CHEST

Official publication of the American College of Chest Physicians

Continuous Positive Airway Pressure Requirement During the First Month of Treatment in Patients With Severe Obstructive Sleep Apnea

Ruzica Jokic, Artur Klimaszewski, Guruswamy Sridhar and Michael F. Fitzpatrick

Chest 1998;114;1061-1069
DOI 10.1378/chest.114.4.1061

ISSN:0012-3692

Continuous Positive Airway Pressure Requirement During the First Month of Treatment in Patients With Severe Obstructive Sleep Apnea*

Ruzica Jokic, MD; Artur Klimaszewski, MD; Guruswamy Sridhar, MD; and Michael F. Fitzpatrick, MD

Objectives: **(1) To compare the continuous positive airway pressure (CPAP) requirement at the time of diagnosis (T_0), after 2 weeks (T_2), and after 4 weeks (T_4) of CPAP treatment, in patients with severe obstructive sleep apnea (OSA); and (2) to assess whether any alteration in CPAP requirement over the first 4 weeks of CPAP treatment would influence daytime alertness, subjective sleepiness, or mood.**

Design: **A prospective, controlled, single-blind crossover study.**

Setting: **University teaching hospital.**

Patients: **Ten patients with newly diagnosed and previously untreated severe OSA (aged 52±9 years, apnea hypopnea index [AHI] of 99±31) and subsequently 10 control patients (aged 52±11 years, AHI 85±17).**

Measurements: **Overnight polysomnography with CPAP titration to determine the CPAP requirement, which was standardized for body position and sleep stage, on all three occasions (T_0, T_2, T_4). Objective sleep quality, daytime alertness, subjective sleepiness (Epworth Sleepiness Scale), and mood (Hospital Anxiety and Depression Scale).**

Results: **CPAP requirement decreased from T_0 to T_2 (median difference, 1.5 cm H_2O, 95% confidence interval [CI], 1.1 to 2.7 cm H_2O, p=0.0004) and did not differ between T_2 and T_4. Use of the lower CPAP pressure during T_2 to T_4 was associated with a decrease in Epworth scale (mean difference, 2.6, 95% CI, 1.2 to 4; p=0.01) and anxiety (median change, 2; 95% CI, 0.5 to 2.9, p=0.03) scores, as compared with the first 2 weeks. Daytime alertness did not differ between T_0 to T_2 and T_2 to T_4.**

Conclusion: **CPAP requirement falls within 2 weeks of starting CPAP treatment. A change to the lower required CPAP was not associated with any deterioration in daytime alertness but was associated with *small* subjective improvements in sleepiness and mood.**

(CHEST 1998; 114:1061–1069)

Key words: CPAP; sleep apnea; treatment

Abbreviations: AHI=apnea hypopnea index; ANOVA=analysis of variance; CI=confidence interval; CPAP=continuous positive airway pressure; EMG=electromyogram; ESS=Epworth Sleepiness Scale; MWT=Maintenance of Wakefulness Test; NS=not significant; OSA=obstructive sleep apnea; REM=rapid eye movement

Continuous positive airway pressure (CPAP),[1] which has become the standard first treatment for patients with moderate and severe obstructive sleep apnea (OSA) syndrome,[2] has been shown to significantly reduce sleep apnea-related morbidity and mortality.[3–5] It is a safe treatment and results in several important benefits to patients with OSA—elimination of apneic events and nocturnal oxygen desaturations, improvement in sleep quality, daytime alertness, and cognitive performance, and reduction in arterial hypertension.[4,6–8]

However, many patients with OSA complain of discomfort from CPAP and 20 to 30% reject CPAP treatment, usually during the first 2 to 4 weeks of treatment.[9,10] Many of the common complaints with CPAP are pressure related—nasal or sinus pressure, flatulence, and chest discomfort,[11,12] which may be a result of pressure-related elevation of the resting lung volume during therapy. These side effects can preclude patient acceptance of long-term CPAP use.

*From the Division of Respiratory Medicine (Drs. Jokic, Klimaszewski, and Fitzpatrick), University of Saskatchewan, Saskatoon, and Regina Health District (Dr. Sridar), Regina, Saskatchewan, Canada.

Performed at the Sleep Research Laboratory, Royal University Hospital, Saskatoon, Saskatchewan, Canada.

Supported by the Heart and Stroke Foundation of Saskatchewan.

Manuscript received December 2, 1997; revision accepted April 1, 1998.

Correspondence to: Michael F. Fitzpatrick, MD, Division of Respiratory and Critical Care Medicine, Richardson House, Queen's University, Kingston, Ontario, Canada, K7L 3N6; email: mf19@post.queensu.ca

There has been no reported correlation between the prescribed CPAP pressure and CPAP compliance,[11,13] but difficulty with mask fitting and air leaks are more common with higher CPAP pressures.[12,14] For this reason most patients with OSA undergo careful CPAP titration in a sleep laboratory to ensure a CPAP setting that is at the lowest pressure necessary to overcome upper airway obstruction during sleep. Indeed, reducing the mask pressure by using bilevel positive airway pressure (with expiratory pressure lower than the previous CPAP pressure) or an automatically adjusting CPAP system (which tracks the lowest CPAP pressure required to maintain airway patency) are strategies that have been advocated for helping patients intolerant of CPAP.[12]

Repeated upper airway obstruction and snoring in patients with OSA is associated with thickening and narrowing of the upper airway, which appears to be due, at least in part, to mucosal edema.[15] Regular nocturnal CPAP use in these patients is associated with widening of the awake pharyngeal dimensions (off CPAP) and reduction in mucosal edema.[15] It is logical to consider that such an increase in general or regional upper airway dimensions after regular CPAP use might, with a concomitant reduction in upper airway resistance, lead to a reduction in the effective CPAP pressure required to maintain airway patency during sleep. Such a change in CPAP pressure requirement could, for the reasons mentioned above, be important in the clinical management of OSA, particularly in patients with pressure-related discomfort from CPAP.

