Original Article

A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-adherent with continuous positive airway pressure

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A R T I C L E   I N F O

A B S T R A C T

Background: While continuous positive airway pressure (CPAP) effectively treats obstructive sleep apnea (OSA), adherence to CPAP is suboptimal. The short-term efficacy of and adherence with a convenient expiratory positive airway pressure (EPAP) nasal device was evaluated in OSA patients non-adherent with CPAP.
Methods: Participants were OSA patients who refused CPAP or used CPAP less than 3 h per night. After demonstrating tolerability to the EPAP device during approximately 1 week of home use, patients underwent a screening/baseline polysomnogram (PSG1) and a treatment PSG (PSG2). Patients meeting pre-specified efficacy criteria underwent PSG3 after about 5 weeks of EPAP treatment.
Results: Forty-seven of 59 eligible patients (80%) tolerated the device and underwent PSG1. Forty-three patients (27 m, 16 f; 53.7 ± 10.9 years) met AHI entry criteria and underwent PSG2. Mean AHI decreased from 43.3 ± 29.0 at baseline to 27.0 ± 26.7 ($p < 0.001$) at PSG2. Twenty-four patients (56%) met efficacy criteria; their mean AHI was 31.9 ± 19.8, 11.0 ± 7.9, 16.4 ± 12.2 at PSG1, PSG2, and PSG3, respectively ($p < 0.001$, PSG1 vs. both PSG2 and PSG3). Mean Epworth Sleepiness Scale (ESS) scores were 12.3 ± 4.8 at baseline, 11.1 ± 5.1 at PSG1, and 8.7 ± 4.4 at PSG3 ($p = 0.001$ compared to baseline). Device use was reported an average of 92% of all sleep hours.
Conclusions: The improvements in AHI and ESS, combined with the high degree of treatment adherence observed, suggest that the convenient EPAP device tested may become a useful therapeutic option for OSA.

1. Introduction

Continuous positive airway pressure (CPAP) is usually first-line treatment for obstructive sleep apnea (OSA) in adults [1–3]. But tolerability of CPAP devices is suboptimal and the degree of adherence among CPAP users is low [4–6]. The proportion of patients for whom CPAP is recommended who do not tolerate use of the device sufficiently to begin home treatment is not well established but is thought to be substantial. In studies using a criterion for adherence of at least 4 h per night, adherence rates are frequently less than 50% of CPAP users. Thus, alternative OSA management approaches are needed.

More than 25 years ago, expiratory positive airway pressure (EPAP) was reported to reduce the apnea index in patients with OSA, although the mechanism involved remains unclear [7]. A convenient, mechanical, disposable EPAP nasal device (Fig. 1) has re-cently been developed for the treatment of OSA (Provent™ Therapy; Ventus Medical, Inc., Belmont, CA). A small mechanical valve attaches over each naris with an adhesive collar to form a seal. The valve produces increased resistance during expiration with minimal resistance during inspiration. Expiratory resistance results in modest levels of EPAP and increased expiratory time, either or both of which may make the airway more resistant to collapse on subsequent inspiration. Early studies indicate that EPAP applied with this device using expiratory resistances of 50–110 cm H_2O/l/s at a flow rate of 100 ml/s may be an effective treatment for some OSA patients [8,9].

The objective of the current investigation was to evaluate tolerability, efficacy, and short-term adherence of this EPAP device in a sample of OSA patients who have either refused or reported minimal adherence with CPAP treatment.

2. Methods

Patients were recruited from the study site's patient population and via media advertisement. Inclusion criteria included males and females at least 18 years old with current signs and symptoms of

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Fig. 1. Photograph of the EPAP device in place.

OSA who, within the past 5 years, had refused CPAP treatment, discontinued CPAP, or had been minimally adherent with CPAP, or defined as reported use less than 3 h per night. On screening/baseline PSG patients were required to have an AHI > 15, or AHI > 10 with evidence of excessive daytime sleepiness, impaired cognition or mood, or hypertension. Exclusion criteria included persistent blockage of one or both nostrils, frequent and/or poorly treated severe nasal allergies or sinusitis, use of any device that interfered with nasal or oral breathing, chronic sores or lesions of the nose, chronic use of nasal decongestants other than nasal steroids, severe respiratory or cardiovascular disorders, severe cardiac rhythm disturbance, pathologically low blood pressure, sleep disorders other than OSA, psychiatric disorder with psychotic features, work schedule which included night shift, excessive caffeine consumption, and pregnancy.

