

Interventions to Improve Compliance in Sleep Apnea Patients Previously Non-Compliant with Continuous Positive Airway Pressure

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Study Objectives: Despite widespread agreement that continuous positive airway pressure is effective therapy for obstructive sleep apnea, it is estimated that 50% of patients recommended for therapy are noncompliant 1 year later. Interventions to improve compliance in such patients have not been studied. We evaluated a 2 phase intervention program to improve compliance in sleep apnea patients previously noncompliant with continuous positive airway pressure.

Methods: 204 patients with previously diagnosed obstructive sleep apnea and noncompliant with continuous positive airway pressure were enrolled. Phase 1 evaluated standard interventions to improve therapy compliance, including mask optimization, heated humidification, topical nasal therapy, and sleep apnea education. Persistently noncompliant patients proceeded to phase 2, where compliance was compared in double-blind randomized fashion between standard continuous positive airway pressure and flexible bilevel positive airway pressure.

Results: 49 (24%) of 204 previously noncompliant patients became compliant (average nightly use ≥ 4 hours) after standard interventions.

Then 104 of the 155 persistently noncompliant patients agreed to continue and were randomized to either CPAP or flexible bilevel positive airway pressure retreatment and treatment for an additional ninety days. At follow-up 15 (28%) of the 53 randomized to CPAP and 25 (49%) of the 51 randomized to flexible bilevel positive airway pressure ($p = 0.03$) achieved compliance.

Conclusions: A two phase intervention program, first employing standard interventions, followed by a change to flexible bilevel airway pressure, can achieve improved compliance in patients previously noncompliant with continuous positive airway pressure.

Keywords: Obstructive sleep apnea, continuous positive airway pressure, bilevel positive airway pressure, compliance, heated humidification, CPAP mask, nasal corticosteroids

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Obstructive sleep apnea (OSA) is highly prevalent, conservatively estimated to affect 2%-4% of the middle-aged adult population in the United States.¹ OSA is widely believed to contribute to impaired cognition,² hypertension,³ cardiovascular disease,⁴ cerebrovascular disease,⁵ and increased risk for accidents.⁶ The most effective therapy is continuous positive airway pressure (CPAP), which improved select signs and symptoms of OSA in several randomized, placebo-controlled trials.^{7,8} However, the efficacy of CPAP may be limited by poor compliance. It has been estimated that as many as 50% of OSA patients for whom CPAP is initially recommended are not using this therapy one year later.⁹ Common reasons for discontinuation include mask discomfort, nasal drying or irritation, and intolerance of the pressure.¹⁰

Disclosure Statement

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Numerous studies have evaluated the benefits of various interventions at initial CPAP set-up to improve acceptance and compliance. Such interventions include intensified education and follow-up programs,¹¹ the addition of humidification to CPAP,¹² and alternative pressure delivery systems.¹³ Gay and colleagues have recently reviewed in detail factors that can affect initial CPAP tolerance and adherence, and interventions that might improve initial CPAP efficacy.¹⁴ However, few studies have evaluated interventions to improve CPAP compliance in OSA patients previously unable to comply with CPAP therapy.

We evaluated a two phase intervention program intended to improve CPAP compliance in previously noncompliant OSA patients. The first phase assessed several standard interventions to improve CPAP comfort, while the second phase compared the efficacy of flexible bilevel positive airway pressure (BiFlex, Respiroics Inc., Murrysville, PA) to standard CPAP. BiFlex differs from standard bilevel positive airway pressure (PAP) devices in that it allows reductions of the late inspiratory and early expiratory pressures.¹⁵

METHODS AND MATERIALS

Subjects

Potential candidates were adult patients (age ≥ 18 y) with OSA and a polysomnography (PSG) confirmed apnea-hypopnea index (AHI) of ≥ 10 events/h (established within 24 months prior to enrollment), who estimated their current average nightly CPAP

