A Randomized, Double-blind Clinical Trial Comparing Continuous Positive Airway Pressure with a Novel Bilevel Pressure System for Treatment of Obstructive Sleep Apnea Syndrome

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Study Objectives: To obtain efficacy, objective compliance, and self-assessment data from obstructive sleep apnea syndrome (OSAS) patients treated with continuous positive airway pressure (CPAP) or a novel bilevel (NBL) therapy.

Design: Randomized, controlled, double-blind trial.

Setting: Home treatment after diagnosis and titration by split-night polysomnography (PSG) in a sleep laboratory.

Patients: Twenty-seven adults (22 men) newly referred for suspected OSAS but without concomitant medical or sleep disorders.

Interventions: If the subject's apnea-hypopnea index was greater than 10 and less than 100, the CPAP was titrated during PSG and then followed by NBL titration. Treatment was randomly and blindly set to either CPAP or NBL mode for 1 month.

Measurements & Results: There were no significant baseline group differences in age, body mass index, apnea-hypopnea index (mean ± SD, CPAP group vs NBL group of 46.1 ± 23.1/hour vs 41.8 ± 25.8), CPAP requirement, or scores on the Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire. Treatment with CPAP and NBL equivalently reduced the apnea-hypopnea index during the laboratory titration (7.6 ± 11.9/hour vs. 3.7 ± 4.4, respectively). At 1 month, there were no significant group compliance differences as determined by percentage of nights with at least 4 hours of use (CPAP, 80.5 ± 24 vs NBL, 77.6 ± 24.8) and hours of use per night (CPAP, 5.6 ± 1.4 hours/night vs NBL, 5.6 ± 1.7). Similar improvements were seen in scores on the Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire.

Conclusions: The NBL appeared to be as effective as CPAP for the treatment of OSAS but offered no advantages in patients receiving first-time therapy for OSAS.

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INTRODUCTION

OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS), A CONDITION CHARACTERIZED BY BRIEF REDUCTIONS IN VENTILATION DURING SLEEP DUE TO EPISODIC NARROWING OF THE UPPER AIRWAY, IS WIDESPREAD AND MAYBE ASSOCIATED WITH IMPAIRED QUALITY OF LIFE AND ADVERSE EVENTS, SUCH AS HYPERTENSION AND AUTOMOBILE CRASHES.[1] Continuous positive airway pressure (CPAP) has been shown in randomized placebo-controlled trials to produce objective and subjective improvements in patients with OSAS.[2,3] Many OSAS patients have difficulty with long-term acceptance of CPAP despite its demonstrable efficacy. [4,5] Several intervention strategies have been suggested to improve adherence to CPAP, including use of specialized education and follow-up programs[6,7] and added airway humidification.[8] Others have suggested that modifications of the airflow delivery pattern, as with continuously auto-adjusting CPAP[9] or bilevel devices capable of varying inspiratory and expiratory levels,[10] may boost compliance in more difficult-to-treat OSAS patients. Although some patients may prefer these more sophisticated modes over standard CPAP, profound improvements in compliance rates have not been demonstrated, especially in first-time users.[11,12]

There are reasons why the use of alternative positive airway flow patterns may have limited impact on compliance. With auto-adjusting CPAP, the proprietary algorithms that govern pressure variations may not respond quickly enough to fluctuations in upper airway patency resulting in re-emergence of airway obstruction, sleep fragmentation, or both. Conventional bilevel devices only allow fixed pressure changes for either phase of the respiratory cycle. Furthermore, bilevel devices may at times have trouble cycling from inspiration to expiration levels, resulting in discomfort to patients from dyssynchrony. Patients may also express concern over too much airflow at the beginning of expiration, a time when the upper airway is not in jeopardy of collapse.

