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Importance of sleep stage- and body position-dependence of sleep apnoea in determining benefits to auto-CPAP therapy

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Importance of sleep stage- and body position-dependence of sleep apnoea in determining benefits to auto-CPAP therapy. F.Sériès, I. Marc. ©ERS Journals Ltd 2001.

ABSTRACT: The influence of sleep stage- and body position-dependence of sleep apnoea on treatment efficacy and compliance between conventional continuous positive airway pressure (CPAP) and auto CPAP therapy was evaluated.

Thirty-three newly treated sleep apnoea hypopnoea syndrome (SAHS) patients were randomly allocated to conventional or auto-CPAP therapy. Six patients of each treatment group were classified as having sleep stage- and body position-dependent obstructive breathing abnormalities according to the results of the baseline sleep study.

After 3 weeks of treatment, the Epworth sleepiness score tended to be higher ($p = 0.08$) and the ability to stay awake lower ($p = 0.02$) in patients with dependent breathing abnormalities treated with fixed CPAP, than in the other patients. The effective pressure/time index was significantly lower in sleep stage- and body position-dependent patients treated with fixed CPAP, than in the other patients ($p = 0.02$). The number of hours the machine was turned on and a positive pressure applied, tended to be smaller in dependent patients treated with fixed CPAP than in independent patients of this treatment group and in patients treated with auto-CPAP. A night-to-night variability index (VI) of positive pressure changes was obtained in the auto-CPAP group. This index significantly decreased with time in the dependent patients while it remained unchanged in the independent group.

It is concluded that auto-continuous positive airway pressure may have specific indications in a subset of obstructive sleep apnoea patients with sleep stage- and body position dependent nocturnal breathing abnormalities.
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Nasal continuous positive airway pressure (CPAP) is one of the most effective treatments of the sleep apnoea/hypopnoea syndrome (SAHS). The effective positive pressure level (P_{eff}) is conventionally identified during attended or unattended titration sleep studies and indicates the pressure level required to normalize sleep and respiration in all sleep stages and body positions during the first treatment night. However, this pressure level is influenced by several physiological and clinical situations, including sleep stages, changes in body, neck and jaw position, variations in upper airway vascular tone, hysteresis of the upper airway, duration of CPAP therapy, and weight loss [1–7]. Because of the aforementioned factors, positive pressure requirements may dramatically change over time. CPAP therapy should take into account for the intra-night and inter-night variability in positive pressure requirements. This has led to the development of automatic positive pressure devices that have the ability to continuously adapt the positive pressure level during the night.

Only a few studies have been conducted to explore the applicability and accuracy of these newly developed apparatus, most of those performed having been conducted in a sleep laboratory or in hospital [8–10] instead of the home environment [11, 12]. Most studies demonstrated a normalization of sleep and respiratory variables during auto-CPAP therapy with a similar improvement in subjective and objective diurnal sleepiness and in neuropsychological performances compared to fixed CPAP [12, 13]. With these auto-CPAP machines, a significant percentage of total sleep time can be spent below the effective pressure level [8, 11], with significant changes in the positive pressure level within the different sleep stages and body positions [12, 13]. Another important potential advantage of auto-CPAP therapy is that it is associated with an increase in short term treatment compliance [12, 13].

Besides these potential benefits of auto-CPAP therapy, it must be acknowledged that the specific place of auto-CPAP therapy in SAHS treatment strategy is not clearly defined, *i.e.* should it be prescribed in every patient or only in a subset of patients who would particularly benefit from this new therapeutic alternative? According to the present authors' experience with auto-CPAP and knowing the influence of sleep stages and body positions on the required positive pressure needs, it was hypothesized that patients who have sleep stage- and/or body position-dependent obstructive breathing abnormalities would be more likely to benefit from auto-CPAP therapy.

The aim of the present study was to evaluate

the influence of sleep stage- and body position-dependence of sleep apnoea on treatment efficacy and compliance between conventional CPAP and auto-CPAP therapy. For this purpose, since the sample sizes of recently published trials on auto-CPAP were too small to conduct the present study [12, 13], the patients who participated to those previous studies were pooled together and a new cohort of patients was enrolled.

Material and methods

Subjects

Forty-eight newly treated SAHS patients, identified by conventional sleep recordings were studied. Forty of them participated in recently published studies on home auto-CPAP [12, 13]. They did not receive any medication at the time of the study. None had previous upper airway surgery. The protocol was accepted by the internal review board of Laval University, Quebec, Canada, and each patient signed an informed consent form for acceptance to participate to the study.

