

## IMPROVEMENT OF SLEEP APNEA IN PATIENTS WITH CHRONIC RENAL FAILURE WHO UNDERGO NOCTURNAL HEMODIALYSIS

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### ABSTRACT

**Background** Sleep apnea is common in patients with chronic renal failure and is not improved by either conventional hemodialysis or peritoneal dialysis. With nocturnal hemodialysis, patients undergo hemodialysis seven nights per week at home, while sleeping. We hypothesized that nocturnal hemodialysis would correct sleep apnea in patients with chronic renal failure because of its greater effectiveness.

**Methods** Fourteen patients who were undergoing conventional hemodialysis for four hours on each of three days per week underwent overnight polysomnography. The patients were then switched to nocturnal hemodialysis for eight hours during each of six or seven nights a week. They underwent polysomnography again 6 to 15 months later on one night when they were undergoing nocturnal hemodialysis and on another night when they were not.

**Results** The mean ( $\pm$ SD) serum creatinine concentration was significantly lower during the period when the patients were undergoing nocturnal hemodialysis than during the period when they were undergoing conventional hemodialysis ( $3.9 \pm 1.1$  vs.  $12.8 \pm 3.2$  mg per deciliter [ $342 \pm 101$  vs.  $1131 \pm 287$   $\mu$ mol per liter],  $P < 0.001$ ). The conversion from conventional hemodialysis to nocturnal hemodialysis was associated with a reduction in the frequency of apnea and hypopnea from  $25 \pm 25$  to  $8 \pm 8$  episodes per hour of sleep ( $P = 0.03$ ). This reduction occurred predominantly in seven patients with sleep apnea, in whom the frequency of episodes fell from  $46 \pm 19$  to  $9 \pm 9$  per hour ( $P = 0.006$ ), accompanied by increases in the minimal oxygen saturation (from  $89.2 \pm 1.8$  to  $94.1 \pm 1.6$  percent,  $P = 0.005$ ), transcutaneous partial pressure of carbon dioxide (from  $38.5 \pm 4.3$  to  $48.3 \pm 4.9$  mm Hg,  $P = 0.006$ ), and serum bicarbonate concentration (from  $23.2 \pm 1.8$  to  $27.8 \pm 0.8$  mmol per liter,  $P < 0.001$ ). During the period when these seven patients were undergoing nocturnal hemodialysis, the apnea-hypopnea index measured on nights when they were not undergoing nocturnal hemodialysis was greater than that on nights when they were undergoing nocturnal hemodialysis, but it still remained lower than it had been during the period when they were undergoing conventional hemodialysis ( $P = 0.05$ ).

**Conclusions** Nocturnal hemodialysis corrects sleep apnea associated with chronic renal failure. (N Engl J Med 2001;344:102-7.)

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**S**LEEP disorders are common in patients with chronic renal failure.<sup>1-5</sup> The reported prevalence of sleep apnea in such patients ranges from 50 percent to 70 percent.<sup>2</sup> Although conventional hemodialysis does not reduce the prevalence or severity of sleep apnea in patients with chronic renal failure, renal transplantation has been reported to correct both obstructive and central sleep apnea.<sup>6-8</sup>

Nocturnal hemodialysis is a new technique that enables patients to undergo hemodialysis seven nights per week at home while sleeping.<sup>9</sup> Since nocturnal hemodialysis provides better clearance of uremic toxins than conventional hemodialysis, it may improve sleep disorders, such as sleep apnea, that are associated with chronic renal failure. We performed a study to determine the effect of nocturnal hemodialysis on sleep apnea.

### METHODS

#### Study Subjects

Between November 1993 and November 1998, we studied 14 of the first 15 patients recruited to our nocturnal-hemodialysis program; the remaining patient declined to participate in the study after being switched to nocturnal hemodialysis. These patients were not assessed for the presence of sleep apnea before enrollment. Eligible patients had central venous access available for hemodialysis; had no contraindications to systemic anticoagulation; were able to learn the technique of nocturnal hemodialysis, in the opinion of the investigators; had a home environment appropriate for the support of nocturnal hemodialysis; and were English-speaking and thus able to respond to a telephone call prompted by remote monitoring. The study protocol was reviewed and approved by the research ethics board at St. Michael's Hospital, and all the patients gave written informed consent to participate in the study.

