

# Type 2 Diabetes, Glycemic Control, and Continuous Positive Airway Pressure in Obstructive Sleep Apnea

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**Background:** Sleep-disordered breathing (SDB) is a prevalent condition associated with significant comorbidities, including hypertension, obesity, cardiovascular disease, and insulin resistance. It has been previously shown that the severity of insulin resistance is related to the severity of SDB.

**Methods:** Using a 72-hour continuous glucose monitoring system, we studied changes in interstitial glucose levels and measured hemoglobin A<sub>1c</sub> levels in 25 patients with type 2 diabetes mellitus before and after continuous positive airway pressure (CPAP) treatment for SDB.

**Results:** With a mean±SD CPAP treatment period of 83±50 days, the mean±SD 1-hour postprandial glucose values were significantly reduced for breakfast (191±68 mg/dL to 130±41 mg/dL [10.6±3.8 mmol/L to 7.2±2.3

mmol/L]), lunch (196±70 mg/dL to 138±49 mg/dL [10.9±3.9 mmol/L to 7.7±2.7 mmol/L]), and dinner (199±66 mg/dL to 137±48 mg/dL [11.0±3.7 mmol/L to 7.6±2.7 mmol/L]). In the 17 patients with a baseline hemoglobin A<sub>1c</sub> level greater than 7%, there was a significant reduction in hemoglobin A<sub>1c</sub> level (9.2%±2.0% to 8.6%±1.8%). Furthermore, in subjects who used CPAP for more than 4 h/d, the reduction in hemoglobin A<sub>1c</sub> level was significantly correlated with days of CPAP use. There was no such correlation in subjects who used CPAP for 4 h/d or less.

**Conclusions:** These findings suggest that SDB is pathophysiologically related to impaired glucose homeostasis, and that CPAP can be an important therapeutic approach for diabetic patients with SDB.

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**O**BSTRUCTIVE SLEEP APNEA syndrome is a common disorder, estimated to occur in 4% of men and 2% of women.<sup>1</sup> Recently published data from large studies indicate that sleep-disordered breathing (SDB) is an independent risk factor for the development of hypertension and other cardiovascular diseases, including strokes and ischemic heart disease.<sup>2-6</sup> The association between SDB and diabetes mellitus was noted several decades ago. More than 20 years ago, Rees et al<sup>7</sup> reported the presence of obstructive sleep apnea in patients with type 1 diabetes. Shortly thereafter a report appeared of a high incidence of breathing disorders in diabetic patients with autonomic neuropathy.<sup>8</sup>

Recently, there has been increased interest in the metabolic effects of SDB and the association of SDB with impaired glucose tolerance, insulin resistance, and type 2 diabetes. One study found a 2-fold increased risk of developing type 2 diabetes in subjects with habitual or regular snoring who were followed up for a 10-year period.<sup>9</sup> Two recent reports indicated that SDB is independently associated with glucose intolerance and insulin resistance.<sup>10,11</sup> In patients with established type 2 diabetes, there

is a significant relationship between SDB and fasting insulin, glucose, and hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels, that is independent of obesity as determined by the waist-hip ratio.<sup>12</sup>

Several studies have examined the effects of SDB treatment with continuous positive airway pressure (CPAP) on insulin sensitivity. One study of 10 patients treated with CPAP for 4 months found an improvement in insulin responsiveness as measured by hyperinsulinemic euglycemic clamp analysis.<sup>13</sup> A larger sample of 40 patients that used the euglycemic clamp technique also found that insulin sensitivity was improved with CPAP treatment.<sup>14</sup> Insulin sensitivity in nonobese patients improved within 2 days, while a significant change in the obese group was not identified until the 3-month follow-up. This improvement in insulin sensitivity occurred without any change in body mass index. However, in another study measuring glucose tolerance, HbA<sub>1c</sub> level, and insulin resistance, no significant improvement was observed after 2 months of CPAP treatment.<sup>15</sup> A recent review reported that in 8 of 9 published studies, CPAP treatment did not produce a consistent improvement in metabolic values in patients with SDB.<sup>16</sup>

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The strong association between insulin resistance and SDB<sup>10-12</sup> suggests that treatment of SDB should lead to improved glucose control in patients with diabetes. Although controversial, published data suggest that insulin responsiveness improves with CPAP treatment of SDB.<sup>13,14</sup> However, the clinical significance of these findings for patients with diabetes requires further investigation. The aim of this study was to assess the effects of CPAP treatment of SDB on glycemic control in a group of obese patients with type 2 diabetes. Important aspects of our study included the ability to monitor CPAP treatment adherence and 24-hour glucose levels.