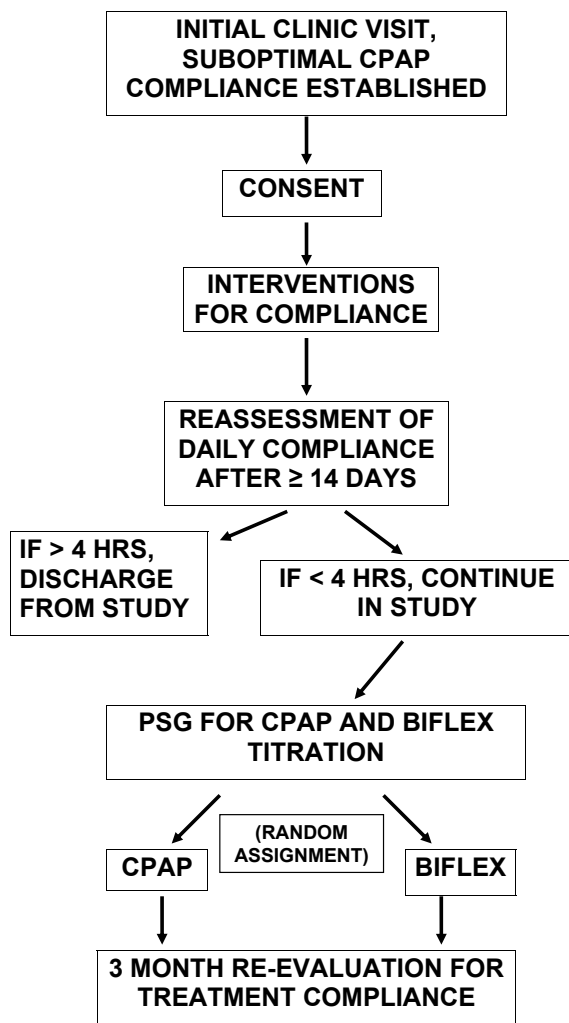


Figure 1—Flow Chart Demonstrating Protocol Organization

use was <4 h. Objective CPAP compliance monitoring was not required for enrollment and was not obtained from any candidate. Exclusion criteria included previous utilization of bilevel positive airway pressure; nocturnal supplemental oxygen therapy; central sleep apnea; upper airway surgery since previous diagnostic PSG; facial dermatitis, eczema, and other facial skin disorders; psychiatric disorders; and other complicating medical conditions. The protocol was approved by participating institutional review boards, and patients provided informed consent before study entry.

Phase 1

Patients were first interviewed by a physician investigator (Figure 1). This visit addressed possible contributors to CPAP intolerance: 1) Mask fit and size—if air leak or discomfort persisted after adjustment, an alternate mask was fitted and provided; 2) Nasal or oropharyngeal dryness—all patients were provided with a heated humidifier for use with CPAP; 3) Rhinitis or nasal congestion—patients with clinically significant rhinitis were provided nasal rinse kits and/or nasal corticosteroid sprays; 4) All patients received education and counseling about OSA and its therapy. This counseling session included a review of the previous sleep study results, education about the potential neurocognitive² and

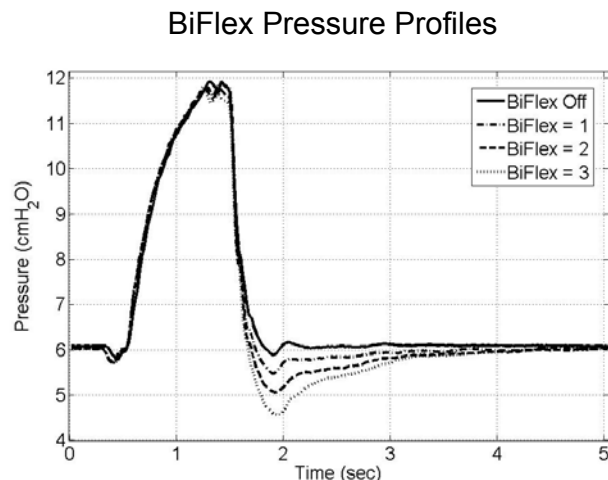


Figure 2—Comparison of BiFlex pressure profiles to standard bilevel profile. Upward deflection corresponds to increased pressure during inspiration. BiFlex Off = standard bilevel profile. BiFlex = 1, gain or “comfort setting” of 1. BiFlex = 2, gain or “comfort setting” of 2. BiFlex = 3, gain or “comfort setting” of 3.

cardiovascular³⁻⁵ risks associated with untreated sleep apnea, and a discussion about potential OSA therapy, with a focus upon the proven efficacy of CPAP therapy.^{7,8}

Patients were then provided a loaner CPAP machine (REMStar Pro, Respironics Inc.), set to their previously recommended CPAP level and incorporating heated humidification plus compliance monitoring technology (Smart Card). After ≥ 2 weeks of therapy, CPAP compliance data were downloaded. Patients averaging ≥ 4 h CPAP use per night were encouraged to continue CPAP use and discharged from the study. Patients averaging <4 h CPAP use per night were invited to enter phase 2.