#### Nocturnal Hemodialysis

The nocturnal-hemodialysis program was a pilot study designed to assess this form of hemodialysis, which the patient undergoes at home, during sleep, for 8 to 10 hours every night. Vascular access was achieved through a long-term internal jugular catheter (Udall catheter, Cook Critical Care, Bloomington, Ind.). A low flow of dialysate (100 ml per minute) was used to avoid excessive dialysis. A low-surface-area (0.7 m<sup>2</sup>) polysulfone dialyzer was used (Fresenius Medical Care, Lexington, Mass.). All the main functions displayed on the front panel of the dialysis machine (Fresenius 2008H) were monitored remotely each night by modem. Nocturnal hemodialysis provided clearance of small molecules at a rate at least twice that provided by conventional hemodialysis, excellent control of serum phosphate concentrations without the use of phosphate binders, improved clearance of medium-sized molecules, hemodynamic stability, control of blood pressure without the use of antihypertensive drugs, and an improved quality of life.<sup>10-14</sup>

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### Study Protocol

All patients entered the study while they were being treated with conventional hemodialysis for four hours on each of three days per week (Fig. 1). Base-line measurements consisting of polysomnography and biochemical studies were performed in the sleep laboratory on two different nights during one week. On one occasion, the measurements were performed after the patient had undergone conventional hemodialysis during the day, and on the other occasion, they were performed after a two-day interval during which the patient had not undergone conventional hemodialysis. The two nights when the studies were performed were scheduled in random order. Over the subsequent six weeks, the treatment was changed to nocturnal hemodialysis. After their condition had become stabilized while they were undergoing this treatment, the patients returned to the sleep laboratory for follow-up measurements performed on two different nights during one week; a night when the patient was being treated with nocturnal hemodialysis and a night when the patient was not undergoing nocturnal hemodialysis. Once again, the nights were scheduled in random order.

### Study Measurements

The measurements consisted of comprehensive overnight polysomnography performed in a sleep laboratory and biochemical studies, which included measurements of serum creatinine and bicarbonate. The biochemical studies were performed just before and after polysomnography, and the values were averaged.

During overnight polysomnography, we obtained a two-channel electroencephalogram, an electro-oculogram, and a submental electromyogram using surface electrodes. The airflow was measured by monitoring expired carbon dioxide at the nose and mouth through nasal cannulas adapted for this purpose and attached to a carbon dioxide analyzer (CD 102, Normocap, Datex, Helsinki, Finland). Respiratory effort was measured by inductance plethysmography with transducers placed on the chest and abdomen (Respirace, Ambulatory Monitoring, Ardsley, N.Y.). Arterial oxygen saturation was recorded with a pulse oximeter (Biox 3740, Ohmeda, Boulder, Colo.). The transcutaneous partial pressure of carbon dioxide was recorded by a sensor placed on the anterior chest wall and attached to a carbon dioxide monitor (Micro Gas 7640, Kontron Instruments, Watford, United Kingdom). Leg movements were measured by anterior tibialis electromyography from both legs with the use of surface electrodes. All variables were recorded continuously by a computerized data-acquisition system and stored on an optical disk for later analysis (Sandman, Mallinckrodt/Nellcor-Puritan Bennet, Melville, Ottawa, Ont., Canada).

All polysomnograms were scored manually according to established criteria.<sup>15</sup> An arousal was defined as an awakening from sleep for 3 to 15 seconds, as reflected by simultaneous alpha activity on the electroencephalogram, electromyographic evidence of

activation, and eye movements. A respiratory arousal was defined as an arousal that occurred within three seconds after the termination of an episode of apnea or hypopnea. Apnea was defined as the absence of airflow for more than 10 seconds. Hypopnea was defined as a reduction for more than 10 seconds in the amplitude of respiratory effort to a value between 10 and 50 percent of the base-line level during sleep, with or without an associated decrease in oxygen saturation. Episodes of apnea and hypopnea were classified as central if the chest wall and abdomen moved synchronously, as obstructive if they moved paradoxically, and as mixed if a central event was terminated by two or three obstructed breaths. The apnea-hypopnea index was defined as the number of episodes of apnea and hypopnea per hour of sleep. Cheyne-Stokes respiration was defined as an episode of central apnea (or hypopnea) alternating with breathing that had a pattern of crescendo and decrescendo.

