

# Cost-Effectiveness Analysis of Automatic Titration of Continuous Positive Airway Pressure at Home in 1 Night Versus 2 Nights

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**OBJECTIVE:** To assess the cost-effectiveness of automatic continuous positive airway pressure (CPAP) titration at home on 1 night or 2 consecutive nights in patients with the sleep apnea-hypopnea syndrome (SAHS).

**PATIENTS AND METHODS:** A home titration study was performed using automatic CPAP for 2 consecutive nights on 100 patients with SAHS and an indication for CPAP. The number of successful studies and the costs of the first night and both nights were analyzed. The pressure requirements on each night and the agreement between the pressures selected visually by 2 different observers were compared.

**RESULTS:** CPAP titration was successful in 85% and 80% of patients on the first night and second night, respectively, and in 88% of patients after both nights. No significant differences between the 2 nights were found for the following parameters: 95th percentile pressure (mean [SD], 10.2 [1.8] cm H<sub>2</sub>O and 10.2 [1.6] cm H<sub>2</sub>O on the first and second nights, respectively), mean pressure (7.8 [1.7] cm H<sub>2</sub>O and 7.7 [1.7] cm H<sub>2</sub>O), or the pressure selected visually (9.4 [1.5] cm H<sub>2</sub>O and 9.4 [1.4] cm H<sub>2</sub>O). Interobserver agreement on the pressure selected was good: the  $\kappa$  statistics were 0.956 for the first night and 0.91 for the second night. The 1-night study cost €232.63 and the 2-night study cost €227.93.

**CONCLUSIONS:** Automatic CPAP titration at home for 1 night enables a substantially greater number of patients to be studied at a similar cost than is possible when titration is accomplished in 2 consecutive nights.

**Key words:** Apnea-hypopnea syndrome. Home CPAP titration. Automatic CPAP titration. Cost-effectiveness.

Análisis de coste-eficacia de la graduación automática de la presión positiva continua de la vía aérea en el domicilio: ¿una o 2 noches?

**OBJETIVO:** Evaluar el coste-eficacia de la graduación automática de la presión positiva continua de la vía aérea (CPAP) en el domicilio, en una y 2 noches consecutivas, en pacientes con síndrome de apneas-hiponeas durante el sueño.

**PACIENTES Y MÉTODOS:** Se practicó un estudio de graduación domiciliaria con un equipo de CPAP automática (APAP) durante 2 noches consecutivas a 100 pacientes con síndrome de apneas-hiponeas durante el sueño e indicación de tratamiento con CPAP. Se evaluaron el número de estudios satisfactorios y el coste resultante de la primera noche y de las 2 noches. Se compararon las necesidades de presión durante cada noche y la concordancia entre la presión seleccionada visualmente por 2 observadores.

**RESULTADOS:** La graduación de CPAP fue satisfactoria en el 85 y el 80% de los pacientes en la primera y la segunda noches, respectivamente, y en el 88% después de las 2 noches. No hubo diferencias significativas entre las 2 noches en la presión percentil 95% (media  $\pm$  desviación estándar: 10,2  $\pm$  1,8 y 10,2  $\pm$  1,6 cmH<sub>2</sub>O), la presión media (7,8  $\pm$  1,7 y 7,7  $\pm$  1,7 cmH<sub>2</sub>O) y la presión visual (9,4  $\pm$  1,5 y 9,4  $\pm$  1,4 cmH<sub>2</sub>O). Se obtuvo un buen grado de concordancia entre 2 observadores en la selección de presión ( $\kappa$  = 0,956 para la noche 1;  $\kappa$  = 0,91 para la noche 2). El coste de los estudios fue 232,63 € para la primera noche y 227,93 € para las 2 noches consecutivas.

**CONCLUSIONES:** Con un coste similar, la adopción de un protocolo de graduación automática de la CPAP una noche en el domicilio permite incrementar sustancialmente el número de pacientes estudiados, respecto a 2 noches consecutivas.

**Palabras clave:** Síndrome de apneas-hiponeas. Graduación domiciliaria de CPAP. Graduación automática de CPAP. Coste-eficacia.

