Clinical Medicine

Compliance and Side Effects in Sleep Apnea Patients Treated With Nasal Continuous Positive Airway Pressure

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Nasal continuous positive airway pressure (CPAP) is an effective therapy for sleep apnea. We treated 144 patients with nasal CPAP and observed them for periods of as long as 25 months. No pneumothoraces occurred in any patient. Compliance rates were between 65% (90/139) and 83% (90/108), depending on the patient population considered. Demographic factors unrelated to discontinuing using CPAP included age, sex, and the presence of a housemate. Better-educated patients were less able to tolerate the equipment. Dry throat and nose and sore eyes were the most common side effects, but only sore eyes related to the amount of pressure. Side effects were unrelated to the number of months on the treatment, and obesity was related to higher pressures. Our study provides optimistic intermediate-term follow-up observations of patients on nasal CPAP therapy for sleep apnea. Whether adverse consequences occur over longer periods of time remains to be seen.

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Nasal continuous positive airway pressure (CPAP) therapy for sleep apnea was originally described in 1981[1] and is now a well-recognized, effective therapy for impaired respiration in sleep.[2-4] The long-term consequences of this intervention, however, and even the natural history of untreated sleep apnea, remain unclear. Until such data are available, the widespread use of CPAP by many thousands of patients requires a thorough evaluation of its compliance, side effects, and adverse reactions. Preliminary work on 24 cases suggests good compliance rates during the first year.[5] We report here on the intermediate-term efficacy and side effects in a larger group of patients followed up systematically.

Patients and Methods

We defined our sample as adult patients, 18 years or older, with diagnosed sleep apnea and originally treated with CPAP between July 1984 and June 1986 (N = 144). Patients were followed up by a questionnaire in August 1986 to allow a minimum of two months' experience for those (N = 90) who continued to use CPAP (Figure 1). Of the 144 patients, there were 3 deaths: brain-stem hemorrhage (a 68-year-old man), metastatic gastrointestinal carcinoma (a 52-year-old woman), and myocardial infarct (a 35-year-old morbidly obese man with a body mass index greater than 80). The first two patients used CPAP regularly. Two additional patients were excluded from follow-up analyses because they showed predominantly central apneas that did not respond initially in such a way as to justify the continued usage of CPAP. The demographics for the remaining 139 patients are shown in Table 1. A total of 42 of the patients had pulmonary disease. Of these, 37 suffered daytime dyspnea and 28 morning sputum production at least occasionally and 36 had a history of smoking in excess of 20 pack-years. Pulmonary function testing was not done routinely in our patients; however, 13 of the 42 patients routinely used theophylline or bronchial inhalers.

The patients who underwent our two-night CPAP protocol (to be described) represented an unselected, but certainly not random, subset of patients with sleep apnea seen in our clinic. We routinely presented CPAP as a treatment option to all patients judged to have clinically significant sleep apnea. Whether or not a patient then agreed to undergo the protocol—as did the 144 patients on whom this report is based—depended on many factors, including but not limited to third-party-payment issues; anxiety to the point of being unwilling to even attempt the protocol; a clear preference for surgical treatment to the point of being unwilling to even consider any other treatment option; and general recalcitrance. A comparison of our CPAP sample with all remaining adult patients undergoing an evaluation for sleep apnea during the aforementioned 24-month period is shown in Table 2. The CPAP group was significantly more obese and had more severe indices of sleep apnea than did the remaining clinic patients. To reiterate, the patients reported on here in no way represent a random sample of patients with sleep apnea, nor do they represent a random sample of sleep apnea patients seen in our clinic.

