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Comparison of conventional nighttime with automatic or manual daytime CPAP titration in unselected sleep apnea patients: study of the usefulness of daytime titration studies

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Summary Daytime CPAP titration studies with full polysomnography have been successfully performed in patients with severe sleep apnea–hypopnea syndrome (SAHS). The implementation of daytime studies in unselected SAHS patients could help to reduce the waiting lists for CPAP titrations. The main purpose of this study was to compare the effectiveness of conventional versus manual or automatic daytime CPAP titration in unselected patients with SAHS.

Ninety-three consecutive patients with SAHS in whom CPAP was indicated were assigned to conventional titration or to manual or automatic (AutoSet) daytime CPAP titration, after sleep deprivation. The number of valid studies, sleep architecture, final pressure selected and mean pressure in the different sleep stages were compared. Changes in sleepiness (Epworth sleepiness score) and hours of CPAP use were assessed after 3 months of treatment.

Four patients did not sleep (3 AutoSet, 1 conventional daytime groups). Sleep latency was shorter during automatic daytime titration whereas REM latency was shorter in daytime studies; the percentage of sleep stages was similar during all types of titration. CPAP requirements were significantly higher during REM sleep in conventional and manual daytime titrations while mean pressure was unchanged throughout sleep stages during AutoSet titration. CPAP pressure selected with conventional or daytime manual titration (7.5(2.2) cm H_2O and 7.4(1.5) cm H_2O, ns) were significantly lower ($P<0.001$) than with AutoSet (9.4(1.6) cm H_2O. All groups showed similar decrease of sleepiness and hours of use of CPAP at 3 months of follow-up.

Automatic and manual daytime PSG studies after sleep deprivation are useful for CPAP titration in unselected patients with SAHS. Pressure selected with AutoSet is significantly higher than with conventional daytime or nighttime titration, although not significant in terms of treatment compliance and symptom improvement.

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Introduction

Continuous positive airway pressure (CPAP) is the treatment of choice for adult patients with the sleep apnea–hypopnea syndrome (SAHS).[1] It has a proven effect in preventing upper airway collapsibility during sleep and normalizing sleep architecture,[2] thus improving daytime somnolence,[3] cognitive function impairment[4] and nocturia.[5] Additionally, CPAP can contribute to better control of coexistent systemic hypertension[6,7] and heart failure.[8]

The effective CPAP pressure is determined during a titration study conducted during a full polysomnography (PSG) study at the sleep laboratory where a trained technician progressively increases airway pressure until apneas, hypopneas and snoring are abolished, oxyhemoglobin saturation is normalized and sleep fragmentation disappears. The guidelines of the American Sleep Disorders Association (ASDA) establish that CPAP titration must be performed during one night under full PSG control and using a manual protocol.[9] However, this practice is not available or is insufficient in many hospitals owing to its cost and to the long waiting lists. This has led to the development of alternative methods of CPAP titration, including split-night studies,[10,11] predictive equations,[12] monitoring of respiratory variables[13] and titration with automatic CPAP systems in hospital[14–19] and at home.[20] Daytime CPAP titration studies with full PSG[21,22] have been successfully performed in severe SAHS patients. However, the applicability of daytime CPAP titration, conventional or automatic, in unselected SAHS patients has not been studied to date. It is our current clinical practise to perform daytime titration studies, manual and automatic. In our center, the implementation of daytime studies has achieved a reduction of the CPAP titration waiting list. The main purpose of this study was to assess the effectiveness of this practise in unselected SAHS patients, in whom CPAP treatment was indicated, by comparing the acute effect of conventional versus manual or automatic daytime CPAP titration on sleep architecture, mean pressure during sleep stages and final pressure selected. As secondary outcomes, we compared the decrease in sleepiness and the hours of use of CPAP, after 3 months, in patients treated according to the results of the three titration procedures.

Methods

Study subjects

The study population consisted of 93 consecutive SAHS patients referred to the sleep unit of our hospital for CPAP titration between January and June 2000. All patients had undergone a diagnostic PSG in the same laboratory, prior to the study. Criteria for apneas were cessation of airflow for at least 10 s, and for hypopneas, a discernible reduction in airflow followed by 3% oxygen desaturation and/or arousal. If thoraco-abdominal effort was present the respiratory events were scored as obstructive; if there was no respiratory effort, they were scored as central events. According to the recommendations of the Spanish Respiratory Society, CPAP was indicated in patients with an apnea–hypopnea index (AHI) higher than 30 with co-existing clinical symptoms (witnessed apneas, nocturnal choking, daytime somnolence, tiredness) or systemic hypertension or cardiac disease.[23] CPAP treatment in patients with an AHI lower than 30 was considered on an individual basis, depending on clinical symptoms and coexisting cardiovascular disease.