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## Introduction

Sleep-apnea hypopnea syndrome (SAHS) is a highly prevalent disease that affects 2% to 4% of the population.<sup>1,2</sup> The treatment of choice for symptomatic patients is continuous positive airway pressure (CPAP).<sup>3,4</sup> Manual titration of CPAP with conventional polysomnography in

the sleep laboratory is the standard procedure; however, it is expensive, requires monitoring by a technician, and is too expensive for many centers. Given the long waiting lists for diagnostic tests and CPAP titration, using only the conventional approach delays the start of therapy in many patients. Several alternative strategies have been developed to solve this problem. These include prediction formulas,<sup>5,6</sup> split-night protocols,<sup>7</sup> daytime studies,<sup>8</sup> and titration with the assistance of the sleep partner.<sup>9</sup> The application of automatic CPAP to select a fixed pressure for long-term treatment is increasingly common and has been shown to be as effective as CPAP titration with conventional polysomnography.<sup>10-19</sup> Automatic CPAP can be carried out with or without a monitor in the sleep laboratory or on the ward. Several studies have evaluated the efficacy of CPAP at home, although most use automatic CPAP for relatively long periods ranging from 3 days to several weeks.<sup>20-25</sup> A recent study has shown that a single night with automatic CPAP at home can be as efficient as titration using conventional polysomnography in most patients.<sup>6</sup>

A national health system must adopt a prudent approach to spending on health care protocols, yet no studies in Spain have evaluated the cost of automatic CPAP titration at home. Therefore, we analyzed the cost-effectiveness of a 2-night protocol for automatic CPAP titration at home by comparing the results after the first night with those of 2 consecutive nights in a large series of untreated patients with SAHS. The secondary outcome measures were differences in the automatically and visually determined pressures between the 2 nights and the level of agreement on the pressure selected visually by 2 observers.

## Patients and Methods

### Patient Selection

We included 100 consecutive patients aged between 18 and 75 years with SAHS for whom CPAP was indicated. CPAP had been recommended 1 month after the diagnostic study by respiratory polygraphy, in which the criteria applied were those of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)<sup>26</sup> and a Spanish National Consensus Statement on SAHS.<sup>27</sup> Patients requiring continuous home oxygen therapy, those who had undergone uvulopalatopharyngoplasty,<sup>28</sup> and those who lived outside the city of Barcelona were excluded from the study. The ethics committee of our hospital approved the study and all the patients gave their informed consent.

### Study Design

Patients arrived at the sleep laboratory in the morning. A technician explained how the automatic CPAP device worked in a 20-minute session during which the importance of the correct adjustment of the nasal mask was stressed. The patients took the device home and returned it to the hospital after using it for 2 consecutive nights. They were asked to complete a simple questionnaire on the subjective quality of their sleep on each of the 2 nights (How did you sleep last night? Well, average, or badly). The device used was the AutoSet Spirit (ResMed, Sydney, Australia). The pressure limits were set at between 4 cm H<sub>2</sub>O and 16 cm H<sub>2</sub>O, with a ramp time of 15 minutes at 4 cm H<sub>2</sub>O. The same model of nasal mask (UltraMirage,

ResMed) was used by all the patients. When the device was returned, a technician transferred the recorded data to a computer and printed the graph and the automatic pressure analysis from the 2 nights. Two separate observers analyzed the results of the 2 studies.

### Outcome Measures

*Acceptable recordings.* The recordings were considered acceptable if they met the following requirements: *a)* automatic CPAP data were recorded for at least 4 hours per night and *b)* any significant leaks (>0.4 L/min) occurred during less than 25% of the recorded time.

*Results of titration with the AutoSet device.* We analyzed 2 pressures—the mean pressure and the 95th percentile pressure—from the automatic analysis by the AutoSet Spirit device. Information on significant leaks was obtained graphically and numerically. Two specialist physicians visually analyzed the recordings independently and selected the pressure considered satisfactory for 90% of the time (ie, the pressure required to abolish snoring, apnea, hypopnea, or airflow limitation), after excluding periods when leaks exceeded 0.4 L/sec.