The study protocol and procedures were approved by the St. Luke's Hospital Institutional Review Board. All patients signed informed consent prior to initiation of study procedures.

2.1. Study procedures

Screening visit procedures included obtaining informed consent, sleep and medical histories, physical examination, Epworth Sleepiness Scale (ESS) [10], and the Functional Outcomes of Sleep Questionnaire (FOSQ) [11]. Patients who met inclusion and exclusion criteria were single-blindedly supplied with EPAP devices having two different expiratory resistances (50 [R50] and 80 [R80] cm H_2O/l/s at a flow rate of 100 ml/s) for home use. Patients recorded hours of device use and sleep duration on a diary each morning. After using each device type for up to three nights, device preference was ascertained. If no preference was declared, device resistance was assigned with the goal of having at least 40% of completing patients using each resistance level. Patients continued with their preferred or assigned device type for the remainder of the study. Patients meeting a criterion for device use of at least 70% of sleep time during three consecutive nights of home use underwent a screening/baseline PSG (PSG1) without EPAP to assess AHI inclusion criteria and obtain baseline data.

Patients meeting AHI entry criteria continued using EPAP at home and underwent a second PSG (PSG2) within 10 days of PSG1 to assess initial EPAP efficacy, defined as >50% reduction in AHI (compared to PSG1), or AHI < 10, or >30% reduction in AHI if ESS during that visit decreased 2 or more from a baseline of <12. Patients meeting PSG2 efficacy criteria continued using EPAP nightly at home for approximately 5–6 weeks until returning for PSG3 to

evaluate durability of efficacy. ESS and FOSQ were also administered at that time. Patients not meeting efficacy criteria completed ESS and FOSQ at the end of their study participation. Device adherence was monitored by diary throughout the study as there is no current method to objectively measure use of the EPAP device.

PSGs were conducted according to published American Academy of Sleep Medicine guidelines [12]. PSG bedtime and wake time were chosen by each patient and kept constant for all PSGs. Respiration was monitored via nasal pressure transducer and chest and abdominal impedance belts. A custom cannula connected to the pressure transducer was used for the nasal signal when the EPAP devices were in place. Respiratory events were scored according to published guidelines [12] by a single registered PSG technologist using the VIII.4.A definition for hypopneas (>4% decrease in oxygen saturation [SaO_2]) to compute the AHI. Additional computations included respiratory disturbance index (RDI: apneas, hypopneas, respiratory events meeting the VIII.4.B definition of hypopnea [>3% decrease in SaO_2] and respiratory effort-related arousals as defined by VIII.5), oxygen desaturation index (ODI: number of times SaO_2 decreased by >3% per hour of sleep), and arousal index (number of arousals per hour of sleep). Respiratory indices were also tabulated by sleep position (supine or non-supine) and sleep state (REM or NREM).

2.2. Data analyses

All patients who met AHI inclusion criteria at the screening/baseline PSG (PSG1) and completed PSG2 were included in the initial efficacy analyses. Patients meeting efficacy criteria at PSG2 were included in analyses of short-term efficacy (PSG3). Adverse events are reported for all patients using the EPAP device.

Analyses were performed using general linear model or linear mixed model (Systat), with Bonferroni correction for multiple comparisons. Log transformation was applied to normalize distributions for most respiratory variables including AHI, RDI, and ODI. Untransformed mean values and standard deviations are presented in the text. Percent of sleep time spent supine and in REM were used as covariates in analyses of overall AHI, RDI, and ODI. Analyses of indices by sleep position (supine, non-supine) and sleep state (REM, NREM) were conducted without covariates. Initial analysis included a factor for EPAP resistance (R50 or R80); because there were no significant differences between resistance types for any respiratory variable, this factor was dropped from analyses and is not reported here. Comparisons of percentage change in AHI were made using Wilcoxon tests. Proportions were compared with either Chi square or Mann–Whitney U.