Design

Patients were assigned, in order of presentation, by the administrative staff of the sleep laboratory, to conventional or daytime manual or automatic CPAP titration. Patients assigned to daytime studies were asked not to sleep the night before and to attend the sleep unit at 8 a.m., although this recommendation was not assessed objectively. Before titration, patients were instructed on the rationale and action of CPAP. All patients went home with a fixed pressure CPAP generator, without differences according to the titration performed.

Methods

Conventional nighttime CPAP titration

EEG (C3-A2, C4-A1), chin EMG, EOG and ECG were recorded continuously on a polygraph (Nightinghale, Judex, Copenhagen, Denmark). SaO_2 was measured using a finger pulse-oximeter (model 504, Critical Care Systems, Inc., Waukesha, WI). Mask pressure and thoracic and abdominal effort were monitored. Sleep stages were manually scored according to standard criteria.[24]

When patients had achieved stable sleep, pressure was gradually increased from 4 cm H_2O in increments of 1 cm H_2O at intervals of approximately 10 min until apneas, hypopneas, snoring and desaturations disappeared. After abolition of the respiratory events, pressure was slowly decreased until the respiratory events resumed to ascertain

the lowest effective pressure, while making sure that the patient had achieved REM sleep and was in the supine position. A night staff technician different than the one attending daytime studies attended the nighttime titration. In nighttime studies, the duration of the study is set by staff schedules to last around 8 h.

Conventional daytime titration

Manual titration with full PSG was performed in the same manner as nighttime titration. Titration began at 9 a.m. The technician decided to end daytime studies in agreement with a physician if patients achieved at least one REM period, which usually occurred during the first 4 h.

Automatic daytime CPAP titration

The AutoSet Clinical CPAP system version 3.02 (ResMed, Sydney, Australia) was used. AutoSet was designed to automatically increase pressure in response to apneas, hypopneas, snoring and airflow limitation. The principles and algorithms of performance of the device were described by Teschler.[18] At the end of the study, a printed summary was obtained displaying the fluctuations in oximetry, snoring, mask pressure, index of flattening of the inspiratory flow contour (indicating inspiratory flow limitation), breathing irregularities and mask leaks. Effective CPAP pressure was selected visually by the same physician as the repetitive pressure that eliminated apneas, snoring, airflow limitation and SaO_2 desaturations, after ruling out occasional peak pressures and portions of the study in which the leak exceeded 0.4 l/s. Auto-CPAP titration was performed in automatic mode from the outset. Simultaneously with AutoSet titration, EEG (C3-A2, C4-A1), chin EMG, EOG and ECG were recorded continuously using the same procedure as with conventional titration.

The same technician attended conventional and automatic daytime titration.

Acute effects of titration on sleep architecture

Duration of the study, sleep efficiency, sleep latency, REM latency, percentage of time at different sleep stages and the number of awakenings per hour of recording were compared in the 3 titration studies.

Pressure changes throughout the night in nighttime and daytime CPAP titration

The same investigator selected, by visual inspection, in each patient and all types of titration, the mean pressure corresponding to each sleep stage. The visually selected mean pressures for each stage throughout the study were totaled and then divided by the number of times the patient entered each sleep stage.

Follow-up of CPAP treatment

After three months of treatment with CPAP, Epworth sleepiness score and objective CPAP use (hour-counter in the CPAP device) were recorded.

Analysis

Data were expressed as means and standard deviation. The One-Way Anova and the *t*-test for independent variables, when appropriate, were used to compare continuous variables from the different studies. The post hoc Scheffe test was performed to assess significant differences between the 3 groups. Qualitative variables were compared by a χ^2 test. A P value lower than 0.05 was considered significant.

Results

Results of CPAP titration

Thirty one patients were assigned to each titration mode. Patients in the 3 groups had similar characteristics (Table 1). In the conventional titration group, 1 patient could not sleep, but the study was successful in 30 patients (97%). In the AutoSet group, 3 patients (2 men, 1 woman) were not able to sleep and 1 did not attend; thus, 27 were suitable for final analysis (90% successful studies). In the manual daytime group, 1 man was not able to sleep and 2 did not attend; thus, 28 remained for final analysis (96.5% successful studies).