Phase 2

Patients repeated a nocturnal PSG to titrate effective levels of both CPAP and BiFlex. Figure 2 demonstrates the pressure waveform modifications available in the BiFlex mode. PSGs were performed using standard methodology.¹⁶ Studies were initiated as CPAP titration, beginning at 4 cm H₂O. Pressure was increased to eliminate obstructive apneas and hypopneas, snoring, airflow limitation, and oxygen desaturation. Therapy was then switched to BiFlex mode, with a gain (“comfort setting”) of 2 (Figure 2) and inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) both set to the previous effective level of CPAP. EPAP was reduced in 1-2 cm H₂O decrements until obstructive apneas recurred, and then increased back to the minimum pressure eliminating apneas. IPAP was then increased to eliminate hypopneas, snoring, airflow limitation, and oxygen desaturation. As per standard clinical protocol, every effort was made to confirm both optimal CPAP and BiFlex settings during supine, REM sleep.

Patients were then provided a modified positive airway pressure device (BiPAP Pro, Respironics Inc.) randomly set to either CPAP or BiFlex mode at appropriate pressure(s). Both patients and the investigators were blinded as to the specific mode assigned to each patient. Patients were interviewed after 1 week of therapy and made scheduled returns for reevaluation and down-

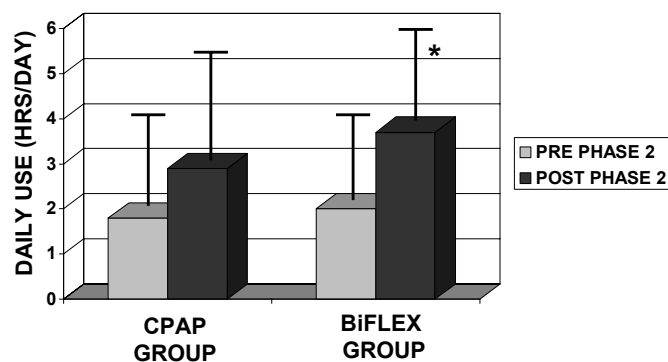


Figure 3—Mean daily therapy usage (h/day) at completion of phase 1 and completion of phase 2 for patients randomly assigned to CPAP (left bars) or BiFlex (right bars) during phase 2. * $p < 0.05$, BiFlex at completion of phase 2 vs. BiFlex at completion of phase 1 and CPAP at conclusion of phase 2.

load of compliance data 1 month and 3 months after initiation of therapy.

Measurements

During phase 1, we monitored CPAP compliance (average nightly use and percentage all nights used) and specific interventions (CPAP mask change, addition of a heated humidifier, addition of nasal rinses and/or corticosteroid sprays). During phase 2, we monitored CPAP/BiFlex compliance and impact of sleep upon daytime function as assessed by the Functional Outcomes of Sleep Questionnaire (FOSQ).¹⁷

Statistical Analysis

Acceptable compliance with therapy was defined as average nightly use ≥ 4 hours. Our primary hypothesis was that at the 3-month time point during phase 2, the proportion of patients compliant with therapy would differ between CPAP and BiFlex treated patients. With the assumption that a 20% difference in the proportion of compliant patients between the two treatment groups would be clinically important, we calculated that to provide $\geq 80\%$ power for a two-sided test of the null hypothesis at a Type 1 error rate (alpha level) of 5%, 93 patients in each therapy group would need to complete phase 2. Proportions of compliant patients were compared with a chi-square test. Secondary variables, including average daily use of therapy and increased hours of average daily use during phase 2 were nonnormally distributed, and these were compared using the Wilcoxon rank-sum test. Proportions of patients receiving specific interventions during phase 1 were compared with chi-square tests. FOSQ scores were compared using the Wilcoxon rank-sum test. Linear regression analyses with baseline demographic data (including age, gender, body mass index [BMI], previous AHI, prescribed level CPAP, and days elapsed from initial diagnosis) as independent variables and therapy daily use as dependent variables were also performed to study whether baseline characteristics were predictive of ultimate compliance. All data are reported as mean \pm standard deviation (SD), unless otherwise noted. To account for dropouts we analyzed on an intent-to-treat basis. Statistical analysis was performed using SPSS (SPSS, Inc., Chicago, IL).