Differences between the results on the 2 nights were evaluated by comparing the pressures from the automatic analysis with the AutoSet device (95th percentile pressure and mean pressure), the pressure selected visually by each observer, the number of hours the device was in use, and the subjective quality of sleep according to the questionnaire completed after the study.

*Cost analysis.* The costs of polysomnography and staffing were those in force at our hospital. The cost of 1 night's titration with AutoSet at home was obtained by adding up the staff costs, 3-year depreciation of the AutoSet Spirit device, and the cost of the disposable material. The cost of the technician's time (20 minutes for the initial explanation and 15 minutes to enter the recorded data), at €15 per hour (ie, €8.75), was calculated to be the same for 1 and 2 consecutive nights. The time required by a physician to review the printouts and present a report was calculated to be 15 minutes, both for 1 night and for 2 nights at a cost of €21.50 per hour (€5.38). The depreciation of an AutoSet Spirit device (cost €4000) was calculated based on 240 studies per year at 3 years (ie, €5.55 per night), and the cost of the disposable material (nasal mask, tubing, and valve) was €161.74 per study. The cost of the CPAP titrations that had to be performed using conventional polysomnography (€341.60 per study) in the case of a failed automatic CPAP titration was added to the overall cost.

### Statistical Analysis

Quantitative data are expressed as the mean (SD). Relative frequencies and percentages were used for the qualitative variables. Inferential statistical analysis was performed using the *t* test for paired samples and the  $\chi^2$  test for quantitative and qualitative variables, respectively. The Wilcoxon signed rank test for paired samples was used to compare the subjective evaluation of sleep quality between the 2 nights. Agreement between the 2 observers in the visual selection of optimal pressure after 2 nights was evaluated using the  $\kappa$  statistic. The mean pressure, 95th percentile pressure, and the pressure selected visually by each observer on each night were compared using a Bland-Altman plot.<sup>29</sup> For all tests, statistical significance was set at a *P* value less than .05. The statistical analysis was performed using SPSS version 13.0 (SPSS Inc, Chicago, Illinois, USA) for Windows.