The mean oxygen saturation and transcutaneous partial pressure of carbon dioxide during sleep were calculated by averaging the high and low values for each 30-second period. The mean minimal oxygen saturation was calculated by averaging the lowest oxygen value for each 30-second period. Periodic leg movements were defined as four or more involuntary leg movements during sleep, each lasting 0.5 to 5.0 seconds, with 5 to 90 seconds between movements.<sup>16</sup>

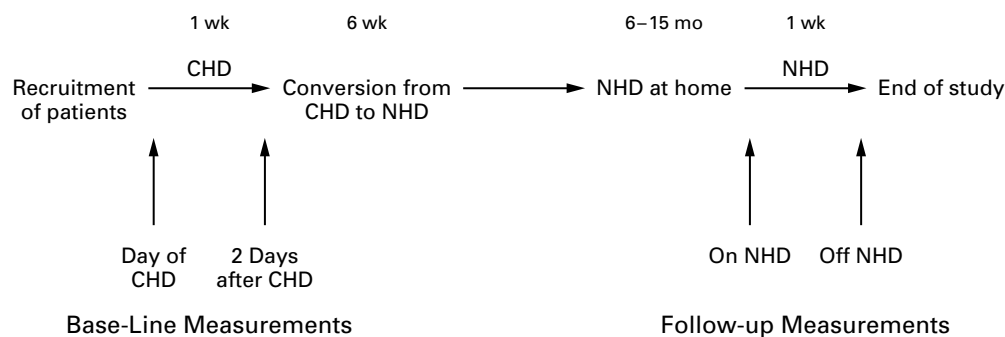
### Statistical Analysis

Comparisons of two groups of mean values were made with Student's *t*-tests. Comparisons of three or four groups of mean values were made by analysis of variance for repeated measures with a Bonferroni test. All reported *P* values are two-sided.

### RESULTS

The patients were 10 men and 4 women with a mean ( $\pm$ SD) age of  $45 \pm 9$  years. They had been treated by conventional hemodialysis for 1 to 15 years. The cause of renal failure was chronic glomerulonephritis (in three patients), diabetes mellitus (in two), polycystic kidney disease (in two), hypertensive nephrosclerosis (in one), and reflux nephropathy (in one); the cause was unknown in five patients.

While the patients were undergoing conventional hemodialysis, the prevalence of sleep apnea, defined as an apnea-hypopnea index higher than 15, was 57 percent (Table 1). One patient had Cheyne-Stokes respiration associated with an estimated left ventricular ejection fraction of 50 percent. Episodes of cen-



**Figure 1.** The Study Protocol.

CHD denotes conventional hemodialysis, and NHD nocturnal hemodialysis. The two sets of base-line measurements were scheduled in random order, as were the two sets of follow-up measurements.

**TABLE 1. PREVALENCE OF SLEEP APNEA DURING TREATMENT WITH CONVENTIONAL HEMODIALYSIS IN 14 PATIENTS WITH END-STAGE RENAL DISEASE.**

VARIABLE	APNEA-HYPOPNEA INDEX*		
	5-10	11-15	>15
	no. of patients (%)		
Obstructive sleep apnea	1	1	7
Cheyne-Stokes respiration	0	0	1
Total	1 (7)	1 (7)	8 (57)

\*The apnea-hypopnea index is the total number of episodes of apnea and hypopnea per hour of sleep. The mean ( $\pm$ SD) value for the index was  $25 \pm 25$  in all 14 patients and  $46 \pm 19$  in those with an index higher than 15 (whom we categorized as having sleep apnea). Only patients with 5 or more episodes per hour are shown.

tral, obstructive, and mixed apnea and hypopnea were equally distributed among the other patients. However, sleep apnea was diagnosed before enrollment in only one patient, who was treated with nasal continuous positive airway pressure throughout the study.

