Comparison between Automatic and Fixed Positive Airway Pressure Therapy in the Home

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We tested the hypothesis that continuous positive airway pressure (CPAP) use and outcomes can be improved by an autotitrating CPAP device in patients with obstructive sleep apnea–hypopnea syndrome (OSAHS) who require higher CPAP (10 cm H_2O or more). In this multisite randomized single-blind cross-over study, 44 patients (mean age, 49 ± 10 years) were randomized to 6 weeks at laboratory-determined fixed pressure and 6 weeks on autotitrating CPAP. Average nightly use was greater in automatic mode (306 versus 271 minutes, p = 0.005); median and 95th centile pressures in automatic mode were lower (p < 0.002). Automatic CPAP resulted in better SF-36 Vitality scores (65 ± 20 versus 58 ± 23, p < 0.05) and mental health scores (80 ± 14 versus 75 ± 18, p < 0.05), but no significant difference in Epworth score (p = 0.065). During automatic therapy, patients reported more restful sleep, better quality sleep, less discomfort from pressure, and less trouble getting to sleep for both the first week of therapy and for the averaged scores for Weeks 2–6 (all p values < 0.006). Patients who require higher fixed CPAP use autotitrating CPAP more and report greater benefit from this therapy.

Keywords: adverse effects; compliance; continuous positive airway pressure; obstructive sleep apnea

Obstructive sleep apnea–hypopnea syndrome (OSAHS) is associated with excessive daytime sleepiness, impaired quality of life, and hypertension (1, 2). Continuous positive airway pressure (CPAP) is an effective treatment for OSAHS symptoms (3, 4), and may also decrease hypertension and vascular risk (5). Rates of nightly use are suboptimal in both short-term and long-term studies, averaging 3 to 5 hours per night (6, 7). Use may be limited by side effects such as pressure intolerance, difficulty in exhaling, mask dislodgement, mask leak, and air leak through the mouth (7, 8).

Changes in weight, body position, alcohol use, or nasal patency can alter acute and chronic CPAP requirements (9, 10). The AutoSet T (ResMed, San Diego, CA) is an autoadjusting CPAP device designed to provide the minimum pressure at each time point of treatment to eliminate apneas, hypopneas, and upper airway resistance (11). Providing a lower mean pressure level during treatment may attenuate side effects associated with pressure intolerance and enhance compliance. This might benefit patients who require high CPAP levels. Studies comparing the AutoSet with fixed pressure delivery at laboratory titration have demonstrated lower median pressures with the AutoSet (12, 13). The AutoSet ameliorates sleep-disordered breathing, while preserving sleep architecture and continuity (12).

The present study assessed whether objective CPAP use, quality of life, and daytime sleepiness can be improved with the use of the AutoSet in automatic mode for patients who require higher CPAP (10 cm H_2O or more) as determined by manual laboratory titration. Secondary outcome measures included self-reported sleep quality and satisfaction with CPAP use.

METHODS

Design

In a five-site randomized single-blind cross-over study, patients received fixed pressure and autotitrating therapy for two 6-week limbs, using the AutoSet. In automatic mode, the CPAP could range from 4 to 20 cm H_2O. Fixed pressure used was determined by a board-certified sleep specialist or equivalent on the basis of minimization of apneas, hypopneas, snoring, hypoxemia, and arousals during either all-night CPAP titration or a split-night study according to American Academy of Sleep Medicine standards (14). Heated humidification was not used during the study.

Institutional review board approval was obtained from each site and written informed consent was obtained. Patients completed the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (15) and the Epworth Sleepiness Scale (ESS) (16). Patients were fitted with a ResMed Mirage or alternative nasal mask, and prospectively completed a sleep diary. Patients were given detailed instructions on using the CPAP equipment. They were not informed of the type of therapy they were receiving, but were informed that compliance was being monitored.

