Constant vs Auto-Continuous Positive Airway Pressure in Patients With Sleep Apnea Hypopnea Syndrome and a High Variability in Pressure Requirement*

André Noseda, MD, PhD; Chantal Kempenaers, MS; Myriam Kerkhofs, PhD; Stéphanie Braun, MS; Paul Linkowski, MD, PhD; and Ernest Jann, MD

Study objectives: Auto-continuous positive airway pressure (CPAP) has been reported to have no more efficacy than constant CPAP in unselected patients with sleep apnea hypopnea syndrome (SAHS). The aim of this study was to evaluate patients judged to be good candidates for auto-CPAP because of a high within-night variability in pressure requirement.

Design: Single-blind, randomized, cross-over study (2 × 8 weeks) to compare auto-CPAP with constant CPAP.

Patients: Outpatients with moderate-to-severe SAHS attending the chest clinic.

Interventions: Patients were equipped at home in the auto-CPAP mode (model GK418A; Malinckrodt; Nancy, France), using a 4- to 14-cm H2O pressure range. Those individuals having a high within-night variability in pressure requirement, assessed at the end of a 14-day run-in period, were included in the cross-over study. Auto-CPAP was compared with constant CPAP (according to a titration night in the sleep laboratory) in terms of compliance, efficacy on apneas (assessed from the pressure monitor), and sleepiness (assessed on the Epworth sleepiness scale).

Measurements and results: Of 90 consecutive patients with SAHS, 27 patients were selected for a within-night variability in pressure requirement exceeding a given threshold. After completion of the cross-over, 24 patients were evaluable. The median percentage of nights the machine was used was 95.5% (range, 45 to 100%) on constant CPAP, and 96.5% (range, 40 to 100%) on auto-CPAP; the median apnea index recorded by the device was 0.40/h (range, 0 to 2.40/h) on constant CPAP, and 0.45/h (range, 0 to 5.80/h) on auto-CPAP (differences not significant). The mean Epworth sleepiness score was significantly (p < 0.01) lower on auto-CPAP (5.1; SD, 2.8) than on constant CPAP (6.1; SD, 2.8).

Conclusions: In patients selected for a high within-night variability in pressure requirement, auto-CPAP administered via a GK418A device was equivalent to constant CPAP based on a titration night in the sleep laboratory. Subjective ratings for sleepiness were slightly lower on auto-CPAP.

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Key words: auto-continuous positive airway pressure; compliance; constant continuous positive airway pressure; sleep apnea hypopnea syndrome; sleepiness

Abbreviations: AHI = apnea hypopnea index; AI = apnea index; CPAP = continuous positive airway pressure; MAI = microarousal index; SAHS = sleep apnea hypopnea syndrome; TST = total sleep time; VI = variability index

Nasal continuous positive airway pressure (CPAP), first introduced by Sullivan et al,1 has become the most effective treatment for patients with sleep apnea hypopnea syndrome (SAHS). Traditionally, the effective pressure is titrated in the sleep laboratory by means of polysomnography, and is defined as a pressure level able to eliminate most apneas, hypopneas, and snoring. However, this effective pressure can vary in a given subject from night to night and even during a given night, depending on body position, fatigue level, sleep stage, nasal patency, upper airway edema, ingestion of alcohol, or sedative agents. Furthermore, regular maintenance CPAP therapy itself and weight loss may alter the effective pressure in the long term.2 As a conse-
quence, there has been considerable interest in the recent years in auto-CPAP devices capable of continuously adjusting the pressure to the effective level. Some studies have been published comparing auto-CPAP vs conventional constant CPAP as home therapy in patients with SAHS. Most of them have reported that patients slept on auto-CPAP at a mean pressure lower than on constant CPAP, but compliance was better on auto-CPAP in only one study. No study was able to report a gain in efficacy with auto-CPAP. In view of these rather disappointing results in studies performed in unselected patients with SAHS, some opinion leaders have emphasized the need to study subgroups of patients selected on basis of some criterion thought to make them good candidates for treatment with auto-CPAP.