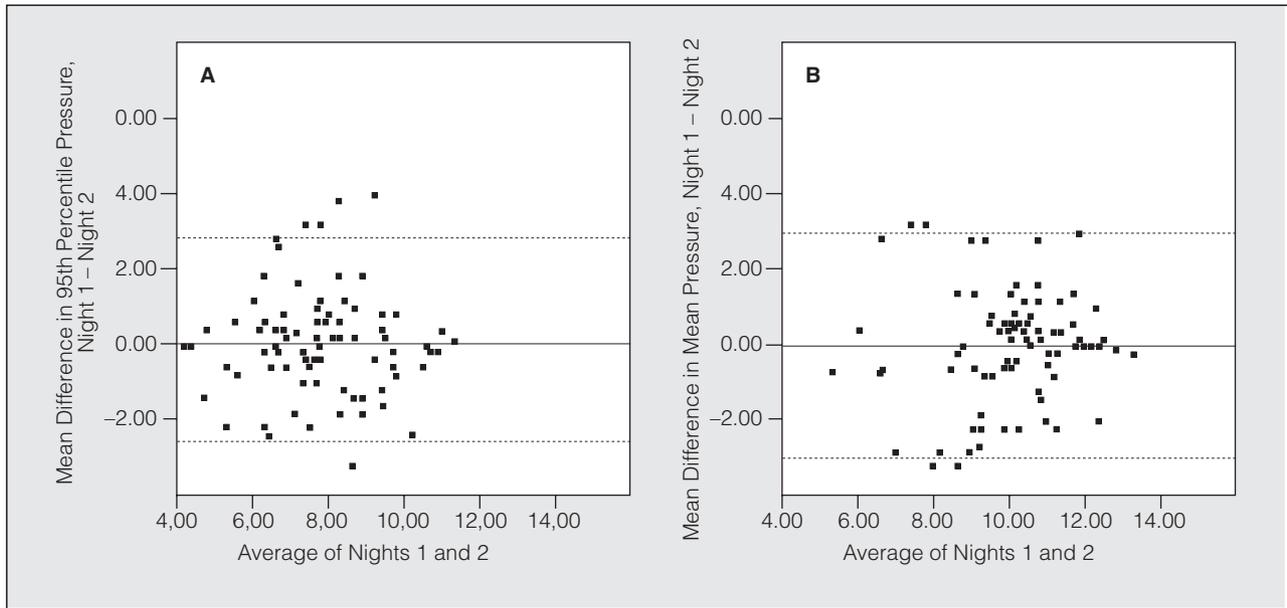


Figure 1. A, Mean difference in 95th percentile pressures between the 2 nights plotted against the mean of the 95th percentile pressures on those 2 nights. B, Mean difference in mean pressures between the 2 nights plotted against the mean pressure on those 2 nights of automatic continuous positive airway pressure titration.

## Results

The mean (SD) age was 54.7 (12) years, the body mass index was 35.5 (9.3) kg/m<sup>2</sup>, the apnea-hypopnea index was 43 (24.6)/h, and the score on the Epworth Sleepiness Scale was 8.7 (4.5).

### Outcome Measures

**Acceptable recordings.** CPAP titration was valid in 85 patients (85%) on the first night and in 80 (80%) on the second night. Overall, titration was successful in 88 patients (88%), taking into consideration the valid result of the first or second night. In 3 cases, a valid titration was not achieved on the first night, but it was on the second. The reasons for failed titration were the same on both nights for 10 patients (inability to tolerate the nasal mask, 3 patients; excessive leakage, 5 patients; and insufficient duration of use of the device, 2 patients). In the remaining cases, the reason for failure was different on each night.

**Results of titration with AutoSet.** Twenty-nine patients (34.1%) reported that they had slept well on the first night and 34 patients (42.5%) reported that they had slept well on the second night ( $P < .01$ ). Patients used automatic CPAP for significantly longer on the first night than on the second (6.9 [2.0] hours and 6.1 [1.9] hours;  $P < .0001$ ). On the first night, mean use of CPAP was the same in patients who reported having slept well or badly (6.9 [1.6] hours and 6.9 [2.2] hours, respectively), although on the second night, the patients whose sleep was good or average used CPAP for longer than those who slept badly (6.8 [1.5] hours and 5.5 [2.0] hours, respectively;  $P < .001$ ).

Table 1 shows the pressures obtained using the AutoSet algorithm and resulting from visual analysis by the 2 observers for each night. Neither the 95th percentile pressures nor the mean pressures were significantly different on the 2 nights. The 95th percentile pressure was significantly greater than the pressure selected visually by both observers on both nights.

The  $\kappa$  statistic for agreement between observers was 0.956 for the first night, 0.91 for the second, and 0.957 for the final pressure taking into consideration the results of both nights. The difference in the 95th percentile pressure and the mean pressure between the 2 nights did not vary

TABLE 1  
Results of 2 Consecutive Nights of Automatic Titration of Continuous Positive Airway Pressure<sup>a</sup>

|  | No. of Patients | Night 1    | Night 2    | P <sup>b</sup> |
|--|-----------------|------------|------------|----------------|
| Visual pressure, observer 1, cm H <sub>2</sub> O | 81              | 9.6 (1.7)  | 9.6 (1.5)  | .864           |
| Visual pressure, observer 2, cm H <sub>2</sub> O | 81              | 9.4 (1.5)  | 9.4 (1.4)  | .831           |
| 95th percentile pressure, cm H <sub>2</sub> O    | 83              | 10.2 (1.8) | 10.2 (1.6) | .994           |
| Mean pressure, cm H <sub>2</sub> O               | 83              | 7.8 (1.7)  | 7.7 (1.7)  | .786           |
| Mean leakage, L/s                                | 84              | 0.08 (0.1) | 0.08 (0.1) | .562           |
| Time in use of automatic CPAP, h                 | 85              | 6.9 (2.0)  | 6.10 (1.9) | <.0001         |

<sup>a</sup>Values are expressed as the mean (SD).  
<sup>b</sup>t test for paired data.