Table 1—Population Demographics (n=204)

Age (years)	52.7 \pm 12.2
Male (%)	64
BMI (kg/m ²)	34.2 \pm 8.7
Previous ahi (events/h)	41.9 \pm 28.6
Prescribed CPAP (cm h ₂ O)	9.1 \pm 2.3
Days from initial diagnosis (Median; interquartile range)	118 (61; 300)
Estimated daily use (hr)	2.0 \pm 1.1

Values are mean \pm standard deviation, excepting days from initial diagnosis (nonnormal distribution).

RESULTS

Phase 1

Prestudy calculations had projected a total enrollment of 232 patients. However, due to difficulty identifying and enrolling acceptable candidates, study enrollment was terminated early. We therefore had a combined enrollment from the 3 sites (Denver, CO; Rochester, MN; Pittsburgh, PA) totaling 204 patients (131 males, 73 females). Population demographics are demonstrated in Table 1. Table 2 demonstrates that 49 (24%) of the patients utilized CPAP ≥ 4 h daily during phase 1, whereas 155 (76%) remained noncompliant. Combined interventions during phase 1 included the addition of heated humidification in 36 (18%) of all patients, a new mask in 76 (38%) of all patients, and the addition of nasal washes and/or nasal corticosteroids in 69 (34%) of all patients. The only intervention that differed between the 2 outcome groups was the provision of a new mask, as 65 (86%) of all patients receiving a new mask remained CPAP noncompliant. Other patient characteristics (age, gender, BMI, previous AHI, CPAP level, previously estimated CPAP use, days from initial diagnosis) did not differ between compliant and noncompliant patients and were not predictive of CPAP compliance.

Phase 2

Of 155 patients who remained noncompliant from phase one, 104 (67%; 71 males, 33 females) proceeded to phase 2. Fifty-one patients declined to continue the study, primarily due to reluctance to continue with positive pressure therapy; 53 of those proceeding to phase 2 were randomly assigned to continue CPAP therapy, while 51 were randomly assigned to BiFlex therapy. Figure 3 illustrates the increases in mean daily use of CPAP (1.1 \pm 2.1 h, NS) vs. BiFlex (1.7 \pm 1.7 hrs, $p < 0.05$) from the beginning to end of phase 2. Figure 4 illustrates that 25 (49%) patients assigned to BiFlex therapy were compliant with therapy after ≥ 90 days of treatment, as opposed to only 15 (28%) of those assigned to continue CPAP ($p = 0.03$). Table 3 demonstrates that patients assigned to BiFlex had a higher mean daily usage ($p = 0.03$) and a greater increase from phase 1 in mean daily usage ($p = 0.02$) than patients assigned to CPAP.

Some patients in both arms discontinued their assigned therapy during phase 2, although none formally withdrew from the protocol. However, several of these patients did not complete the FOSQ at the conclusion of phase 2 (5 assigned to BiFlex, 10 assigned to CPAP). Eighty-nine patients completed FOSQs at both the beginning and conclusion of phase 2. Mean FOSQ total score

Table 2—Outcomes from Phase 1 Interventions: Compliant (CPAP Use ≥ 4 H/day) vs. Noncompliant (CPAP Use < 4 H/day)

