Supplemental material

Sleep study and CPAP pressure titration

Each participant was subjected to a sleep study, either full standard polysomnography (PSG) (Alice 5. Respironics, Inc), or respiratory polygraphy (RP) (Alice Pdx, Respironics, Ins) with a device previously validated against PSG [1]. PSG included continuous recording of electro-encephalogram, electro-oculogram, electro-myogram, electro-cardiogram, evaluations of the nasal airflow, thoracic and abdominal band movements, and arterial oxygen saturation (SaO2), according to standard criteria [2]. RP included continuous recording of oronasal flow and pressure, heart rate, thoracic and abdominal respiratory movements, and SaO2. All the patients undergoing RP who showed recording artefacts, discrepancy between the result of the RP and the pre-test clinical probability (pre-test clinical suspicion) of sleep apnea (especially in patients with high pre-test probability and unaltered RP results), predominance of central events, or a subjective sleep time of <3 h had a full PSG. Apnea was defined as interruption (>90%) of oronasal airflow for ⩾10 s, and it was classified as obstructive or central, depending on whether respiratory effort was present or absent. Hypopnea was defined as a 30–90% reduction in the oronasal airflow for ⩾10 s associated with a desaturation of ⩾3% (and/or an arousal in the case of a PSG study). The AHI was defined as the number of apneas plus hypopneas per hour of sleep (PSG) or recording (RP). All data were recorded manually by the investigators.

Optimal CPAP pressure was titrated by an auto-CPAP device (S9 Autoset, Resmed Ltd) over three consecutive nights. The optimal pressure was determined, based on the visual evaluation of the raw data recording from the night study, with no significant leaks (<0.40 leaks/s^{-1}). This fixed pressure was then maintained throughout the study in those patients assigned to the CPAP arm.

Per protocol analysis

Per protocol analysis was also perfomed by comparing those patients with good adherence to CPAP treatment (n=66) with the control group without CPAP (n=72). For quantitative variables, baseline characteristics were compared using the t-test or U-Mann Whitney test, depending on the normal or non-normal distribution, and the x2 test was used for dichotomic variables. Intra-group and inter-group differences were analyzed using the same protocol as that used in the ITT analysis, in this case adjusting the results not only for the corresponding baseline measures but also for those baseline variables that demonstrated a statistical difference between groups ($p<0.1$), or for those variables that the researchers considered as clinically meaningful, regardless of the presence or otherwise of differences between groups.

When those patients who tolerated CPAP for at least 4 hours per day (n=53) were compared with the control group without CPAP (n=71), a statistically significant difference was observed in their baseline variables with respect to the domains of quality of life (except for that of diurnal symptoms, which was better in patients with poor tolerance), without any differences in any other parameter, although the EES value was 1.1 points higher in those who tolerated CPAP (without reaching statistical significance) (Table 1 suppl). When a PP analysis was applied, however, the treatment with CPAP improved significantly, not only in the parameters observed in the ITT but also in those related to all the quality-of-life domains (Table 2 suppl). The EES values were 9.7 (4.1) and 8.9 (3.7) at baseline and 5.2 (2.7) and 8.3 (3.8) at the end of the follow-up for the CPAP (effect size 1.1) and control groups (effect size 0.2), respectively. After adjusting for the baseline ESS value, a significant decrease of -3.5 (95%CI -4.5 to -2.5) points was observed in the CPAP group compared with the control group. Furthermore, CPAP was shown to provide protection against nocturia (OR 0.37 [95%CI: 0.2-0.9], p=0.025). However, there were no significant improvements, even in the PP analysis, in any of the neurocognitive tests analyzed (including those for anxiety and depression), or in the incidence of nightmares or in the blood pressure readings (Table 3 suppl)

References

1. Nilus G, Domanski U, Schroeder M, Franke KJ, Hogrebe A. Margarit L. Ensayo controlado aleatorio para validar el equipo ambulatorio Alice Pdx. El sueño de Nat Sci. 2017;9:171-180.
2. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages Q5 Q6 of human subjects. Los Angeles, University of California, 1968.

Table S1. Comparative baseline characteristics of those patients randomized to CPAP with good (at least 4 hours/day) and bad compliance with the treatment.