## METHODS

### SUBJECTS

Subjects were recruited from a sleep clinic studying patients for the presence of SDB. Potential subjects were those with type 2 diabetes mellitus, on a stable medication regimen, who were referred for evaluation of sleep apnea based on clinical criteria. To detect an improvement in glucose control, the primary intent was to focus our analysis on patients with an HbA<sub>1c</sub> level greater than 7%. However, subjects with an HbA<sub>1c</sub> level of 7% or less were not excluded. Forty-two subjects were initially screened and enrolled; 3 subjects did not require CPAP on the basis of polysomnography, 4 subjects refused to initiate CPAP treatment, 8 subjects refused to return for repeat glucose monitoring after CPAP, and 2 subjects had incomplete glucose monitoring data. A sample size of 25 was available for final analysis. Of these 25 subjects, 24 used CPAP machines that allowed for treatment adherence monitoring. No medication adjustments were permitted during the study period.

Subjects underwent baseline testing of glucose and HbA<sub>1c</sub> levels and 72-hour continuous glucose monitoring with completion of a food diary before initiation of CPAP treatment. Patients were asked to return for repeat blood analysis and 72-hour continuous glucose monitoring with a food diary after 30 to 90 days of CPAP treatment. This protocol was approved by the Institutional Review Board for Protection of Human Subjects. Written consent was obtained from subjects by one of us (A.R.B. or J.H.).

### CONTINUOUS GLUCOSE MONITORING SYSTEM

The continuous glucose monitoring system (CGMS) (Guardian; Medtronic-MiniMed, Northridge, Calif) is a device used to measure interstitial glucose levels.<sup>17</sup> The CGMS records sensor signals every 5 minutes, providing 288 glucose level readings per day. The typical measurement period is up to 3 days (72 hours). The average difference between glucose sensor and glucose meter is  $-5.4$  mg/dL ( $-0.3$  mmol/L). It has a daily median correlation coefficient of 0.92 and a coefficient of variation of 5%.<sup>18</sup> The sensor is calibrated with fingerstick blood glucose measurements 3 to 4 times per day.

After a complete history was obtained and physical examination performed, the glucose sensor was inserted subcutaneously with aseptic precautions. All sensor insertion, removal, and troubleshooting were performed by a single physician (A.R.B.). The patients recorded a diet diary while they were undergoing glucose monitoring. Patients entered 3 to 4 blood glucose readings from their glucometer to the CGMS to maintain calibration. At the conclusion of the monitoring period, the subjects returned to the clinic for removal of the sensor. After the data from the CGMS were downloaded, the manufacturer's software was used for analysis.

## POLYSOMNOGRAPHY

Laboratory-based 16-channel polysomnography was performed with 1 of 2 sleep monitoring systems (Telefactor or Sandman Elite; Nellcor Puritan Bennett, Ottawa, Ontario). Each study included standard placement of electrodes for continuous monitoring of the central and occipital electroencephalograms, electro-oculogram, submental electromyogram, and one chest lead for cardiac rhythm; nasal and oral respiration measured with a thermistor; and bilateral leg (anterior tibialis) electromyograms. Each polysomnography recording was scored manually in 30-second epochs according to standard criteria.<sup>19</sup> Patients demonstrating significant SDB who were thought to be best treated with CPAP underwent laboratory-based CPAP titration.

### MONITORING OF CPAP USAGE

Microchip downloadable CPAP machines were used during the study (ResMed S6 Elite [Resmed Corp, San Diego, Calif] or RemstarPro [Respironics Inc, Pittsburgh, Pa]). Both machines allow recording of CPAP use for at least 3 consecutive months, based on time the mask was actually applied to a subject's face (not machine-run time). Data collection by the machine is not influenced by the type of mask used by the subject as long as leakage in the system is not excessively high. Compliance with CPAP treatment was prospectively defined as an average use of CPAP for more than 4 hours per night. Twenty-four of the 25 patients available for analysis used CPAP equipment that allowed for monitoring of compliance.

