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Treatment with Continuous Positive Airway Pressure Is Not Effective in Patients with Sleep Apnea but No Daytime Sleepiness

A Randomized, Controlled Trial

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Background: **The sleep apnea–hypopnea syndrome is defined by a pathologic number of respiratory events during sleep (the apnea–hypopnea index, defined as the number of apnea and hypopnea episodes per hour) and daytime symptoms (mostly, excessive sleepiness). In patients with the sleep apnea syndrome, treatment with continuous positive airway pressure (CPAP) normalizes both the apnea–hypopnea index and diurnal symptoms. However, the effect of CPAP in persons with a pathologic apnea–hypopnea index without daytime sleepiness is unclear.**

Objective: **To investigate the short-term effects of CPAP on quality of life, objective sleepiness, cognitive function, and arterial blood pressure in nonsleepy patients with a pathologic apnea–hypopnea index.**

Design: **Multicenter randomized, placebo-controlled, parallel-group study.**

Setting: **Six teaching hospitals in Spain.**

Patients: **55 patients with an apnea–hypopnea index of 30 or greater who did not have daytime sleepiness (Epworth Sleepiness Scale score ≤ 10).**

Intervention: **Patients were randomly assigned to receive optimal ($n = 29$) or sham ($n = 25$) CPAP and were observed for 6 weeks.**

Measurements: **Quality of life, objective sleepiness (Multiple Sleep Latency Test score), cognitive function, and arterial blood pressure.**

Results: **The intervention and control groups were similar in terms of mean (±SE) age (54 ± 2 vs. 52 ± 2 years), apnea–hypopnea index (54 ± 3 vs. 57 ± 4), Epworth Sleepiness Scale score (7.0 ± 0.4 vs. 7.0 ± 0.4) and adherence to CPAP treatment (5.0 ± 0.4 vs. 4.0 ± 0.5 hours/d). Other variables, such as quality of life, cognitive function, and arterial blood pressure, were also similar in both groups before treatment. After 6 weeks of CPAP or sham CPAP, none of these variables changed significantly.**

Conclusion: **In patients with an apnea–hypopnea index of 30 or greater and no subjective daytime sleepiness, CPAP does not modify quality of life, objective sleepiness, vigilance, attention, memory, information processing, visuomotor coordination, or arterial blood pressure. Treatment with CPAP is therefore not indicated in nonsleepy patients with a pathologic apnea–hypopnea index.**

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See editorial comment on pp 1065-1067.

The sleep apnea–hypopnea syndrome is currently defined by the presence of a pathologic number of episodes of cessation (apnea) or reduction (hypopnea) of respiratory flow during sleep (the apnea–hypopnea index, defined as the number of apnea and hypopnea episodes per hour). This syndrome is normally associated with arterial desaturation, sleep disruption (arousals), severe snoring, and excessive daytime sleepiness (1). Nasal continuous positive airway pressure (CPAP) is the treatment of choice for the sleep apnea–hypopnea syndrome (2, 3). Several randomized, placebo-controlled studies have shown that CPAP improves subjective and objective daytime sleepiness, quality of life, cognitive performance, and psychological well-being in patients with this syndrome (4–9). The effects of CPAP on other clinically relevant variables, such as prognosis and incidence of cardiovascular events or traffic accidents, are unclear (10). The available evidence therefore supports the notion that CPAP is an effective symptomatic treatment for patients with the sleep apnea–hypopnea syndrome.

Epidemiologic studies report that many persons with an apnea–hypopnea index of at least 5 do not experience daytime sleepiness (11). In clinical practice, these patients are commonly referred to consultation by their partner (who observed apneas during sleep) or by an otorhinolaryngologist (who ordered a polysomnographic study before surgery for snoring). Whether these nonsleepy patients with a pathologic apnea–hypopnea index require treatment with CPAP is unclear (12, 13).

On the one hand, it may be argued that they do not need treatment because they do not have symptoms; moreover, the available evidence relates only to the efficacy of CPAP treatment on such symptoms. On the other hand, because the sleep apnea–hypopnea syndrome is a chronic, slowly progressing disease, patients with this syndrome may perceive their symptoms poorly. If this is the case, treatment with CPAP may substantially improve their well-being and quality of life. In addition, CPAP treatment of nonsleepy patients may have other potentially relevant biological effects, such as control of arterial hypertension, which is common in the sleep apnea–hypopnea syndrome (14) but often goes unnoticed.

We designed a multicenter randomized, placebo-controlled, parallel-group study to evaluate the short-term (6 weeks) effects of CPAP on quality of life, objective sleepiness, cognitive function, and arterial blood pressure in nonsleepy patients with a pathologic apnea–hypopnea index.