A new bilevel mode (NBL) differs from conventional bilevel positive airway pressure devices in several ways (Figure 1). First, the inspiratory pressure is reduced slightly near the *end* of inspiration, and the expiratory pressure is slightly reduced near the *beginning* of expiration. The reduction of the late inspiratory and early expiratory pressures may help facilitate cycling to expiratory positive airway pressure (EPAP) and optimize patient-ventilator synchrony without jeopardizing upper airway patency. As Figure 1 demonstrates, the EPAP automatically rises during the later portion of expiration to the target basal pressure (P_{base}; can also be thought as the optimal CPAP) and thus maintains pressure above the critical airway opening pressure to ensure airway patency. Second, the magnitude of change of the inspiratory positive airway pressure (IPAP) and EPAP is proportional to patient effort. During inspiration, a positive inspiratory gain ($Gain_{insp}$) helps determine the peak IPAP achieved up to a preset maximum IPAP ($IPAP_{max}$). The greater the $Gain_{insp}$, the greater the IPAP reached for a given inspiratory effort. During expiration, a negative expiratory gain ($Gain_{exp}$) modulates the degree of EPAP reduction at the beginning of expiration down to a set minimum EPAP ($EPAP_{min}$). The greater the $Gain_{exp}$, the greater the initial reduction in the EPAP for a given patient effort. The gains are governed by proprietary electronic algorithms. The NBL design could result in an overall reduction in the mean airway pressure if the $Gain_{insp}$ is set to the minimum, which locks the highest-level airflow delivery to P_{base}. On the other hand, the IPAP can be adjusted upward to raise the IPAP peak when it is most needed,

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giving a more typical bilevel profile, and either approach might be more comfortable for the patient.

In this prospective study comparing NBL with standard CPAP, we sought to 1) demonstrate equivalent efficacy of NBL and CPAP to resolve obstructive sleep- disordered breathing events during polysomnography (PSG) in patients with newly diagnosed OSAS and 2) obtain objective compliance (hours of patient use recorded by internal machine software) and self-assessment (questionnaires) data after 30 days of therapy applied in a randomized double-blind trial design.

We hypothesized that NBL would show a better (> 10%) compliance rate (percentage of nights with more than 4 hours of use per night over 30 days) and reveal at least an equivalent patient-reported clinical improvement in scores on the Epworth Sleepiness Scale (ESS)[13] and Functional Outcomes of Sleep Questionnaire (FOSQ).[14]

METHODS

This study was approved by our Institutional Review Board.

Subjects

Consecutive patients referred by their primary community physician to the sleep disorders center (SDC) with a possible diagnosis of OSAS and seen by 1 of the investigators (PCG or EJO) were approached for recruitment if the interview and examination suggested a high likelihood of a diagnosis of OSAS. Inclusion criteria were age greater than 18 (years); apnea-hypopnea index (AHI) greater than 10 but less than 100 (obstructive events); ability to follow instructions and provide informed consent; willingness to return for a follow-up visit 30 days after being randomly assigned to receive treatment with CPAP or NBL, and, preferentially, residence within 200 miles of the SDC for easier follow-up.

Exclusion criteria were an inability to wear a nasal mask due to facial or other anatomic abnormalities or claustrophobia; prior uvulopalatopharyngoplasty or other surgical procedures for the treatment of snoring or OSAS; the use of devices, including prior or current use of positive airway pressure devices for snoring or previously diagnosed OSAS; and complicating medical conditions (echocardiogram and pulmonary function tests utilized when available) including cardiac disease (cardiomyopathy [left ventricular ejection fraction < 50%]; dysrhythmias; uncontrolled hypertension [diastolic blood pressure >110]; angina); chronic obstructive pulmonary disease (forced expiratory volume in 1 second [FEV1]/forced vital capacity < 70% and FEV1 < 50% predicted); suspected or documented hypercapnia ($PaCO_2$ > 45); restrictive lung disease (total lung capacity and/or vital capacity < 80% predicted); very severe OSAS (AHI > 100 with desaturation (< 80% lasting > 5 minutes during the diagnostic portion of PSG); psychiatric disorders that in the opinion of the investigators would possibly interfere with cooperation in the study; and neuromuscular disease.