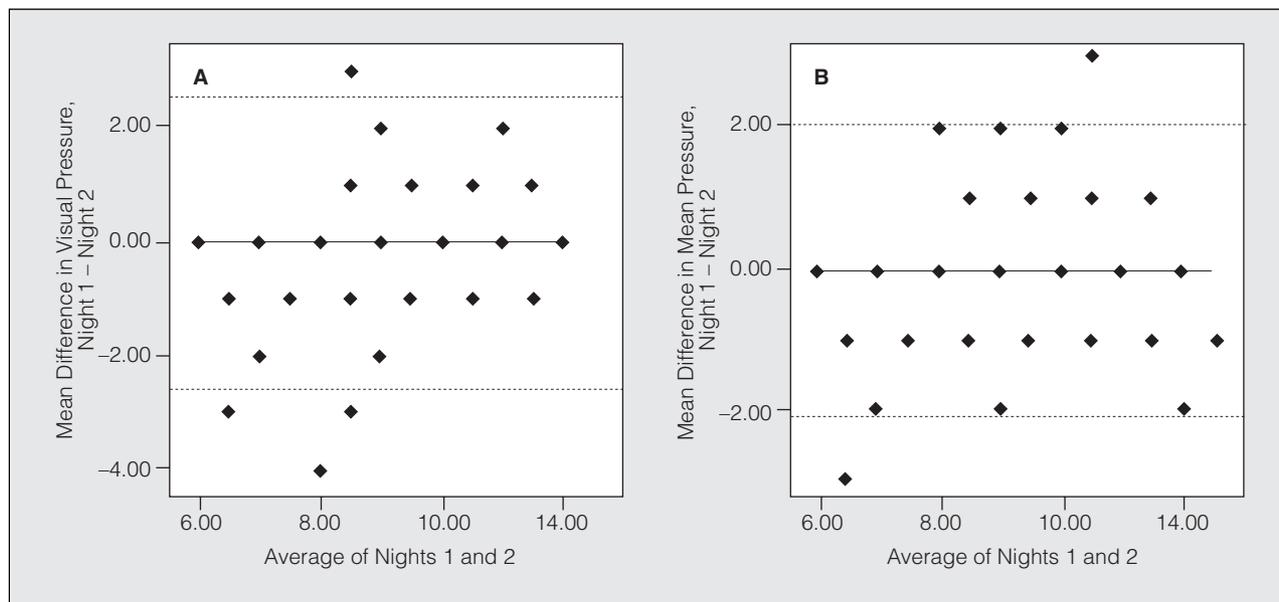


Figure 2. A, Mean difference in the mean visually assessed pressure as read by observer 1 between the 2 nights plotted against the average of the visual pressures on those nights. B, Mean difference in the mean visually assessed pressure as read by observer 2 between the 2 nights plotted against the average of the visual pressures on those 2 nights of automatic titration of continuous positive airway pressure.

significantly from zero, with a mean difference of  $-0.006$  ( $1.56$ )  $\text{cm H}_2\text{O}$  (limits of agreement,  $\pm 3.05$ ) for the 95th percentile pressure and  $0.04$  ( $1.38$ )  $\text{cm H}_2\text{O}$  (limits of agreement,  $\pm 2.70$ ) (Figure 1). The mean difference in visually assessed pressure selected for both nights was  $-0.025$  ( $1.30$ )  $\text{cm H}_2\text{O}$  (limits of agreement,  $\pm 2.60$ ) for observer 1 and  $-0.025$  ( $1.04$ )  $\text{cm H}_2\text{O}$  (limits of agreement,  $\pm 2.08$ ) for observer 2 (Figure 2).