	CPAP ≥ 4 h/day	CPAP < 4 h/day
N	49 (24%)	155 (76%)
Daily use @ 2 weeks (hr)	5.8 \pm 1.4 *	1.9 \pm 1.3
% Days used @ 2 weeks	93.9 \pm 30.2	62.6 \pm 42.1
Age (y)	52.0 \pm 12.2	54.6 \pm 12.3
Male (%)	60	66
Bmi (kg/m ²)	34.3 \pm 8.9	34.0 \pm 8.1
Previous AHI (events/h)	42.2 \pm 28.0	40.6 \pm 30.5
Prescribed CPAP (cm h ₂ o)	9.1 \pm 2.6	9.1 \pm 2.2
Days from initial diagnosis (median; interquartile range)	134 (53; 367)	112 (64; 274)
Estimated entry use (h/day)	2.1 \pm 1.1	2.0 \pm 1.1
Changed mask	11 (23%)	65 (43%) *
Added heated humidity	6 (13%)	30 (20%)
Added nasal steroids	15 (31%)	54 (36%)
No intervention	22 (45%)	53 (34%)
One intervention	19 (39%)	63 (41%)
Two interventions	7 (14%)	32 (21%)
Three interventions	1 (2%)	7 (4%)

Values are mean \pm standard deviation, excepting days from initial diagnosis (non-normal distribution). * $p < 0.0001$

did not differ significantly at baseline between those assigned to CPAP (15.31 \pm 3.55) and BiFlex (14.22 \pm 3.27, $p = 0.06$). Ninety days of ongoing therapy was associated with an increase in mean FOSQ total score of 1.45 \pm 4.52 in the BiFlex treated group ($p = 0.0038$), but a nonsignificant increase of only 0.45 \pm 4.42 in the CPAP treated group ($p = 0.34$). Mean FOSQ total scores were similar in the CPAP treated (15.76 \pm 4.00) and BiFlex treated (15.67 \pm 4.12) groups after 90 days of therapy.

DISCUSSION

We evaluated specific interventions in OSA patients previously intolerant of and/or noncompliant with CPAP therapy to determine if a comprehensive change in PAP approach can ultimately improve therapy compliance. Our findings suggest that standard interventions (mask refitting, heated humidification, adding nasal saline rinses and/or nasal corticosteroids) were modestly helpful, achieving subsequent tolerance and compliance in only 24% of patients restarted on CPAP therapy. A subsequent change to BiFlex therapy yielded a significant advantage in treatment com-

pliance when compared to continuing standard CPAP (49% vs. 28%). BiFlex therapy was also associated with improved functional outcome, indicated by improvement in FOSQ score.

Early studies suggested that most CPAP-treated OSA patients were compliant, but such studies were based upon questionnaires and subjective reporting. Kribbs and colleagues used clandestine compliance monitoring incorporated into CPAP machines to demonstrate that only 46% of treated OSA patients used CPAP ≥ 4 hours nightly, 70% of all nights.¹⁸ More recent studies suggest that educational and supportive efforts focused upon problem solving yield long-term compliance rates ranging from 65% to 89%.¹⁹ It is unlikely that most OSA patients prescribed CPAP therapy receive such intensive efforts to promote CPAP acceptance, and it has been estimated that over 50% of patients started on CPAP may not be using this therapy 1 year later.⁹ Many such patients are ultimately referred to sleep specialists for further management, but little is known about the efficacy of reinitiating CPAP in previously noncompliant patients.

Phase 1 of the study assessed standard interventions previously demonstrated to improve compliance in OSA patients when initially treated with CPAP. Seventy-six percent of patients remained noncompliant after the minimum 2-week monitoring period, and no specific intervention was predictive of a better outcome. Conversely, we observed that changing to an alternate mask²⁰ was associated with reduced compliance. This suggests that problems with specific masks were unlikely to be important determinants of initial noncompliance in our population, although patients frequently focused upon general mask discomfort as a factor limiting CPAP tolerance.