The aim of this study was to compare the CPAP requirement at the time of diagnosis and after 2 and 4 weeks of commencing CPAP treatment (we reasoned that resolution of mucosal edema would likely occur soon after commencing CPAP treatment for OSA). In addition, we sought to evaluate if these changes influence outcome measures such as daytime alertness, subjective sleepiness, and mood in patients with severe OSA.

Materials and Methods

Hypothesis

CPAP requirement in patients with severe OSA will fall during the first month of treatment.

Study Design

This study was performed in two consecutive parts: part 1—prospective single-blind crossover study in 10 consecutive patients with newly diagnosed and previously untreated severe OSA; and part 2—comparison with 10 consecutive (unmatched) patients with newly diagnosed and previously untreated severe OSA, in whom no CPAP alteration was made.

Part 1

All subjects were recruited from outpatients referred for the investigation of daytime somnolence to the Sleep Disorders Centre, Royal University Hospital, Saskatoon, Canada, and were diagnosed as having severe OSA (see below) by overnight polysomnography. The criteria for participation in this study were (1) newly diagnosed OSA with apnea hypopnea index (AHI)>40, and (2) CPAP required to abolish all obstructive respiratory events during sleep≥9 cm H_2O.

Patients (seven men, three women) had a mean age of 52.4 (SD 9.1) years, a body mass index of 38 (5.5) kg/m^2, and an AHI of 99 (31), and range of 46 to 144. All patients gave written informed consent to participate in the study. The University of Saskatchewan Advisory Committee on Ethics in Human Experimentation approved the research protocol and the consent form. Patients with other conditions that might interfere with sleep (respiratory tract infections, uncontrolled allergies, heart failure, narcolepsy, periodic leg movements) were excluded from the study.

Outcome Measures

Primary: CPAP requirement—standardized for body position (lateral or supine) and sleep stage at the time of diagnosis (T_0) and after 2 weeks (T_2) and 4 weeks (T_4).

Secondary: Daytime alertness (Maintenance of Wakefulness Test [MWT]);[16–18] subjective sleepiness (Epworth Sleepiness Scale [ESS]);[19,20] and mood (Hospital Anxiety Depression Scale).[21]

The protocol for the study is summarized on Figure 1. CPAP titration on the diagnostic night (T_0) established the minimum CPAP required to alleviate obstructive respiratory arousals dur-

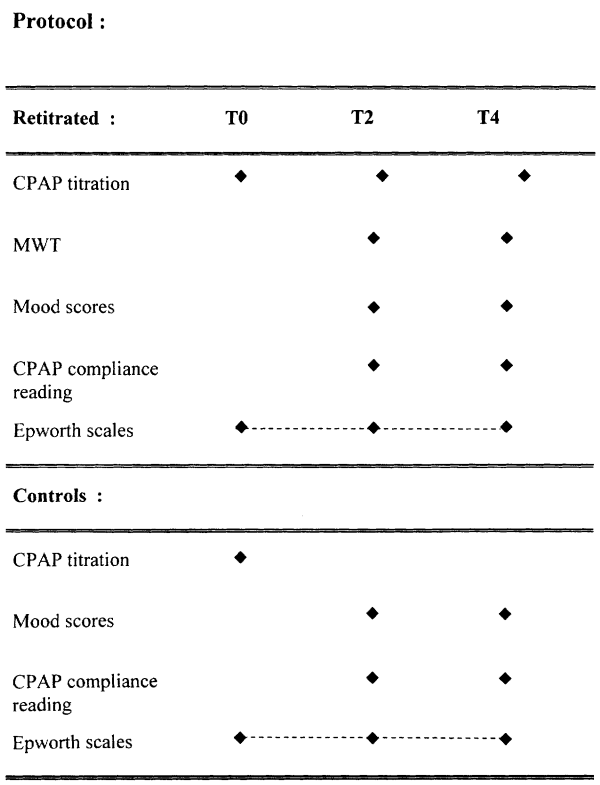

Figure 1. Study protocol.

ing sleep at the time of diagnosis (CPAP 1). Patients were familiarized with the CPAP apparatus on the morning after the overnight study, and received a CPAP machine preset at the required pressure. They were instructed to use the CPAP device all night, every night, during the study, and were given a contact telephone number in case of problems with CPAP treatment. This pressure (CPAP 1) was used during the first 2 weeks of the study. Overnight CPAP titration was repeated at T_2 (night 15, CPAP 2) and each patient's CPAP machine was adjusted accordingly on the morning after the overnight sleep study. CPAP 2 was the pressure used during the second 2 weeks of the study. On night 29 (T_3), after 4 weeks of CPAP treatment, overnight polysomnography with CPAP titration was repeated (CPAP 3). During the second and third CPAP titrations (nights 15 and 29), the technician was advised only of the position and sleep stage (not the CPAP pressure) at which the patient's highest CPAP requirement could clearly be determined in the diagnostic study, and asked to titrate CPAP for this circumstance. (For example, if the patient's highest CPAP requirement during the diagnostic study was clearly defined in supine rapid eye movement [REM], the technician was requested to titrate for this circumstance in the second and third studies.)

On days 15 and 29, following a normal night's sleep at home, and before the second and third overnight studies, daytime alertness (MWT)[16–18] and mood (Hospital Anxiety and Depression Scale)[21] were measured.

Subjective sleepiness was assessed during the study with a daily ESS score.[19,20] Nasal CPAP compliance was monitored through hour meter readings on the CPAP units at the time of issue and again on days 15 and 29, and a urine toxicology screen was performed on days 15 and 29 of each study limb, as part of the MWT protocol.