METHODS

Patients

Participants were recruited prospectively from patients attending the sleep units of six teaching hospitals in Spain from August 1999 to March 2000. All participants had an apnea–hypopnea index of 30 or greater, as determined during a full, supervised, standard polysomnographic study; had Epworth Sleepiness Scale scores of 10 or less (15); and had no or mild daytime sleepiness, according to the International Classification of Sleep Disorders (16). Patients were excluded if they had cognitive deterioration of any cause, a chronic underlying disease that may affect their quality of life, or severe cardiac disease; had less than 8 years of formal education; or used illicit drugs or drank excessive alcohol.

The ethics committee of all participating institutions approved the study protocol, and all participants gave written consent after they were informed of the characteristics of the investigation. However, participants remained blinded to the hypothesis of the study.

Design

We designed a multicenter randomized, placebo-controlled, parallel-group study. A computer-generated random-number list generated with SPSS software (SPSS, Inc., Chicago, Illinois) was used to assign patients to receive CPAP or sham CPAP. In all participants, we measured the following variables at baseline and after 6 weeks of treatment with CPAP or sham CPAP: 1) quality of life; 2) degree of sleepiness; 3) different psychological variables, such as attention, vigilance, visual memory, coordination, and mental control; 4) arterial blood pressure on ambulatory monitoring; and 5) drug intake and alcohol consumption, as potential confounding variables.

Patients assigned to the CPAP group received treatment with optimal nasal CPAP at home for 6 weeks (Respironics, Inc., Murrisville, Pennsylvania). The optimal nasal CPAP pressure was determined during a full-night polysomnographic study as the pressure necessary to abolish all respiratory events and snoring, secondary arousals, and episodes of oxyhemoglobin desaturation during rapid eye movement sleep and in the supine position. Patients assigned to sham CPAP received this treatment at home during 6 weeks, using the method described by Farré and colleagues (17). These patients also underwent a sham titration polysomnographic study in which no pressure was added.

According to the randomization schedule, the morning after the CPAP trial, patients were sent home with a CPAP or sham CPAP device. During the study, all participants had telephone access to researchers for advice if required.

Measurements

Polysomnographic studies included recording of oronasal flow and thoracoabdominal movements, electrocardiography, submental and pretibial electromyography, electroculography, electroencephalography (C_4–A_1 and C_3–A_2), and transcutaneous measurement of arterial oxygen saturation. A polysomnographic study was considered valid for scoring if the total sleep time was longer than 240 minutes. Sleep scoring was standardized according to international criteria (18). Respiratory events (apneas and hypopneas) were scored according to criteria proposed by the Spanish Respiratory Society (19), which defined apneas as cessation of respiratory flow for more than 10 seconds and hypopneas as a significant reduction in respiratory flow followed by an arousal (as defined by Collard and associates [20]) or an episode of arterial oxygen desaturation greater than 4%.

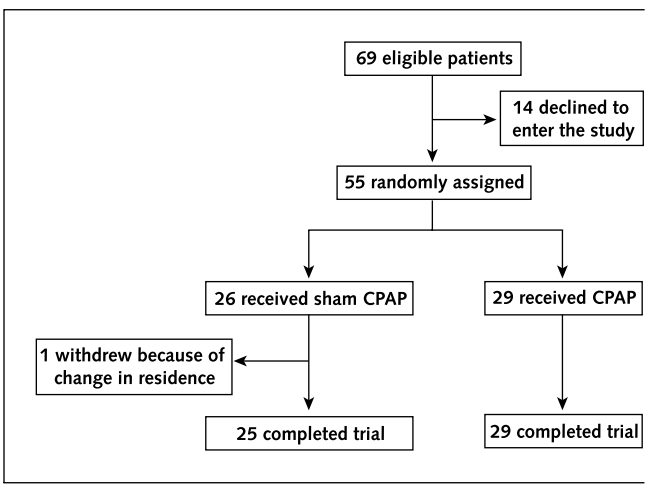
The apnea–hypopnea index was defined as the sum of the number of apneas plus hypopneas per hour of sleep. The arousal index indicates the number of arousals per hour of sleep.

Quality of life was quantified by using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (21) and the Functional Outcomes of Sleep Questionnaire (FOSQ) (22). The degree of sleepiness was assessed by using the Multiple Sleep Latency Test (1) (MSLT) and the Epworth Sleepiness Scale (15). The technicians who scored the MSLT were blinded to the patients' treatment assignments. Patients filled out the Epworth Sleepiness Scale themselves, without input from family or friends. Attention, vigilance, visual memory, and coordination were assessed by using the following psychological tests: digit span, block design, and digit symbols from the Wechsler Adult Intelligence Scale (23); mental control and verbal paired associates from the Wechsler Memory Scale (24); the Paced Auditory Serial Addition Test (PASAT); and the trail making test (25). A psychologist administered or supervised (in the case of the SF-36, the FOSQ, and the Epworth Sleepiness Scale) these tests between 9 a.m. and noon and in the absence of family or friends. Psychologists were aware of the study hypothesis but were blinded to patient treatment assignments.