During the period when the patients were undergoing conventional hemodialysis, the mean serum cre-

atinine concentration was elevated both two days after hemodialysis ( $12.8 \pm 3.2$  mg per deciliter [ $1131 \pm 287$   $\mu$ mol per liter]) and on the day of dialysis ( $7.4 \pm 2.5$  mg per deciliter [ $652 \pm 223$   $\mu$ mol per liter]). Although the serum creatinine concentrations were lower during nocturnal hemodialysis ( $3.9 \pm 1.1$  mg per deciliter [ $342 \pm 101$   $\mu$ mol per liter],  $P < 0.001$ ), the concentration tended to increase on the single night when the patients were not undergoing nocturnal hemodialysis ( $5.7 \pm 1.7$  mg per deciliter [ $506 \pm 148$   $\mu$ mol per liter],  $P < 0.001$ ). The mean serum bicarbonate concentration was lowest ( $22.9 \pm 2.6$  mmol per liter) two days after conventional hemodialysis, indicating greater metabolic acidosis in patients who had not undergone dialysis for more than 48 hours.

There were no substantial changes in sleep patterns during the study (Table 2). The frequency of arousals and periodic leg movements was higher than normal<sup>16</sup> but remained stable. The apnea-hypopnea index decreased substantially after the treatment was converted from conventional to nocturnal hemodialysis, and it tended to increase during the single night when the patient was not undergoing nocturnal hemodialysis. The mean transcutaneous partial pressure of carbon dioxide during sleep was lowest two days af-

**TABLE 2. MEAN ( $\pm$ SD) POLYSOMNOGRAPHIC DATA ACCORDING TO THE TYPE OF HEMODIALYSIS.\***

VARIABLE	2 DAYS AFTER CHD	DAY OF CHD	OFF NHD	ON NHD
Total sleep time (hr)	$5.7 \pm 0.7$	$5.6 \pm 0.7$	$5.4 \pm 0.5$	$5.0 \pm 0.6$
Sleep efficiency (%)†	$85 \pm 10$	$87 \pm 10$	$87 \pm 11$	$80 \pm 8$
Type of sleep (% of total sleep time)				
Non-rapid eye movement				
Stage 1	$9 \pm 5$	$10 \pm 7$	$6 \pm 3$	$12 \pm 5$ ‡
Stage 2	$48 \pm 4$	$47 \pm 11$	$42 \pm 10$	$47 \pm 12$
Slow-wave	$26 \pm 13$	$24 \pm 10$	$30 \pm 7$	$27 \pm 10$
Rapid eye movement	$17 \pm 8$	$19 \pm 6$	$22 \pm 8$	$14 \pm 5$ ‡
Arousals (no./hr)	$25 \pm 22$	$23 \pm 20$	$25 \pm 24$	$24 \pm 21$
Periodic leg movements (no./hr)	$40 \pm 52$	$37 \pm 54$	$37 \pm 33$	$40 \pm 38$
Apnea-hypopnea index§	$25 \pm 25$	$25 \pm 25$	$13 \pm 13$	$8 \pm 8$ ¶
Oxygen saturation during sleep (%)	$93.8 \pm 2.0$	$93.2 \pm 3.0$	$94.7 \pm 1.9$	$95.9 \pm 1.7$
Transcutaneous PCO <sub>2</sub> (mm Hg)**	$39.6 \pm 3.9$ ††	$46.2 \pm 4.2$	$45.6 \pm 5.6$	$45.5 \pm 5.4$

\*The two sets of measurements performed during conventional hemodialysis (CHD) and the two sets performed after the conversion to nocturnal hemodialysis (NHD) were scheduled in random order.

†Sleep efficiency is the total sleep time expressed as a percentage of the total duration of the sleep study.

‡ $P = 0.003$  for the comparison with the study when the patient was not receiving nocturnal hemodialysis, by Student's t-test.

§The apnea-hypopnea index is the total number of episodes of apnea and hypopnea per hour of sleep.