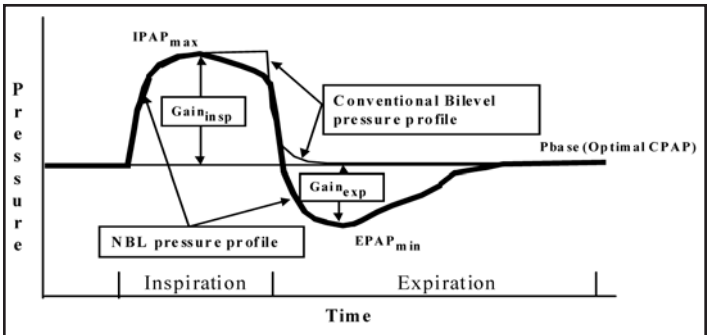

Figure 1—Novel bilevel (NBL) pressure waveform (heavy line) is compared to conventional bilevel pressure waveform (fine line). The inspiratory positive airway pressure (IPAP) profile identifies the inspiratory period, and the expiratory positive airway pressure (EPAP) profile corresponds to the expiratory period, which terminates at the set baseline P_{base} level. P_{base} is the optimal continuous positive airway pressure (CPAP). The NBL pressure waveform automatically bends down the IPAP profile toward the latter half of inspiration to facilitate cycling to EPAP while still providing the intended peak inspiratory pressure support. During any given breath, the peak inspiratory positive airway pressure ($IPAP_{max}$) is determined by a combination of patient effort and an adjustable inspiratory gain ($Gain_{insp}$), while the initial reduction in the EPAP is determined by patient effort and an adjustable negative expiratory "gain" ($Gain_{exp}$). The greater the gains and/or patient effort, the greater the pressure swings during the respiratory cycle. The range of allowable pressures is governed by the $IPAP_{max}$ and $EPAP_{min}$. The EPAP always returns to P_{base} by end-expiration to maintain upper airway patency.

For patients in our protocol, the $IPAP_{max}$ was 5 cm H_2O above P_{base}, and the $Gain_{insp}$ was adjusted such that the actual peak IPAP was 2 cm H_2O above the P_{base} for the majority of breaths. During expiration, the $EPAP_{min}$ was 5 to 7 cm H_2O, and the $Gain_{exp}$ was adjusted such that a 2- to 4-cm H_2O early expiratory pressure drop occurred during the majority of breaths. The reader can assume that the mean airway pressure of NBL was 1 to 2 cmH_2O higher than CPAP, but this was all accounted for during inspiration, and the mean expiratory pressure was lower by design. See text.

Subject Preparation

After agreeing to participate and signing informed consent, subjects were scheduled for standard split-night diagnostic and therapeutic laboratory-based PSG study at the earliest mutually convenient time. All patients eventually enrolled in the home-going trial had to complete the split-night protocol and receive titration with both CPAP and NBL. Our laboratory has been doing split-night protocols for nearly 2 decades, and personnel are skilled and efficient at performing these protocols. The purpose of the study was explained to the subject as intending to assess their compliance, tolerance, and perceived benefit from the treatment of OSAS from either standard CPAP or a "different airflow delivery device." They participated in our standard, daytime pre-PSG preparation protocol consisting of a tour of the SDC, oral and video education about OSAS and CPAP, and choice sampling of at least 2 types of CPAP nasal interfaces. Patients were not allowed to formally compare CPAP and NBL during wakefulness. The ESS and FOSQ were completed before the PSG.

The FOSQ is a 30-question self-reported instrument that seeks to assess the impact of sleepiness on daily living in the realms of activity level, vigilance, intimacy and sexual relations, general productivity, and social outcome.[14] The FOSQ can successfully discriminate normal subjects from those seeking medical attention for a sleep problem. The reported internal reliability ($\alpha = 0.96$) and test-retest reliability ($r = 0.91$) are excellent.