Ambulatory blood pressure (Spacelabs Medical, Redmond, Washington) was recorded 3 days before the MSLT was administered. Systolic and diastolic blood pressure values were measured for 24 hours. At least 60 data points were recorded in each patient. The average daytime (8:00 to 22:00) and nighttime (22:00 to 8:00) values were calculated. Patients were classified as "non-dippers" if the systolic or diastolic blood pressure at night did not decrease by more than 10% of diurnal values (26).

Adherence to CPAP or sham CPAP was assessed by using the timer built into each CPAP device. At the end of the study period, we recorded the presence or absence of several potential side effects of therapy, such as claustrophobia, morning headache, insomnia, nose or ear pain, skin lesions, bleeding, and dryness of the oropharyngeal mucosa.

Figure 1. **Trial design.**



CPAP = continuous positive airway pressure.

Table 1. **Anthropometric Data at Baseline in Study Participants***

Characteristic	CPAP Group (n = 29)	Sham CPAP Group (n = 25)
Age, *y*	54 ± 2	52 ± 2
Women, *n*	3	2
Body mass index, kg/m^2	29 ± 1	29 ± 0.4
Apnea index†	30 ± 4	34 ± 5
Apnea–hypopnea index†	54 ± 3	57 ± 4
Arousal index†	44 ± 3	49 ± 4
Adherence to therapy, *h/d*	5 ± 0.4	4 ± 0.5
CPAP pressure, $cm\ H_2O$	8 ± 0.2	–
Alcohol consumption, *g/d*		
Daily	11 ± 4	17 ± 4
Weekends	19 ± 4	25 ± 5

* Unless otherwise indicated, data are the mean ± SE. CPAP = continuous positive airway pressure.
† Number of events per hour.

Statistical Analysis

The study was powered according to the findings of Jenkinson and colleagues (8). In brief, quality of life (assessed by the SF-36 questionnaire) was the main outcome variable. We expected a mean difference of 9 in the change in the SF-36 questionnaire score after treatment between the CPAP and the sham CPAP group. Accordingly, we calculated that for a two-sided test, 25 patients in each group had to complete the study if a standard deviation of 9.5, an α error of 0.5, and a β error of 0.1 were assumed.

Results are given as the mean (±SE). For the main outcome variables, the 95% CI is also given. A two-tailed *t*-test for independent samples or a chi-square test was used to compare anthropometric and clinical vari-

Table 2. **Quality of Life, Daytime Sleepiness, and Results on Psychological Tests before and after 6 Weeks of Treatment***

Measure	CPAP		
	Before	After	Difference
SF-36			
PCS score	49 ± 1 (46 to 51)	51 ± 1 (49 to 53)	2 ± 1 (0 to 5)
MCS score	51 ± 2 (48 to 55)	51 ± 2 (47 to 54)	−1 ± 2 (−4 to 2)
FOSQ score	102 ± 3 (95 to 108)	108 ± 2 (104 to 113)	7 ± 2 (2 to 12)
Epworth Sleepiness Scale score	7 ± 0.4 (6 to 8)	8 ± 0.6 (7 to 10)	1 ± 1 (0 to 2)
MSLT score, *min*	12 ± 1 (9 to 14)	13 ± 1 (11 to 15)	1 ± 1 (−1 to 3)
Hits on Steer-Clear test, %	5 ± 1 (2 to 7)	4 ± 1 (2 to 5)	−1 ± 1 (−3 to 0)
Wechsler Adult Intelligence Scale			
Digit symbols	42 ± 2 (37 to 47)	43 ± 3 (38 to 48)	1 ± 1 (−1 to 3)
Block design	33 ± 1 (30 to 36)	34 ± 1 (31 to 36)	1 ± 1 (−1 to 3)
Digit span	9 ± 0.3 (8 to 10)	9 ± 0.3 (8 to 10)	0 ± 0.3 (−1 to 1)
PASAT 1	15 ± 1 (14 to 16)	15 ± 1 (13 to 17)	0 ± 1 (−2 to 1)
PASAT 2	14 ± 1 (12 to 16)	16 ± 1 (14 to 17)	2 ± 1 (1 to 3)
PASAT 3	10 ± 1 (8 to 12)	12 ± 1 (11 to 14)	2 ± 1 (1 to 3)
PASAT 4	5 ± 1 (3 to 6)	5 ± 1 (4 to 7)	1 ± 0.4 (0 to 1)
Trail making test, *s*			
Part A	49 ± 4 (41 to 56)	47 ± 3 (41 to 53)	−2 ± 2 (−7 to 3)
Part B	122 ± 16 (89 to 155)	96 ± 6 (83 to 109)	−27 ± 14 (−55 to 2)
Wechsler Memory Scale			
Mental control	6 ± 0.4 (5 to 6)	6 ± 0.4 (5 to 7)	0 ± 0.3 (−1 to 1)
Verbal paired associated	14 ± 1 (12 to 16)	15 ± 1 (14 to 17)	1 ± 1 (0 to 3)