¶ $P = 0.03$  for the comparison with two days after conventional hemodialysis, by Student's t-test;  $P = 0.01$  for the comparison with the day of conventional hemodialysis, by Student's t-test.

|| $P = 0.01$  for the comparison with two days after conventional hemodialysis, by Student's t-test;  $P = 0.004$  for the comparison with the day of conventional hemodialysis, by Student's t-test.

\*\*PCO<sub>2</sub> denotes the partial pressure of carbon dioxide. The normal range is 40 to 50 mm Hg.

†† $P = 0.003$  for the comparison with the day of conventional hemodialysis, by analysis of variance.

ter conventional hemodialysis, a result consistent with the ventilatory response to metabolic acidosis noted above.

The polysomnographic data in the seven patients who had sleep apnea (apnea-hypopnea index greater than 15), excluding the single patient who continued to receive nasal continuous positive airway pressure throughout the study, are shown in Table 3. There was a reduction in the apnea-hypopnea index after conversion from conventional to nocturnal hemodialysis, accompanied by an increase in oxygen saturation during sleep. The mean transcutaneous partial pressure of carbon dioxide was significantly higher during the period when the patients were undergoing nocturnal hemodialysis, whereas their serum bicarbonate concentration was lowest two days after a session of conventional hemodialysis. Although the frequency of all arousals (respiratory plus nonrespiratory) remained high, the frequency of respiratory arousals fell significantly, from  $25 \pm 14$  per hour when measured two days after conventional hemodialysis to  $6 \pm 7$  per hour during nocturnal hemodialysis ( $P = 0.008$ ). In the single patient with Cheyne-Stokes respiration, the apnea-hypopnea index remained elevated

(Fig. 2), but the pattern of breathing became more characteristic of obstructive sleep apnea.

There was an even and consistent distribution of central, obstructive, and mixed episodes of apnea and hypopnea during the period when the patients were being treated by conventional hemodialysis (Table 4). Furthermore, the reduction in the apnea-hypopnea index after treatment was changed to nocturnal hemodialysis was similar for all categories of apnea and hypopnea.

The body-mass index (the weight in kilograms divided by the square of the height in meters) did not change significantly in patients with sleep apnea ( $25.9 \pm 5.6$  during conventional hemodialysis and  $25.9 \pm 5.0$  during nocturnal hemodialysis) or in those without sleep apnea ( $25.5 \pm 4.1$  and  $25.6 \pm 3.6$ , respectively).

## DISCUSSION

Our findings confirm the high prevalence of sleep apnea in patients with end-stage renal disease<sup>1-4</sup> and demonstrate that nocturnal hemodialysis improves sleep apnea. Although sleep apnea is clearly associated with chronic renal failure, the natural history of the association has not been determined. In the majority

**TABLE 3.** MEAN ( $\pm$ SD) POLYSOMNOGRAPHIC DATA IN SEVEN PATIENTS WITH AN APNEA-HYPOPNEA INDEX ABOVE 15.\*

VARIABLE	2 DAYS AFTER CHD	DAY OF CHD	OFF NHD	ON NHD
Total sleep time (hr)	$5.6 \pm 0.7$	$5.8 \pm 0.5$	$5.3 \pm 0.6$	$5.2 \pm 0.7$
Sleep efficiency (%)	$83 \pm 9$	$88 \pm 7$	$84 \pm 15$	$79 \pm 8$
Type of sleep (% of total sleep time)				
Non-rapid eye movement				
Stage 1	$9 \pm 3$	$10 \pm 8$	$8 \pm 4$	$15 \pm 6$
Stage 2	$54 \pm 15$	$48 \pm 14$	$43 \pm 11$	$48 \pm 15$
Slow-wave sleep	$19 \pm 9$	$21 \pm 10$	$28 \pm 8$	$24 \pm 12$
Rapid eye movement	$18 \pm 9$	$20 \pm 6$	$21 \pm 9$	$13 \pm 4$
Arousals (no./hr)	$30 \pm 22$	$22 \pm 8$	$34 \pm 30$	$28 \pm 25$
Periodic leg movements (no./hr)	$43 \pm 48$	$23 \pm 25$	$42 \pm 35$	$57 \pm 40$
Apnea-hypopnea index (no./hr)	$46 \pm 19$	$44 \pm 22$	$19 \pm 15^\dagger$	$9 \pm 9^\ddagger$
Oxygen saturation during sleep (%)	$92.6 \pm 2.0$	$91.7 \pm 3.1$	$93.7 \pm 1.6$	$95.3 \pm 1.3^\S$
Minimal oxygen saturation during sleep (%)	$89.2 \pm 1.8$	$87.9 \pm 4.9$	$92.0 \pm 2.3$	$94.1 \pm 1.6^\P$
Transcutaneous PCO <sub>2</sub> (mm Hg)	$38.5 \pm 4.3$	$43.9 \pm 4.6$	$46.2 \pm 7.2$	$48.3 \pm 4.9^\parallel$
Serum bicarbonate (mmol/liter)	$23.2 \pm 1.8$	$26.0 \pm 3.2$	$27.0 \pm 2.8$	$27.8 \pm 0.8^{**}$