At the second visit, each patient returned with the AutoSet machine and the sleep diary. Compliance data were downloaded from the AutoSet (AutoScan, version 3.1; ResMed) and use time was derived from the "time at pressure" data. The SF-36 and ESS were reassessed, sleep diaries were reviewed, and new diaries were issued. The AutoSet was then switched to the alternate mode and returned to the patient. At the final visit, outcomes were reassessed and patients were debriefed regarding the nature of the study and given feedback regarding use data. A stipend was given to patients who successfully completed the 12-week protocol.

Subjects

At each site, consecutive eligible patients were invited to participate in the study immediately after their overnight laboratory CPAP titration study, if it showed the need for higher CPAP (10 cm H_2O or more). Other entry criteria were symptomatic OSAHS with an apnea–hypopnea index of 15 or more (17) and age between 18 and 65 years. None had received CPAP previously. Exclusion criteria included preexisting lung disease, awake resting Sa_{O_2} < 90%, or 10 or more central apnea–hypopnea events per hour; patients were also excluded if they

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TABLE 1. SLEEP DIARY QUESTIONNAIRE

1.	How much trouble did you have with mask leak?
2.	Did you have air leaking out of your mouth?
3.	How well did your mask fit?
4.	How restful was your sleep?
5.	How much did the noise of the machine disturb your sleep?
6.	How well did you sleep?
7.	How alert do you feel this morning?
8.	Are you having problems with a blocked, runny or stinging nose?
9.	Did you have a sore or dry mouth or throat?
10.	How much discomfort did you get from the pressure?
11.	How much trouble did you have getting to sleep?
12.	Did you have trouble staying asleep during the night?

were taking medications known to significantly interfere with sleep or respiration.

Questionnaires

Patients completed the SF-36, a general quality of life survey designed to assess a patient's perception of his or her health status. The SF-36 has been used extensively, including in sleep apnea (18), and its reliability and validity are documented (19). The ESS is a self-administered questionnaire that measures a patient's subjective sleepiness (16). Patients completed, daily for the first week, and then weekly thereafter, a sleep diary comprising 12 sleep-related questions rated on 100-mm visual analog scales (Table 1). A mean value was calculated for the first week of each treatment and for Weeks 2–6.

Statistical Analyses

Values are given as means ± standard deviation. Comparisons between treatments were performed by two-way analysis of variance with treatment order as a between-subjects factor and treatment type as a within-subjects factor for normally distributed data and by Wilcoxon tests for nonnormally distributed data.

RESULTS

Patient Characteristics

Forty-six patients were enrolled in the study. One patient dropped out at the end of the first limb because he did not wish to continue with CPAP therapy, and another patient's CPAP machine did not provide compliance data. Three patients had fixed pressures decreased from 10, 14, and 11 cm H_2O to 8, 8, and 9 cm H_2O, respectively, after beginning the fixed pressure limb because of pressure intolerance. Forty-four patients (36 men and 8 women) completed the 12-week protocol and their data are reported. Their mean age was 49 ± 10 years, with a mean body mass index of 32 ± 4 kg/m^2.

CPAP Use Data

Patients used the AutoSet in automatic mode an average of 35 minutes more per night compared with the fixed mode ($p = 0.005$; Table 2). During automatic therapy lower median and 95th centile pressures were delivered (both p values < 0.001). Neither the percentage of nights that CPAP was used nor the apnea–hypopnea index differed significantly between fixed mode and automatic mode (Table 2).

Quality of Life Questionnaires

Automatic CPAP resulted in significantly ($p < 0.05$) better SF-36 Vitality scores (65 ± 20 versus 58 ± 23) and SF-36 Mental Health scores (80 ± 14 versus 75 ± 18) than fixed pressure CPAP. There were no differences between treatment type in the outcomes on the other six SF-36 domains: Physical Function, Role-physical, Bodily Pain, General Health, Social Function, and Role-emotional (all p values > 0.07). There was only a trend to improvement of ESS scores among patients receiving automatic pressure (automatic mode, 8 ± 4; fixed mode, 9 ± 4).