In the present study, we selected patients with SAHS showing a high level of within-night variability in pressure requirement. Variability was studied extensively during a 2-week run-in period while the patients slept with a machine in auto-CPAP mode. At the end of the run-in period, those patients with a level of variability superior to a given threshold were selected. Subsequently, these patients were enrolled in a single-blind, randomized, cross-over study comparing 8 weeks on constant CPAP, according to the effective pressure titrated in the sleep laboratory, and 8 weeks on auto-CPAP, using a large 4- to 14-cm H2O pressure range.

**Materials and Methods**

**Study Design**

The study protocol was approved by the Ethics Committee of the Hôpital Erasme, and all patients gave informed consent. All patients went to the sleep laboratory for baseline polysomnography and a classical CPAP titration, in order to assess an effective pressure. Treatment with CPAP at home was initiated at the chest clinic by a respiratory physician (A.N.). In the run-in period, all patients were given a machine in the auto-CPAP mode with a 4- to 14-cm H2O pressure range. The recorded data were downloaded after 14 ± 2 days (± SD) at the biomedical technical department of the hospital. Within-night variability in pressure was analyzed, and those subjects with a variability exceeding a given threshold were included. The study itself was a single-blind, randomized, cross-over trial. Subjects were told that they would sleep with a machine functioning in two distinct modes, and that a comparison would be made between the two modes. No further explanation was given, and specific questions were not answered. A randomization table was used. Every effort was made to solve any technical problem with CPAP interface, if present. At the end of the first 8 weeks, recorded data were downloaded to assess compliance and efficacy, as well as pressure requirement, in patients on the auto-CPAP mode. Quality of sleep was assessed using the Pittsburgh questionnaire, and diurnal vigilance was assessed using the Epworth sleepiness scale. Subsequently, the patient was switched to the alternate mode for a further 8-week period. At the end of this second period, the same evaluation was made as at the end of the first period. Each patient was also asked whether he (or she) preferred the first or the second period and was further treated with CPAP at home in the mode that was preferred during the cross-over study.

**Patients**

We investigated patients with moderate-to-severe obstructive sleep apnea. Only those patients with an apnea hypopnea index (AHI) > 20/h and a microarousal index (MAI) > 20/h were included. Exclusion criteria were previous treatment with CPAP, central sleep apnea syndrome or Cheyne-Stokes respiration, major facial or pharyngeal anatomic abnormalities likely to require surgery, night or rotating shift work, severe chronic heart failure or COPD, seizure disorder, mental retardation, and sedative, hypnotic, or antidepressant therapy. Additional exclusion criteria related to the use of auto-CPAP were previous uvulopalatopharyngoplasty (a potential cause of failure with auto-CPAP in detecting snoring and, possibly, flow limitation) and the presence of prolonged hypoventilation during rapid eye movement sleep, as seen in some subjects with COPD and/or major obesity (not usually detected by auto-CPAP).

**Sleep Studies**

An all-night baseline polysomnography was performed using standard sleep recording leads (electro-oculogram, EEG, chin electromyogram, ECG, nasobuccal thermistor, thoracic and abdominal belts, and transcutaneous oximetry). Sleep staging was performed according to the criteria of Rechtschaffen and Kales. Sleep period time was defined as the time from the onset of sleep to the last awakening in the morning, and total sleep time (TST) was defined as sleep period time minus any time the subject was awake after falling asleep. Microarousals were defined as an abrupt change in EEG frequency (mostly in the range of 16 Hz) of 2 to 10 s in duration, accompanied by an increase in electromyogram amplitude. The MAI was calculated as the sum of all microarousals divided by the TST, and was expressed as per hour.

Apnea was defined as a cessation of flow at the nose and mouth for at least 10 s, and hypopnea was defined as a decrease for at least 10 s in the amplitude of airflow signal to < 50% of the level prevailing before the event, coupled with a fall in oxyhemoglobin saturation of at least 3%. The apnea index (AI) and AHI were calculated, respectively, as the sum of all apneas, and the sum of all apneas and hypopneas, divided by the TST, and were expressed as per hour.

In each patient, CPAP titration was performed on a subsequent night in the sleep laboratory. The pressure was gradually increased—by steps of 1 cm H2O—until such a level that most apneas and hypopneas were abolished and snoring was eliminated in all sleep stages and all body positions.