Following AutoSet titration, mean visual pressure (9.4 (1.6) cm H_2O) was significantly higher ($P<0.001$) than pressure obtained with conventional nighttime and manual daytime titration, which did not differ significantly (7.5 (2.2) and 7.4 (1.5) cm H_2O, respectively).

Effects on sleep architecture

All patients in the manual daytime titration group reached REM sleep but 2 in the AutoSet group and 1

in the conventional group did not. Six patients of the AutoSet group experienced an inconvenient pressure increase while awake without significant air leaks at the beginning of the study. This required technician intervention to switch from auto to manual mode for approximately 30 min and until the patient was asleep and to change back to auto-mode, with no further difficulties in achieving titration. In all cases, sleep latency was calculated from the beginning of the recording.

In nighttime studies, study duration was significantly longer compared with daytime studies. REM latency was significantly shorter during daytime studies compared with conventional nighttime studies and sleep latency was significantly shorter during AutoSet compared with the other types of titration. The percentage of time in the different sleep stages and number of awakenings per hour of sleep were similar in all groups.

Table 2 shows mean CPAP levels in the different sleep stages during all titration studies. CPAP pressure requirements throughout sleep were similar during conventional nighttime and manual daytime titration, with significantly higher pressures in REM and stages 3 and 4, compared with stages 1 and 2. In contrast, during AutoSet titration, mean CPAP pressure was the same in the different sleep stages and was significantly higher except in REM sleep compared with the other titration modes.

Clinical outcomes at 3 months of follow-up

Outcome data at 3 months of follow-up are shown in Table 3. The number of patients lost, those not starting CPAP or who rejected it and those who decided on surgery were excluded from the final analysis. Thus, compliance data were available for 77% of the initial patients, 25 in the AutoSet group, 24 and 23 in the daytime and nighttime conventional groups, respectively.

Objective use of CPAP and subjective sleepiness assessed by the Epworth sleepiness scale did not differ significantly between all groups. No significant differences were found between all groups concerning side effects after 3 months of CPAP treatment: 5, 2 and 2 patients referred excessive pressure sensation according to AutoSet, conventional daytime and conventional nighttime titrations, 2, 4 and 1 patients complained of rhinitis and 2, 2 and none experienced dry mouth, respectively.

Discussion

This study shows that daytime CPAP titration studies after night sleep deprivation, manual or automatic, are useful in unselected SAHS patients. This is the first prospective study assessing the efficacy of daytime CPAP titration, including

Table 1 Patient characteristics in the 3 CPAP titration groups.

	AutoSet daytime ($n = 27$)	Manual daytime ($n = 28$)	Conventional titration ($n = 30$)	*P*
Sex (M/F)	22/5	24/4	23/7	ns
Age (years)	53.9 (7.7)	56.4 (10.2)	58.6 (8,7)	ns
BMI (kg/m^2)	32.0 (5.8)	31.5 (5.1)	31.1 (6.7)	ns
Epworth	13.3 (5.1)	12.6 (4.6)	11.6 (5.2)	ns
AHI	55.2 (24.2)	49.8 (26.9)	52.6 (22.7)	ns

Results are expressed as mean (SD).

Table 2 Comparison of mean CPAP pressures in the different sleep stages obtained in conventional and manual or automatic daytime titration studies.

	AutoSet daytime	Manual daytime	Conventional nighttime	*P*
Visual pressure	9.4 (1.6)*	7.4 (1.5)	7.5 (2.2)	0.001
REM pressure	7.8 (2)	6.7 (2)	7.1(1.5)	0.056
Stage 1 pressure	7.6 (1.6)*	4.9 (0.9)	5.5(1.1)	0.0001
Stage 2 pressure	7.9 (1.9)*	6 (1.3)	6.1(1.1)	0.0001
Stages 3 and 4 pressure	7.9 (1.9)*	6.4 (1.8)	6.2(1.4)	0.006

Data are expressed as mean (SD). The *P* values correspond to differences between pressures in the different sleep stages between AutoSet titration and manual daytime or conventional CPAP titration.

Table 3 Outcome measures at 3 months of follow up in the 3 CPAP titration groups.

