Auto-Adjusting Versus Fixed Positive Pressure Therapy in Mild to Moderate Obstructive Sleep Apnoea

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Study Objectives: To determine if auto-adjusting positive airway pressure (APAP) would be better tolerated on the basis of delivering a lower mean pressure in patients with mild to moderate obstructive sleep apnoea syndrome (OSAS).

Design: Patients spent 8 weeks on continuous positive airway pressure (CPAP) and 8 weeks on APAP in a randomized crossover design.

Setting: Respiratory Sleep Disorders Unit in a University Hospital and the patient's home.

Participants: Twenty-nine patients with newly diagnosed mild to moderate OSAS (apnoea-hypopnoea frequency of 5-30 events/hour) were studied.

Interventions: N/A.

Measurements and Results: Overnight polysomnography and Epworth Sleepiness Scale were recorded at baseline and at the end of each treatment period in addition to patient preference for device, side effects, and objective compliance. No differences were found in polysomnographic variables or Epworth Sleepiness Scale scores between the 2 treatment modes, but all variables were significantly improved from baseline values. Mean APAP pressure levels were significantly lower than CPAP (6.3 ± 1.4 vs 8.1 ± 1.7 cm H_2O, p < .001). Patient compliance was similar with both treatments. More patients requiring higher fixed pressure (≥ 8cm H_2O) preferred APAP, whereas those requiring lower pressure (< 8 cm H_2O) preferred CPAP (p = .03). Follow-up after 18 months of therapy indicated that 76% of subjects continued to be compliant, with a nightly use of 5.8 ± 1.9 hours per night, despite high levels of minor side effects.

Conclusions: APAP and CPAP are equally effective in managing patients with mild to moderate OSAS, but device preference may be influenced by fixed pressure requirements.

Keywords: Obstructive sleep apnoea, positive airway pressure, CPAP

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INTRODUCTIONS

OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS) IS A COMMON MEDICAL DISORDER AFFECTING 2% TO 4% OF THE ADULT MIDDLE-AGED POPULATION.[1] Recent studies have suggested that even patients with mild breathing abnormalities during sleep (apnoea-hypopnoea index, [AHI] < 15) may have associated hypertension,[2] neurocognitive deficits,[3] and excessive daytime sleepiness leading to an increased risk of motor vehicle accidents.[4] Continuous positive airway pressure[5] (CPAP) has become the standard treatment for OSAS, particularly in moderate to severe cases, and has also been shown to produce significant benefits in patients with mild disease.[6,7] However, despite its efficacy, nasal CPAP is not fully accepted by all patients.[8] Initial acceptance rates are generally in the region of 80%, and nightly use averages about 5 hours per night,[9] although some studies have shown hourly usage rates as low as 3 hours per night.[10] Furthermore, compliance with CPAP has been shown to be lower in patients with mild to moderate OSAS, particularly when not associated with daytime sleepiness.[11]

Auto-adjusting positive airway pressure (APAP) devices are a more recently developed alternative modality of therapy that continuously adjust the pressure to the optimal level, and many studies have shown the mean nightly pressure to be lower on APAP, as compared with fixed-pressure devices.[12,13] Thus, it is possible that APAP devices could increase compliance by reducing side effects associated with air leaks and noise at higher pressures. To date, many studies have shown that APAP can control OSAS as effectively as CPAP, but whether these devices improve patient compliance is still not clear.[14] However, a recent report has shown improved compliance with APAP therapy in patients with OSAS who require high pressure levels on CPAP to control their condition.[15]

In our clinical experience, patients with mild to moderate OSAS (AHI < 30 events per hour of sleep) are less likely to tolerate nasal CPAP therapy than are those with severe OSAS. We hypothesized that the lower treatment pressures delivered by APAP could improve compliance, as compared with CPAP, in patients with mild to moderate disease. Thus, in a randomized crossover study, we compared treatment efficacy, compliance, and device preference between APAP and CPAP therapy in patients with mild to moderate OSAS. The primary endpoint was patient compliance and device preference at the end of the initial 4-month crossover study. A secondary endpoint was long-term compliance with the selected device after 18-months of therapy.