**CPAP at Home**

The machine used was the GK418A device (Malinckrodt; Nancy, France), which can easily be switched from the constant mode to the auto-CPAP mode. In the constant mode, the pressure was that judged to be effective during the titration night at the sleep laboratory. In the auto-CPAP mode, the reference pressure was 7 cm H2O, the pressure being allowed to change inside a 4- to 14-cm H2O range. The GK418A device has a pressure monitor coupled with a real-time clock, able to function as a control operating system. Compliance was assessed as in a previous study by our group, as the percentage of nights the...
subject used the machine and the mean effective time the device was on pressure during nights of effective use. Efficacy was evaluated on basis of the AI recorded by the control system. In the auto-CPAP mode, within-night pressure variability was assessed using the variability index (VI) as proposed by Series and Marc. In this mode of reporting variability, the weighted mean of pressure (A) is calculated as A = Σ i Pi, where i represents the pressure from 4 to 14 cm H₂O in 1-cm H₂O increments, and Pi the fraction of time spent at the different pressure levels, and the VI is calculated subsequently as follows:

According to this index calculation, the minimal theoretical value of VI is 0, when the whole night is spent at the same pressure level, while its maximal theoretical value is 5 cm H₂O and is reached when 50% of time is spent at the two extreme pressure values, respectively. In the case the time spent at each pressure level within the 4- to 14-cm H₂O range is identical, VI amounts 3.16 cm H₂O. In the present study, variability in pressure was assessed during the run-in period. At the end of this period, patients with a VI > 2.75 cm H₂O (calculated as the mean on the last 5 nights) were included in the cross-over study. During the cross-over study, variability in pressure was also assessed during the period the patient was in the auto-CPAP mode.

Statistical Analysis

Samples were described as mean (SD) values, or, when not normally distributed, as median (range). In the cross-over study, variables recorded on constant CPAP vs auto-CPAP were compared using a Student t test for paired values or, when the distribution was not normal, a nonparametric Wilcoxon test.

RESULTS

Patients

Ninety-three patients attending the chest clinic were eligible for the study on the basis of their polysomnographic results and absence of exclusion criteria. Three patients refused CPAP as treatment at home. Of the remaining 90 patients, 27 patients had at the end of the run-in period a within-night pressure variability exceeding the required threshold (VI > 2.75 cm H₂O) and were randomized. All but one were men. Their anthropometric features were as follows: age, 49 years (SD, 10); height, 176 cm (SD, 7); weight 99.7 kg (SD, 16.0); and body mass index, 32.3 (SD, 4.9). The baseline score on the Epworth sleepiness scale, assessed on admission at the sleep laboratory, was 10.7 (SD, 2.4). Fifteen of 27 patients had a score > 10. The results of the sleep studies are shown in Table 1. The patients studied were characterized by moderate-to-severe SAHS, with—as expected—spectacular improvement during the CPAP titration night. Thirteen patients were randomized on constant CPAP during the first period; one patient was not evaluated because the data could not be downloaded from the monitor. Two of 14 patients randomized in the auto-CPAP mode first dropped out, as 1 patient did not tolerate the machine, and 1 patient felt very well and refused to switch to the alternate mode at the end-period visit. To correct nasal discomfort, a cold humidifier was necessary in three patients in each group, and a heated humidifier was necessary in one additional patient in each group. No dropouts occurred during the second period, so that 24 patients (12 patients receiving constant CPAP first, and 12 patients receiving auto-CPAP first) were evaluable.

Assessment of Within-Night Variability in Pressure Requirement

As shown in Figure 1, the within-night variability in pressure requirement on auto-CPAP during the run-in period, expressed as the VI, tended to decrease with time. The run-in period included 12 nights (n = 1), 13 nights (n = 3), most often 14 nights (n = 83), 15 nights (n = 2) or 16 nights (n = 1). In each patient, a mean VI value was calculated on the last 5 nights. For the whole group, this mean VI amounted to 2.16 cm H₂O (SD, 0.25). Twenty-seven of 90 patients (30%) had a mean VI at the end of the run-in period exceeding a threshold of 2.75 cm H₂O and were selected for the cross-over study. The threshold was set at 2.75 cm H₂O, as we observed that in all the patients with a VI > 2.75 cm H₂O the distribution of pressure was curved inwards, whereas it was curved outwards in all the patients with a VI < 2.75 cm H₂O. Figure 2 shows typical examples of a subject with a mean VI below the threshold (not enrolled) vs a subject with a mean VI above the threshold (enrolled).