	AutoSet daytime	Manual daytime	Conventional nighttime	*P*
Patients on CPAP	25(92.6%)	24(85.7%)	23(83%)	
Objective CPAP use (hours)	4.8(1.9)	4.8(2.1)	3.9(2)	ns
Epworth	6.4(2.8)	6.7(3)	7.4(4)	ns
Epworth difference respect to baseline	6,9(3.9)	5,9(8)	4,2(6)	
Patients never on CPAP	0	0	3(10%)	
Patients who discontinued CPAP	0	1(3.5%)	2(6.6%)	
Patients deciding on surgery	2(7%)	2(7%)		
Patients lost to follow-up	0	1(3.5%)	2(6.6%)	

Data are expressed as mean (SD) or numbers and percentages in parenthesis.

automatic titration, in unselected SAHS patients. The number of failed studies due to the difficulty in sleeping was low in daytime studies and no significant differences were observed in sleep efficiency among the three procedures. Although the pressure selected after daytime titration with AutoSet was significantly higher than that selected with manual daytime or conventional titration, reduction of sleepiness and hours of CPAP use were not different between titration modes at three months of follow up.

Failure rate in CPAP titrations with the AutoSet system are low. Teschler described 27 failed titration studies with the AutoSet system in a series of 1000 patients owing to mouth respiration or severe air leak.[18] In our study, despite of the pressure increase during wakefulness in six patients at the beginning of the AutoSet titration, mean sleep latency was significantly shorter compared with manual nighttime and daytime titration. In the study by Marrone et al.[25] 88% of rapid CPAP augmentations were observed during sleep–wake transitions or after arousals/awakenings and without any detectable respiratory abnormality. Therefore, we suggest that auto-CPAP studies should begin at a low pressure in a ramp mode, for 15–20 min, until the patient is asleep.

Few studies have compared daytime and nighttime CPAP titration in patients with severe SAHS.[21,22] In these studies, diurnal and nocturnal manual titration resulted in comparable therapeutic pressures, comparable resolution of sleep-disordered breathing and improvement in subjective sleepiness, after 1 week of treatment[21] or after a longer follow up period (<3 months).[22] We have shown that these results are also applicable in unselected SAHS patients referred for a CPAP titration study, either conventional or automatic. Although most of our patients have an AHI >30 and then could be considered as severe, this is the population we usually treat and thus the results of this study are clinically relevant.

Since our SAHS patients were not selected on the basis of an extreme daytime hypersomnolence, sleep deprivation was indicated before daytime titration, to enhance the probability of sleeping in the morning. Although we cannot objectively confirm the compliance to this recommendation of sleep deprivation, the shorter sleep latency observed in daytime studies may have been due to the acute sleep deprivation prior to the study.[26]

We were concerned about the possibility of finding higher pressures during daytime titrations. It has been suggested that sleep deprivation can worsen sleep apnea,[27] perhaps through a depressive effect on the upper airway dilator muscle activity.[28] However, the 3 groups had similar percentages of REM sleep, and higher pressures were only found with AutoSet titration.

During AutoSet titration, mean pressure did not differ throughout the different sleep stages. In contrast, during conventional titration, mean CPAP pressure during REM and stages 3 and 4 was significantly higher than in stages 1 and 2. The most likely explanation for this and for the higher pressure obtained during AutoSet titration is that the AutoSet algorithm for detection and response to snoring, apneas, hypopneas and silent flow limitation is more sensitive than the conventional CPAP titration applied by sleep laboratory technicians, acting preventively before respiratory disturbances occur, even during REM sleep and that in conventional titrations we treated apneas, hypopneas and snoring but not airflow limitation.

The higher CPAP pressures selected with AutoSet, compared with manual titration, have already been documented during night studies.[17–20] The last consensus statement for CPAP treatment does not specify the best method for measuring airflow.[29] However, the authors recommend the elimination of respiratory related arousals, measured with esophageal catheter or other novel technologies, probably referring to the inclusion of a pneumo-

tachograph between the nasal mask and the expiratory port. In our center, at the time of performing this study we did not use the pneumotachograph technology, which possibly could explain the pressure difference between manual and AutoSet titration.

The therapeutic usefulness of indicating a higher level of pressure versus the lower obtained with manual titration is unknown. Automatic CPAP nighttime titration results in compliance rates similar to those obtained after manual titration, when the same levels of pressure are achieved.[30] We found that AutoSet daytime titration and conventional nighttime or daytime titration result in comparable compliance rates, daytime somnolence improvement and side effects, despite the mean higher pressure obtained with AutoSet.

In summary, automatic and manual daytime PSG studies after sleep deprivation are useful for CPAP titration in unselected patients with SAHS. Pressure selected with AutoSet is significantly higher (1.9 cm H_2O) than with conventional daytime or nighttime titration, although not significant in terms of treatment compliance, symptom improvement or side effects. AutoSet produces increments in pressure from the outset which are not significantly modified during the different sleep stages, in contrast to conventional titration, in which REM pressure is significantly higher than during the other sleep stages.

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