* Data are shown as the mean ± SE (95% CI). CPAP = continuous positive airway pressure; FOSQ = Functional Outcomes of Sleep Questionnaire; MCS = mental component summary; MSLT = Multiple Sleep Latency Test; PASAT = Paced Auditory Serial Addition Test; PCS = physical component summary; SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.
† By *t*-test comparing the change over time (difference) observed in each group (CPAP vs. sham CPAP).

ables at baseline in the two groups. The effects of treatment were analyzed on an intention-to-treat basis by using a two-sided *t*-test for independent samples to compare the change over time in different variables between the two groups. A *P* value less than 0.05 was considered significant.

RESULTS

Baseline Data

Figure 1 shows the trial design. During the study, 69 patients who fulfilled all inclusion criteria were recruited from the six participating institutions. Fourteen patients declined to participate in the study. The remaining 55 patients underwent randomization. One patient initially assigned to the sham CPAP group was lost to follow-up after his first evaluation owing to a change in residence (**Figure 1**). Thus, the final study sample comprised 54 patients (29 in the CPAP group and 25 in the sham CPAP group).

Table 1 shows the patients' main anthropometric and clinical characteristics at the start of the study. The CPAP and sham CPAP groups did not differ significantly for any variable (**Table 1**). By design, all patients had an apnea–hypopnea index of 30 or greater (ranging from 30 to 91) and no excessive daytime sleepiness (**Table 2**). Adherence to treatment was similar in both groups. The number of patients receiving benzodiazepines (1 vs. 2) or treatment for arterial hypertension (β-blockers [4 vs. 2], angiotensin-converting enzyme inhibitors [3 vs. 4], or diuretics [2 vs. 1]) was similar in the CPAP and sham CPAP groups. Likewise, alcohol consumption was modest in both groups (**Table 1**).

Table 2 shows scores on the SF-36, FOSQ, Epworth Sleepiness Scale, and MSLT and results of tests of cognitive function. On average, all findings were within the normal range in both groups and did not differ significantly between groups. However, 12 patients in the CPAP group and 13 patients in the sham CPAP group had pathologic MSLT scores (<10 minutes). As shown in **Figure 2**, there was no relationship at baseline between Epworth Sleepiness Scale scores and MSLT scores.

Table 2—**Continued**

Sham CPAP			*P* Value†
Before	After	Difference	
48 ± 1 (45 to 51)	50 ± 1 (47 to 52)	1 ± 1 (−1 to 4)	>0.2
50 ± 2 (49 to 53)	52 ± 2 (48 to 55)	1 ± 1 (−2 to 4)	>0.2
107 ± 3 (102 to 113)	110 ± 2 (106 to 114)	3 ± 3 (−3 to 9)	>0.2
7 ± 0.4 (7 to 8)	8 ± 1 (6 to 9)	0 ± 1 (−1 to 2)	0.2
10 ± 1 (7 to 12)	11 ± 1 (9 to 14)	1 ± 1 (−1 to 3)	>0.2
6 ± 2 (2 to 10)	5 ± 2 (2 to 9)	−1 ± 1 (−2 to 1)	>0.2
44 ± 4 (36 to 52)	47 ± 4 (39 to 55)	3 ± 2 (0 to 6)	>0.2
32 ± 2 (29 to 36)	33 ± 2 (29 to 37)	1 ± 1 (−1 to 3)	>0.2
10 ± 0.4 (9 to 11)	10 ± 1 (9 to 11)	0 ± 0.3 (−1 to 1)	>0.2
14 ± 1 (12 to 16)	15 ± 1 (14 to 17)	1 ± 1 (0 to 3)	>0.2
15 ± 1 (13 to 17)	15 ± 1 (13 to 17)	0 ± 1 (−2 to 2)	0.04
11 ± 1 (9 to 13)	12 ± 1 (9 to 14)	0 ± 1 (−1 to 2)	0.09
4 ± 1 (3 to 5)	5 ± 1 (4 to 6)	1 ± 1 (0 to 2)	>0.2
49 ± 4 (41 to 56)	47 ± 3 (41 to 53)	−1 ± 3 (−8 to 5)	>0.2
108 ± 11 (84 to 132)	110 ± 10 (89 to 131)	2 ± 11 (−21 to 25)	0.1
6 ± 1 (5 to 7)	7 ± 0.4 (6 to 8)	1 ± 0.3 (0 to 1)	>0.2
15 ± 1 (13 to 16)	15 ± 1 (14 to 17)	0 ± 1 (−1 to 1)	>0.2

Table 3 shows the results of ambulatory blood pressure monitoring in both groups at baseline. On average, results were in the normal range. However, 12 patients in the CPAP group and 12 patients in the sham CPAP group were classified as nondippers.