ESS and FOSQ data were analyzed separately for patients meeting and not meeting efficacy criteria at PSG2 because the final administration of these instruments occurred at different time points for the two groups.

Subjective estimates of sleep duration and the number of hours EPAP was worn were reported for the 7 nights prior to PSG2 for the entire group and for the 28 nights following PSG2 for the group who met efficacy criteria. EPAP was considered as not used if diary data were missing. Missing data for sleep duration were imputed.

The primary endpoint was AHI at PSG2 compared to PSG1. Secondary endpoints were AHI, percent of sleep time with SaO_2 <90%, and ESS at PSG3 compared to PSG1 in the subsample with pre-defined efficacy at PSG2.

3. Results

3.1. Participants

Fig. 2 shows the disposition of patients. Sixty-nine patients provided informed consent. Ten patients did not meet one or more

inclusion/exclusion criteria at the screening office visit (nasal obstruction, 5; CPAP use >3 h per night or willing to reconsider CPAP, 3; insomnia, 2; OSA symptoms negligible following significant weight loss, 1; nasal decongestant use, 1) and 59 patients proceeded with home trial of EPAP. Fifty-eight of these patients reported prior attempt to use CPAP at home an average of 12 months (range 2 days to intermittent use over 18 years) following a sleep laboratory CPAP titration. One patient refused home CPAP after intolerance in the sleep lab. At the initial visit the majority ($N = 36$) had not used CPAP for 2 months or more, and the remaining 21 patients reported an average of 2.2 h of current nightly CPAP use.

Forty-seven of the 59 patients given EPAP (80%) tolerated the device and met criterion to continue with PSG1. Twelve patients did not tolerate the device (see Adverse Events, below). Twenty-four patients preferred R50, 15 preferred R80, and 8 expressed no preference (R50 assigned to one and R80 assigned to 7).

Three patients did not meet AHI > 10 inclusion criterion at PSG1. One patient withdrew after PSG1 because of scheduling difficulty. Thus the final sample evaluated for initial efficacy included 43 patients (27 males, 16 females; mean age 53.7 ± 10.9, range 24–79 years). Mean BMI was 34.9 ± 6.7 (range 22.7–51.1). Mean ESS was 12.5 ± 5.1 and mean total FOSQ was 15.1 ± 2.8.

PSG1 occurred 10.4 ± 4.2 days following the screening office visit. PSG2 and PSG3 occurred 18.0 ± 4.8 and 49 ± 10.3 days, respectively, after the screening office visit.

3.2. Polysomnography

3.2.1. Initial efficacy

Table 1 contains demographic data and AHI for individual patients for each PSG. Mean AHI was 43.3 ± 29.0 at baseline PSG1 and 27.0 ± 26.6 at PSG2 ($p < 0.001$); the median decrease was 45.2%. There were also significant improvements in mean arousal index, percent sleep time with $SaO_2 < 90\%$, RDI, and ODI (Table 2). While AHI was significantly decreased from PSG1 to PSG2 during both supine and non-supine sleep ($p < 0.001$ for both) as well as during REM ($p = 0.002$) and NREM ($p < 0.001$), the median percent decrease was larger for non-supine sleep (63.6% vs. 35.8% supine,

Fig. 2. Disposition of patients. N = number, m = male, f = female.

Table 1
Apnea–hypopnea index (AHI) and demographic data for each patient in order of decreasing AHI at PSG1.