Polysomnography

Polysomnography was conducted using a Network Concepts, Inc., Dimensions acquisition system with QNX (version 2.4.08) operating software (Network Concepts, Inc., Middleton, WI). The following parameters were recorded: electrooculogram, electroencephalogram (C4A1/C3A2; FzCz; CzOz), submental and anterior tibialis electromyogram, electrocardiogram, oral and nasal airflow by thermocouple, snoring (laryngeal microphone, Radio Shack sound level meter, model 330-2050), oxygen saturation (finger or ear pulse oximeter, Ohmeda 3700, Datex-Ohmeda, Madison, WI), and respiratory effort (thoracic, abdominal, and summated inductive plethysmography signals, Respitrace, Ambulatory Monitoring Inc., Ardsley, NY). The sampling rate of the oximeter was set in the 'fast' mode for a saturation averaging time of 3 seconds with display data updating every 1/3 seconds. Sedatives and hypnotics were not used.

The PSGs were scored manually. Sleep stages and arousals were analyzed per the criteria of Rechtschaffen and Kales[15] and the American Sleep Disorders Association.[16] Arousals were defined as respiratory-related when they occurred at the termination of an apnea or hypopnea. An obstructive apnea was defined as the cessation of respiratory flow despite ongoing respiratory effort for at least 10 seconds. A hypopnea was defined as a reduction in airflow of at least 50% compared to baseline and lasting at least 10 seconds, together with a decrease in oxygen saturation of at least 2%.

Titration and Randomized Setting of Positive Airway Pressure Modes

The prototype devices had 3 modes from which to choose: "Set

CPAP," "Set NBL," and "A." The first 2 "set" options were used by the technologist to titrate the modes during the PSG. In all patients, CPAP was initially titrated while in the "Set CPAP" mode, and then the NBL was titrated in the "Set NBL" mode. While realizing the nonrandom application of the modes might introduce confounding factors, this order was intentionally chosen for patient safety reasons. In case the PSG was unexpectedly complicated (insomnia, difficult positive airway pressure titration, etc.) we wanted to be sure that we would at least have robust CPAP data by the end of the PSG that could be used to clinically manage OSAS patients regardless of their eventual participation in the study. If the patients could not complete all portions of the titration with the split-night protocol, they were not enrolled in the full study (see ineligible patients under 'Results').

After the diagnostic portion demonstrated the presence OSAS (AHI >10 and < 100/hour), CPAP was initiated at 5 cm H_2O and increased at 1-cm H_2O increments until snoring and respiratory-related arousals were abolished and the AHI decreased to less than 5 per hour. The CPAP titration was considered complete ('optimal CPAP' level obtained) when the patient obtained non-rapid eye movement (NREM) and rapid eye movement (REM) sleep in a lateral decubitus position and at least 20 minutes of sleep, preferably with REM, in the supine position. The device was then seamlessly switched to "Set NBL," which did not result in arousal of the patient.

In the NBL mode, adjustable settings included the P_{base}, $Gain_{insp}$, maximum IPAP ($IPAP_{max}$), the $Gain_{exp}$, and the minimum EPAP ($EPAP_{min}$). In the prototype used for this protocol, the gain choices ranged from levels 1 thorough 5. With $Gain_{insp}$ and $Gain_{exp}$ both set at 1, NBL delivers optimal CPAP. The optimal CPAP became the P_{base} at the beginning of the NBL titration. The $Gain_{exp}$ was then titrated in 1- to 2-step increments until there was reemergence of sleep-disordered breathing or arousals, at which time the $Gain_{exp}$ was returned to the previous setting 1 to 2 steps prior to this setting. The $EPAP_{min}$ (lowest allowable drop in the early expiratory pressure) was set at 5 to 7 cm H_20. We targeted an early expiratory drop below P_{base} of about 2 to 4 cm H_20 for the majority of breaths. The $IPAP_{min}$ was targeted to allow approximately 2 cm H_20 of pressure above the P_{base}, primarily in response to an assessment made of the quality of the inspiratory flow profile.[17] If the inspiratory flow profile suggested flow limitation, the $Gain_{insp}$ was gradually increased incrementally. If the inspiratory flow profile remained unchanged or equivocal after about a 4-cm H_2O increase, then the IPAP level was moved toward a minimum level of about 2 cm H_2O above the P_{base}. The $IPAP_{max}$ was set at 5 cm H_20 above P_{base} to prevent excessive inspiratory pressure exposure that might lead to unwanted arousals. The overall plan was to obtain an IPAP of at least 2 cm H_2O above the P_{base} and an initial EPAP fall of 2 to 4 cm H_2O in all patients for the majority of breaths.