### QUESTIONNAIRES

Subjects were provided questionnaires assessing daytime sleepiness (Epworth Sleepiness Scale) and eating behavior (food diary). The Epworth Sleepiness Scale is an 8-question scale, scored from 0 to 3, that measures sleepiness as a reflection of a subject's tendency to fall asleep during specific, nonstimulating situations, as assessed during an interval of time. This scale has been validated and correlated with disease severity and change over time with CPAP use.<sup>19-22</sup> The food diary was validated by comparison with glucose peaks detected with the continuous glucose monitoring sensor and used to monitor dietary intake.

### STATISTICAL ANALYSIS

SPSS for Windows, version 11 (SPSS Inc, Chicago, Ill), was used for data management and statistical analysis. Because the measurements of interest had statistically nonnormal distributions that could not be transformed to statistical normality, nonparametric statistical methods were used. The Mann-Whitney test was done to compare independent groups with respect to noncategorical variables. The Friedman test was used to compare pretreatment and posttreatment glucose measurements. Scatterplots and Spearman rank correlation coefficients were obtained to investigate relationships between noncategorical variables. A .05 significance level was used for all statistical tests. No 1-sided statistical tests were done. Results in the text and tables are presented as mean  $\pm$  SD.

## RESULTS

**Table 1** gives the patient characteristics for the entire patient population, patients compliant or noncompliant with CPAP, and patients with a baseline HbA<sub>1c</sub> level greater than 7%. Of the 25 total patients, compliance information was available for 24. Eight patients had a base-

**Table 1. Baseline Patient Characteristics**

Characteristic	All Patients (N = 25)	Patients With CPAP Use >4 h/d (n = 12)	Patients With CPAP Use ≤4 h/d (n = 12)	Patients With HbA <sub>1c</sub> >7% (n = 17)
Age, mean ± SD, y	50.7 ± 9.0	52.2 ± 9.1	49.4 ± 9.5	49.5 ± 7.2
Sex, No. (%) M	16 (64)	9 (75)	6 (50)	11 (65)
BMI	42.7 ± 8.7	45.2 ± 10.8	40.6 ± 6.0	42.9 ± 7.9
Duration of diabetes, mean ± SD, y	8.3 ± 6.8	11 ± 8	5 ± 3	9.9 ± 6.7
Baseline HbA <sub>1c</sub> , mean ± SD, %	8.3 ± 2.2	7.9 ± 2.0	8.7 ± 2.5	9.2 ± 2.0
Diabetes treatment, No.				
Oral	17	7	10	10
Insulin	4	2	1	3
Insulin and oral	4	3	1	4

Abbreviations: BMI, body mass index (expressed as weight in kilograms divided by the square of height in meters); CPAP, continuous positive airway pressure; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>.

**Table 2. Patient Sleep Characteristics**

Characteristic	All Patients (N = 25)	Patients With CPAP Use >4 h/d (n = 12)	Patients With CPAP Use ≤4 h/d (n = 12)	Patients With HbA <sub>1c</sub> >7% (n = 17)
Epworth score, mean ± SD	14 ± 6	15 ± 7	13 ± 6	14 ± 6
Sleep hours, mean ± SD	6.0 ± 1.5	5.9 ± 1.5	6.3 ± 1.6	5.8 ± 1.7
Sleep efficiency, mean ± SD, %	75 ± 15	72 ± 14	79 ± 15	74 ± 14
Apnea + hypopnea index, mean ± SD	56 ± 37	48 ± 26	60 ± 44	54 ± 38
Lowest oxygen saturation, mean ± SD, %	76 ± 9	78 ± 10	73 ± 9	76 ± 9
Effective CPAP pressure, mean ± SD, cm H <sub>2</sub> O	12.4 ± 2.4	12.5 ± 2.3	12.2 ± 2.5	12.9 ± 2.0

Abbreviations: CPAP, continuous positive airway pressure; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>.