Patient number	Age (years)	Sex	Body mass index	AHI (PSG1)	AHI (PSG2)	AHI (PSG3)[a]
10	42	M	51.1	118.7	114.1	
56	29	M	46.8	113.4	101.0	
45	48	F	35.6	97.7	54.1	
41	54	M	29.8	95.6	95.0	
64	61	F	35.7	86.8	33.6	55.7
61	62	F	39.6	85.2	49.3	
63	53	M	40.9	77.2	42.3	
1	57	M	32.1	70.9	31.0	25.7
29	64	M	30.7	65.5	60.9	
21	79	M	33.4	64.5	49.3	
46	55	F	29.7	57.4	22.0	19.7
19	44	F	44.4	57.3	5.3	5.4
35	53	M	44.9	54.0	44.3	
54	54	M	28.3	48.1	34.1	
42	41	M	29.2	48.1	17.2	13.4
2	38	M	38.7	48.1	37.6	
6	54	F	46.5	46.4	43.7	
17	60	F	37.3	42.7	14.3	14.6
25	53	M	27.2	39.9	11.7	6.6
52	58	M	33.1	37.5	41.1	
34	71	F	32.2	36.2	27.3	
44	39	M	33.0	33.4	32.8	
7	59	F	29.3	32.4	12.6	30.6
33	56	F	26.6	31.3	6.2	14.8
51	57	M	35.4	30.0	8.4	36.3
2	41	M	37.0	28.9	6.9	17.6
24	52	M	34.0	28.7	5.2	16.9
68	57	M	26.0	28.6	19.4	
12	24	M	46.2	27.4	5.1	16.5
14	66	M	34.9	26.6	15.0	15.9
67	59	F	42.2	25.8	19.4	
48	39	F	31.4	22.3	8.1	26.8
50	60	M	22.7	18.9	3.7	0.9
16	51	F	30.4	17.9	8.7	6.6
49	67	M	28.6	17.7	5.9	11.5
57	47	F	45.9	15.9	7.7	7.5
22	54	F	39.9	15.3	3.8	11.7
8	66	M	32.1	14.6	7.8	7.4
32	60	M	35.5	14.6	5.4	1.3
15	62	M	31.0	11.0	9.6	20.1
38	58	M	34.0	10.2	8.7	8.9
69	63	F	28.7	10.2	19.8	
37	44	M	28.9	10.0	10.5	
Mean (SD)	53.7 (10.9)		34.9 (6.7)	43.3 (29.0)	27.0 (26.6)	16.4 (12.2)
Median	55.0		33.4	33.4	17.2	14.7

[a] PSG3 data were obtained only for patients who met pre-defined efficacy criteria at PSG2.

$p = 0.005$) and for NREM (51.3% vs. 22.2% for REM; Table 3). Sleep architecture showed less stage N1, more stage N2, and slightly lower sleep efficiency on PSG2 (Table 2).

Twenty-four patients (56%) met the efficacy criteria at PSG2 (14 males, 10 females, mean age 53.8 years [range 24–67]). Sixteen of these patients (37%) had AHI < 10 at PSG2.

3.2.2. Short-term efficacy

PSG data for the 24 patients who met efficacy criteria are presented in Tables 1, 3 and 4. Compared to PSG1 (AHI = 31.9 ± 19.8), mean AHI was significantly lower at both PSG2 (11.0 ± 7.9) and PSG3 (16.4 ± 12.2; $p < 0.001$ for both), with median decreases of 64.0% and 45.2%, respectively. AHI at PSG3 was slightly increased compared to PSG2 ($p = 0.023$), likely the result of regression to the mean. Examination of individual data showed that, for most patients, AHI at PSG3 was similar to AHI at PSG2. However, four patients had AHI at PSG3 which was similar to baseline. RDI and ODI data were similar to AHI data, with median decreases of 47.8% and 61.2% at PSG2, and 37.0% and 45.1% at
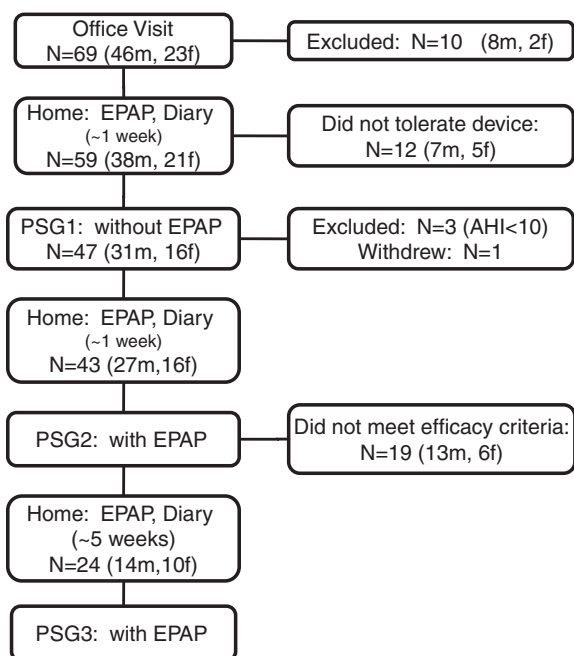
Table 2
Polysomnography (PSG) data for all patients for PSG1 and PSG2 (*N* = 43)[a].