This technology was a prototype and differs from the currently available BiFlex mode (Respironics Inc Murrysville, PA) in several ways and should not be considered clinically identical. There is no $Gain_{insp}$ or $IPAP_{max}$ setting in the newly available BiFlex. A fixed IPAP setting is used, and the rise time and flow profile are determined by proprietary algorithms. The $Gain_{exp}$ is more similar, but the range of our prototype was larger (5 vs 3 for BiFlex). The only other settings are fixed IPAP and EPAP levels.

The following morning, after successful titration of both modes, the technician selected the "A" mode, which, in a double-blinded and selective way, locked in the optimal settings for either CPAP or NBL. A sealed list of the identity of the "A" mode was kept based on the serial number of the device. This serial number was recorded on each subject's case report form, but the true identification of the "A" mode was not revealed until the end of the trial.

Table 1—Mean baseline Demographic and Diagnostic Polysomnogram Data

	CPAP	NBL
N	15	12
Age (years)	45.1 ± 9.3	43.6 ± 13.4
BMI (kg/m^2)	34.1 ± 4.7	36.6 ± 6.0
ESS	13.5 ± 3.4	14.2 ± 3.4
FOSQ	88.4 ± 21.2	89.7 ± 11.1
AHI (#/hour)	46.1 ± 23.1	41.8 ± 25.8
Arousal Index (#/hour)	36.8 ± 18.5	35.9 ± 20.4
Sleep Efficiency (%)	75.4 ± 15.5	79.1 ± 12.7
Total Sleep Time (minutes)	126.3 ± 36.1	158.3 ± 36.8

No significant differences were noted between groups (P= NS). CPAP, continuous positive airway pressure; NBL, novel bilevel pressure; BMI, body mass index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcome of Sleep Questionnaire; AHI, apnea-hypopnea index.

Home Dismissal and Follow-up

After reviewing their PSG data with 1 of the investigators (PCG or EJO) and receiving oral and written instructions on how to use the equipment, subjects returned home for an expected trial period of 30 days with the unit mode set. Subjects were contacted by telephone at 2 weeks by 1 of the investigators (PCG or EJO), and any pertinent obstacles to their personally assessed progress were addressed. Humidification was not routinely offered at the outset. However, if subjects were admitting difficulty, then typical interventions, such as a mask change or treatment for nasal congestion, were offered. Patients were also encouraged to call the SDC at anytime if further difficulties were encountered.

At the end of the trial, whether by failure or at 30 days, subjects returned to the SDC for retrieval of compliance data from the device and completion of the ESS and FOSQ. "Failure" was pre-defined as voluntary withdrawal anytime before 30 days on positive airway pressure or physician-requested withdrawal if clinical judgment suggested alternative interventions for OSAS. When subjects were dismissed from the protocol, they continued with standard CPAP at the level determined during their split-night PSG or other treatments as suggested by their primary physicians.

Statistics

A power analysis was calculated based on results from an auto-adjusting CPAP study that indicated a compliance difference of 81% with standard CPAP versus 93% with an auto-adjusting device.[18] We predicted that NBL would produce results similar to those from the auto-adjusting CPAP when compared to standard CPAP. Therefore, a total of 12 patients would be needed in each group to detect a 10% compliance difference with at least a 90% power. We analyzed on an intent-to-treat basis to account for dropouts. Dropouts were expected to be a high as 20%. Student's *t* test was used to determine statistical significance between group means.

RESULTS

Forty patients consented to participate in the study after their initial history and physical examination. Thirteen patients subsequently became ineligible after their PSG for the following reasons: AHI of 10 or less (4 patients); AHI of 100 or greater (4 patients); insufficient time during the PSG to titrate NBL (1 patient); central sleep apnea (1 patient); marked periodic limb movement disorder (1 patient); psychiatric disorder acknowledged after the PSG (1 patient); and travel issues felt to be a barrier to completing the protocol (1 patient).