Variable	**Good CPAP tolerance (n=53)**	**Bad CPAP tolerance (n=20)**	**p**
Age, yrs	74.6 (4.2)	75.5 (4.3)	0.46
Gender, n, (% males)	35 (66%)	15 (75%)	0.58
BMI, Kg/m2	30.8 (4.8)	31.9 (8.9)	0.49
AHI, events/hour-1	22.2 (4.2)	22.1 (4.9)	0.99
Tc90%, %	14.6 (30.9)	13.1 (19.6)	0.83
ODI3%, events/hour-1	21.5 (8.1)	20.6 (7.3)	0.67
CPAP pressure, cmH20	7.9 (1.9)	7.5 (1.6)	0.47
EES	9.7 (4.1)	8.6 (4.2)	0.28
QSQ domains			
Hipersomnolence	5.3 (1.4)	5.8 (1)	0.13
Diurnal symptoms	4.7 (1.5)	5.4 (1.4)	0.08
Nocturnal symptoms	4.1 (1.4)	5 (1)	0.01
Emotions	5 (1.4)	5.9 (1.3)	0.01
Social aspects	5.4 (1.6)	6.2 (0.9)	0.03
SBP, mmHg	128.7 (14.7)	128.4 (12.7)	0.32
DBP, mmHg	73.5 (8.7)	74 (8.8)	0.33
Neurocognitive measures			
TMT-A	108.5 (71.5)	88.6 (60.1)	0.27
TMT-B	215.2 (82.7)	197 (79.4)	0.39
Digital spam	8.4 (4.6)	8 (1.4)	0.68
Digital symbol	20.8 (11.7)	22.1 (9.4)	0.65
HADS test			
Depression	7 (4.8)	5.9 (5.2)	0.41
Anxiety	7.1 (4.2)	5.2 (4.6)	0.09

ESS: Epworth Sleepiness Scale; BMI: Body Mass Index; AHI: Apnea-hypopnea index; ODI3%: Oxygen desaturation index at 3%; CPAP: Continuous positive airway pressure; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; QSQ: Quebec Sleep Questionnaire; HADS: Hospital Anxiety-Depression Scale

Table S2. Changes in sleep-related quality of life (Quebec Sleep Questionnaire) between randomized groups in a per-protocol principle, adjusted for baseline measurements and baseline ESS value.

Variables	**CPAP treatment (n=53)**				**Conservative treatment (n=72)**				**Intergroup difference (95% CI)***	**p-value**
	Baseline	Follow-up	Effect size	Intragroup difference	Baseline	Follow-up	Effect size	Intragroup difference		
QSQ, quality of life										
Hypersomnolence	5.3 (1.4)	5.9 (1.2)	0.4	-0.6 (1.4)	5.7 (1.1)	5.8 (1.3)	0.1	-0.1 (1)	0.4 (0.02-0.8)	0.04
Diurnal symptoms	4.7 (1.5)	5.4 (1.3)	0.1	-0.7 (1.3)	5.3 (1.4)	5.4 (1.3)	0.1	-0.1 (0.1)	0.4 (0.06-0.8)	0.023
Nocturnal symptoms	4.1 (1.4)	5.5 (1.2)	1	-1.4 (1.5)	5 (1.3)	5.2 (1.3)	0.2	-0.2 (0.2)	0.8 (0.4-1.2)	0.0001
Emotions	5 (1.4)	5.8 (1.3)	0.6	-0.8 (1.2)	5.7 (1.2)	5.6 (1.3)	0.1	0.1 (0.1)	0.7 (0.3-1.1)	0.001
Social interaction	5.4 (1.6)	6.2 (0.9)	0.5	-0.8 (1.6)	5.8 (1.3)	6 (1.1)	0.2	-0.2 (0.2)	0.3 (0.1-0.65)	0.04

Data are expressed as mean (SD), unless otherwise stated. QSQ: Quebec Sleep Questionnaire.

*Adjusted by baseline measure and baseline EES (Epworth Sleepiness Scale).

Table S3. Changes in neurocognitive tests between randomized groups in a per-protocol principle, adjusted for baseline measurements and baseline EES value.

Variables	**CPAP treatment (n=53)**				**Conservative treatment (n=72)**				**Intergroup difference (95% CI)***	**p-value**
	Baseline	Follow-up	Effect size	Intragroup difference	Baseline	Follow-up	Effect size	Intragroup difference		
HADS Anxiety	7.1 (4.2)	6.3 (4.9)	0.2	0.8 (3.6)	6.1 (4.9)	5.8 (4.6)	0.1	0.3 (2.4)	-0.6 (-1.7, 0.5)	0.28
HADS Depression	7 (4.8)	6.3 (4.6)	0.1	0.7 (2.7)	5.8 (4.5)	6.1 (4.9)	0.1	-0.3 (2.1)	-0.5 (-1.3, 0.3)	0.23
Digit Span	8.4 (4.6)	8.6 (2.2)	0	-0.2 (4)	8.4 (2.7)	8.3 (2.6)	0	0.1 (1.6)	0.2 (-0.5,0.9)	0.58
Digit Symbol	20.8 (11.7)	23.1 (11.9)	0.1	-2.3 (6.9)	20.4 (10)	21.7 (11.2)	0.1	-1.3 (7.2)	0.7 (-3,1, 4.5)	0.68

*Adjusted for baseline measurements and baseline EES (Epworth Sleepiness Scale). HADS: Hospital Anxiety-Depression Scale