	PSG1	PSG2	*p* value [b] PSG1 vs. 2
Apnea–hypopnea index	43.3 (29.0); 33.4	27.0 (26.6); 17.2	<0.001
Respiratory disturbance index	57.8 (27.3); 53.1	41.2 (27.1); 32.5	<0.001
Oxygen desaturation index	38.8 (27.2); 32.2	25.6 (24.7); 15.6	<0.001
Percent sleep with SaO_2 <90%[c]	13.6 (19.3); 4.6	9.7 (19.7); 2.3	<0.001
Apnea–hypopnea index supine	66.1 (34.6); 70.3	46.6 (41.6); 33.1	<0.001
Apnea–hypopnea index non-supine	34.3 (31.9); 22.9	19.0 (26.3); 5.8	<0.001
Apnea–hypopnea index REM	55.6 (34.5); 51.4	42.4 (28.6); 37.9	0.002
Apnea–hypopnea index NREM	41.7 (29.8); 34.5	24.9 (27.1); 16.0	<0.001
Arousal index	50.3 (23.3); 43.8	40.7 (22.4); 34.9	<0.001
Total sleep time (min)	378.4 (50.1); 375.0	362.8 (66.4); 367.0	0.059
Sleep efficiency (%)	82.1 (8.1); 84.0	78.9 (12.0); 81.7	0.004
Percent stage N1	36.6 (16.7); 35.2	32.4 (16.5); 28.4	0.006
Percent stage N2	42.9 (13.5); 41.3	48.5 (13.0); 47.2	<0.001
Percent stage N3	7.6 (9.1); 5.1	8.1 (8.4); 7.5	>0.3
Percent stage REM	12.9 (4.7); 11.9	11.1 (4.2); 11.0	0.030
Percent sleep supine	39.6 (25.0); 41.3	42.0 (26.6); 39.8	>0.7

[a] Values are means (standard deviations); medians, unless otherwise indicated.
[b] *p* values are Bonferroni-corrected values.
[c] SaO_2 = oxygen saturation.

Table 3
Median Percent Change in AHI from PSG1 to PSG2 and PSG3 by sleep position and sleep state.

Group/PSG	Supine	Non-supine	REM	NREM
All patients (*N* = 43) at PSG2	−35.8	−63.6 [a]	−22.2	−51.3 [b]
Non-efficacious patients (*N* = 19) at PSG2	−9.4	−39.1 [a]	−14.0	−18.4
Efficacious patients (*N* = 24) at PSG2	−59.2	−71.8	−35.6	−68.3 [b]
Efficacious patients (*N* = 24) at PSG3	−43.5	−63.9	−46.6	−57.0

[a] Significantly different from supine, *p* < 0.05, Wilcoxon.
[b] Significantly different from REM, *p* < 0.05, Wilcoxon.

PSG3. The arousal index and percent of sleep time with SaO_2 < 90% were also lower on both PSG2 and PSG3. Decrease in AHI was larger for NREM than REM on both PSG2 and PSG3, but not significantly different for supine compared to non-supine sleep (Table 3). On both nights with EPAP, percent stage N1 was lower and percent stage N2 was greater than on PSG1.

3.3. ESS, FOSQ

Patients meeting efficacy criteria had mean ESS of 12.3 ± 4.8 at baseline, 11.1 ± 5.1 at PSG1 (ns, *p* > 0.5), and 8.7 ± 4.4 at PSG3 (*p* = 0.001 vs. baseline, *p* = 0.03 vs. PSG1) indicating reduced sleepiness with treatment (Fig. 3). FOSQ total score was 15.3 ± 3.1 at baseline and improved to 17.3 ± 1.7 at PSG3 (*p* = 0.001). All individual FOSQ subscale scores with the exception of the intimacy scale (*p* = 0.076) improved from baseline to the end of the study (*p* < 0.005).