Twenty-seven patients (5 women, 22 men) were randomly assigned to receive treatment with standard CPAP (15 patients) or NBL (12 patients). An uneven number of patients in each group resulted because randomization took place before the PSG and slightly more patients became ineligible for the NBL than the CPAP treatment limb. Table 1 provides the baseline demographic and diagnostic PSG data. Patients were typically middle-aged, overweight men with moderately severe OSAS and with questionnaire scores revealing excessive daytime sleepiness and compromised function. There were no significant differences in any of the clinical or diagnostic PSG data between the groups.

Table 2 reveals the data from the titration portion of PSG. There were no differences in the optimal CPAP requirement, sleep efficiency, or total sleep time between the 2 groups. Apneas and hypopnea and arousals were substantially and equivalently reduced with CPAP and NBL. Statistical comparisons were not done for all sleep architecture parameters because of the nonrandom application of CPAP and NBL.

All 27 of the randomly assigned patients completed the 30-day trial. There were no dropouts. The mean follow-up occurred at 30.9 days and 30.4 days for the CPAP and NBL groups, respectively. Figure 2 depicts the compliance information and represented time at pressure rates. The 30-day compliance rates were high and statistically equal. All but 1 patient used the device at least 80% of the days. Compliance was essentially determined within the first week of treatment. There were no group mean differences (P= NS) between compliance at 1 week versus 30 days, for CPAP versus NBL, respectively, in percentage of days used (96.4% vs 95.2), percentage of days with more than 4 hours of use per night (79% vs 80.5), or average hours of use per night (5.7 hours vs 5.6). Accordingly, no patient required early return to the SDC for optimization of the originally provided care plan. Telephone contact did not reveal complications necessitating additional interventions. No patients required added humidification. Self-assessment questionnaires demonstrated statistically significant improvements from baseline to follow-up (P<0.05) for both groups per the ESS and FOSQ, but the improvements for CPAP and NBL groups were equivalent.

DISCUSSION

Composite international data indicate the extensive prevalence and implications of sleep-disordered breathing. An estimated 20% of adults may have borderline or mild OSAS, and nearly 7% have at least moderate disease.[19] Obstructive sleep apnea syndrome is associated with significant cardiovascular and neurobehavioral consequences that may have a profound impact on the economy and healthcare system. Several large studies have demonstrated a dose-dependent association between OSAS and systemic hypertension.[20-22] A retrospective study of 704 Scandinavian workers with OSAS compared to an employed, age-matched, random sample of 580 subjects revealed that the risk of being involved in an occupational accident was increased by 50% in men with OSAS.[23] A Spanish study reported an adjusted odds ratio of 8.1 for automobile crashes if the AHI exceeded 15.[24] Not surprisingly, a strong association can be shown between subjective complaints related to poor sleep quality or objective measures of sleep-disordered breathing and healthcare utilization.[25] There is clearly a need to identify OSAS and optimize its treatment.

Continuous positive airway pressure is the therapeutic mainstay for OSAS and has been shown to produce subjective[2,3] and objective[26,27] improvements, even in patients with mild disease. Despite the proven value of CPAP, compliance remains a management obstacle in a significant minority of OSAS patients. Studies have shown variably and arbitrarily defined CPAP compliance rates ranging from 65 to 85%.[28-33] Patients with OSAS who develop side effects use CPAP less frequently.[34] Troublesome side-effects of CPAP use include those related to inconvenience, noise, the nasal interface, the upper airway, and pressure.[35]

The use of bilevel positive airway pressure with independently adjusted IPAP and EPAP levels has been proposed as a plausible alternative to standard CPAP. If the pressure requirement to maintain upper airway patency during sleep is lower during expiration than inspiration,[36] it follows that a reduction in the EPAP relative to the IPAP might decrease pressure-related side effects and improve compliance with positive airway pressure therapy. While there is a consensus statement supporting its use during sleep in restrictive thoracic disorders with chronic hypercapnic respiratory failure,[37] the role of bilevel positive airway pressure in otherwise uncomplicated OSAS remains unclear.