METHODS

Consecutive patients attending the Sleep Disorders Unit at St Vincent's University Hospital with newly diagnosed mild to moderate OSAS (AHI ≥ 5 and < 30) and compatible clinical features, and who were awaiting a trial of CPAP therapy, were offered the protocol. Patients were required to have a score on the Epworth Sleepiness Scale (ESS) of 7 or higher.[16] Exclusion criteria were known cardiovascular disease other than hypertension, previous CPAP therapy, preexisting chronic airways disease, or previous upper-airway surgery. Ethics approval was obtained from the hos-

Disclosure Statement

This was not an industry supported study. Drs. Nolan, Doherty, and Mc Nicholas have indicated no financial conflicts of interest.

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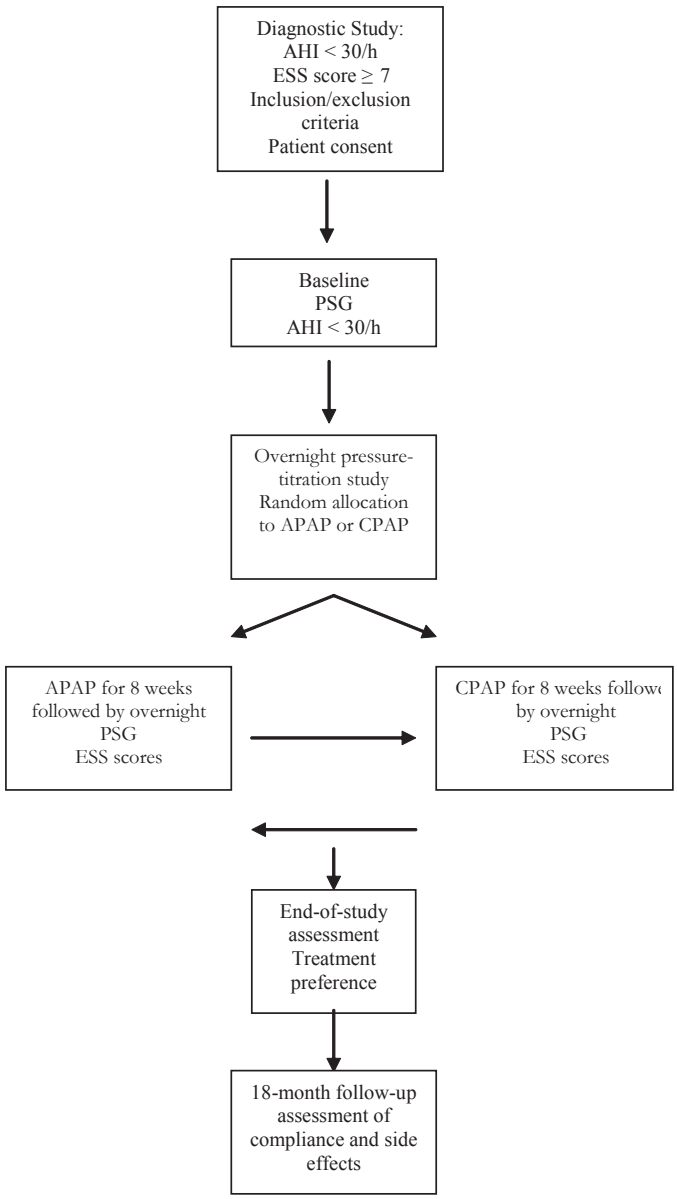

Figure 1—Flow chart of study protocol. AHI refers to apnoea-hypopnoea index; ESS, Epworth Sleepiness Scale; PSG, polysomnography; APAP, auto-adjusting positive airway pressure; CPAP, continuous positive airway pressure.

pital ethics committee, and informed consent was obtained from each patient.

In a randomized crossover design, patients received 8 weeks of CPAP therapy at a fixed pressure calculated from the 95th percentile pressure of an overnight laboratory-based autotitration study[17] and 8 weeks of APAP therapy at a variable pressure between 4 and 20 cm H_2O (Figure1). The Sullivan Elite 6 (ResMed Ltd, Abington, UK) CPAP device was selected as the fixed-pressure device and the Auto T (ResMed) as the APAP device. Although the latter device (APAP) is no longer commercially available, the same algorithm is used in the APAP devices currently available from this manufacturer (Autoset Spirit and S 8 Auto). This APAP device assesses the inspiratory flow-time curve on a breath-by-breath basis. The device delivers variable positive pressure, starting at a minimum of 4 cm H_2O, with the system algorithm responding to obstructive and snoring events by increasing treatment pressure to a maximum upper limit of 20 cm H_2O. Patients were instructed in the use of the devices, and the same nasal mask was used during both parts of the study.