Addition of heated humidification had no detectable effect upon outcome, but this may reflect the fact that 82% of all patients had previously received heated humidification with their CPAP, thus limiting our intervention sample size. Inflammatory rhinitis is common in OSA patients,^{21,22} and recent studies suggest that nasal corticosteroid therapy can improve OSA in both adults²¹ and children.²³ We found no evidence that this intervention improved compliance with CPAP, although the minimum 2 week monitoring period for phase 1 may be too brief to demonstrate a beneficial effect. As no specific directed intervention pre-

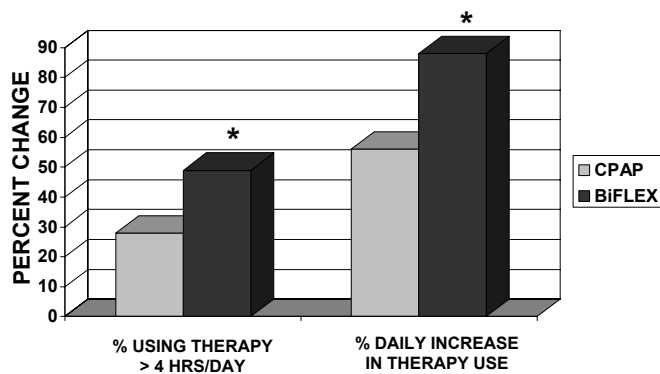


Figure 4—Percentage (%) of patients using CPAP or BiFlex therapy ≥ 4 h/day at the conclusion of phase 2 (left bars), and percent increase in therapy daily use from the completion of phase 1 to the completion of phase 2 for patients assigned to CPAP or BiFlex (right bars). * $p < 0.05$.

Table 3—Outcomes from Phase 2: CPAP vs. BiFLEX

	BiFLEX	CPAP
N	51	53
Age (y)	51.9 ± 11.3	52.5 ± 12.5
Male (%)	65	72
Bmi (kg/m ²)	33.4 ± 7.9	32.6 ± 6.3
Previous AHI (events/h)	40.4 ± 23.4	44.0 ± 26.1
Recommended cpap (Cm h ₂ o)	9.2 ± 2.9	9.1 ± 2.6
Recommended BiFLEX (inspiratory/Expiratory pressure - cm h ₂ o)	10.9 ± 2.3/6.9 ± 2.1	11.0 ± 2.8/7.2 ± 2.5
# Using ≥4 h/day (%)	25 (49%) *	15 (28%)
Daily use (h/day)	3.7 ± 2.0 *	2.9 ± 2.3
% Days used during phase 2	70.9 ± 23.2	63.5 ± 35.0
Increased daily use from phase 1 (h/day)	1.7 ± 1.7 *	1.1 ± 2.1
Daily use (h/day) in therapy compliant subgroups	5.4 ± 1.1	5.7 ± 1.2

Values are mean ± standard deviation. * p < 0.05

dicted improved compliance, but all patients received education about OSA plus supportive counseling, it is likely that this latter intervention was an important contributor to the improved compliance in 24% of previously noncompliant patients. However, it must be acknowledged that the specific content and structure of counseling may substantially affect subsequent compliance,²⁴ and alternative approaches to education and counseling may be more or less successful.

Phase 2 of the study compared differing effects upon compliance from changing to BiFlex or continuing standard CPAP for an additional 90 days. Two observations deserve comment. First, 28% of patients previously noncompliant with CPAP therapy became compliant with the same CPAP therapy after an additional 90 days of treatment. This suggests that continued support of previously CPAP noncompliant OSA patients can ultimately lead to acceptable compliance. Second, patients assigned to BiFlex in phase 2 had a superior compliance rate after 90 days (49% vs. 28%, p = 0.03), averaging a higher mean daily usage and a greater mean daily increase in usage from phase 1 than those assigned to CPAP. It is likely that this increased compliance with therapy accounts for the improvement in FOSQ score demonstrated in the BiFlex treated group.

Combined data from phases 1 and 2 indicate that 89 of 204 (44%) of all patients reinitiated on CPAP and/or BiFlex therapy ultimately became therapy compliant. Of the 155 patients who remained noncompliant with CPAP after phase 1, only 104 proceeded to phase 2. It is likely that the other 51 patients received no further CPAP therapy, although some may have proceeded to alternative therapies such as oral appliances or surgery. Therefore, of 155 patients remaining CPAP noncompliant after phase 1, we ultimately achieved targeted CPAP or BiFlex compliance in only 40 (26%) of these patients. Twenty-five of the newly compliant patients (16% of the total) had been assigned to BiFlex, while 15 (10%) had been assigned to CPAP during phase 2.