Most patients underwent a full night of baseline polysomnography in our sleep laboratory, although 20 polysomnograms were done elsewhere. Our CPAP protocol consists of two consecutive nights of polysomnography with pressure adjustments made on the first night and uninterrupted sleep with CPAP on the second. Conventional procedures for poly-

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ABBREVIATIONS USED IN TEXT

CPAP = continuous positive airway pressure
NS = not significant
RDI = respiratory disturbance index

somnography outlined elsewhere[6,7] were used on all nights, and Biox II or III ear oximeters were used. For convenience in sleep stage scoring,[7] we combined stages 1 and 2 and stages 3 and 4. We calculated desaturation indices of less than 90% and less than 80% by dividing the number of desaturation measurements by hours of sleep. In 28 patients, CPAP was started on the baseline night because of extreme severity of apnea. In these cases the baseline sleep measurements were calculated only for the first portion of the night. All sleep measurements during CPAP were based on the second night of CPAP of our two-night protocol. The pressure was delivered through the Respironics Nasal CPAP System (model SleepEasy).

The follow-up questionnaire is shown in Figure 2. Although any such survey instrument is limited by the veracity of self-reporting, a questionnaire does provide some cursory estimate of the frequency of side effects. Such estimates might also be a useful first step in examining the frequency of usage—for example, by more objective means[8]—or in designing clinical trials aimed at reducing the side effects of nasal CPAP. Our response rate on the mail questionnaire was relatively high (80.5%) because of telephone follow-up of the initial mailing. For those patients unwilling to complete the form, the reason for discontinuing CPAP was ascertained from a telephone interview for every case.

TABLE 1.—*Demographics of 139 Patients Using Continuous Positive Airway Pressure*

Sex	121 men, 18 women
Age, yr (range)	Mean 52.8, SD±12.4 (19-80)
Height, cm	Mean 176, SD±9.2
Weight, kg	Mean 117, SD±28.0
Body mass index	Mean 35.4, SD±8.4
Education	47.8% graduated high school or less 52.2% partial college education or higher
Housemate	13% lived alone

SD=standard deviation

Data were analyzed with parametric or nonparametric tests depending on the normality of distribution of the dependent variable. For normally distributed data, we used *t* tests for between-group comparisons and matched-pair *t* tests for within group comparisons. For non-normally distributed data, we used Mann-Whitney tests for between-group comparisons and Wilcoxon signed rank tests for within-group comparisons. We used χ^2 tests for comparing categoric data across groups. In the χ^2 tests, Yates' corrections were used when expected cell frequencies were less than 5.

Results

Pneumothorax did not develop in any of our patients. The polysomnographic data confirmed the efficacy of nasal CPAP in improving oxygenation substantially, reducing the number of disturbed breathing events, and restoring the sleep architecture to normal (Table 3). Despite this efficacy, only 90 patients continued to use CPAP when followed up in August 1986. Of the 49 persons giving up CPAP, 7 had undergone an unsuccessful upper airway operation in the past and elected not to resume the use of CPAP, 18 had no other current or past treatment, and 24 underwent other apparently successful treatments as of August 1986. These treatments included the following: an upper airway operation either successfully carried out in the past or in progress (15 patients); a tracheostomy done elsewhere after a trial with CPAP (4 patients); a tongue-retaining device prescribed elsewhere (2); gastric stapling associated with a significant weight loss (2); and low-flow oxygen (1). In some of these 24 patients, alternative treatments may have been chosen because of dissatisfaction with nasal CPAP.

Several different estimates of compliance can be derived from these figures. For example, if we assumed the patients choosing other treatments did so primarily because of dissatisfaction with CPAP, we obtained a somewhat strict compliance estimate of 64.7% (90/139). A more liberal compliance estimate (83.3%) related only those patients able to tolerate CPAP to those who chose no other treatment (90/108). An intermediate estimate of compliance (78.3%) included the 18 patients who did not use CPAP and the 7 who had an unsuccessful operation and did not resume using CPAP (90/115). For purposes of further analysis, we used the latter 25 cases as a comparative CPAP-discontinued group.