Overnight Sleep Study

Polysomnography included EEG (C_4–A_1, C_3–A_2, and O_2–A_1 derivations), electro-oculogram (two channels), submental electromyogram (EMG), pulse oximetry, oronasal airflow (oronasal thermistor), chest and abdominal movement (respiratory inductance plethysmography), snore (vibration sensor), intercostal EMG and anterior tibialis EMG ("Sandman," Nellcor Puritan Bennett [Melville Diagnostics] Limited; Ottawa, Canada). A position sensor was used to monitor position continuously on-line (Rochester Electro-Medical Inc; Tampa, FL). Sleep and arousals were scored according to conventional criteria.[22,23]

CPAP Titration Procedure

CPAP was administered via machines (Tranquility model 7201 CPAP machines; Healthdyne Technologies; Marietta, GA) with remote control adjustment. CPAP titrations were performed by two experienced sleep technologists. The CPAP titration procedure used was similar to that described by Sanders and colleagues[12] (1993)—CPAP was initiated at 4 cm H_2O and was titrated upwards in 2-cm H_2O increments to eliminate gross obstructive apneas and hypopneas, and then 1-cm H_2O adjustments (up and down) were made with sleep stage and position until the minimum CPAP necessary to eliminate respiratory arousals (obstructive apneas and hypopneas and repetitive snoring-associated arousals) had been carefully defined. The first (T_0) CPAP titration was conducted as part of a "split night" study, *ie*, diagnostic study followed by therapeutic study.

Blinding Procedure

The 30 complete polysomnograms with CPAP titrations were then recoded into random numbers and each polysomnogram was evaluated independently by a clinical polysomnographer to determine the minimum CPAP required to abolish obstructive respiratory events during sleep. The CPAP requirement was standardized for body position (lateral, supine) and sleep stage on all three occasions (T_0, T_2, T_4). The decision of the blinded clinical polysomnographer was taken as final.

Maintenance of Wakefulness Test

Objective daytime sleepiness was measured using the 40-min version of the MWT.[16–18] Sleep onset latency was defined as the time from lights out to the first of three consecutive 30-s epochs of stage 1 sleep or any single 30-s epoch of another sleep stage. Four trials were given at 2-h intervals with the first trial beginning 2 h after awakening.

Part 2

We compared 10 newly diagnosed and previously untreated patients with severe OSA whose CPAP was left unaltered after diagnosis.

After completing the first part of the study (in which each patient served as his/her own control subject), we then compared the secondary outcome measures at T_2 and T_4 between the 10 patients from part 1 with another group of 10 consecutive patients with newly diagnosed severe OSA (criteria the same as for group 1 subjects), whose CPAP was left unaltered during the first 4 weeks after diagnosis. The mean age of the patients in this second group was 52.3 (SD 10.7) years, body mass index was 38.1 (4.4) kg/m^2, and AHI was 85 (16.9) (AHI range, 45 to 100).

Clinician Contact

The study plan included an equal number of encounters with the responsible sleep physician (M.F.F.) during both parts of the study—each patient was seen on three occasions—before diagnosis, after diagnosis and CPAP titration, and at the end of the study period (4 weeks after commencement of treatment).

Data Analysis

Data were analyzed using a statistical package (SPSS version 6.0; SPSS Inc; Chicago, IL).

Part 1: Analysis of variance (ANOVA) (one-way) was used to compare CPAP requirements at the three time points. Paired *t* tests were used to compare MWT sleep latencies at different time points. Wilcoxon sign ranks test was used to compare differences in ordinal scales (mood questionnaires). ANOVA (two-way) was used to compare ESS data at the three time points and between the groups.

Part 2: Unpaired *t* tests and Mann-Whitney *U* tests were used to compare data between groups. The Bonferroni correction factor was used when more than one comparison was made on a single variable.

Results

Part 1

The CPAP requirement was higher during REM sleep than non-REM sleep in each of the 10 patients studied. Thus, the CPAP requirement was standardized for REM sleep at T_0, T_2, and T_4 in each of the 10 patients. In seven patients, the CPAP require-

ment was standardized for the supine position at T_0, T_2, and T_4, and in the other three patients for the lateral position.

ANOVA revealed a significant fall in CPAP requirement over the 4 weeks of the study (ANOVA, p=0.002) (Fig 2). As is evident from Figure 2, there was a significant fall in CPAP requirement between T_0 (median, 12; range, 9 to 15 cm H_2O) and T_2 (9.5 cm H_2O; range, 8 to 11 cm H_2O; median difference, 1.5 cm H_2O; 95% confidence interval [CI], 1.1 to 2.7 cm H_2O; p=0.0004), but CPAP requirement did not change significantly between T_2 and T_4 (9.5 cm H_2O; range, 8 to 11 cm H_2O; median change, 0; 95% CI, −0.5 to 0.3 cm H_2O; p=0.59). The median difference between T_0 and T_4 was 2 cm H_2O; 95% CI, 1.2 to 2.8 cm H_2O; p=0.0004. The CPAP requirement was lower after 2 weeks of CPAP treatment in all 10 patients.

Although the first CPAP titration was undertaken as a "split-night" study, the total sleep time during the CPAP titration part of this study was 259 (SD 62) min. No patient had <3.5 h of CPAP titration time during the split-night study. The time spent in REM sleep (in the same body position) was similar on all three CPAP titrations (diagnostic study, 64±30 min; after 2 weeks, 74±31 min; and after 4 weeks, 64±28 min). There was no difference in sleep architecture between the second and the third overnight studies, as shown in Table 1. There were no changes in the body weight or alterations in medication over the 4-week study period.

Maintenance of Wakefulness Test

The MWT sleep latencies at T_2 (mean, 35.7 [2.2] min) and T_4 (mean, 34.6 [2.7] min; mean change, 1.1 min; 95% CI, −2.4 to 4.6 min; p=0.5) were similar, as shown in Figure 3. Epworth Sleepiness Scale scores were lower for the second 2 weeks (T_2 to T_4) of CPAP treatment (mean, 4.1 [1.1]) than for the first 2 weeks (T_0 to T_2) (mean, 6.7 [1.2]; mean change, 2.6; 95% CI, 1.2 to 4, p=0.01) (Fig 4).