Patients who did not meet the efficacy criteria had mean ESS 12.7 ± 5.5 at baseline, 11.8 ± 5.5 at PSG1, and 12.2 ± 5.7 at the end of their participation which occurred shortly after PSG2, indicating no change in sleepiness (*p* > 0.8 for all comparisons; Fig. 3). FOSQ total score was 14.9 ± 2.7 at baseline and improved to 16.5 ± 2.8 at study end (*p* = 0.002). There were increases in the activity and intimacy subscales (*p* = 0.003 and 0.034, respectively), but no significant differences in the other three subscales.

3.4. Device use

During the week prior to PSG2 EPAP was used on 94.2% of nights, assuming non-use on nights with missing diary data, and 97.2% of nights for nights with diary data, (*N* = 43). Mean nightly EPAP use was 6.5 ± 1.3 h for all nights and 6.9 ± 1.1 h for nights with available diary data. Reported sleep duration was 7.1 ± 1.0 h nightly. Thus EPAP was used 91% of sleep time for all nights and

97% of sleep time on nights with diary data. Device detachment or removal during the night was reported on a total of 24 nights (9.5% of nights with diary data). Twenty-two patients reported 100% adherence (wearing EPAP all night every night).

During the week prior to PSG2 plus the following 4 weeks combined, the 24 patients meeting efficacy criteria used EPAP 95.5% of nights (once again assuming non-use when diary data were missing) and 97.0% of nights with diary data, 6.7 ± 1.0 h per night for all nights and 7.0 ± 1.1 h on nights with diary data. With average sleep duration of 7.2 ± 1.0 h, EPAP use comprised 92–97% of sleep time. Device detachment or removal during the night was reported on a total of 80 nights (10.6% of nights with diary data). Four patients reported wearing EPAP all night every night.

3.5. Predictors of efficacy

There were no differences in age, sex, BMI, weight, neck circumference, percent time spent supine, or baseline ESS and FOSQ measures between patients who met efficacy criteria at PSG2 and those who did not. Mallampati scores were higher in the non-efficacious group (*p* = 0.015, Mann–Whitney *U* = 143). Fourteen of 18 patients (78%) with Mallampati scores <4 met efficacy criteria while only 10 of 25 patients (40%) with scores of 4 met efficacy criteria (*p* = 0.014, chi square = 6.1). The non-efficacious group had higher AHI and lower SaO_2 at baseline than the efficacious group (AHI: 57.7 ± 32.7 vs. 32.0 ± 19.8, *p* = 0.006; percent of sleep time with SaO_2 < 90: 24.0 ± 25.2 vs. 5.3 ± 4.8, *p* = 0.024). However it is notable that six patients who met efficacy criteria (25%) had baseline AHI > 40 including two patients with AHI > 60.

EPAP use during the week prior to PSG2 was similar for the two groups (94.2% of nights, 6.6 ± 1.3 h per night for the non-efficacious group and 94.2% of nights, 6.4 ± 1.4 h per night for the efficacious group).

Table 4
Polysomnography (PSG) data for patients who met efficacy criteria (N = 24)[a].