In this study, we sought to assess and compare a modified bilevel positive airway pressure prototype referred to herein as NBL in OSAS. The NBL reduces the inspiratory pressure near the end of the inspiratory phase, as well as the expiratory positive airway pressure near the beginning of the expiratory phase (Figure 1). This is not simply a trivial modification of existing bilevel technology. As many clinicians have heard, NBL bilevel users may understandably complain of too much airflow at the beginning of expiration. The NBL pressure adjustments may enhance comfort as the patient transitions from the inspiratory to the expiratory phase and may reduce expiratory effort that is perceived in some cases. We found that in randomized groups of treatment-naive OSAS patients matched for age, weight, subjective sleepiness, and OSAS severity, NBL eliminated obstructive sleep-disordered breathing events during PSG at the same level that CPAP eliminated these events and produced equivalent, objectively documented treatment compliance at 30 days.

Sanders and Kern[38] initially reported that a bilevel pressure device could treat OSAS. Reeves-Hoche et al[39] monitored compliance via covert monitors in 83 OSAS patients randomly assigned to receive treatment with CPAP or Bilevel positive airway pressure BiPAP (Respironics Inc, Murrysville, PA) and found no differences in compliance rates or

Table 2—Polysomnogram data from titration of CPAP and NBL in 27 patients

	CPAP	NBL
Optimal CPAP & baseline pressure (cm H_2O)	8.8 ± 1.1	8.9 ± 1.6
AHI (# / hour)	7.6 ± 11.9	3.7 ± 4.4
Arousal Index (#/hour)	16.5 ± 14.6	11.8 ± 5.8
Sleep Efficiency (%)	73.4 ± 15.0	84.4 ±14.4
Total Sleep Time (minutes)	115.2 ± 36.9	89.6 ± 42.5

No significant differences were noted between groups in the parameters presented (P = NS). CPAP, continuous positive airway pressure; NBL, novel bilevel pressure; AHI, apnea-hypopnea index

Table 3—Mean (± SD) self-assessment data of daytime sleepiness from 27 patients with obstructive sleep apnea syndrome

	CPAP	NBL
ESS		
Pretreatment	13.5 ± 3.4	14.2 ± 3.4
Posttreatment	8.0 ± 4.8	7.8 ± 3.8
FOSQ		
Pretreatment	88.4 ± 21.2	89.7 ± 11.1
Posttreatment	103.7 ± 18.4	107.2 ± 7.7

Pretreatment versus posttreatment self-assessment data regarding daytime sleepiness in 27 patients randomly assigned to receive treatment with continuous positive airway pressure (CPAP) or novel bilevel pressure (NBL). There were statistically significant reductions in the scores on the Epworth Sleepiness Scale and increases in the scores on the Functional Outcomes of Sleepiness Questionnaire (P < 0.05) of similar magnitude in both groups.

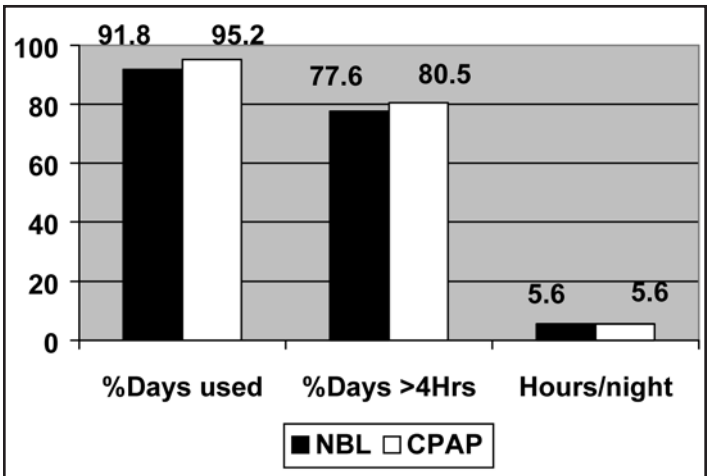

Figure 2—Compliance data downloaded from the device's inboard, pressure-actuated software for 27 patients randomly assigned to 30 days of treatment with continuous positive airway pressure (CPAP) or novel bilevel pressure (NBL). No significant differences were noted between groups in the 3 compliance parameters (P=NS). Percentage of days used equals number of days when any amount of use was recorded divided by total number of follow-up days.