**Table 3. Sleep Apnea Treatment Characteristics**

Characteristic	All Patients (N = 25)	Patients With CPAP Use >4 h/d (n = 12)	Patients With CPAP Use ≤4 h/d (n = 12)	Patients With HbA <sub>1c</sub> >7% (n = 17)
AHI at CPAP treatment pressure, mean ± SD	8 ± 10 (median, 4)	14 ± 20	7 ± 9	10 ± 18
CPAP treatment period, mean ± SD, d	83 ± 50	74 ± 37	100 ± 62	94 ± 58
Daily CPAP use, mean ± SD, h/d	4.2 ± 2.9	6.6 ± 2.0*	1.8 ± 1.1*	4.3 ± 3.3

Abbreviations: AHI, apnea + hypopnea index; CPAP, continuous positive airway pressure; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>.

\*P < .001 between high and low CPAP users.

line HbA<sub>1c</sub> level of 7% or less after initial enrollment but were included in the study. The entire patient population (N=25) had a mean age of 50.7±9.0 years, and 16 (64%) were men. The patient group was very obese, with a body mass index (calculated as weight in kilograms divided by the square of height in meters) of 42.7±8.7, and had a diabetes duration of 8.3±6.8 years and baseline HbA<sub>1c</sub> level of 8.3%±2.2%. Of the 25 patients, 17 were taking oral hypoglycemic agents, 4 were taking insulin, and 4 were using both insulin and oral agents. Patients with CPAP use greater than 4 h/d tended to be male, be heavier, and have a longer duration of diabetes. However, there were no significant differences in characteristics between high and low CPAP users.

**Table 2** gives the baseline sleep characteristics of the entire patient population and subgroups of interest. The Epworth score was 14±6 (normal, <10), consistent with significant daytime sleepiness. The degree of SDB was

somewhat variable but, in general, was moderate to severe, with an apnea-hypopnea index of 56±37. No significant differences were found between high and low CPAP users for these sleep characteristics.

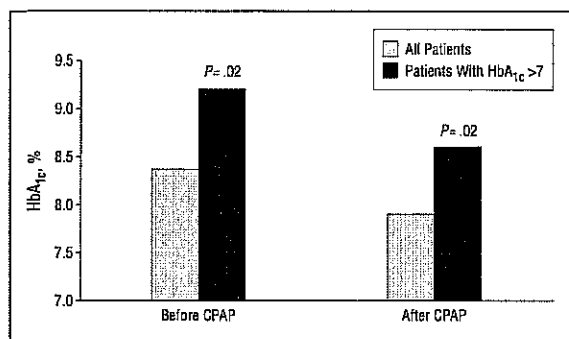
**Table 3** gives the sleep apnea treatment characteristics for the entire group and subgroups. In the entire group, the apnea-hypopnea index was significantly reduced at the effective treatment pressure to a mean of 8 and a median of 4. Nineteen patients (76%) had an apnea-hypopnea index less than 11 at their prescribed CPAP pressure. Patients with CPAP use greater than 4 h/d tended to have a higher apnea-hypopnea index with treatment and fewer days of CPAP use at the time of analysis. However, the only significant difference in patient subgroups was the daily CPAP use in compliant compared with noncompliant patients (6.6±2.0 vs 1.8±1.1 h/d).

Diabetes control was measured by means of the CGMS and HbA<sub>1c</sub> values at the beginning and end of the study pe-

**Table 4. Postprandial Glucose Control Before and After CPAP Therapy**

Variable	Glucose, Mean ± SD, mg/dL					
	All Patients (N = 25)		Patients With CPAP Use >4 h/d (n = 12)		Patients With CPAP Use ≤4 h/d (n = 12)	
	Pretherapy	Posttherapy	Pretherapy	Posttherapy	Pretherapy	Posttherapy
Breakfast	191 ± 68	130 ± 41*	200 ± 82	123 ± 34*	188 ± 53	138 ± 49*
Lunch	196 ± 70	138 ± 49	203 ± 89	136 ± 56	195 ± 47	144 ± 42
Dinner	199 ± 66	137 ± 48	206 ± 85	130 ± 49	197 ± 43	150 ± 47

Abbreviation: CPAP, continuous positive airway pressure.  
 SI conversion factor: To convert glucose to millimoles per liter, multiply by 0.0555.  
 \* $P < .05$  for within-group pre-CPAP vs post-CPAP treatment values.