Anxiety scores were lower during the T_2 to T_4 period (median, 3; range, 0 to 4) as compared with T_0 to T_2 (median, 4.5; range, 1 to 6; median difference, 2; 95% CI, 0.5 to −2.9; p=0.03), as shown in Figure 5. Depression scores were similar between the two periods of CPAP treatment (T_0 to T_2 median, 2; range, 1 to 8; T_2 to T_4, 2.5; range, 0 to 7; median difference, 1; 95% CI, −0.9 to 1.7, p=not significant [NS] (Fig 5).

Part 2

ESS scores tended to decrease in the control group during T_2 to T_4 (mean, 6.3 [1.4]) as compared

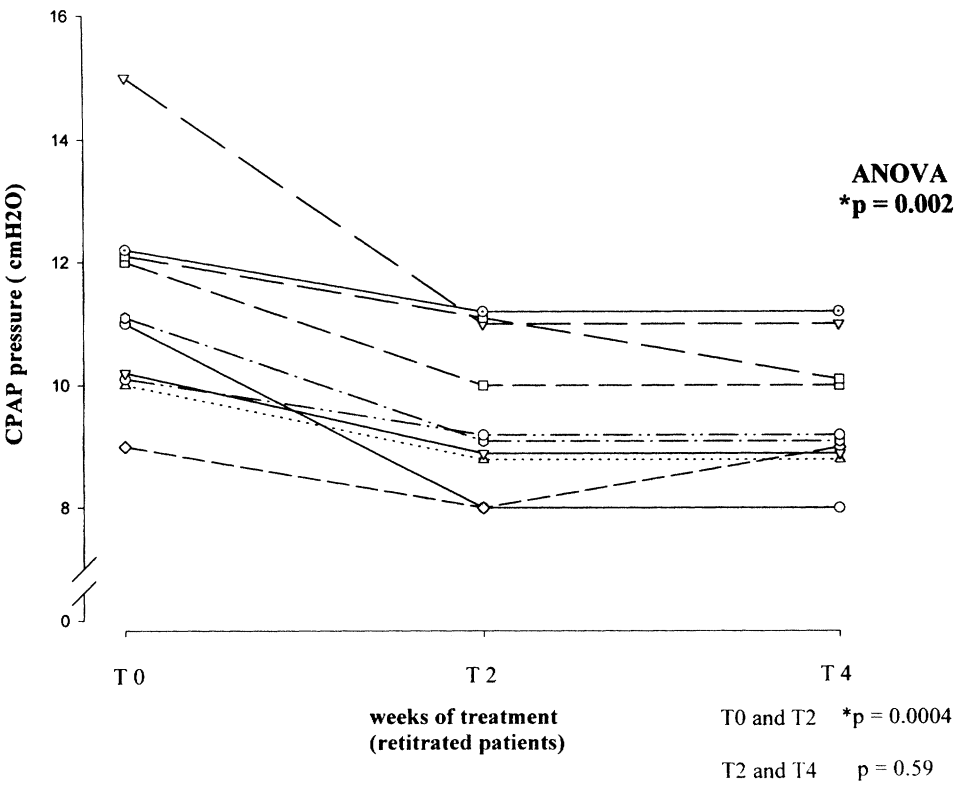

FIGURE 2. CPAP requirement from the time of diagnosis until 4 weeks after commencing CPAP treatment.

Table 1—*Sleep Architecture and Respiratory Variables at Overnight Polysomnography After 2 and 4 Weeks of CPAP Treatment

	2 wk	4 wk	p Value
Wakefulness (% TRT)	17.9 (10.6)	14.2 (11.9)	0.51
Stage 1 (% TST)	9.3 (5.1)	6.9 (4.2)	0.13
Stage 2 (% TST)	43.6 (9.2)	43.8 (10.1)	0.95
Stage 3 (% TST)	12.7 (5.9)	11.6 (4.8)	0.61
Stage 4 (% TST)	10.5 (6.1)	12.5 (7.4)	0.43
Slow-wave sleep (% TST)	23.2 (7.4)	24.1 (7.0)	0.80
REM (% TST)	23.9 (6.1)	23.6 (6.3)	0.89
Time in REM, same position (min)	74.6 (34.3)	64.1 (35.4)	0.22
Total sleep time (min)	334 (62)	328 (69)	0.78
Sleep efficiency (TST/TRT)	77.5 (12.7)	78.0 (13.7)	0.92
AHI	13.3 (10.9)	13.9 (9.3)	0.86
Nonrespiratory arousals	6.8 (3.9)	7.0 (3.9)	0.80
Arousal index	24.2 (11.6)	22.9 (10.6)	0.69
Mean oxygen saturation NREM sleep (%)	94 (1.3)	94 (0.9)	0.78
Minimum oxygen saturation NREM sleep (%)	89 (1.6)	88 (1.3)	0.14
Mean oxygen saturation REM sleep (%)	94 (1.3)	94 (1.3)	0.9
Minimum oxygen saturation REM sleep (%)	89 (2.7)	88 (3.4)	0.46

*TRT=total recorded time; TST=total sleep time; NREM=non-REM. Values are mean and SD.

with T_0 to T_2 (8.3 [1.3]), but this difference was not statistically significant (mean difference, 2.1; 95% CI, 0.3 to 4, p=0.17).

Two-way ANOVA showed no significant group-wise difference between patients (who underwent a change in CPAP at T_2) and control subjects (who did not) at the three different time points (p=0.9). As expected, there was a significant fall in ESS scores after T_0 in both groups (p<0.001) (Fig 4).

Anxiety scores at T_2 (median, 4.5; range, 0 to 11) and T_4 (median, 5; range, 0 to 12) were similar in the control group of patients (median change, 0; 95% CI, −1.9 to 1.5; p=NS). Similarly, there was no difference in depression scores between T_2 (median score, 4; range, 0 to 18) and T_4 (3.5; range, 0 to 13; median change, 0.5; 95% CI, −1.2 to 2.2; p=NS) in the control patients (Fig 5). No statistically significant differences were observed in either the anxiety or the depression scale scores at T_2 or T_4 between patients and control subjects.