Table 1—Baseline Characteristics of the 29 Subjects in the Study

Parameter	Results
Men	26
Age, y	52.8 ± 8.3
BMI, kg/m^2	29.9 ± 4.7
Neck circumference, cm	42 ± 2
Blood pressure, mm Hg	132/84 ± 23/13

Data are presented as mean ± SD, except men, which is number. BMI refers to body mass index.

The trial was fully blinded to the investigator performing the analysis, as this person was not involved in the immediate patient contact and was also blinded to the randomization. It was not possible to fully blind the patients because of the different appearances of the devices, but patients were not informed about the different technologies used in the devices. An independent person not involved in the study design, protocol, or analysis assigned the devices to the patients in random order. A microprocessor in the 2 devices recorded compliance data, which were downloaded using the Autoscan (ver.3.1) software, (ResMed). Both polysomnography studies (PSG) and ESS were completed at baseline and on the last night of each treatment period. Patients were asked which machine they preferred at the end of the trial.

PSG studies were recorded on an automated system (SleepLab, Viaysis, Wurzburg, Germany) using standard techniques and manually analyzed according to the criteria of Rechtschaffen and Kales.[18] A thermistor recorded oronasal flow. Thoracic and abdominal movements were monitored by inductive plethysmography, and events were classified as obstructive or central based on the presence or absence, respectively, of respiratory effort during apnoea or hypopnoea. Arterial oxyhemoglobin saturation (Spo_2) was measured with a pulse oximeter (BMI, Viaysis, Wurzburg, Germany). A surface microphone attached above the sternal notch detected snoring.

All numerical variables are given as means ± SD. Power-analysis calculations showed that 28 patients were required to demonstrate a change of 20% in the hours used per night with at least 80% power. Statistical significance was taken at the $p < .05$ level. Comparison of APAP versus CPAP modes of therapy and the baseline data were analyzed by the Wilcoxon matched-pair test. Group comparisons were performed using the student's t test. The statistical calculations were performed using SPSS (version 11, SPSS, Inc., Chicago, IL).

RESULTS

Thirty-four patients enrolled in the study, but 5 subsequently dropped out, 1 because of unacceptable side effects and 4 failed to attend follow-up assessments without explanation. Twenty-nine patients (26 men) completed the 16-week protocol, and their baseline characteristics are given in Table 1.

Neither body weight (88.1 ± 13.3 kg) nor neck circumference changed during the course of the study. Six patients (20%) were taking antihypertensive medications at the time of enrollment and a further 10 (34%) had elevated blood pressure levels (> 140 mm Hg systolic and/or 90 mm Hg diastolic) taken in the supine position while at rest. There was no significant change in blood pres-

Table 2—Respiratory and Sleep Variables

Parameter	Baseline (B)	APAP Therapy (A)	CPAP Therapy (C)	p Value		
				B vs A	B vs C	A vs C
AHI, no./h	14.7 ± 8.0	2.7 ± 2.1	3.5 ± 3.5	< 001*	< .001*	.15
Total desaturation, no.	82 ± 45	15 ± 15	15 ± 11	< .001*	< .001*	.68
Mean SaO_2%	92.0 ± 2.1	93.2 ± 1.8	93.3 ± 1.7	.001*	< .001*	.44
Minimum SaO_2%	79.0 ± 11.5	87.5 ± 3.5	82.7 ± 11.0	<.001*	.055	.16
Total snore events, no.	313 ± 259	16 ± 11	17 ± 16	.001*	.001*	.72
Respiratory arousals, no./h	16 ±14	2 ± 3	5 ± 4	< .001*	< .001*	.03*
TST, min	343 ± 48	335 ± 43	349 ± 55	.32	.42	.09
Sleep efficiency, %	79 ± 9	83 ± 8	84 ± 10	.15	.02*	.39
SWS, %	13.7 ± 7.8	15.0 ± 7.4	14.7 ± 8.4	.45	.47	.87
REM, %	17.6 ± 5.1	17.1 ± 7.3	19.6 ± 6.5	.21	.40	.06
ESS score	12.3 ± 4.0	8.6 ± 4.0	7.7 ± 4.6	< .001*	< .001*	.35