**Figure 1.** Mean hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels before and after continuous positive airway pressure (CPAP) treatment in the entire study population and patients with a baseline HbA<sub>1c</sub> level greater than 7%. Groups were compared by Friedman test.

riod. Fasting glucose analysis was performed with values obtained by CGMS between 4 and 6 AM. For this period, the mean glucose level was 137 mg/dL (7.6 mmol/L) before CPAP treatment and 122 mg/dL (6.8 mmol/L) after CPAP treatment. Although all subgroups demonstrated a reduction of fasting glucose level after CPAP treatment, this reduction did not reach statistical significance for the entire group or any of the subgroups.

**Table 4** gives the postprandial CGMS data obtained for all patients and patients with high and low CPAP compliance. The data represent the mean glucose values obtained by the CGMS for 1 hour after each meal (12 data points) before and after CPAP treatment. On the basis of correlation with the food diary, these were the highest post-meal glucose values. As shown, mean 1-hour postmeal glucose values were significantly reduced after use of CPAP. For the entire study population, the mean postbreakfast glucose value decreased from 191 ± 68 mg/dL to 130 ± 41 mg/dL (10.6 ± 3.8 mmol/L to 7.2 ± 2.3 mmol/L), the postlunch glucose level decreased from 196 ± 70 mg/dL to 138 ± 49 mg/dL (10.9 ± 3.9 mmol/L to 7.7 ± 2.7 mmol/L), and the postdinner glucose level decreased from 199 ± 66 mg/dL to 137 ± 48 mg/dL (11.0 ± 3.7 mmol/L to 7.6 ± 2.7 mmol/L).

Subgroup analysis also demonstrated significant post-meal glucose reduction for all 3 mealtimes in subjects using CPAP greater than 4 h/d. In patients using CPAP for 4 h/d or less, postmeal glucose values were generally lower at all 3 meals after CPAP use, but only the breakfast mealtime demonstrated a significant reduction in glucose level.

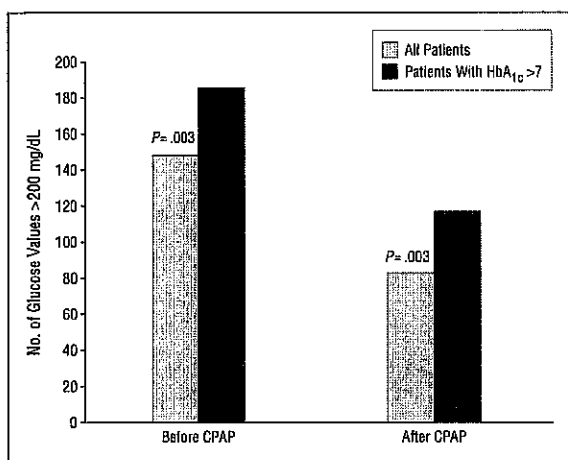
**Figure 1** presents the HbA<sub>1c</sub> values before and after CPAP treatment. For the entire patient population, the HbA<sub>1c</sub> level was 8.3% ± 2.2% at baseline and 7.9% ± 1.8% after CPAP treatment ( $P = .06$ ). However, in the analysis of the 17 patients with an initial HbA<sub>1c</sub> level greater than 7% at enrollment (our prespecified analysis), the baseline HbA<sub>1c</sub> level was 9.2% ± 2.0%, and this was reduced to 8.6% ± 1.8% after CPAP treatment ( $P = .02$ ).

**Figure 2** presents the absolute change in the number of glucose values greater than 200 mg/dL (11.1 mmol/L) before and after CPAP in the entire study group and in patients with an HbA<sub>1c</sub> level greater than 7%. A value of 200 mg/dL was chosen because this represents unequivocal hyperglycemia irrespective of dietary intake. In this analysis, glucose values before and after CPAP were compared by means of an identical number of glucose values matched for the same period. This was done to maintain an identical number of meal and fasting periods before or after CPAP treatment. The figure illustrates that there was a significant reduction in the number of glucose values greater than 200 mg/dL in the entire study population (baseline, 148 ± 200; after CPAP, 83 ± 117;  $P = .003$ , Friedman test). There was also a reduction in the number of glucose values exceeding 200 mg/dL in the subgroup of patients with HbA<sub>1c</sub> levels greater than 7%; however, this did not reach statistical significance.