The primary reasons for discontinuing treatment in the

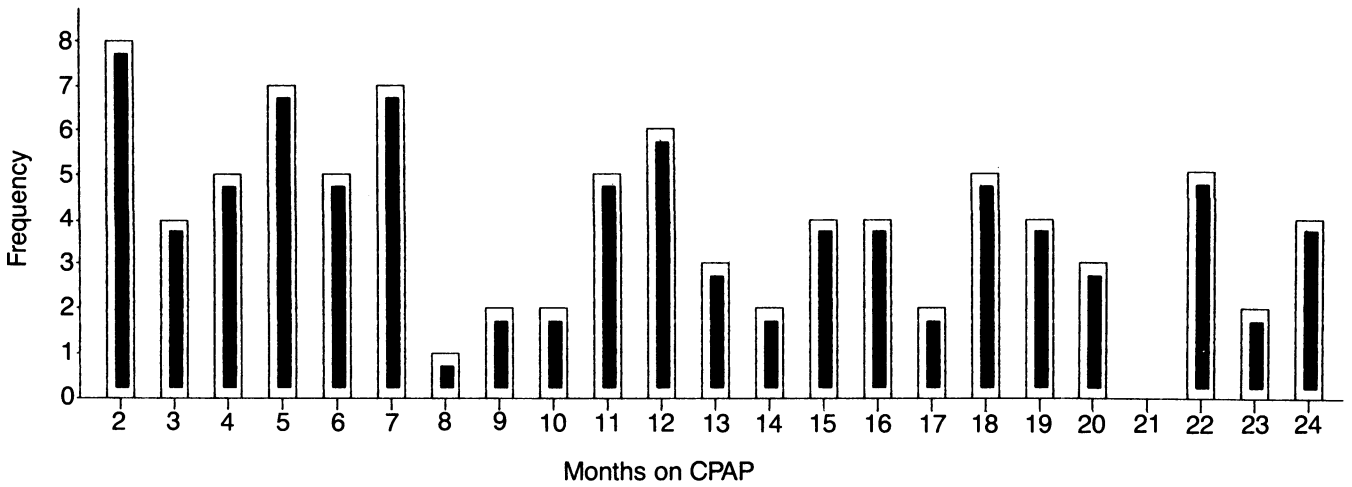

Figure 1.—The frequency histogram shows the number of months on nasal continuous positive airway pressure (CPAP) therapy for 90 patients with at least two months of use (current CPAP group).

TABLE 2.—*Patients Using Continuous Positive Airway Pressure (CPAP) and Remaining Patients Undergoing Sleep Apnea Evaluation*

Descriptor	Evaluation: CPAP Patients, N=139 Mean±SD	Evaluation: Other Patients, N=523 Mean±SD	Significant Difference
Male, %	87.1	80.9	NS
Age, yr	52.8±12.4	50.5±12.9	NS
Body mass index	35.4± 8.4	30.5± 7.2	t= 7.28, P<.0001
Respiratory disturbance index	80.8±38.8	37.1±36.0	t=11.78, P<.0001
Lowest SaO_2 % REM sleep	63.6±17.8	79.9±14.4	t=10.19, P<.0001
Lowest SaO_2 % non-REM sleep	72.3±14.2	83.3±11.0	t= 9.24, P<.0001
SaO_2 <90% index	62.4±53.2	18.3±34.2	t=11.14, P<.0001
SaO_2 <80% index	24.4±43.2	6.1±19.8	t= 6.85, P<.0001

NS=not significant, REM=rapid eye movement, SaO_2=arterial oxygen saturation, SD=standard deviation

comparative group were physical side effects (7 patients), dislike of the system (5 patients), and insomnia or anxiety (5 patients). The other eight patients discontinued using CPAP for miscellaneous reasons. The physical side effects included tinnitus, otitis media, dry mouth, and mask-induced facial pain. Of the 25 comparative cases, 10 used CPAP at home for two weeks or less, though one person used it for 17 months (mean, 3.6 months). Those patients who discontinued using CPAP within two weeks did so because of anxiety or dislike of the system.