Effects of Treatment with CPAP

Table 2 and **Figure 3** show the effects of treatment with CPAP or sham CPAP on quality of life, subjective and objective sleepiness, and results of psychological tests. The change over time in these variables did not differ between the groups, except for scores on PASAT 2. However, the small absolute value of this difference, the lack of differences observed when the same test was performed at a different speed (PASAT 1, PASAT 3, and PASAT 4), and its borderline statistical significance ($P = 0.04$) minimize the clinical relevance of this observation. When the same variables were analyzed in the subgroup of patients with a pathologic MSLT score (<10 minutes) at baseline, the difference was not significant (data not shown).

Figure 2. **Lack of relationship between daytime sleepiness according to Epworth Sleepiness Scale score (a subjective measure) or Multiple Sleep Latency Test score (an objective measure) before treatment with actual or sham continuous positive airway pressure.**

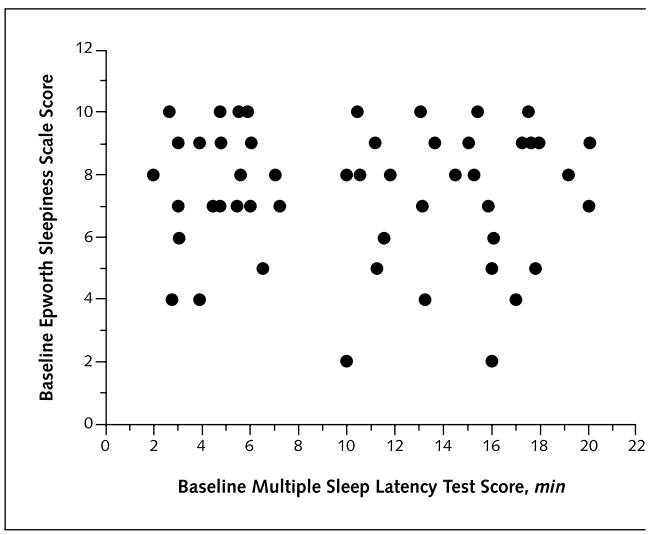


Table 3. **Mean Arterial Blood Pressure before and after 6 Weeks of Treatment***

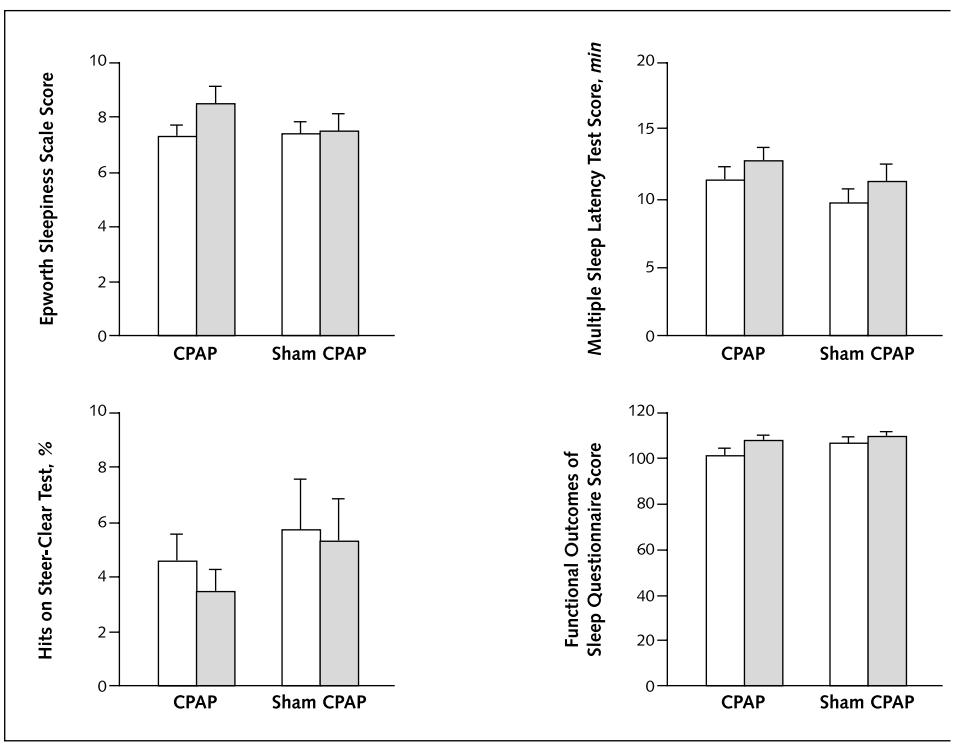
Measure	CPAP			Sham CPAP			*P* Value†
	Before	After	Difference	Before	After	Difference	
24-hour systolic blood pressure, *mm Hg*							
Overall	126 ± 2 (122 to 130)	124 ± 2 (120 to 128)	−2 ± 2 (−5 to 3)	123 ± 2 (118 to 128)	122 ± 3 (117 to 127)	1 ± 2 (−4 to 5)	>0.2
Diurnal	130 ± 2 (126 to 134)	127 ± 2 (123 to 131)	−3 ± 2 (−7 to 2)	127 ± 2 (122 to 133)	124 ± 3 (119 to 129)	−1 ± 2 (−6 to 3)	>0.2
Nocturnal	118 ± 2 (114 to 122)	117 ± 2 (112 to 122)	−1 ± 2 (−5 to 3)	118 ± 3 (113 to 123)	116 ± 3 (109 to 122)	−1 ± 2 (−6 to 3)	>0.2
24-hour diastolic blood pressure, *mm Hg*							
Overall	79 ± 1 (76 to 81)	79 ± 1 (77 to 82)	0 ± 1 (−2 to 3)	77 ± 2 (74 to 80)	77 ± 2 (74 to 81)	1 ± 1 (−2 to 3)	>0.2
Diurnal	82 ± 1 (79 to 84)	81 ± 1 (79 to 83)	−1 ± 1 (−4 to 2)	80 ± 2 (77 to 83)	80 ± 2 (76 to 83)	0 ± 1 (−2 to 2)	>0.2
Nocturnal	73 ± 1 (70 to 75)	73 ± 2 (69 to 77)	0 ± 1 (−3 to 2)	73 ± 2 (68 to 77)	72 ± 2 (68 to 76)	−1 ± 1 (−4 to 2)	>0.2