Bilevel PAP therapy has been previously compared to CPAP in newly diagnosed OSA, and was not observed to yield better compliance or symptom relief.¹³ More recently, Gay and associates assessed a prototype therapy to BiFlex, and found no clear advantage when compared to CPAP in newly treated patients.¹⁵ This was a relatively small study, with unusually high compliance rates with both modes of therapy. Aloia and colleagues subsequently

reported improved compliance from the use of a similar pressure adaptation to CPAP, which also allows the reduction of pressure during early expiration (C-Flex, Respironics Inc.).²⁵ However, a subsequent prospective, randomized crossover trial demonstrated no difference in compliance between conventional CPAP and pressure relief CPAP (C-Flex).²⁶ We therefore hypothesized that BiFlex, which incorporates bilevel positive airway pressure with late inspiratory with early expiratory pressure relief, might be a more effective positive pressure mode for patients who remain noncompliant with conventional CPAP, despite standard interventions to correct perceived problems with this mode of therapy. Our findings appear to confirm this hypothesis.

When considering our results, one must consider potential limitations of our study design. First, it must be emphasized that the design of this study does not allow us to make any conclusion regarding the relative merits of BiFlex vs. standard bilevel PAP. Standard bilevel PAP was not a treatment option in our study. Although previous studies found no advantage to standard bilevel PAP¹³ or BiFlex¹⁵ when compared to CPAP in newly diagnosed OSA patients, the current study has a very different objective and design. We therefore cannot speculate whether the improved compliance in our BiFlex treated group resulted from the standard bilevel PAP mode, the BiFlex-specific pressure reductions during late inspiration and early expiration, or a combination of these features. Given this limitation and the relatively small size of the current study, we believe that a larger study designed to also compare standard bilevel PAP with BiFlex is clearly warranted.

Second, our study enrolled a diverse group of patients. A median of 118 days had elapsed since diagnosis, with a very large interquartile range (Table 1). The majority of patients had already returned the CPAP systems provided to them after their initial diagnosis. Separate analyses confirmed that duration of OSA diagnosis was not predictive of outcome in either phase 1 or 2 of the study, and did not differ between compliant and noncompliant patients during either phase 1 or 2. This suggests that patients were as likely to benefit from these interventions irrespective of time elapsed after the initial diagnosis.

Third, mean FOSQ total scores increased significantly during phase 2 only in the group assigned to BiFlex. There was no statistical difference in mean FOSQ total scores at baseline between those assigned to CPAP and BiFlex, but the numerical difference

was nearly significant ($p = 0.06$). One possible interpretation is that those subjects randomly assigned to the BiFlex treatment group could have had greater baseline impairment of their daytime function from untreated OSA, and may have therefore been more motivated to comply with subsequent therapy. However, there were no differences in OSA severity or demographics between the CPAP and BiFlex groups, and this interpretation remains speculative.

Finally, although patients were randomly assigned in a double-blinded fashion to either CPAP or BiFlex during phase 2 of the study, all patients had been treated previously with CPAP in an unblinded fashion. It is therefore possible that subjects may have been able to perceive the presence or absence of a changed pressure waveform during phase 2, which may have alerted them to their assigned therapy. We know of no way to correct for this potential limitation, but the minimum 90-day follow-up during phase 2 suggests that final outcomes are not necessarily a result of transient exposure to a novel pressure waveform.

In conclusion, a 2 phase intervention program is a useful approach to improve CPAP compliance in previously noncompliant CPAP patients. The first phase should focus upon standard interventions to improve CPAP comfort, with an emphasis upon education about OSA and supportive counseling. Although the design of our study precludes any conclusion regarding the relative merits of BiFlex vs. standard bilevel PAP, patients remaining noncompliant after such interventions may then be considered for alternative forms of pressure therapy, including flexible bilevel positive airway pressure. Larger studies should be conducted to allow specific comparisons between BiFlex and standard bilevel PAP in this role.