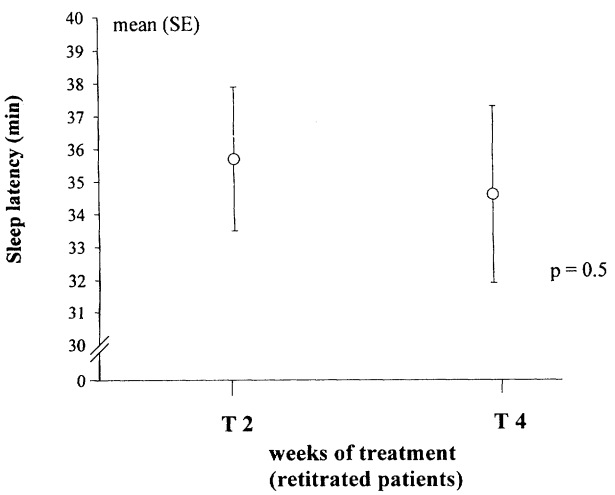

FIGURE 3. Maintenance of wakefulness test sleep onset latencies after 2 weeks and 4 weeks of CPAP treatment.

CPAP Compliance

Nightly CPAP compliance over time was similar in both groups: part 1—first 2 weeks mean, 6.6 (0.5) h; second two weeks, 6.5 (0.4) h; mean difference, 0.1 h; 95% CI, −0.8 to 1; p=NS; part 2 (control subjects)—first 2 weeks, 6.9 (0.4) h; second 2 weeks, 6.6 (0.4) h; mean difference, 0.7 h; 95% CI, −0.6 to 1.2; p=NS. In the second 2 weeks of treatment, CPAP compliance between the two groups was not significantly different (patients, 6.5 h; control subjects, 6.6 h; mean difference, 0.7 h; 95% CI, −1.4 to 2.8, p=NS).

DISCUSSION

Our results demonstrate a fall in CPAP requirement of approximately 2 cm H_2O within 2 weeks of starting CPAP treatment in patients with severe OSA. Why should this be? One plausible explanation for this finding, which has gleaned considerable support from recent studies, is that the upper airway in patients with OSA undergoes anatomic change resulting in an improved upper airway caliber soon after commencing CPAP treatment. In 24 male patients with OSA who underwent erect and supine cephalometry before and after treatment with CPAP for at least 3 months, Mortimore et al[24] demonstrated a widening of the posterior airway space while awake in the supine position after CPAP treatment. The magnitude of the change in upper airway caliber in the latter study correlated strongly with CPAP compliance. Using MRI, the pharyngeal airway of five patients with OSA has been measured in the awake state before and after 4 to 6 weeks of CPAP therapy.[15] After CPAP treatment, the pharyngeal airway volume increased significantly, primarily because the volume of the oropharyngeal airway doubled, on average.[15] Similarly, in the latter study, the minimum upper airway cross-sectional area also increased markedly (by 186% on average) after using CPAP.[15] A marked decrement in upper airway water

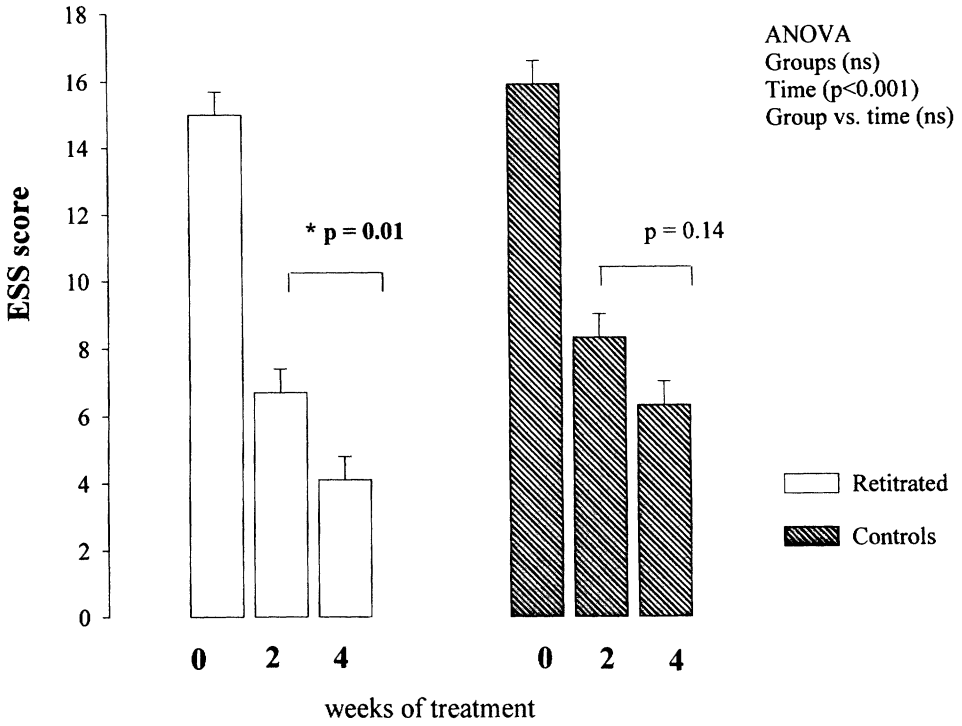

FIGURE 4. ESS scores from the time of diagnosis until 4 weeks after commencing CPAP treatment.

content on the MRI images after CPAP treatment suggested that at least some of this improvement in upper airway caliber was due to resolution of edema. In addition, Sforza and colleagues[25] reported that the *length* of the soft palate (measured by cephalometry in 22 patients) was a major determinant of the level of effective CPAP in OSA. Thus, a change in upper airway morphology with CPAP treatment is a plausible mechanism for the reduction in CPAP requirement observed during the current study.