Cross-over Study of Auto-CPAP vs Constant CPAP

Data Downloaded From the CPAP Device: The median percentage of nights the machine was used was 95.5% (range, 45 to 100%) with constant CPAP, and 96.5% (range, 40 to 100%) with auto-CPAP (difference not significant). Individual data are shown in Figure 3. The mean use per effective night was not significantly different either (5.5 h; SD, 1.5) with constant CPAP, vs 5.3 h (SD, 1.9) with auto-CPAP. Where efficacy is concerned, the AI recorded by the control operating system was not significantly different: median 0.40/h (range, 0 to 2.40) on constant CPAP and 0.45/h (range, 0 to 5.80) on auto-

Table 1—Polysomnographic Results in the 27 Patients Randomized in the Cross-over Study*

<table>
<thead>
<tr>
<th>Variables</th>
<th>AI</th>
<th>AHI</th>
<th>MAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline night</td>
<td>24.6 (22.6)</td>
<td>50.9 (25.2)</td>
<td>43.0 (12.9)</td>
</tr>
<tr>
<td>CPAP night</td>
<td>4.0 (5.0)</td>
<td>10.3 (8.2)</td>
<td>8.5 (2.1)</td>
</tr>
</tbody>
</table>

*Data are presented as mean (SD)/h.
CPAP. Mean pressure on auto-CPAP was significantly (p < 0.05) lower than on constant CPAP: 7.6 cm H2O (SD, 2.3) vs 8.5 cm H2O (SD, 2.2). As shown in Figure 4, the within-night variability in pressure, expressed as the VI, remained stable during the 8-week study period in the auto-CPAP mode. The pattern of pressure distribution remained curved inwards in all but one patient.

Data Obtained From Questionnaires: Individual scores on the Epworth sleepiness scale are shown in Figure 5. The score, which was > 10 before treatment in 13 of 24 patients, remained abnormal in 3 patients receiving constant CPAP, and in 1 patient receiving auto-CPAP. The mean score on auto-CPAP (5.1; SD, 2.8) was significantly (p < 0.01) lower than on constant CPAP (6.1; SD, 2.8). Self-estimated sleep latency (Pittsburgh questionnaire) was very similar on constant CPAP (14 min; SD, 12) and on auto-CPAP (12 min; SD, 12), the difference being not significant. Similarly, the self-estimated duration of effective sleep was not significantly different between the constant CPAP (6.2 h; SD, 1.3) and the auto-CPAP (6.1 h; SD, 1.3) mode. At the end of the cross-over trial, 16 patients claimed they preferred the auto-CPAP mode and 8 patients pre-

![Figure 1](image1.png)

**Figure 1.** Within-night variability in pressure requirement on auto-CPAP in 90 patients with SAHS. The variable plotted is the mean (SD) VI assessed every night during a 2-week run-in period.

![Figure 2](image2.png)

**Figure 2.** Individual examples of variability in pressure requirement at the end of the run-in period on auto-CPAP, with a 4- to 14-cm H2O pressure range. These histograms represent an average on the last 5 nights. Left: the histogram is curved outwards. The subject spent 67% of the night in the 7- to 11-cm H2O range; his VI was 1.76, and he was not selected. Right: the histogram is curved inwards. The subject spent only 18% of the night in the 7- to 11-cm H2O range; his VI was 3.46, and he was selected.
ferred the constant CPAP mode. The preferred period was the first period in 11 patients, and the second period in 13 patients.

**DISCUSSION**

In the present study, we evaluated the GK418A device with a nose mask for home treatment, using a single-blind, randomized, cross-over design to compare auto-CPAP with constant CPAP, in 24 patients with SAHS selected on the basis of a high within-night variability in pressure requirement. We have found that a short run-in period on auto-CPAP with a large 4- to 14-cm H$_2$O pressure range showed markedly different individual patterns in pressure requirement, and allowed for the selection of a subgroup of patients with high within-night variability. In these patients, auto-CPAP, using the same large 4- to 14-cm H$_2$O pressure range over a 8-week period, was as effective as constant CPAP based on a titration night in the sleep laboratory. Furthermore, auto-CPAP provided a slight subjective benefit over
constant CPAP, with a slightly lower sleepiness score and more subjects preferring the auto-CPAP mode.