**Figure 3** relates the improvement (reduction) of HbA<sub>1c</sub> levels to the number of days of CPAP usage among patients with either high or low CPAP treatment compliance. For this analysis, the change in HbA<sub>1c</sub> level was calculated as the baseline value minus the post-CPAP value, so that a positive result represents an improvement in HbA<sub>1c</sub> during CPAP treatment. In the high-compliance CPAP group (average use, >4 h/d; n = 12), there was a highly significant correlation between HbA<sub>1c</sub> improvement and the number of days of CPAP use (Figure 3A; Spearman correlation,  $r = 0.74$ ,  $P = .006$ ). In the low-compliance CPAP group (average use, ≤4 h/d; n = 12), there was no correlation between HbA<sub>1c</sub> improvement and the number of days of CPAP use (Figure 3B; Spearman rank correlation,  $r = 0.28$ ,  $P = .32$ ).

#### COMMENT

The results in this report demonstrate that effective treatment of SDB (ie, the CPAP pressure that best eliminated

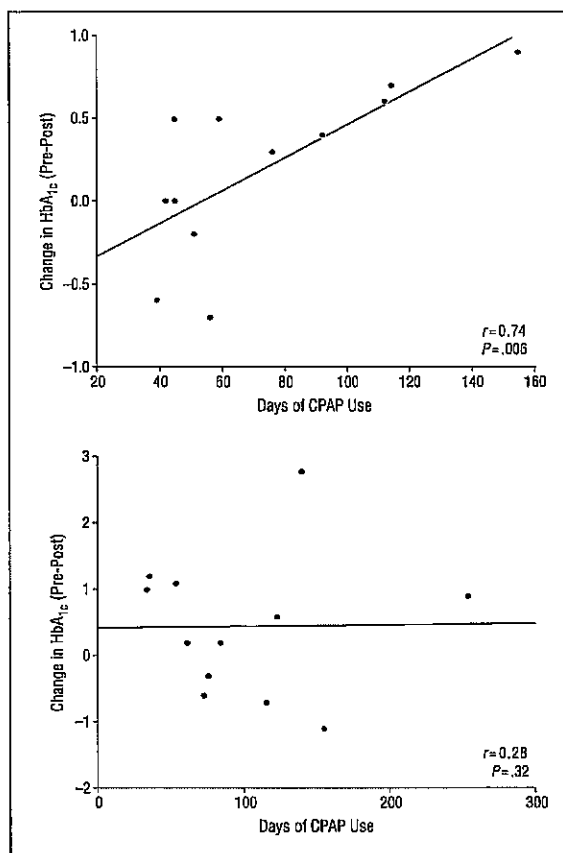


**Figure 2.** Number of glucose values greater than 200 mg/dL (11.1 mmol/L) before and after continuous positive airway pressure (CPAP) treatment for the entire study population and patients with an initial hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) level greater than 7%. Glucose values before and after CPAP were matched for number and time of day for each patient. Groups were compared by Friedman test.

SDB) led to improved glycemic control in a group of very obese subjects with type 2 diabetes mellitus. Improvement in overall glycemic control was documented by measuring interstitial glucose levels every 5 minutes and by observing changes in HbA<sub>1c</sub> level. Treatment with CPAP significantly reduced postprandial hyperglycemia and the total number of glucose values that were greater than 200 mg/dL (11.1 mmol/L). In a group of patients with baseline poor glycemic control, CPAP treatment also significantly reduced HbA<sub>1c</sub> level. Finally, the strong correlation between HbA<sub>1c</sub> improvement and days of CPAP use among compliant CPAP users, but not noncompliant CPAP users, supports an important CPAP treatment effect.