*indicates significance. Data presented as mean ± SD. APAP refers to auto-adjusting positive pressure; AHI, apnoea-hypopnoea index; SpO_2, oxygen saturation; TST, total sleep time; SWS, slow-wave sleep, as a percentage of TST; REM, rapid eye movement sleep, as a percentage of TST; ESS, Epworth Sleepiness Scale.

sure with either CPAP or APAP during the course of the study, compared with baseline. However, given the relatively small number of subjects and the relatively simple assessment of blood pressure by an office device, this finding may not be surprising.

Sleep architecture, sleep-related respiratory abnormalities, and daytime sleepiness at baseline and after each treatment modality are given in Table 2. There was no significant difference in sleep quality or sleep architecture between baseline and either of the 2 therapy nights. Table 2 also demonstrates that both forms of treatment improved measures of OSAS severity. The changes in AHI, number of snoring events, and respiratory-related arousals during both treatment nights were all significantly lower ($p < .001$), compared with the baseline night, but were not different from each other. The mean Spo_2 during sleep increased significantly ($p < .001$) on both forms of therapy, and ESS scores also fell significantly ($p < .0001$) from baseline, but there was no difference between the 2 treatments in either of these variables.

Compliance data are presented in Table 3, which demonstrate no difference between the 2 treatment modes, averaging approximately 5 hours per night. Mean mask pressure level during APAP was significantly lower than the mean fixed CPAP level ($p < .0001$). The order of administration of the treatment had no significant effect on compliance.

Thirteen patients (44.8%) indicated a preference for APAP device for long-term use at the end of the study, whereas an equal number preferred CPAP. Only 3 patients (10.3%) did not express a preference for either device. End preference was strongly influenced by the order of treatment, with the majority of patients preferring the machine they had received for the first leg of the trial (85% who received APAP during leg 1 preferred this therapy, as compared with 77% who received CPAP).

Analysis of baseline variables such as OSAS severity (AHI), ESS, age, body mass index, and fixed-pressure requirements revealed that only fixed-pressure requirement for CPAP therapy influenced patient preference at the end of the trial (Table 4). In particular, a significantly higher proportion of patients requiring 8 cm H_2O (12/18) or higher preferred APAP therapy, whereas most of those requiring less than 8 cm H_2O (7/8) preferred CPAP therapy ($p = .03$).

Side effects from treatment were monitored subjectively at the end of each treatment mode (Figure 2). Although all patients

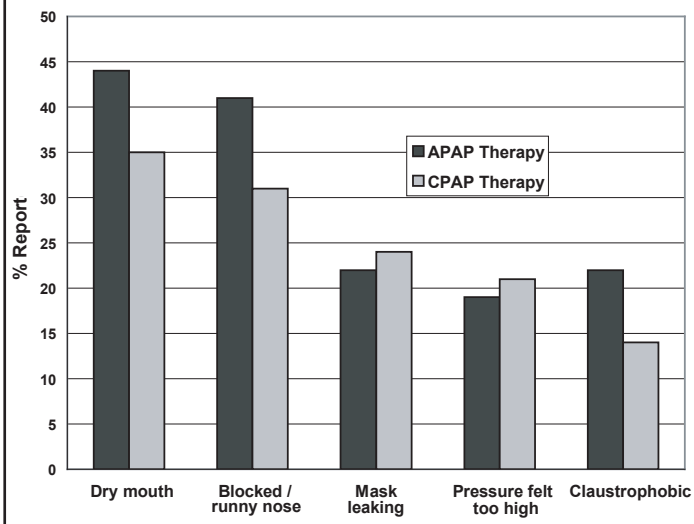

Figure 2—Reported side effects after 8 weeks on auto-adjusting positive airway pressure (APAP) and continuous positive airway pressure (CPAP) therapies.

experienced some side effects on each treatment, there was no significant difference between APAP and CPAP in terms of side effects. Humidification was added to the device in selected cases based on clinical circumstances (7 of 29 patients in total, of which 4 patients continued with this intervention during the course of the treatment period). Overall, patients tolerated treatment even in the presence of nasal problems (up to 45% reported experiencing nasal problems).