### Cost-Effectiveness Analysis

Table 2 shows the estimated comparative cost of 1 and 2 consecutive nights of CPAP titration at home. A conventional titration of CPAP due to the failure of titration with automatic CPAP would have been indicated in

TABLE 2  
Cost in Euros of 1 and 2 Consecutive Nights of Automatic Titration of Continuous Positive Airway Pressure

|  | 1 Night                              | 2 Nights                              |
|--|--------------------------------------|---------------------------------------|
| Technician's time                            | 8.75                                 | 8.75                                  |
| Physician's time                             | 5.35                                 | 5.35                                  |
| Depreciation of AutoSet device <sup>a</sup>  | 5.55                                 | 11.10                                 |
| Need for conventional titration <sup>b</sup> | ( $341.6 \times 15$ )<br>100 = 51.24 | ( $341.6 \times 12$ )<br>/100 = 40.99 |
| Disposable material <sup>c</sup>             | 161.74                               | 161.74                                |
| Total cost per patient                       | 232.63                               | 227.93                                |

<sup>a</sup>Based on 240 studies per year over 3 years. <sup>b</sup>Cost of conventional titration of continuous positive airway pressure in patients with failed automatic titration. The cost is for 1 patient, based on the number of studies necessary the group of 100 patients. <sup>c</sup>Disposable material (nasal mask, tubing, valve).

15 patients after the first night. With the 2-night protocol, conventional titration would have been necessary in 12 patients. The overall cost of 1 night and 2 consecutive nights was  $\text{€}232.63$  and  $\text{€}227.93$  per patient, respectively, and both options were less expensive than titration using conventional polysomnography ( $\text{€}341.60$ ).

### Discussion

We found that automatic CPAP titration at home on the first night was effective in 85% of patients. On the second night, titration was effective for the 3 patients whose titration had failed on the first night (3% more). The cost of automatic CPAP titration on 1 or 2 consecutive nights was the same. The variability in the pressures obtained on the 2 nights was not significant, and interobserver agreement on the visually selected optimal pressure on each night was good.

In the first version of the AutoSet device (AutoSet Clinical), the algorithm had already proven useful for titrating effective pressure in 96% of a series of patients with SAHS in a sleep laboratory.<sup>30</sup> The pressure recommended by the device showed little variation over time, and adherence to treatment was good after 8 months of follow-up.<sup>31</sup> Seven randomized trials<sup>6,11,24,25,31-33</sup> and several clinical series<sup>11-19,25,34,35</sup> have found that automatic CPAP systems can be used to select a fixed CPAP pressure to reduce the apnea-hypopnea index to less than 10 per hour. This procedure has been effective in 80% to 95% of the patients studied in the sleep laboratory, whether they were monitored or not. Titration with automatic CPAP systems has also proven useful in the home. Most studies

have used such systems over several days, however. Fletcher et al<sup>22</sup> found that titration with an automatic device was efficacious in 78% of patients, but that a mean of 2.4 studies per patient were required to achieve a satisfactory treatment pressure. In a trial lasting from 1 to 2 weeks, Serié<sup>23</sup> evaluated automatic CPAP titration and showed that testing for 1 week was as effective as testing for 2 when attempting to set an acceptable pressure. West et al<sup>24</sup> compared conventional CPAP titration in the laboratory with the pressure selected after using an automatic system for 1 week at home and with a fixed pressure determined by an algorithm. They found no significant differences in the outcome measures between the 3 techniques, and concluded—as did Planes et al<sup>25</sup>—that automatic CPAP titration in the home reduces costs and time between diagnosis and treatment in comparison with conventional titration. A recent study comparing CPAP titration by the AutoSet Spirit device in the sleep laboratory and for 3 consecutive nights at home found that both methods were equally effective.<sup>20</sup> Titration was effective in 100% of the patients in that study and there were no differences in the CPAP pressures between the 3 nights. A single previous study has shown that 1 night with an automatic CPAP device at home is successful in 82% of patients and that the effective pressure using this procedure is no different from that determined using conventional polysomnography.<sup>6</sup> Our study corroborates this success rate.

According to our calculation, the cost of 2 consecutive nights was €4.70 less than the cost of a single night. However, a study over 2 consecutive nights proved more efficient than that of the first night in only 3 patients (3%). Given the long waiting lists for most sleep laboratories, and the fact that the use of 1-night titration would mean that the device could be used every night, the number of studies that could be carried out would be twice the number possible with a 2-night protocol and treatment would be put in place faster. Consequently, we believe that single-night automatic CPAP titration is more cost-effective than automatic titration on 2 consecutive nights. The cost of the test was calculated based on the use of disposable material (nasal mask, tubing, and valve), although it could be significantly reduced by reusing sterilized material. If this were the case, the reduction in cost would also have to be taken into account. Such a procedure would not modify the differences between 1 and 2 nights, although it would reduce the overall cost of the test.