We were able to study the effect of CPAP on 24-hour glucose control in subjects during routine daily activities by using CGMS. Accuracy studies for the CGMS have been reported in healthy volunteers, as well as in patients with type 1 and type 2 diabetes.<sup>23-27</sup> The CGMS accurately tracked acute changes in plasma glucose level across a wide range of plasma glucose and insulin values in healthy volunteers. In patients with diabetes, concordance between self-monitored blood glucose levels and CGMS results were reported to be as high as 96.2%. The validity of the CGMS in our study is supported by concordant changes in HbA<sub>1c</sub> level.

Snoring (a clinical marker for SDB) and SDB have been associated with the development of diabetes in several population studies.<sup>9,28-31</sup> Sleep-disordered breathing has been associated with the development of insulin resistance and its related metabolic and cardiovascular risk factors.<sup>10,11,32,33</sup> However, the effect of CPAP treatment on glucose control in subjects with SDB and diabetes has been inconsistent.<sup>16,34,35</sup> In published studies, however, objective measures of compliance with CPAP were not included. Our results demonstrate the importance of compliance for metabolic improvement with CPAP therapy. These results provide support for use of CPAP as a therapeutic approach in patients with type 2 diabetes and SDB,



**Figure 3.** Change in hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels by number of days of continuous positive airway pressure (CPAP) use in patients who used CPAP more than 4 h/d (A) or 4 h/d or less (B). Pre and Post refer to values before and after CPAP treatment. A positive change in HbA<sub>1c</sub> represents an improvement (reduction). The patients using CPAP more than 4 h/d demonstrated a significant correlation between number of days of CPAP use and improvement in HbA<sub>1c</sub> level ( $r=0.74$ ,  $P=.006$ , Spearman rank correlation).

and are consistent with the previously reported association between SDB and glucose intolerance. In addition, the current results provide support for a causal relationship between SDB and impaired glucose homeostasis. We believe that failure to account for poor compliance may have masked a positive treatment effect of CPAP in previous studies of diabetic subjects with SDB.

Because we monitored blood glucose every 5 minutes for several days, we were able to document a much larger CPAP treatment effect on postprandial compared with fasting blood glucose levels. This result could reflect the fact that our subjects had more substantial elevation of postprandial than fasting glucose values. This would make a treatment effect easier to detect for a given sample size. Alternatively, these results could also reflect the effect of CPAP treatment on insulin resistance and sympathetic activity.<sup>36,37</sup> Increased sympathetic activity caused by frequent sleep arousals and hypoxemia, with release of counterregulatory stress hormones, may be one mechanism for increasing insulin resistance in SDB.<sup>37-40</sup>

The interpretation of our study is limited by the absence of a placebo group, ie, we did not randomize sub-

jects to sham CPAP treatment. We used patients as their own controls and compared them before and after CPAP treatment. However, the ability to monitor compliance, and to identify patients with low CPAP compliance, allowed a direct comparison between high- and low-use groups. This comparison helps to address the issue of regression to the mean as an explanation of our results. There was a strong and significant correlation between days of CPAP use and HbA<sub>1c</sub> improvement in compliant CPAP users but not in noncompliant users (Figure 3). There was also a larger impact on postprandial blood glucose values in compliant than noncompliant CPAP users (Table 4). These results are consistent with a significant treatment effect. Although it remains possible that patients compliant with CPAP may also be more compliant with their medication regimen, our design did not allow medication adjustment during the study period, and it is unlikely that new compliance issues arose during the study to affect our results.

In view of the high prevalence of obesity and SDB in diabetic patients, our results suggest that treatment of SDB in these patients will have important therapeutic benefit. The degree of HbA<sub>1c</sub> reduction that we observed with treatment of SDB could have important implications for development of diabetic complications. Even more provocatively, the efficacy of CPAP treatment of SDB in improving glucose homeostasis suggests an important pathophysiologic role for SDB in producing, or worsening, impaired glucose homeostasis. The results of our study, therefore, also support the hypothesis that treatment of significant SDB in patients with impaired glucose tolerance, or impaired fasting glucose levels, might prevent or delay progression to diabetes. Evaluating this hypothesis could have significant implications for reducing cardiovascular risk in the large number of patients with SDB, obesity, and insulin resistance.

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