A follow-up assessment 18 months after the patients completed the study (Table 5) found that more than 76% of the patients, who had all chosen to continue with treatment after the study period (26/29), were still on treatment; 59% of those continuing therapy were on APAP, compared with 41% on CPAP therapy. Although more than 50% of patients were still experiencing side effects with treatment, compliance data confirmed an average usage of 6 hours per night. This value was higher than the original 4.9 hours observed at the end of the study period in the group of 29. However, when the usage data from the 22 patients who had remained on treatment after 18 months, were compared with the subjects'

Table 3—Compliance and Treatment-Pressure Data

Compliance data	APAP Therapy	CPAP Therapy	p Value
Nights used, %	79 ± 29	81 ± 25	.87
Mean hours used per night used	4.9 ± 2.1	4.9 ± 1.9	.94
Total clock hours	242 ± 128	245 ± 117	.91
Mean mask pressure, cm H_2O	6.3 ± 1.4	8.1 ± 1.7	.0001*
Leak, L/sec[a]	0.29 ± 0.16		

*indicates significance. Data are presented as mean ± SD. CPAP refers to continuous positive airway pressure. [a]Leak at the 95th percentile when using auto-adjusting positive pressure (APAP).

Table 4—Baseline Data and Patient Preference at the End of the Study

Parameter	Preferred APAP (n = 13)	Preferred CPAP (n = 13)	p Value
AHI, no./h	16.3 ± 6.6	14.3 ± 9.2	.49
Age, y	51.9 ± 9.8	53.1 ± 6.8	.74
BMI, kg/m^2	30.6 ± 3.8	28.5 ± 5.1	.27
Neck circumference, cm	41.9 ± 1.8	41.5 ± 1.9	.32
ESS score	13.3 ± 3.8	11.5 ± 4.3	.26
Fixed Pressure (CPAP) cmH_2O	8.9 ± 1.3	7.4 ± 1.4	.01*

*indicates significance. Data are presented as mean ± SD. APAP refers to auto-adjusting positive pressure; CPAP, continuous positive airway pressure AHI, apnoea hypopnoea index; BMI, body mass index; ESS, Epworth Sleepiness Scale.

original study-period usage data (5.5 ± 1.6 hours, both APAP and CPAP), there was no significant difference demonstrated. None of the variables of AHI, ESS, or initial fixed-pressure requirements influenced long-term compliance with either APAP or CPAP.

DISCUSSION

The present report represents the first study comparing CPAP and APAP therapy in patients with mild to moderate OSAS. The findings indicate no consistent difference in efficacy or preference for APAP over CPAP among patients with mild to moderate OSAS, and most patients expressed a preference for the device initially prescribed. Thus, the study finds no evidence to indicate that such patients would be better managed by APAP. However, posthoc analysis indicated that patients requiring higher fixed-pressure levels tended to prefer APAP, similar to the findings of another report,[15] whereas those requiring lower fixed-pressure levels preferred CPAP. Both devices were equally effective in reducing the level of sleep-disordered breathing, snoring, and arousal frequency, in addition to subjective daytime sleepiness, and were similar in efficacy to previous reports in this regard.[14]

Patients in the present study had mild to moderate OSAS, as defined in the report of a Working Group of the American Academy of Sleep Medicine.[19] They also had anthropometric data similar to those of subjects in this category of OSAS, in regard to age and body mass index, that have been previously published.[20,21] Neither device had a major impact on sleep architecture, although sleep efficiency was similarly improved with each device. There was no tendency toward rapid eye movement (REM) versus non-REM or positional obstructive sleep apnoea. Nor was there evidence that any patients had alcohol- or drug- induced obstructive sleep apnoea. Previous reports have indicated significant improvements in sleep quality with both CPAP and APAP, particularly increased slow-wave and REM sleep,[22-24] but these studies evaluated patients with more-severe OSAS, and, thus, the subjects may have had more-severe sleep disturbances prior to therapy. Only 1 previously published report[25] compared sleep quality before and after CPAP in patients with mild to moderate OSAS, and the authors also reported no difference in slow-wave sleep or REM sleep, similar to the present findings.