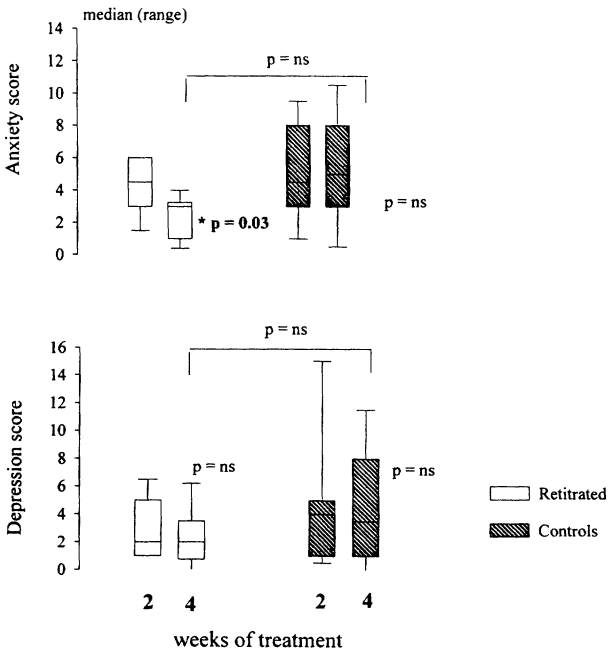

FIGURE 5. Anxiety and depression scores from the time of diagnosis until 4 weeks after commencing CPAP treatment.

Several other possible explanations exist for the improved upper airway patency noted after CPAP treatment in patients with OSA. These include (1) improved upper airway dilator muscle activity,[26,27] (2) reduced upper airway muscle fatigue,[28–30] and (3) a reduction in upper airway vascularity.[31]

Others have also demonstrated changes in CPAP requirement over more prolonged follow-up studies of OSA. Series and colleagues[32] demonstrated that the required CPAP progressively decreased (from 9.6 to 7.7 cm H_2O) during the first 8 months of treatment in patients with OSA. Similarly, Boecker and colleagues[33] found a reduction in the effective CPAP in 57% of 30 OSA patients, over a follow-up period of 6 to 15 months. The authors of these two studies, however, did not standardize the CPAP requirement for sleep stage and position, and did not assess the effect of the alteration in CPAP requirement on other outcome measures. It is also important to control for changes in weight, ventilatory control, and nasal obstruction over longer follow-up periods, as these factors may also contribute to a change in CPAP requirements.[32]

One potential criticism of the current study is that

the initial CPAP determination could have been deleteriously influenced by the split-night study protocol employed during the first CPAP titration (night 1). Single-night studies have been shown to provide a reliable estimate of the required CPAP in approximately 78% of patients, particularly those with severe OSA.[34] There was only one subject in the current study (in part 2) in whom the clinical polysomnographer believed that a full overnight polysomnogram for CPAP titration was indicated because of inability to clearly discern an optimal CPAP during the first (split-night) study. Furthermore, the major problem with split-night polysomnography is a tendency to underestimate the CPAP requirement in OSA.[12,34] Such an error, with a low initial CPAP determination, would bias against a positive result in the current study.

As an additional criticism of this study, it could be argued that the use of an automatically titrating CPAP device would provide a more objective determination of the change in CPAP requirement over time. Certainly, the lack of any operator involvement is an attractive aspect of such a protocol. Our decision to perform CPAP titrations by an experienced technician, rather than to use the autosetting CPAP device, was based on several arguments: (1) lack of validation studies against standard manual CPAP determination in OSA; (2) lack of long-term outcome studies of patients with OSA titrated using automatic CPAP titration; (3) philosophical differences—our concern in treating patients with OSA is to optimize sleep quality—not necessarily to eliminate minor obstructions such as snoring without arousals. We attempted to minimize any operator bias by (1) performing the study in single-blind fashion such that the technician performing the titrations was not informed of the optimal pressure determination by the clinical polysomnographer, and (2) recoding all studies into random numbers and using the opinion of the blinded clinical polysomnographer as to the optimal CPAP pressure in a given body position and sleep stage.

One weakness of the current study is that the control group of patients was not studied concurrently. Indeed, it was the intention of the authors to use patients as their own control subjects in single-blind crossover fashion. However, when the differences in outcome measures became apparent during analysis of part 1 of the study, the question arose as to whether the observed improvements in subjective sleepiness and mood were related to time receiving CPAP treatment or to CPAP reduction. Although the authors could not have preempted this outcome, we attempted to address this question by studying a group of control subjects (patients with OSA in whom CPAP was left unaltered) over an identical period.

Possibly as a result of high CPAP compliance rates, the functional outcome in this study was excellent. This excellent result in terms of daytime alertness in the current study testifies to the accuracy of the CPAP titrations performed. Indeed, the MWT mean sleep onset latencies in this study, after each 2-week treatment limb, were within the range for normal subjects.[17]

This is a better outcome from CPAP treatment than others have reported in patients with less severe OSA.[8,35] Furthermore, whereas even a single night without adequate CPAP treatment results in significant daytime sequelae from OSA,[7] the adjustment to lower CPAP after 2 weeks in the present protocol was not associated with any subjective or objective deterioration.

Patients (parts 1 and 2) in this study complied satisfactorily with CPAP (average use >6 h) both before and after reducing the CPAP. It has been suggested that patients with severe OSA may be more motivated to use CPAP because of greater disease-related sequelae.[10] As mentioned earlier, most patients who decline CPAP treatment for OSA do so early.[9,10] Subjective sleepiness tended to decrease in the second 2-week period as compared with the first, in both parts of the study, but this reduction in subjective sleepiness was statistically significant only in part one of the study. Our two-way analysis revealed no group effect on ESS related to CPAP reduction. Furthermore, analysis of the change in ESS scores for the total patient group studied (20 patients) shows significantly lower ESS scores at T_4 (5.2 [SD 5.1]) than T_2 (7.5 [SD 3.9]; $p=0.0002$). This leads the authors to believe that there is a time-dependent effect in the decrement in ESS scores in addition to any putative effect related to pressure reduction. For example, acclimatization to the CPAP machine may improve comfort with its use over time and may thus improve subjective sleepiness over the 2 weeks between T_2 and T_4.