The group currently using CPAP and the CPAP-discontinued group are compared in Table 4. Except for educational level, no other demographic feature distinguished the groups. In addition, no differences were seen between the groups in the proportion suffering from pulmonary disease. The CPAP-discontinued group had relatively less severe sleep apnea on baseline polysomnography but still showed substantial sleep-disordered breathing and oxygen desaturation, and it also showed less improvement in sleep oxygenation measures than the current CPAP group.

The mean weight for the group currently using CPAP was 117 kg at baseline and 110 kg at follow-up (t=4.38, P < .001). Although this was a statistically significant decrease, pronounced weight loss was infrequent. Only 17 patients lost more than 10% of their baseline weight, and only 5 lost more than 20% of their baseline weight. There was no relationship between months on CPAP treatment and weight loss (r = −.09, not significant [NS]).

The continuous positive airway pressure was delivered at pressures between 7.5 and 15.0 cm of water. The amount of pressure was unrelated to age but was correlated with body mass index at baseline (ρ = .32, P < .001) as well as with severity of sleep apnea on baseline (ρ = .32 with the respiratory disturbance index; ρ = .37, with < 90% O_2 index; ρ = .38 with < 80% O_2 index; all P < .001).

We examined by checklist the side effects experienced by the 90 patients regularly using CPAP at follow-up (Table 5) and the reasons for not using CPAP nightly (Table 6). None of the factors in Tables 5 and 6 were related to sex or having a housemate. A dry nose was more frequently reported by the older patients (r = .24, P < .05), but age was generally unrelated to side effects. The amount of pressure was also unre-

TABLE 3.—*Baseline and Continuous Positive Airway Pressure (CPAP) Sleep Data*

Sleep Variable	Baseline Mean±SD	CPAP Mean±SD	Significant Difference*
RDI†	80.8±38.8	9.9±14.3	z= 9.3
Stages 1 and 2, %	88.0± 9.2	70.8±14.6	z= 8.5
Stages 3 and 4, %	2.3± 6.7	9.6±10.5	z= 7.6
REM, %	8.2± 6.1	19.6± 9.4	t=10.6
Lowest SaO_2 % REM sleep	63.6±17.8	87.3±10.6	z= 8.4
Lowest SaO_2 % non-REM sleep	72.3±14.2	88.9± 5.6	z= 9.2
SaO_2 <90% index‡	62.4±53.2	2.5± 7.2	z= 9.1
SaO_2 <80% index‡	24.4±43.2	0.1± 0.6	z= 7.8

REM=rapid eye movement, SaO_2=arterial oxygen saturation, SD=standard deviation

*All differences significant at P<.0001.
†Respiratory disturbance index (number of episodes of apnea and hypopnea per sleep hour).
‡Desaturation index (number of desaturations per sleep hour).

1. If you are *not* using the CPAP device on a regular basis, please state reasons for discontinuing the treatment _____.

   If you *are* currently using the CPAP device on a regular basis, please *continue* to answer this form.
2. Since you began to use the CPAP device, what percentage (%) of nights have you *not* used it?__%. (Although we do not expect an absolutely exact figure, try to be as accurate as possible.)
3. After using the device for a night, do you experience any of the following (circle whichever applies):
   (a) confusion and disorientation after waking
   (b) unusual sleepiness
   (c) unusual fatigue
   (d) headaches
   (e) dryness of the throat
   (f) dryness of the nose
   (g) buzzing in the ears
   (h) sore eyes
   (i) other; please explain _____
4. On the days when you have not used the device, the reason has been (circle whichever applies):
   (a) severe nasal obstruction caused by allergies or colds
   (b) unavailable electrical outlet
   (c) traveling without the device
   (d) failure of mask
   (e) failure of the device or other elements used apart from mask
   (f) being frightened of the device
   (g) being tired of using the device every night
   (h) disturbs sleep of bed partner
   (i) other; please explain _____

Rate satisfaction with CPAP from 1 to 10

1 2 3 4 5 6 7 8 9 10

(1 = very unhappy; 10 = very satisfied)

Figure 2.—This questionnaire was sent to patients using continuous positive airway pressure (CPAP) for sleep apnea.