Table 5—Long-term Follow-up Assessment

Question	Answer
On PAP treatment after 18 months, no.	22/26
In use after 18 months, no.	
APAP	13/14
CPAP	9/12
Nights used, %	99
Mean hours per night used[a]	5.8 ± 1.9
Side effects with treatment after 18 months, %	52
Side effects on long-term treatment, %	
Nasal only	50
Mask leaking only	25
More than 1 side effect	25
Baseline Epworth Sleepiness Scale, score[a]	12 ± 4
ESS after 18 months PAP therapy	6.1 ± 3

[a]Data are presented as mean ± SD. PAP refers to positive airway pressure; APAP, auto-adjusting positive pressure; CPAP, continuous positive airway pressure.

We performed a single attended overnight study in the sleep laboratory using a proprietary APAP device to determine the optimum CPAP level to use in the study protocol, and the 95th percentile was the chosen pressure after visual inspection of the APAP pressure tracing to exclude artifactually high pressure levels. This approach has been validated in previous studies[17,26,27] and has been the method used in clinical practice in our sleep disorders unit for many years. The mean pressure level delivered on the APAP limb of the trial was significantly lower than the CPAP level prescribed, similar to previous reports.[12,13,15,24,25,28]

Compliance was similar with both devices in terms of percentage of nights used and mean hours usage per night. These findings differ from some reports that have found better compliance with APAP,[15,28-30] although other reports have found similar compliance with APAP and CPAP.[12,24] Side effects were common, but relatively minor in degree, with both devices, and there was no difference between devices in this regard. These findings are similar to previous reports in this respect.[31-33]

Most patients expressed a definite preference for one or the other device, but an equal number (13 patients each) expressed a preference for CPAP or APAP. This finding differs from a study by Marrone et al,[34] in which a significantly higher preference rate for APAP (14/18) was shown in a group of patients with moderate to severe OSAS (mean AHI 60/hour), and this study found that only the AHI related to subjective device preference. The most important indicator of preference in our study was the device initially prescribed, although fixed-pressure level prescribed on the CPAP arm of the trial also had a significant influence on preference. The preference for the device first prescribed likely reflects

that modality being associated with the most notable improvement in symptom level. This influence might have been reduced by the inclusion of a washout period between devices, although we believe that the subjective influence of benefit from the first device would have persisted.

We chose a relatively low threshold for an ESS score of 7 to determine daytime sleepiness, in line with our desire to compare compliance with the 2 devices in patients with mild OSAS. This approach, however, did not bias our findings because the results were the same when the 4 patients with an ESS of 7 or 8 were excluded. We also chose different devices from the same manufacturer to deliver CPAP and APAP rather than a single device that could be switched from CPAP to APAP. However, the same nasal mask was used for both parts of the trial for each patient and, thus, we don't believe that this approach was likely to have influenced our results.

We followed our patients for 18 months after they completed the study to evaluate the long-term outcome, particularly in terms of side effects and compliance. The prevalence of mild side effects remained high, with more than 50% of patients stating that they had ongoing nasal symptoms and more than 25% reporting intermittent mask leak. Seventy-six percent of patients were continuing therapy after the initial study period, the majority of whom were on APAP (59% on APAP compared with 41% on CPAP). While these differences are not significant, they do suggest some trend toward better long-term compliance with APAP compared with CPAP, and the lack of significance may be a reflection of the relatively small number of subjects studied. However, the data do not support the routine prescription of APAP as initial therapy for mild to moderate OSAS, and the authors recommend that, at present, APAP therapy be reserved for use in patients who are having difficulty with standard CPAP, or in selected patients in whom there is objective evidence of APAP superiority, such as those requiring high fixed-pressure levels with CPAP.

In conclusion, the present data indicate that CPAP and APAP are equally effective in managing patients with mild to moderate OSAS, and patients have no consistent preference for either device.

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