\*CHD denotes conventional hemodialysis, NHD nocturnal hemodialysis, and PCO<sub>2</sub> the partial pressure of carbon dioxide. One patient with an apnea-hypopnea index above 15 continued to receive nasal continuous positive airway pressure; data for this patient are not included in the table. Percentages may not total 100, because of rounding.

$^\dagger P = 0.05$  for the comparison with two days after conventional hemodialysis, by Student's t-test.

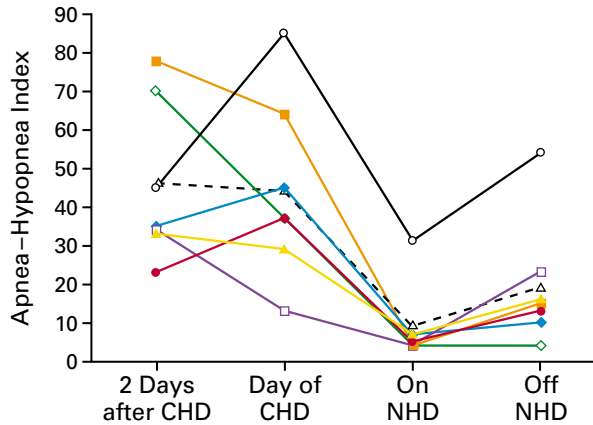
$^\ddagger P = 0.006$  for the comparison with two days after conventional hemodialysis, by Student's t-test;  $P = 0.002$  for the comparison with the day of conventional hemodialysis, by Student's t-test.

$^\S P = 0.02$  for the comparison with the day of conventional hemodialysis, by Student's t-test.

$^\P P = 0.005$  for the comparison with two days after conventional hemodialysis, by Student's t-test.

$^\parallel P = 0.006$  for the comparison with two days after conventional hemodialysis, by Student's t-test.

$^{**} P < 0.001$  for the comparison with two days after conventional hemodialysis, by Student's t-test;  $P = 0.02$  for the comparison with two days after conventional hemodialysis, by analysis of variance.



**Figure 2.** Apnea-Hypopnea Index in Seven Patients with a Base-Line Apnea-Hypopnea Index Higher Than 15.

CHD denotes conventional hemodialysis, and NHD nocturnal hemodialysis. The mean values are represented by the broken black line. Data from the single patient who had Cheyne-Stokes respiration during conventional hemodialysis and persistent obstructive sleep apnea during nocturnal hemodialysis are represented by the solid black line.

ty of our patients, sleep apnea was not apparent until chronic renal failure had become established, the problem persisted during conventional hemodialysis, and snoring and witnessed apnea resolved shortly after conversion to nocturnal hemodialysis. These results contrast with the findings in the single patient who had obstructive sleep apnea before chronic renal failure developed. This patient was treated with nasal continuous positive airway pressure throughout the study and continued to have severe obstructive sleep apnea when this treatment was discontinued (apnea-hypopnea index, 65), despite successful conversion from conventional to nocturnal hemodialysis.