	PSG1	PSG2	PSG3	p value[b] PSG1 vs. 2	p value[b] PSG1 vs. 3	p value[b] PSG2 vs. 3
Apnea–hypopnea index	31.9 (19.8); 28.0	11.0 (7.9); 8.2	16.4 (12.2); 14.7	<0.001	<0.001	0.023
Respiratory disturbance index	46.7 (19.8); 41.8	25.0 (14.0); 20.2	30.1 (15.3); 26.2	<0.001	<0.001	0.034
Oxygen desaturation index	27.9 (17.8); 22.4	11.3 (7.5); 7.9	17.0 (11.3); 14.3	<0.001	<0.001	0.004
Percent sleep with SaO$_2$ < 90%[c]	5.3 (4.8); 3.3	1.5 (2.0); 0.6	2.2 (2.0); 1.4	<0.001	0.072	0.024
Apnea–hypopnea index supine	54.4 (32.5); 50.1	24.8 (26.7); 17.2	32 (30.1); 20.5	<0.001	<0.001	ns
Apnea–hypopnea index non-supine	21.6 (20.1); 16.4	5.5 (5.9); 4.1	8.7 (11.2); 5.4	<0.001	<0.001	ns
Apnea–hypopnea index REM	47.2 (30.2); 39.6	27.9 (20.5); 26.3	28.2 (18.9); 27.2	<0.001	<0.001	ns
Apnea–hypopnea index NREM	29.6 (20.6); 26.4	8.9 (8.5); 5.8	14.3 (14.1); 10.0	<0.001	<0.001	ns
Arousal index	43.1 (17.3); 40.0	30.8 (13.5); 25.7	31.2 (13.7); 29.7	<0.001	<0.001	ns
Total sleep time (min)	375.0 (58.9); 370.3	359.7 (80.8); 358.3	376.4 (53.5); 362.3	ns	ns	ns
Sleep efficiency (%)	81.7 (9.3); 85.0	78.3 (14.6); 82.1	82.4 (8.3); 82.9	ns	ns	ns
Percent stage N1	32.7 (12.2); 32.9	27.1 (13.4); 23.6	25.3 (10.0); 23.1	0.015	0.001	ns
Percent stage N2	47.6 (11.4); 48.5	53.9 (11.2); 54.1	52.6 (10.1); 52.9	0.007	0.009	0.048
Percent stage N3	6.7 (8.8); 3.8	6.9 (7.3); 5.1	6.1 (7.8); 3.4	ns	ns	ns
Percent stage REM	13.1 (4.6); 12.6	12.1 (4.5); 12.3	16.0 (5.3); 15.0	ns	0.041	0.005
Percent sleep supine	43.0 (26.0); 41.3	43.6 (29.9); 32.9	42.2 (24.3); 43.4	ns	ns	ns

[a] Values are means (standard deviations); medians, unless otherwise indicated.
[b] p values are Bonferroni-corrected values; ns = nonsignificant.
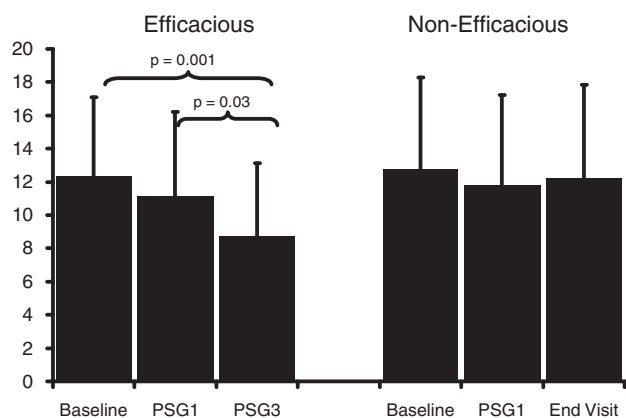[c] SaO$_2$ = oxygen saturation.

Fig. 3. Mean Epworth Sleepiness Scale scores for the efficacious and non-efficacious groups, by time of assessment (see text for explanation). Higher values indicate higher sleepiness. Error bars indicate standard deviations.

Table 5
Adverse events considered possibly, probably, or definitely related to use of EPAP device for efficacious patients, non-efficacious patients, and patients intolerant of the EPAP device. Patients may have reported more than one adverse event.[a]

	Intolerant N = 12	Non-efficacious N = 19	Efficacious N = 24
Difficulty breathing	8	5	8
Difficulty sleeping	7	5	8
Dry mouth	1	5	6
Nasal congestion, drainage, head cold	0	4	8
Itching at device site	1	2	3
Headache	1	3	0
Claustrophobia	1	0	0
Shortness of breath	1	0	0
Dizziness	0	1	0
Dreaming of suffocating	0	0	1
Panicky feeling	0	1	0
Tiredness	0	1	1

[a] Values refer to number of patients.

3.6. Adverse events

There were no serious adverse events. Adverse events judged by the study physician to be possibly, probably, or definitely related to use of the EPAP device are listed in Table 5 separately for patients intolerant of EPAP, those who did not meet efficacy criteria, and those who did. The most common adverse events were difficulty breathing, difficulty falling or staying asleep, and dry mouth. Severity of all adverse events was rated as mild to moderate.

