Hayashi J. Glycated albumin and diabetes mellitus. *Biochim Biophys Acta - Gen Subj.* 2013; 1830: 5509-5514.
29. Freitas PAC, Ehlert LR, Camargo JL. Glycated albumin: A potential biomarker in diabetes. *Arch Endocrinol Metab.* 2017; 6: 296-304.
30. Hsu P, Ai M, Kanda E, et al. A comparison of glycated albumin and glycosylated hemoglobin for the screening of diabetes mellitus in Taiwan. *Atherosclerosis.* 2015; 242: 327-333.
31. Johnson NL, Kirchner HL, Rosen CL, et al. Sleep estimation using wrist actigraphy in adolescents with and without sleep disordered breathing: A comparison of three data modes. *Sleep.* 2007; 30: 899-905.
32. Surani S. Effect of continuous positive airway pressure therapy on glucose control. *World J Diabetes.* 2012; 3: 65-70.
33. Babu AR, Herdegen J, Fogelfeld L, et al. Type 2 diabetes, glycemic control, and continuous positive airway pressure in obstructive sleep apnea. *Arch Intern Med.* 2005; 165: 447-452.
34. Czupryniak L, Loba J, Pawlowski M, et al. Treatment with continuous positive airway pressure may affect blood glucose levels in nondiabetic patients with obstructive sleep apnea syndrome. *Sleep.* 2005; 28: 601-603.
35. Dawson A, Abel SL, Loving RT, et al. CPAP therapy of obstructive sleep apnea in type 2 diabetics improves glycemic control during sleep. *J Clin Sleep Med.* 2008; 4: 538-543.
36. Harsch IA, Schahin SP, Radespiel-Tröger M, et al. Continuous Positive Airway Pressure Treatment Rapidly Improves Insulin Sensitivity in Patients with Obstructive Sleep Apnea Syndrome. *Am J Respir Crit Care Med.* 2004; 169: 156-162.
37. Lam JCM, Lam B, Yao TJ, et al. A randomised controlled trial of nasal continuous positive airway pressure on insulin sensitivity in obstructive sleep apnoea. *Eur Respir J.* 2010; 35: 138-145.
38. Brooks B, Cistulli PA, Borkman M, et al. Obstructive sleep apnea in obese noninsulin-dependent diabetic patients: Effect of continuous positive airway pressure treatment on insulin responsiveness. *J Clin Endocrinol Metab.* 1994; 79:1681-1685.
39. Smurra M, Philip P, Taillard J, et al. CPAP treatment does not affect glucose-insulin metabolism in sleep apneic patients. *Sleep Med.* 2001; 2: 207-213.
40. Sharma SK, Agrawal S, Damodaran D, et al. Retraction: CPAP for the metabolic syndrome in patients with obstructive sleep apnea. *N Engl J Med.* 2011; 365: 2277-86. *N Engl J Med.* 2013; 369: 1770.
41. Chung S, Yoon IY, Lee CH, et al. The effects of nasal continuous positive airway pressure on vascular functions and serum cardiovascular risk factors in obstructive sleep apnea syndrome. *Sleep Breath.* 2011; 15: 71-76.
42. Tsai YW, Kann NH, Tung TH, et al. Impact of subjective sleep quality on glycemic control in type 2 diabetes mellitus. *Fam Pract.* 2012; 29: 30-35.