The reasons for choosing the GK418A apparatus as an auto-CPAP device have to be discussed. Since 1996, we have had a clinical experience with the Rem+ auto device (SeFam; Nancy, France), based on apnea, hypopnea, and snoring detection. Titrating the effective pressure with this device was shown to be feasible in a study in which the apnea/hypopnea detection facility was deliberately disabled, nasal mask pressure vibration detection being the only mode of pressure setting. Later, a flow limitation detection, shown to be a useful marker of changes in upper airway resistance during CPAP titration, was included in the algorithm. This led to an auto-CPAP device based both on snoring and flow limitation detection, the latter being the earliest indicator of obstruction during decreases in CPAP. The GK418A device used in the present study is still very sensitive for detecting snoring but is also able to correct flow limitation, a capability potentially associated with more efficiency in normalizing daytime vigilance.

A few studies have already compared auto-CPAP with constant CPAP as home treatment for patients with SAHS, using a single or double-blind crossover design or a single-blind, parallel-group design, over a period of 2 to 3 months. Efficacy was evaluated using polysomnography, the Epworth sleepiness scale, or the AI recorded by the control system of the CPAP device; all studies concluded that auto-CPAP and constant CPAP have similar efficacy. Compliance was measured as a mean on-pressure time, assessed from a pressure monitor, or from a time counter, and was found to be similar or slightly better with auto-CPAP than with constant CPAP. In all studies, mean pressure on auto-CPAP was found to be lower than the manually titrated effective CPAP used on constant CPAP, the difference ranging on average from 0.9 cm H₂O to 4.2 cm H₂O. However, the clinical significance of this finding has been disputed, as the peak pressure with auto-CPAP is higher than with constant CPAP. All these previous studies included “general patients” with SAHS, the sole inclusion criterion being an AHI > 10/h, or > 20/h.

In our study, we selected 27 patients from a general population of 90 patients with SAHS on the basis of a high within-night pressure variability during the run-in period. In so doing, we followed the recommendation made by some opinion leaders to identify a specific subgroup of patients who might benefit from auto-CPAP. We used a mode of calculation of pressure variability that was successfully used by another group and, as proposed by Levy and Pepin, we based the selection for within-night variability on a short run-in period rather than on a single test night. Indeed, during an initial therapeutic trial with an auto-CPAP device, a highly variable pressure may reflect poor sleep quality. We studied within-night variability during a 2-week period, and found that it decreased with time. This result is in agreement with that of a previous study that controlled for body position and sleep stage, and found that the decrease in pressure variability was typical for those patients with obstructive breathing abnormalities depending on sleep stage and/or body position. However, we found in the patients selected for high variability that pressure variability remained stable during the course of the 8-week study period. It has been suggested that, during CPAP therapy, body position stabilizes over time and that upper airway shape and/or dimension improve over time. These factors may explain why variability in pressure requirement stabilizes after an initial decrease.

Despite selecting a specific subgroup of patients with high within-night variability in pressure requirement, we found no gain in efficacy or in compliance with auto-CPAP as assessed from the data downloaded from the pressure monitor. However, the subjects had a significantly lower score on the Epworth sleepiness scale in the auto-CPAP, with a mean difference of 1 U. As no objective assessment of daytime vigilance was made, this slight difference should be interpreted with caution. Finally, 16 of 24 patients preferred the auto-CPAP mode at the end of the cross-over and chose auto-CPAP for further use at home. Whether auto-CPAP provided more comfortable breathing and could result in better long-term adherence is presently speculative, and should be assessed in a parallel-group prospective trial.

In conclusion, a short trial with the GK418A auto-CPAP device using a large pressure range is a convenient strategy to identify those patients with SAHS having a high within-night variability in pressure requirement. In patients selected for such a high variability, maintenance therapy with auto-CPAP is equivalent, in terms of compliance and efficacy on apneas, to constant CPAP based on a titration night in the sleep laboratory. Furthermore, auto-CPAP is associated in these patients with slightly better subjective ratings for sleepiness than constant CPAP. Our results are specific to the GK418A device, and should not be extrapolated to other auto-CPAP devices.

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