Why was no benefit in objective alertness noted to correspond with the observed subjective improvement in daytime sleepiness in the retitrated patients (part 1), and why were there no significant between-group differences in subjective or objective measures? There are several possible explanations for these findings: (1) a "ceiling effect"—CPAP compliance in this study was better than could have been expected from available literature;[8,10,11,35] perhaps as a result of this, patients may have already achieved an optimal response with CPAP under both conditions, making it very difficult to discern between group differences; (2) an improvement related to

Table 2—*Power Analysis*

Variable	Groups Being Compared	Estimated True Difference	Standardized Difference	Statistical Power, % (α=0.05)
CPAP	Patients: T_0–T_2	2 cmH20[7,32]	1.8	95
ESS score	Control subjects: (T_0–T_2) to (T_2–T_4)	3.5[20]	1.3	95
ESS score change	Patients vs control subjects (T_0–T_2) to (T_2–T_4)	3.5[20]	1.06	90
MWT sleep latency	Patients: T_2–T_4	7 minutes[18]	1.4	95
HAD score*	Patients: T_2–T_4	1.9[8]	1.05	90
HAD score	Control subjects: T_2–T_4	2.5[35]	1.0	90

*HAD=Hospital Anxiety Depression Scale.

duration of CPAP treatment rather than CPAP reduction (see above); and (3) true divergence of subjective sleepiness and objective alertness measures. Available literature shows a loose correlation only between subjective and objective measures of sleepiness and alertness such that it is not surprising to find a change in subjective sleepiness without any corresponding objective change.[36–39] The current study showed some internal consistency in that the ESS scores and the MWT latencies were both in the normal range at 2 and 4 weeks after commencement of CPAP treatment in the retitrated patients, confirming a satisfactory treatment response that was well maintained after reduction of the CPAP. Thus, our findings could be construed as a gradual acclimatization to using CPAP over the first few weeks of treatment, possibly facilitated by eliminating superfluous pressure during part 1 of the current study.

Adverse mood changes such as irritability, impatience, or depressive manifestations are common in patients with OSA.[8,40] These manifestations appear to be related to the severity of OSA, and they improve with CPAP treatment.[8] A decrease in the subjective anxiety level accompanied a reduction in CPAP in patients with severe OSA (part 1). There was no change in the anxiety scores over time in the control group (part 2). Unlike the trend in ESS scores, there was no obvious time-dependent fall in anxiety scores in the total patient group. The fall in anxiety scores in the retitrated group could represent an improvement related to CPAP comfort associated with subjective sleep quality. Previous work in patients with nocturnal asthma, for example, has demonstrated significant differences in Hospital Anxiety Scale scores between patients and normal subjects in association with minor changes in sleep architecture and without any difference in objective daytime sleepiness.[41]

The power analysis for this study is presented in Table 2. Based on previous experience over 8 months[32] and 1 year,[7] it seemed reasonable to expect a decrement in CPAP of around 2 cm H_2O in the current study. The SD for the change in CPAP (part 1) between T_0 and T_2 was 1.1 cm H_2O. Applying this information and adjusting for pairwise comparisons,[42] 10 complete data sets provided a statistical power of 95% (α=0.05) to detect a 2-cm H_2O difference in CPAP requirement between T_0 and T_2/T_4. Similarly, because the data spread among the patient and control groups for the other outcome variables were narrow, the study afforded satisfactory statistical power to detect clinically important change in these variables.

The primary purpose of monitoring CPAP compliance in the current protocol was for quality control—to protect against false assumptions based on differences in CPAP use rather than adjustment of CPAP. A longer-term study would be required to evaluate whether reducing the CPAP by an average of 2 cm H_2O would alter compliance with CPAP treatment in the clinical setting. It is interesting to note, however, that use of a lower expiratory positive airway pressure alone (bilevel positive airway pressure) did not increase compliance or make an obvious improvement to patient comfort in comparison to CPAP, in one group of patients with OSA.[43]

In conclusion, CPAP requirement changes soon after commencing treatment in patients with severe OSA. Reducing the CPAP after 2 weeks was associated with some small subjective improvements in sleepiness and mood over the ensuing 2 weeks, in patients with severe OSA. Reducing the CPAP after 2 weeks was not associated with any deterioration in daytime alertness, which was normal after instituting CPAP treatment. The authors do not recommend routinely repeating CPAP titrations on patients with severe OSA who have recently commenced CPAP treatment. Rather, from a clinical perspective, the findings suggest that it may be safe and reasonable to make a small reduction in the CPAP in those patients with severe OSA who complain of pressure-related discomfort within the first few weeks of CPAP treatment, despite a recent accurate CPAP titration.