side effects. Nonetheless, bilevel devices may play an important role in the management of patients with complicated OSAS. Clinical experience suggests that bilevel positive airway pressure can be a successful rescue strategy in patients with difficulty from exhaling against pressure, mask air leaks, nasal congestion, and chest discomfort.[35] It may also be effective in those requiring an above-average CPAP level (although what absolute continuous pressure constitutes such a level has never been decided). Furthermore, nocturnal bilevel positive airway pressure may be indicated in those patients with OSAS and disturbed diurnal gas exchange. Hypercapnia is rare in uncomplicated OSAS and is most commonly seen with OSAS plus coexisting illness, such as chronic obstructive pulmonary disease or severe obesity. When analyzing their experience with CPAP in OSAS, both Resta et al[40] and Schafer et al[41] reported that bilevel positive airway pressure was an effective option for the subset of OSAS patients with continued sleep-disordered breathing despite treatment with CPAP, namely those with obesity hypoventilation syndrome. In recognition of these potential niches, a consensus report acknowledged the role of bilevel devices in CPAP-intolerant patients with OSAS, obesity hypoventilation, and OSAS with coexisting respiratory disease.[42] Therefore, it seems prudent to seek ways to enhance bilevel pressure delivery, such as with NBL technology.

Despite producing compliance data similar to the studies of Sanders and Kern[38] and Reeeves-Hoche et al,[39] our study still provides several unique insights. This is the first study to demonstrate the efficacy of NBL in the treatment of OSAS. The NBL appeared to be as effective as CPAP over the 30-day study period. Secondly, because NBL differs significantly from conventional bilevel continuous positive pressure , it was not a foregone conclusion that the NBL-CPAP compliance evaluation would be similar to results from previous conventional bilevel-CPAP comparisons. Lastly, currently available equipment for the treatment of patients with OSAS shares the unique early expiratory flow response of the NBL prototype used in our study. The appropriate indications for this technology remain unclear for practicing clinicians. It is possible that future data may show potential benefit of this expiratory flow modulation in patients intolerant of conventional CPAP devices; however, our study suggests that this technology may not offer a significant compliance advantage in first-time CPAP users.

Our trial design had several potential limitations. Patients with uncomplicated OSAS may not have been the optimal patient population to seek an impact on compliance. As stated previously, bilevel devices have never been shown to improve compliance in OSAS patients with normal awake gas exchange. However, a primary goal of this trial was to also demonstrate efficacy of this NBL prototype in eliminating sleep-disordered breathing, and for this, our patient population seemed appropriate. Our relatively short follow-up of 1 month may not have been of sufficient duration to detect a longer-term compliance difference. Usage of CPAP may wane over time,[29] yet it seems unlikely a longer follow-up period would have produced a major difference given the results of Reeves-Hoche et al after 1 year of monitoring CPAP versus bilevel therapy. Compliance was much higher than expected. More than 90% of patients in the CPAP and NBL arms had objectively documented compliance based on delivered pressure, and this adversely affected the power of the study to detect a compliance difference. The patients were provided modest remuneration for travel expenses, but we doubt this was a major influence on compliance rates, since the patients were promised compensation simply on the basis of returning the machine. We arbitrarily chose the IPAP level to be a minimum of 2 cm H2O above the P_{base} to achieve a bilevel airflow delivery profile. This objective was based on our judgment of comfort and bench data generated during the design of the prototype. This probably resulted in at least a 1 to 2 cm H_2O rise in the total mean airway pressure level, which could conceivably negate an advantage of a bilevel device.

CONCLUSION

NBL, a bilevel pressure system that seeks to improve patient comfort by slightly altering the terminal inspiratory pressure and reducing the initial expiratory pressure, eliminates obstructive sleep-disordered breathing events but does not appear to offer a compliance advantage as initial therapy for OSAS. Future directions may include examining the role of NBL in patients with OSAS who are not compliant with CPAP therapy or whose OSAS is otherwise difficult to treat.

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