Despite reductions in the apnea-hypopnea index and associated respiratory arousals after the conversion to nocturnal hemodialysis, the number of total arousals remained high. This observation reflects the multiple causes of sleep disruption in patients with chronic renal failure, which includes sleep apnea, periodic limb movements, and conditioned insomnia associated with many years of sleep disruption. The majority of persistent arousals during nocturnal hemodialysis either were associated with periodic limb movements or were classified as “spontaneous,” in that they were not temporally related to periodic limb movements or environmental noise. Dialysate flow was minimized in this study (100 ml per minute) in order to prevent excessive dialysis. It is possible that higher dialysate and blood flows would further relieve sleep fragmentation.

The pathogenesis of sleep apnea in patients with end-stage renal disease is not clear, although many

**TABLE 4.** TYPE OF EPISODE OF APNEA OR HYPOPNEA.\*

TYPE OF EPISODE	2 DAYS AFTER CHD	DAY OF CHD	OFF NHD	ON NHD
	no. of episodes/hr			
<b>All patients</b>				
Central	11±13	13±22	6±6	3±2†
Obstructive	8±10	9±10	5±7	3±6
Mixed	6±13	4±5	2±5	2±3
Total	25±25	25±25	13±13	8±8‡
<b>Patients with apnea-hypopnea index &gt;15</b>				
Central	21±12	24±27	11±5	4±2§
Obstructive	13±11	13±11	4±6	2±4
Mixed	11±14	7±6	4±6	3±4
Total	46±19	44±22	19±15¶	9±9

\*Values are means ±SD. CHD denotes conventional hemodialysis, and NHD nocturnal hemodialysis.

†P=0.02 for the comparison with two days after conventional hemodialysis, by Student’s t-test.

‡P=0.03 for the comparison with two days after conventional hemodialysis, by Student’s t-test.

§P=0.003 for the comparison with two days after conventional hemodialysis, by Student’s t-test.

¶P=0.05 for the comparison with two days after conventional hemodialysis, by Student’s t-test.

||P=0.006 for the comparison with two days after conventional hemodialysis, by Student’s t-test; P=0.002 for the comparison with the day of conventional hemodialysis, by Student’s t-test.

hypotheses have been considered.<sup>1,2,17,18</sup> It is characterized by features of both obstructive and central apnea.<sup>3,5,6</sup> In our patients with sleep apnea, there was an even distribution of central, obstructive, and mixed respiratory events. These findings support the hypothesis that sleep apnea in patients with chronic renal failure is due both to central destabilization of ventilatory control and to upper-airway occlusion. The respiratory adaption to chronic metabolic acidosis in renal failure promotes the development of hypocapnia,<sup>5,6,19</sup> which has a key role in the pathogenesis of periodic breathing.<sup>20</sup> This destabilization is augmented by increased chemosensitivity, which has been reported in patients with end-stage renal disease<sup>19</sup> and in the pathogenesis of periodic breathing.<sup>20</sup>

During conventional hemodialysis, our patients had relative hypocapnia, reflected by mean values for the transcutaneous partial pressure of carbon dioxide that were at the lower end of the normal range; these values increased significantly after the initiation of nocturnal hemodialysis. The development of periodic breathing can promote upper-airway occlusion both by reducing drive to the upper airway muscles during apnea and by disproportionately increasing drive to the inspiratory muscles.<sup>21,22</sup> This combination is more likely to cause obstructive apnea in patients with

chronic renal failure than in healthy persons, since those with chronic renal failure may be predisposed to upper-airway occlusion because they have airway edema, which is associated with fluid overload, and reduced muscle tone, which is associated with uremia and neuropathy.<sup>1,6</sup>

We did not evaluate every potential mechanism by which nocturnal hemodialysis might improve sleep apnea, although we believe the increase in the transcutaneous partial pressure of carbon dioxide reflects stabilization of ventilatory control. We speculate that the change from Cheyne–Stokes respiration to obstructive sleep apnea in one of our patients resulted from increased respiratory drive in association with an unstable upper airway. However, it is possible that the correction of sleep apnea in our patients was mediated primarily through the effect of nocturnal hemodialysis on the upper airway. Nocturnal hemodialysis improves the control of blood pressure by decreasing the volume of extracellular fluid.<sup>13</sup> Such a decrease, particularly in the upper airway, may have a salutary effect on the pathophysiology of sleep apnea.

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