TABLE 4.—*Groups Currently Using and Discontinued Using Continuous Positive Airway Pressure (CPAP)*

Patient Data	CPAP Use: Currently	CPAP Use: Discontinued	Significant Difference
Age, yr*	52.3±12.5	55.1±12.4	NS
Sex	12 F, 78 M	2 F, 23 M	NS
Body mass index*	37.2± 8.9	32.6± 6.2	t=2.94, P<.01
CPAP pressure, cm water*	12.5± 2.4	11.4± 2.6	z=1.77, P<.08
High school graduate or less, %	55.7	33.3	χ^2=3.77, P<.05
Has housemate, %	87.5	83.3	NS
RDI baseline*	84.8±43.5	69.9±28.9	t=1.95, P<.06
SaO_2<90% index baseline*	71.1±59.1	36.0±34.0	z=2.85, P<.005
SaO_2<80% index baseline*	31.9±50.1	7.0±15.2	z=3.05, P<.003
RDI change on CPAP*†	12.1±12.2	8.8±11.1	NS
SaO_2<90% index change on CPAP, mean†	−67.1	−37.1	z=2.44, P<.02
SaO_2<80% index change on CPAP, mean†	−32.9	− 6.4	z=2.79, P<.01

NS=not significant, RDI=respiratory disturbance index, SaO_2=arterial oxygen saturation

*Numbers are given as the mean ± standard deviation.
†Change score calculated as (post-CPAP value minus pre-CPAP value).

TABLE 5.—*Incidence of Side Effects From Continuous Positive Airway Pressure*

Side Effect	Incidence, %
Dry throat	69
Dry nose	52
Sore eyes	30
Headache	16
Unusual sleepiness	15
Unusual fatigue	15
Tinnitus	12
Other nasal problems including rhinorrhea	14*
Mask discomfort	6*

*Items were not included on checklist but were spontaneously reported.

TABLE 6.—*Incidence of Reasons for Not Using Continuous Positive Airway Pressure Nightly*

Reason	Incidence, %
Nasal obstruction	34
Travel	28
Tired of device	23
Mask failure	20
Inconvenient electrical outlet	12
Device failure	12
Partner disturbed	7
Afraid of device	2

lated to side effects, as were months on treatment, except that the amount of pressure was correlated with the symptom of sore eyes ($\rho = .27$, $P < .02$). Patients were generally satisfied with CPAP, giving a mean rating of 7.5 on a 1-to-10 scale. Satisfaction with CPAP was highest in those patients losing the most weight ($\rho = -.28$, $P < .02$). Nonetheless, only 60 patients reported using CPAP every night or nearly every night (95% or more of the time); far more likely was usage on at least a half-time basis (86 patients). Satisfaction was highly related to the percentage of nights when CPAP was used ($r = .43$, $P < .001$).

On baseline, patients with pulmonary disease did not differ from those without pulmonary disease in their respiratory disturbance index (86.3 versus 77.8, $z = .11$, NS), <90% O_2 index (69.0 versus 58.5, $z = 1.00$, NS) or <80% O_2 index (32.8 versus 20.3, $z = .33$, NS). On CPAP, pulmonary disease patients benefited equally well in terms of disturbed breathing events (for the respiratory disturbance index, 13.0 versus 9.1, $z = 1.14$, NS) though they still showed some mild desaturation (for <90% O_2 index, 4.7 versus 2.0, $z = 2.10$, $P < .05$; for <80% O_2 index, 0.3 versus 0.1, $z = 2.73$, $P < .01$). The pulmonary disease patients did not require higher CPAP pressures (12.7 versus 12.0, $t = 1.52$, NS), nor did they report more side effects than patients without pulmonary disease.