4. Discussion

The results of this study indicate that treatment with a convenient EPAP device is tolerated by 80% of patients with poor adherence to CPAP and improves OSA in 56% of patients based upon PSG2. Moreover, for patients meeting initial efficacy criteria, approximately 7 weeks of EPAP treatment resulted in improvement in clinical status as assessed by ESS and FOSQ. Mean ESS following treatment was in the normal range [13] and mean FOSQ was near normal [14]. This degree of improvement in ESS and FOSQ is similar to that seen in moderate to severe OSA patients treated with CPAP for approximately 1 month [15,16]. Whether these

changes would persist beyond the time period studied remains to be determined.

The magnitude of improvement in PSG efficacy measures is generally less than what is typically reported for CPAP, and certainly the data indicate that many patients are not completely treated. Nevertheless, 16 patients had AHI < 10 at PSG2 (37%), including 6 patients with baseline AHI > 25, and 20 patients had AHI < 15 at PSG2 (47%). The slight increase in mean AHI at PSG3 in the group of patients meeting efficacy criteria at PSG2 is likely the result of regression to the mean, although four patients had AHI at PSG3 similar to baseline. Increases in time spent supine and/or in REM may account for some of the change in these patients, but we cannot rule out factors more directly related to device efficacy.

This study also suggests that poor adherence with or intolerance of CPAP does not generalize to all other treatments. Adherence to the novel EPAP device was exceptionally high in the 80% of patients who tolerated the device, at least as reported by the patients. The observation that patients self-applied EPAP and wore the device all night on all PSG recording nights confirms that patients were able to use the device properly, although the accuracy of the self-report data for home use remains unknown.

While normalization of AHI is a logical and well-accepted efficacy standard for treatment of OSA, a high level of adherence with treatment is needed for a similarly high degree of treatment effectiveness. In some cases less efficacious treatment with high adherence may be a comparable or better alternative than a highly efficacious treatment with poor adherence.

The patients in our sample had more severe sleep apnea and ESS-assessed sleepiness than patients in two prior studies with this EPAP device [8,9]. Nevertheless, mean percent decrease in AHI with EPAP was similar among the three studies (ranging 38–45% for all patients tolerating the device) as was the proportion of patients meeting our criteria for efficacy (ranging 56–70%). Unlike the previous studies, improvement in sleep architecture (fewer arousals and less stage 1 sleep) was observed with EPAP in the current investigation.

It is unclear why EPAP is efficacious in some patients and not others. Whereas patients with higher Mallampati scores and more severe sleep apnea were less likely to show reductions in AHI and other indices of sleep apnea, a number of patients with high Mallampati scores and/or high baseline AHI demonstrated clinically meaningful improvement in OSA with EPAP treatment. Individual differences in the mechanisms contributing to sleep apnea such as ventilatory control instability, airway collapsibility, and arousal threshold probably play a role [17]. Our data indicate that EPAP reduces AHI less in the supine position (relative to non-supine) and in REM sleep (relative to NREM). This may indicate that increasing end-expiratory pharyngeal pressure may be insufficient to completely override mechanical and physiologic changes associated with the supine position and with REM. Thus, reduced lung volume and airway size, heightened airway collapsibility, elevated arousal threshold, and/or changes in respiratory cycle timing may be factors that affect EPAP efficacy.

Adverse events associated with device use were judged to be mild to moderate and did not significantly impact adherence for patients demonstrating initial tolerability of EPAP. Longer term studies are needed to determine if the rate of reported adverse events would decrease over time or might ultimately negatively impact adherence.

Limitations to this study include the absence of a sham or other comparative treatment and lack of counterbalancing of baseline and treatment nights. The adherence data in our sample may be artificially high because the data were obtained by diary rather than by an objective method such as that typically employed to monitor CPAP use [18]. The relatively short duration of the study and frequent interaction by study staff may also have contributed and may not generalize to routine clinical use. It is also possible that motivation may be higher in patients who have had prior difficulty using CPAP or who seek participation in a clinical trial for a new sleep apnea treatment. Future research should include both patients who are naïve to CPAP as well as patients who show good adherence with CPAP treatment. In addition, studies to evaluate longer-duration efficacy and adherence, as well as comparative efficacy studies (e.g., vs. mandibular repositioning devices) should be undertaken.

In conclusion, the improvements in AHI and ESS, combined with the high degree of treatment adherence observed suggest that the convenient EPAP device tested may become a useful addition to current therapeutic options for OSA.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: doi:10.1016/j.sleep.2010.06.011.

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