References

1 Sullivan CE, Issa FG, Berthon-Jones M, et al. Reversal of obstructive sleep apnea by continuous positive airway pres-

sure applied through the nares. Lancet 1981; 1:862–865
2 Kryger MH. Management of obstructive sleep apnea. Clin Chest Med 1992; 13:481–492
3 Lamphere J, Roehrs TR, Wittig F, et al. Recovery of alertness after CPAP in apnea. Chest 1989; 96:1364–1367
4 He J, Kryger MH, Zorick FJ, et al. Mortality and apnea index in obstructive sleep apnea: experience in 385 male patients. Chest 1988; 94:9–14
5 Sforza E, Krieger J, Weitzenblum E, et al. Long-term effects of treatment with nasal continuous positive airway pressure on daytime lung function and pulmonary hemodynamics in patients with obstructive sleep apnea. Am Rev Respir Dis 1990; 141:866–870
6 Rajagopal KR, Bennett LL, Dillard TA, et al. Overnight nasal CPAP improves hypersomnolence in sleep apnea. Chest 1986; 90:172–176
7 Sforza E, Lugaresi E. Daytime sleepiness and nasal continuous positive airway pressure therapy in obstructive sleep apnea syndrome patients: effects of chronic treatment and 1-night therapy withdrawal. Sleep 1995; 18:195–201
8 Engelman HM, Martin SE, Deary IJ, et al. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. Lancet 1994; 343:572–575
9 Guilleminault C, Stoohs R, Clerk A. Daytime somnolence: therapeutic approaches. Neurophysiol Clin 1993; 23:23–33
10 Reeves-Hoche MK, Meck R, Zwillich CW, et al. Nasal CPAP: an objective evaluation of patient compliance. Am J Respir Crit Care Med 1994; 149:149–154
11 Pèpin JL, Leger P, Veale D, et al. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome. Chest 1995; 107:375–381
12 Sanders MH, Kern NB, Constantino JP, et al. Adequacy of prescribing positive airway pressure therapy by mask for sleep apnea on the basis of a partial-night trial. Am Rev Respir Dis 1993; 147:1169–1174
13 Barrone Kribbs N, 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; 147:887–895
14 Mortimore IL, Bradley PA, Murray JAM, et al. Uvulopalatopharyngoplasty may compromise nasal CPAP therapy in sleep apnea syndrome. Am J Respir Crit Care Med 1996; 154: 1759–1762
15 Ryan CF, Lowe AA, Li Det al. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after chronic nasal continuous positive airway pressure therapy. Am Rev Respir Dis 1991; 144:939–944
16 Mitler MM, Gujavarty KS, Browman CP. Maintenance of wakefulness test: a polysomnographic technique for evaluating treatment in patients with excessive somnolence. Electroencephalogr Clin Neurophysiol 1982; 53:658–661
17 Doghramji K, Mitler M, Sangal RB, et al. and The MWT normative study group: a normative study of the Maintenance of Wakefulness Test (MWT): preliminary report. Sleep Res 1996; 25:233
18 Poceta JS, Timms RM, Jeong DU, et al. Maintenance of Wakefulness Test in obstructive sleep apnea syndrome. Chest 1992; 101:893–897
19 Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991; 14:540–545
20 Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992; 15:376–381
21 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983; 67:361–370
22 Rechtschaffen A, Kales A. A manual of standardized terminology: techniques and scoring system for sleep stages of human subjects. Los Angeles, CA: BIS/BRI, University of California at Los Angeles, 1968; 1–15
23 American Sleep Disorders Association. EEG Arousals: scoring rules and examples. Sleep 1992; 15:173–184
24 Mortimore IL, Kochhar P, Douglas NJ. Effect of chronic continuous positive airway pressure (CPAP) therapy on upper airway size in patients with sleep apnoea/hypopnoea syndrome. Thorax 1996; 51:190–192
25 Sforza E, Krieger J, Bacon W, et al. Determinants of effective continuous positive airway pressure in obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151:1852–1856
26 Sullivan C, Issa F, Berthon-Jones M, et al. Home treatment of obstructive sleep apnea with continuous positive airway pressure applied through the nose-mask. Bull Eur Physiopathol Respir 1985; 20:49–54
27 Mortimore IL, Douglas NJ. Effect of CPAP treatment on reflex palatal muscle activity in sleep apnea patients. Am J Respir Crit Care Med 1995; 151:A537
28 Suratt PM, McTier RF, Wilhoit C. Upper airway muscle activation is augmented in patients with obstructive sleep apnea compared with that in normal subjects. Am Rev Respir Dis 1988; 137:889–894
29 Tangel DJ, Mezzanote WS, White DP. Influence of sleep on tensor palatini EMG and upper airway resistance in normal men. J Appl Physiol 1991; 62:2574–2581
30 Alex CG, Aronson RM, Onal E, et al. Effects of continuous positive airway pressure on upper airway and respiratory muscle activity. J Appl Physiol 1987; 62:2026–2030
31 Wasicko NJ, Hutt DA, Parisi RA, et al. Role of vascular tone in the control of upper airway collapsibility. Am Rev Respir Dis 1990; 141:1569–1577
32 Sériés F, Marc I, Cormier Y, et al. Required levels of nasal continuous positive airway pressure during treatment of obstructive sleep apnoea. Eur Respir J 1994; 7:1776–1781
33 Boecker MR, Shaffer JI, Neeb MJ, et al. CPAP pressure changes at follow-up. ASDA, Abstract book, 1995;A7
34 Iber C, O'Brien C, Schluter J, et al. Single night studies in obstructive sleep apnea. Sleep 1991; 14:383–385
35 Engleman HM, Martin SE, Deary IJ, et al. Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. Thorax 1997; 52:114–119
36 Carskadon MA, Dement WC. The multiple sleep latency test: what does it measure? Sleep 1985; 5:S67–S72
37 Pressman MR, Fry JM. Relationship of autonomic nervous system activity to daytime sleepiness and prior sleep. Sleep 1989; 12:239–245
38 Cook Y, Schmitt F, Berry D, et al. The effects of nocturnal sleep, sleep disordered breathing and periodic movements of sleep on the objective and subjective assessment of daytime somnolence in healthy aged adults. Sleep Res 1988; 17:95
39 Sangal RB, Thomas L, Mitler MM. Maintenance of wakefulness test and multiple sleep latency test: measurement of different abilities in patients with sleep disorders. Chest 1992; 101:898–902
40 Derderian SS, Bridenbaugh RH, Rajagopal KR. Neuropsychologic symptoms in obstructive sleep apnea improve after treatment with nasal continuous positive airway pressure. Chest 1988; 94:1023–1027
41 Fitzpatrick MF, Engleman HM, Whyte KF, et al. Morbidity in nocturnal asthma: sleep quality and daytime cognitive performance. Thorax 1991; 46:569–573
42 Altman DG. Statistics and ethics in medical research: III. How large a sample? BMJ 1980; 281:1336–1338
43 Reeves-Hoche MK, Hudgel DW, Meck R, et al. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151:443–449