TABLE 2. CONTINUOUS POSITIVE AIRWAY PRESSURE USE DATA

	Automatic Mode	Fixed Mode
Use		
min/24 h	306 ± 114	271 ± 115*
Nights used, % of total	92 ± 11	88 ± 15
Pressure, cm H_2O		
median	6.9 ± 1.8	10.7 ± 1.8†
95th centile	9.2 ± 2.1	10.9 ± 1.7†
Residual OSAHS		
AHI/h	9.6 ± 5.3	10.7 ± 6.6

Definition of abbreviations: AHI = apnea–hypopnea index; OSAHS = obstructive sleep apnea–hypopnea syndrome.

Data are presented as mean ± SD.

* $p < 0.005$.

† $p < 0.001$.

Sleep Diary

During automatic therapy, patients reported (all p values $<$ 0.006) more restful sleep, overall better sleep quality, less discomfort from pressure, and less trouble getting to sleep for the first week of therapy; the same results were obtained for Weeks 2–6 for averaged scores. All sleep diary comparisons are presented in Table E1 (*see* the online data supplement).

DISCUSSION

This study found that patients who require higher CPAP (10 cm H_2O or more on manual laboratory titration) have greater nightly CPAP use with autotitrating CPAP compared with fixed pressure CPAP. Average autotitrating CPAP levels were lower than fixed pressure CPAP levels, as determined by manual laboratory titration. Autotitrating CPAP was associated with improvements in SF-36 Vitality and Mental Health scores, but no significant improvement in Epworth score. Sleep diary questions showed improvement with automatic therapy, such as less discomfort from pressure, improved sleep quality, more restful sleep, and less trouble getting to sleep.

In this study the ESS score did not improve when SF-36 Vitality, another measure weighted to sleepiness, did improve. The SF-36 Vitality scale may be a more sensitive marker of improvement in OSAHS with treatment than the ESS. Other studies have shown large effect sizes for this measure after CPAP treatment (4). Patients reported better sleep quality and fewer problems with CPAP use during automatic therapy. Sleep diary questions were chosen for their pertinence to CPAP outcome, use in prior studies, and face validity. However, the sleep diary questionnaire was not validated, which limits the generalizability of these results.

The goal of laboratory titration is to determine the minimum pressure required to normalize sleep-disordered breathing and hypoxemia, which must include the higher pressures usually observed during supine rapid eye movement sleep. Patients who require higher fixed pressure levels during laboratory titration may require high pressure levels for only a small percentage of sleep (13). The data regarding an association between pressure level, use, and side effects are equivocal. Some studies have shown decreased CPAP use with higher pressures (20), but most studies have failed to demonstrate a reduction in CPAP use or a higher incidence of side effects with increasing CPAP (21–23). All of these studies included a broad range of CPAP levels, and

did not examine patients who required higher fixed pressures. Few long-term studies of pressure requirements have been performed. Studies with follow-up intervals of 2 to 9 months have failed to demonstrate significant differences in fixed pressure requirements (24, 25), while mean autotitrating CPAP values remained lower than original laboratory fixed pressure determinations (25). Other studies have demonstrated reductions in mean CPAP levels after 2 weeks of treatment (26) and during longer follow-up intervals (27).

Studies comparing the effects of autotitrating CPAP devices with fixed pressure CPAP have consistently found that autotitrating CPAP is as effective at controlling sleep-disordered breathing as fixed pressure CPAP (25, 28–32). Whether there is any extra benefit associated with using autotitrating CPAP is less clear. A few studies have shown improved sleep architecture when using autotitrating CPAP (28, 29) and all but one study (31) found that pressure requirements are lower with autotitrating CPAP compared with fixed pressure CPAP (25, 28, 30, 32, 33). There have been previous suggestions of clinical benefit with the use of auto-CPAP in comparison with the fixed pressure device. In one study, the number of hours per night that positive pressure was applied favored autotitrating CPAP (30), and in another study 75% of patients preferred autotitrating therapy (32). However, in this latter study, as in others, no compliance differences were found between autotitrating and fixed pressure therapy (28, 33). The current study found greater autotitrating CPAP use at effective pressure and extends previous studies by showing that autotitrating CPAP use can improve some quality of life domains. It is postulated that selecting patients who require higher fixed CPAP also selects those who will gain the most clinical benefit, but whether this will be a consistent finding is still unknown. Another aspect is that intelligent CPAP machines perform differently (34). The response to sleep breathing patterns is different among automatic CPAP devices, and therefore results from one machine are not generalizable to others.