* Data are shown as the mean ± SE (95% CI). CPAP = continuous positive airway pressure.
† By *t*-test comparing the change over time (difference) observed in each group (CPAP vs. sham CPAP).

Table 3 and **Figure 4** show the effects of CPAP or sham CPAP on ambulatory blood pressure monitoring. Again, the change over time in these variables was similar in the two groups. Likewise, when the effects of treatment were analyzed in nondippers, CPAP treatment had no clinically or statistically significant effect (data not shown).

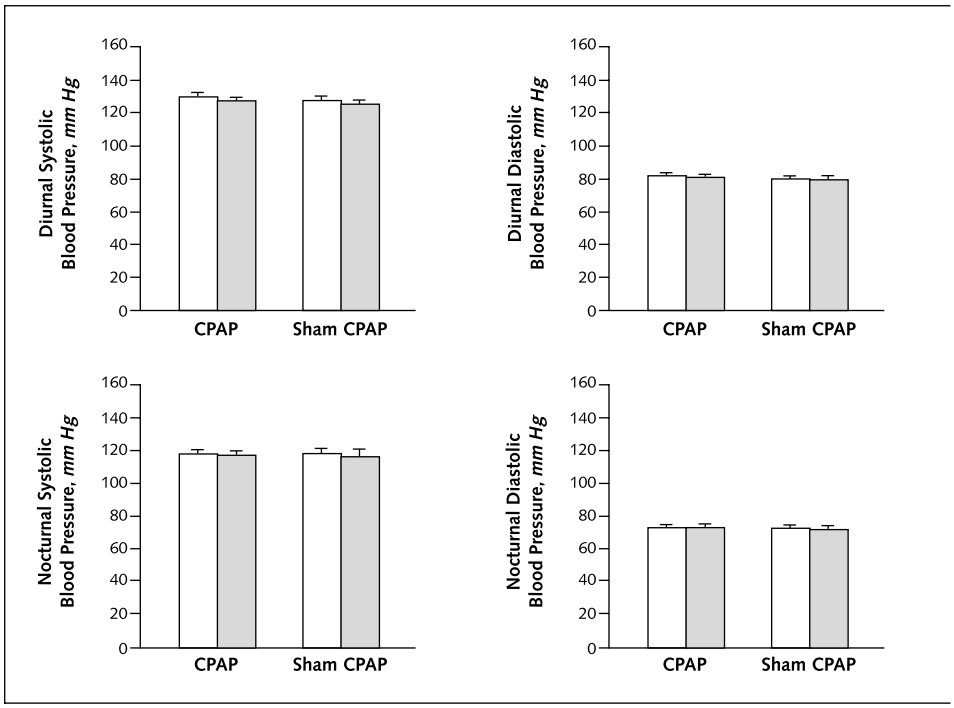
Adverse effects of CPAP or sham CPAP were clini-

Figure 3. **Mean scores on the Epworth Sleepiness Scale, Multiple Sleep Latency Test, the Steer-Clear test, and Functional Outcomes of Sleep Questionnaire (a quality-of-life measure) before (*white bars*) and after (*gray bars*) actual or sham continuous positive airway pressure (*CPAP*).**



Error bars represent SEs.

Figure 4. **Mean blood pressure measurements before (*white bars*) and after (*gray bars*) actual or sham continuous positive airway pressure (*CPAP*).**



Error bars represent SEs.

cally minor in all cases and were equally distributed among groups (data not shown).