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ABBREVIATIONS

Apnea-hypopnea index - AHI
 Body mass index - BMI
 Continuous positive airway pressure - CPAP
 Expiratory positive airway pressure - EPAP
 Flexible bilevel positive airway pressure - BiFlex
 Functional Outcomes of Sleep Questionnaire - FOSQ
 Inspiratory positive airway pressure - IPAP
 Obstructive sleep apnea - OSA
 Polysomnography - PSG
 Positive airway pressure - PAP
 Standard deviation - SD

REFERENCES

- Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-5.
- Engleman H, Martin SE, Douglas NJ. Cognitive function in the sleep apnea/hypopnea syndrome. *Sleep* 2000;23:S102-7.
- Peppard P, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000;342:1378-84.
- Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001;163:19-25.
- Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005;353:2034-41.
- Sassani A, Findley LJ, Kryger M, Goldlust E, George C, Davidson TM. Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome. *Sleep* 2004;27:453-8.
- Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ. Randomized, placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. *Am J Respir Crit Care Med* 1999;159:461-7.
- Jenkinson C, Davies RJ, Mullins R, Stradling JR. Comparison of therapeutic and sub-therapeutic nasal continuous positive airway pressure for obstructive sleep apnea: a randomized prospective parallel trial. *Lancet* 1999;353:2100-5.
- Stepnowsky C, Moore P. Nasal CPAP treatment for obstructive sleep apnea: developing a new perspective on dosing strategies and compliance. *J Psychosom Res* 2003;54:599-605.
- Zozula R, Rosen R. Compliance with continuous positive pressure therapy: assessing and improving treatment outcomes. *Curr Opin Pulm Med* 2001;7:391-8.
- Hoy CJ, Venelle M, Kingshott RN, Engleman HM, Douglas NJ. Can intensive support improve continuous positive airway pressure use in patients with sleep apnea/hypopnea syndrome? *Am J Respir Crit Care Med* 1999;159:1096-1100.
- Massie CA, Hart RW, Peralez K, Richards G. Effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure. *Chest* 1999;116:403-8.
- Reeves-Hoche MK, Hudgel DW, Meck R, Wittman R, Ross A, Zwillich CW. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. *Am J Respir Crit Care Med* 1995;151:443-9.
- Gay P, Weaver RN, Loubé D, Iber C. Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. *Sleep* 2006;29:381-401.
- Gay PC, Herold DL, Olson EJ. A randomized, double-blind clinical trial comparing continuous positive airway pressure with a novel bilevel pressure system for treatment of obstructive sleep apnea syndrome. *Sleep* 2003;26:864-9.
- Rechtschaffen A, Kales A, eds. A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. Los Angeles: Brain Information Service/Brain Research Institute, UCLA;1968.
- Weaver TE, Laizner AM, Evans LK, et al. An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep* 1997;20:835-43.
- Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis* 1993;147:887-95.
- Sin DD, Mayers I, Man GCW, Pawluk L. Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: a population-based study. *Chest* 2002;121:430-5.
- Pepin JL, Leger P, Veale D, Langevin B, Robert D, Levy P. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome: study of 193 patients in two French sleep centers. *Chest* 1995;107:375-81.
- Kiely JL, Nolan P, McNicholas WT. Intranasal corticosteroid therapy for obstructive sleep apnoea in patients with co-existing rhinitis. *Thorax* 2004;59:50-5.
- Brander PE, Soirinsuo M, Lohela P. Nasopharyngeal symptoms in patients with obstructive sleep apnea syndrome. Effect of nasal CPAP treatment. *Respiration* 1999;66:128-35.
- Kheirandish L, Goldbart AD, Gozal D. Intranasal steroids and leukotriene modifier therapy in residual sleep-disordered breathing after tonsillectomy and adenoidectomy in children. *Pediatrics* 2006;117:61-6.
- DeMolles DA, Sparrow D, Gottlieb DJ, Friedman R. A pilot trial

of a telecommunications system in sleep apnea management. *Med Care* 2004;42:764-9.

25. Aloia AM, Stanchina M, Arnedt JT, Malhotra A, Millman RP. Treatment adherence and outcomes in flexible vs. standard continuous positive airway pressure therapy. *Chest* 2005;127:2085-93.
26. Nilius G, Happel A, Domanski U, Ruhle KH. Pressure-relief continuous positive airway pressure vs. constant continuous positive airway pressure: a comparison of efficacy and compliance. *Chest* 2006;130:1018-24.