Discussion

Nasal CPAP appears to be well suited to most subgroups of patients studied here. Although the percentage of women in our study at 15% is greater than that reported in many studies, there was no suggestion that women had any more difficulty with nasal CPAP. This may be noteworthy in that, at least in some studies, women may be more prone to external disruption of sleep than men.[9,10] Of our 90 patients continuing to use CPAP, 15 were older than 65 years, suggesting that aged patients also were well suited for this treatment despite the fact that their sleep is physiologically more likely to be fragmented.[11] With growing concern over sleep apnea in the elderly and its possible consequences,[12,13] more geriatric patients may be using CPAP in the future. Finally, CPAP was effective in patients with pulmonary disease. No evidence of barotrauma has occurred in any of these latter patients, and the mean continuous positive airway pressure was similar.

When considering compliance, estimates should take into account all treatment options when patients discontinue nasal CPAP. In the strictest estimate of compliance (64.7%), those persons using CPAP as a temporary measure while awaiting an upper airway operation were considered noncompliant because such patients, having tried nasal CPAP and finding it effective, still opted for surgical treatment. Such an estimate may be biased against nasal CPAP, however, inasmuch as many patients simply prefer a surgical procedure over the nightly use of bedside equipment on an a priori basis. Obviously, any figures for CPAP compliance must take into account local treatment options available for patients with sleep apnea. Indeed, we think the availability of surgical treatment in our area makes this a more feasible choice than may be the

case elsewhere. Our compliance rates must also take into account our procedures for indoctrinating patients into nasal CPAP. In brief, we specially schedule each patient for an approximately one-hour daytime session with a polysomnographic technologist before the two-night CPAP protocol. This session, together with a weekly phone call from the technologist to the patient, particularly in the first few weeks of CPAP therapy, may promote compliance.

Why some patients discontinued using nasal CPAP and others did not was unclear. The group differences in change in oxygenation (Table 4) imply that those who discontinued may have received less symptomatic relief. As for other factors, none of the obvious demographics (age, sex, presence of a housemate) distinguished the patients who discontinued using nasal CPAP from those who did not. Curiously, the compliant group has had less formal education than the noncompliant group. The meaning of this finding is unclear. We speculate that the psychosocial impact of a mandatory nightly medical appliance is more tolerable to people who may be less skeptical of medical treatment in general. As an additional note, we must point out that even among our compliant group, nightly use was reported in only two thirds of the sample. As Krieger and Kurtz have suggested,[8] the veracity of such self-reported use may be discrepant from measurements of use based on actually using the CPAP unit. Nonetheless, it is clear that many patients apparently titrate their use without supervision by their physician. Whether such titration will ultimately have deleterious effects is unclear. What is clear is that any long-term follow-up study of CPAP patients must evaluate morbidity and mortality relative to the frequency of use.

Many of the physical side effects experienced by patients undergoing nasal CPAP may be ameliorated. For example, dryness of the upper airway and rhinorrhea are often improved with ultrasonic humidification, and soreness of the eyes suggests that an improperly fitting or worn mask should be replaced. We were impressed with the fact that the presence of such side effects was unrelated to the number of months on CPAP therapy. This suggests that the dry nose experienced by many CPAP patients, for example, does not lessen with the passage of time, but neither does it become worse. This is reassuring for those patients with few problems at the initiation of treatment. A simple dislike of the system and insomnia or anxiety played a major role in all of the patients giving up nasal CPAP rapidly. Nearly half of those patients giving up using nasal CPAP and opting for no other treatment did so in the initial two weeks. Apparently this initial period is the most critical and sensitive phase for adjusting to nasal CPAP and the time during which maximum support from the sleep clinic staff is required. Whether or not more frequent, such as daily, contact with staff would further increase compliance remains unanswered.

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