Discussion

Our multicenter randomized, placebo-controlled study demonstrates that 6 weeks of treatment with CPAP had no significant effect on quality of life, subjective and objective sleepiness, cognitive function, or arterial blood pressure in nonsleepy patients with an apnea–hypopnea index of 30. Accordingly, our results do not support use of active treatment with CPAP in such patients.

Because this is a negative study, several methodologic aspects need to be considered. First, because many patients had normal values in many different variables at baseline, it is important to exclude a significant floor effect (27). Such an effect was excluded because the percentage of patients with the lowest score at baseline was lower than 15% for all variables in both groups (27). Second, the virtual absence of changes in the variables investigated could, in theory, be due to a lack of sensitivity of the instruments used (such as the SF-36, FOSQ, or Epworth Sleepiness Scale). However, we believe that this is not the case because many previous randomized clinical trials (4–9) have shown that these instruments detect clinically relevant changes. Third, the multicenter design of our study may have contributed to variability in sleep scoring. To overcome this potential limitation, we ensured that all technicians involved in the study had extensive experience and adhered strictly to international guidelines (18). Fourth, the relatively small sample may have jeopardized our ability to detect a statistically significant difference between groups. However, we calculated the necessary power a priori for the hypothesis being tested. Furthermore, the small absolute difference detected between groups and the overlap between the CIs (**Tables 1, 2,** and **3**) make it unlikely that increasing the number of participants would have revealed a biologically relevant difference. Finally, assessment of CPAP adherence may be inaccurate when estimated from patient self-reports. However, we determined adherence to CPAP by using the timer built

into in each device, both in the CPAP and sham CPAP groups.

Several recent studies have demonstrated that treatment with CPAP improves quality of life, sleepiness, cognitive function, psychological well-being, and perceived health status in patients with the sleep apnea–hypopnea syndrome (4–9). In contrast to findings in symptomatic patients, our results clearly show that CPAP has no effect in nonsleepy patients. Previous studies of patients with only mild sleep apnea–hypopnea syndrome (as defined by the apnea–hypopnea index) also found that scores on neither the MSLT (6) (as in our study) nor the maintenance of wakefulness test (5) were significantly influenced by CPAP.

We also found that CPAP had no significant effect on arterial blood pressure regulation (**Table 3**, **Figure 4**), even in patients classified as nondippers. This observation might seem at variance with findings in previous studies of arterial hypertension in patients with the sleep apnea–hypopnea syndrome (14, 28, 29). However, the lack of effect that we observed must be analyzed cautiously; our sample was small and primarily involved normotensive persons, and we investigated the effects of CPAP in the short term only (6 weeks).

Given the high prevalence of the sleep apnea–hypopnea syndrome in western societies and the costs of CPAP treatment, it is important to rationalize and optimize its use. Our results show that CPAP is not indicated in nonsleepy patients with a pathologic number of apnea–hypopnea episodes per hour of sleep, at least in the short term. Whether these untreated patients will go on to develop full-blown sleep apnea–hypopnea syndrome (with excessive daytime sleepiness and a clear indication for treatment with CPAP) is currently unknown. Until this becomes clear, we recommend periodic follow-up in the clinic if these patients are not treated with CPAP.

Our results also show that patients with frequent apneas during sleep but no excessive daytime sleepiness do not have abnormalities in more objective measures of sleepiness (MSLT), cognitive function, or quality of life. This may not have been the case if patients with the sleep apnea–hypopnea syndrome had lost the ability to perceive their symptoms. In patients with frequent apneas but no daytime sleepiness, scores on the Epworth Sleepiness Scale were not related to MSLT scores (**Figure 2**).

In conclusion, this study demonstrates that in patients with 30 or more episodes of apnea or hypopnea per hour but no subjective daytime sleepiness, CPAP does not influence quality of life, MSLT score, vigilance, attention, memory, information processing, visuomotor coordination, or arterial blood pressure.

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References

1. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Report of an American Academy of Sleep Medicine Task Force. Sleep. 1999;22:667-89.

2. **Loube DI, Gay PC, Strohl KP, Pack AI, White DP, Collop NA.** Indications for positive airway pressure treatment of adult obstructive sleep apnea patients: a consensus statement. Chest. 1999;115:863-6. [PMID: 10084504]

3. Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. American Thoracic Society. Official statement adopted March 1944. Am J Respir Crit Care Med. 1994;150:1738-45. [PMID: 7952642]

4. **Engleman HM, Martin SE, Kingshott RN, Mackay TW, Deary IJ, Douglas NJ.** Randomised placebo controlled trial of daytime function after continuous positive airway pressure (CPAP) therapy for the sleep apnoea/hypopnoea syndrome. Thorax. 1998;53:341-5. [PMID: 9708223]

5. **Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ.** Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1999;159:461-7. [PMID: 9927358]

6. **Redline S, Adams N, Strauss ME, Roebuck T, Winters M, Rosenberg C.** Improvement of mild sleep-disordered breathing with CPAP compared with conservative therapy. Am J Respir Crit Care Med. 1998;157:858-65. [PMID: 9517603]