Patterns of CPAP use are established early in treatment and therefore optimizing CPAP use is paramount. Studies have shown that increased nightly use in the first 1–3 months predicts longer term use (6, 7). Intensive education and support result in improvements in CPAP use, but these interventions can be labor and cost intensive (35). Other interventions that enhance CPAP use are the addition of heated humidity at CPAP initiation (36). Compliance gains with heated humidity were similar in magnitude to those in the present study. Heated humidification reduced side effects related to nasal pathology, but no differences were noted on ESS scores. This is similar to the present investigation; fewer adverse effects, improvements in sleep quality, and energy level (SF-36 Vitality) likely resulted in greater AutoSet use in the automatic mode. However, ESS scores were not improved with autotitrating therapy. Autotitrating CPAP has an advantage over heated humidification in terms of convenience as the humidifier does not need to be cleaned and replenished nightly, while autotitrating CPAP and standard CPAP plus heated humidification may be similar in price.

Quality of life and cognitive functioning are impaired in patients with OSAHS, with degree of impairment being related to OSAHS severity (1). Improvements in quality of life have been observed on SF-36 Physical and Mental Health scales after treatment with CPAP (37–39). Reductions in daytime sleepiness and improved cognitive functioning have been observed with as little as 4 hours of CPAP use per night (40). Furthermore, amount of CPAP use per night is positively correlated with reductions in ESS scores and increased sleep latencies on the Maintenance of Wakefulness Test (41). The question is raised: can further improvements in quality of life be attained by a specific type of CPAP intervention? The current investigation supports this assumption. Autotitrating CPAP resulted in differential improvements in quality of life measures compared with fixed pressure CPAP. As would be anticipated, the quality of life differences between the two forms of active treatment were not as large compared with the differences between CPAP treatment and no therapy. Increased objective use and a reduction in CPAP-specific adverse effects with autotitrating CPAP may be responsible for the greater improvements in quality of life observed, as the apnea–hypopnea index during the time treated was the same with both forms of CPAP.

Limitations of this study include the single-blind study design and the relatively short assessment interval. The study was performed in a single-blind fashion because some investigators had to be involved in the mode settings of the devices. The investigators could have influenced CPAP use by their enthusiasm (knowingly or unknowingly) for the automatic mode of treatment, but were instructed not to convey any bias. Care was taken to ensure that all end points were either objective and unalterably determined by the recording devices or were scored only by the patient, such as visual analog scales and Epworth Sleepiness Scale. In addition, all end points were reviewed by the study monitor. Thus, the investigators had no opportunity to directly influence the results. As the study was performed as a crossover design, patients could theoretically detect the difference between the modes of the device. Patients were blinded to the mode of the device and the hypothesis under test and all were naive to CPAP therapy; thus we do not believe this would have influenced the results. The intervention time of 6 weeks in this study was relatively short. Longer term studies are needed to determine whether benefits in compliance and quality of life are maintained. The ability to compensate for changes in pressure requirements, both acutely and chronically, accompanied by lower mean pressures, may result in long-term gains in CPAP use. Also, this study does not generalize to all patients prescribed CPAP, as patients were selected on the basis of higher CPAP requirements. Mean pressure levels across all patients prescribed CPAP is in the range of 9–10 cm H_2O, and therefore patients in this study are from the top 50% of the distribution. Whether all patients would demonstrate compliance gains with the AutoSet is not yet known.

We conclude that among patients requiring higher CPAP (10 cm H_2O or more) there are improvements in CPAP use, OSAHS symptoms, and quality of life domains when using autotitrating as opposed to fixed pressure CPAP.

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