In our patients, the mean score on the Epworth Sleepiness Scale was 8.7, even though the mean apnea-hypopnea index was 43. The patients were not selected, but were included in the study consecutively and are representative of our SAHS caseload. We think that the low score on the Epworth Sleepiness Scale can be explained by the limitations inherent to the interpretation of this scale (when patients do not read or do not travel by car), although it can also indicate a change in the characteristics of the patients who were referred to the sleep laboratory. Many patients complain of significant excessive sleepiness; however, for others who are being evaluated because of observed apneas, nonrestorative sleep, poor nighttime rest, excessive

sleepiness in relaxed situations or daytime tiredness, hypersomnolence is not a major complaint. The efficacy of CPAP against the symptoms of SAHS has been proven in controlled studies, even in mild-to-moderate cases.<sup>36</sup> On other occasions, patients with cardiovascular disease are referred to the sleep laboratory for evaluation of suspected apnea due to growing evidence of the harmful cardiovascular effects of SAHS.<sup>37,38</sup> In these patients, we recommend CPAP if the apnea-hypopnea index is over 30, and we reevaluate the definitive indication some months later.

A larger number of patients said they had slept better on the second night with the automatic CPAP device than on the first night, indicating that they had adapted well to the treatment. However, the mean time of use of automatic CPAP was shorter on the second night, because the patients who slept badly on the first night used the device for less time than on the second night.

We found no significant variations in the pressures obtained (95th percentile and mean) with the automatic AutoSet analysis between the 2 consecutive nights, although the Bland and Altman plots show that there may be a considerable variation in some cases. These results are consistent with those of Stradling et al,<sup>21</sup> who reported considerable inaccuracy in the 95th percentile pressure (between 1.65 and 2.45 cm H<sub>2</sub>O) achieved using automatic CPAP on 4 different nights; however, there was little error compared with a reference value obtained as the mean of the 95th percentile pressure over 28 nights. Variability was attributed to changes in the quality of sleep<sup>39</sup> more than to an authentic difference in the pressure requirement, and the reproducibility of the measurements is very similar to that of conventional CPAP titration on 2 consecutive nights with polysomnography, where the effective pressure was 0.5 (1.3) cm H<sub>2</sub>O higher on the second night than on the first (limits, -2 to 3 cm H<sub>2</sub>O).<sup>40</sup>

In clinical practice, we visually estimate the 90th percentile pressure as effective in order to avoid excessive pressures for more than 10% of the time. Given the subjective character of this method of evaluation, we decided to assess the level of agreement between 2 observers. In our series, this was good, thus corroborating the results reported after a study of 20 patients.<sup>6</sup>

Our study has several limitations. First, although the primary objective was to compare the efficacy and cost of 1 or 2 consecutive nights of titration with automatic CPAP at home, we did not use a control polysomnography to evaluate the effectiveness of treatment with CPAP pressure determined by automatic CPAP titration. In fact, our study is based on the assumption that the effectiveness of a pressure selected by titration with automatic CPAP has already been demonstrated.<sup>6,10-19,32,33</sup> Furthermore, instead of an alternative randomized design on 1 or 2 nights in 2 groups of patients, we chose a design in which the results for the same patient were compared over 1 and 2 nights. Finally, our study did not enable us to analyze whether the degree of adherence to treatment with long-term CPAP would be any different from that observed using a titration protocol of 1 or 2 nights, although, in principle, the absence of pressure differences between the 2 nights seems to indicate that this would not be the case.

Therefore, we conclude that titration with the AutoSet Spirit at home can be achieved on a single night in most patients with SAHS and that this procedure is more cost-effective than a protocol based on 2 consecutive nights. The variability in pressures over 2 consecutive nights, although evident in some cases, is not significant in the patient population as a whole. The agreement between 2 observers in the visual selection of the effective pressure is good.

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