7. **Ballester E, Badia JR, Hernández L, Carrasco E, de Pablo J, Fornas C, et al.** Evidence of the effectiveness of continuous positive airway pressure in the treatment of sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1999;159:495-501. [PMID: 9927363]

8. **Jenkinson C, Davies RJ, Mullins R, Stradling JR.** Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet. 1999;353:2100-5. [PMID: 10382693]

9. **Muñoz A, Mayoralas LR, Barbé F, Pericás J, Agusti AG.** Long-term effects of CPAP on daytime functioning in patients with sleep apnoea syndrome. Eur Respir J. 2000;15:676-81. [PMID: 10780758]

10. **Wright J, Johns R, Watt I, Melville A, Sheldon T.** Health effects of obstructive sleep apnoea and the effectiveness of continuous positive airways pressure: a systematic review of the research evidence. BMJ. 1997;314:851-60. [PMID: 9093094]

11. **Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S.** The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993;328:1230-5. [PMID: 8464434]

12. **Wright J, Sheldon T.** The efficacy of nasal continuous positive airway pressure in the treatment of obstructive sleep apnea syndrome is not proven [Editorial]. Am J Respir Crit Care Med. 2000;161:1776-8. [PMID: 10852740]

13. **Davies R, Stradling J.** The efficacy of nasal continuous positive airway pressure in the treatment of obstructive sleep apnea syndrome is proven [Editorial]. Am J Respir Crit Care Med. 2000;161:1775-6. [PMID: 10852739]

14. **Davies R, Crosby J, Prothero A, Stradling JR.** Ambulatory blood pressure and left ventricular hypertrophy in subjects with untreated obstructive sleep apnoea and snoring, compared with matched control subjects, and their response to treatment. Clin Sci (Colch). 1994;86:417-24. [PMID: 8168336]

15. **Johns M.** A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14:540-5. [PMID: 1798888]

16. International Classification of Sleep Disorders: Diagnostic and Coding manual. Rochester, MN: American Sleep Disorders Association; 1990.

17. **Farré R, Hernández L, Montserrat J, Rotger M, Ballester E, Navajas D.** Sham continuous positive airway pressure for placebo-controlled studies in sleep apnoea [Letter]. Lancet. 1999;353:1154. [PMID: 10209985]

18. **Rechtschaffen A, Kales A.** A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Washington, DC: U.S. Government Printing Office; 1968.

19 **Barbé F, Amilibia J, Capote F, Durán J, Mangado N, Jiménez A, et al.** [Diagnosis of obstructive sleep apnea syndrome. Consensus report from the Respiratory Insufficiency and Sleep Disorders Group]. Arch Bronconeumol. 1995;31:460-2. [PMID: 8520818]

20. **Collard P, Dury M, Delguste P, Aubert G, Rodenstein DO.** Movement arousals and sleep-related disordered breathing in adults. Am J Respir Crit Care Med. 1996;154:454-9. [PMID: 8756822]

21. **Alonso J, Prieto L, Antó JM.** [The Spanish version of the SF-36 Health Survey (the SF-36 health questionnaire): an instrument for measuring clinical results]. Med Clin (Barc). 1995;104:771-6. [PMID: 7783470]

22. **Weaver TE, Laizner A, Evans LK, Maislin G, Chugh DK, Lyons K, et al.** An instrument to measure functional status outcomes for disorders of excessive sleepiness. Sleep. 1997;20:835-43. [PMID: 9415942]

23. **Wechsler D.** Wechsler Adults Intelligence Scale (WAIS). 13th ed. Madrid: TEA Ediciones; 1998.

24. **Wechsler D.** Wechsler Memory Scale. Paris: Editions du Centre de Psychologie Appliquée; 1981.

25. **Lezack MD.** Neuropsychological Assessment. 3rd ed. New York: Oxford Univ Pr; 1995.

26. **Fagard RH, Staessen JA, Thijs L.** Optimal definition of daytime and nighttime blood pressure. Blood Press Monit. 1997;2:315-21. [PMID: 10234134]

27. **McHorney C, Tarlov A.** Individual-patient monitoring in clinical practice: are available health status surveys adequate? Qual Life Res. 1995;4:293-307. [PMID: 7550178]

28. **Hedner J, Darpö B, Ejnell H, Carlson J, Caidahl K.** Reduction in sympathetic activity after long-term CPAP treatment in sleep apnoea: cardiovascular implications. Eur Respir J. 1995;8:222-9. [PMID: 7758555]

29. **Akashiba T, Minemura H, Yamamoto H, Kosaka N, Saito O, Horie T.** Nasal continuous positive airway pressure changes blood pressure "non-dippers" to "dippers" in patients with obstructive sleep apnea. Sleep. 1999;22:849-53. [PMID: 10566903]