Sleep studies

Sleep recording consisted of the continuous acquisition of: electroencephalogram (C_4A_1, C_3A_2, O_2A_1); electroculogram (EOG); submental and anterior tibialis electromyogram (EMG); electrocardiogram (ECG); combined oro-nasal flow with thermistors placed in front of the nares and the mouth (ONT 2, Grass instruments, Astromed, Longueuil, PQ, Canada); thoracoabdominal movements with inductive plethysmography (Respitrace®, Ambulatory monitoring, Arsdley, NY, USA) calibrated with the isovolume method [14]; arterial oxyhaemoglobin saturation with an ear oximeter (504 pulse oximeter, Criticare systems, Waukesha, WI, USA); and breathing noises with two microphones placed at the head of the bed [15]. Body position was checked during the sleep recordings by the attending technician, according to continuous infrared monitoring. During CPAP nights, flow was measured *via* a pneumotachograph connected to the nasal CPAP mask.

Protocol

Diurnal sleepiness was subjectively assessed by the Epworth sleepiness score (ESS) [16], and the ability to stay awake with the Maintenance of wakefulness test (MWT) [17], before initiating CPAP therapy. Every patient had a conventional titration sleep study to determine the *P*eff level. They were then randomly allocated to fixed (n = 24) or auto-CPAP (n = 24) therapy using the same auto-CPAP machine (Morphée Plus/Cloudnine, Nelcorr Puritan Benett, Minneapolis, MN, USA) for 3 weeks. For the 40 patients who participated in the aforementioned previous auto-CPAP studies, the constant and auto-CPAP groups were paired for the apnoea/hypopnoea index (AHI) and body mass index (BMI) (n = 8) or for *P*eff (n = 12). The eight additional subjects were paired for *P*eff.

In the conventional CPAP group, the machine was set at *P*eff and used in the constant mode. In the auto-CPAP group, the Morphée Plus setting requires the determination of a reference pressure on each side of which the pressure is allowed to change inside upper and lower limits that are separately chosen by the physician. Reference pressure was set at the *P*eff value, with upper and lower pressure limits set at $+2$/-4 cmH_2O in eight subjects, and $+3$/-4 cmH_2O in the 12 others. A control sleep study was obtained at the end of the CPAP trial using the machine and the pressure setting prescribed for the three previous weeks. ESS score and MWT test were obtained during the day following the control sleep study.

Data and statistical analysis

Sleep and respiratory variables were manually interpreted according to standard criteria [18, 19]. Treatment compliance was evaluated by the time the machine was turned on (machine running time), the time a positive pressure was applied (positive pressure-time), and their ratio (effective pressure time index). Patients were classified as having sleep stage- or body position-dependent nocturnal breathing abnormalities when there was a minimum of 100% difference in the apnoea/hypopnoea index between the different sleep positions (lateral, supine) in nonrapid eye movement (REM) sleep or between stages I and II, and REM in the same sleep position. Patients were defined as having sleep stage- and body position-dependent nocturnal breathing abnormalities when both sleep stage-dependence criteria were met.

In patients of the auto-CPAP group, the amount of pressure delivered at the different pressure levels was assessed by a print out of the percentage of the positive pressure-time spent at the different pressure levels for each treatment night during the 3 weeks of home CPAP therapy. The degree of pressure changes was quantified by the VI, which took into account the percentage of positive pressure time spent at the different pressure levels. The same formula that is used to determine the variance of a frequency variable was used: $VI = \Sigma_i\ (i\text{-}A)^2 \cdot P_i$, where i represents the positive pressure value from $4-20$ cmH_2O in 2 cmH_2O increments, P_i is the percentage of positive pressure time spent at the different positive pressure levels, and $A = \Sigma_i\ I \cdot P_i$. According to this index calculation, VI is 0 if the whole night was spent at the same pressure level and 5 if the time spent at the different pressure levels is identical. The maximal possible value of VI is 9 and corresponds to the situation where 50% of the treatment time is spent at the two extreme pressure values respectively.

The different analysed parameters were compared using a two-way ANOVA to evaluate the interaction effects of treatment mode and sleep stage/body position-dependence status. Parameters measured at baseline and after treatment were compared with a

Table 1. – Anthropometric and nocturnal breathing characteristics of the patients in each treatment group

Parameter	Conventional CPAP	Automatic CPAP
Subjects n	16	17
Age yrs	49±6	47±10
Body mass index $kg \cdot m^{-2}$	40±10	39±10

Data are presented as mean±SD. CPAP: continuous positive airway pressure.

repeated measure design. Normality of variance assumptions were verified to validate statistical tests. The distribution of total sleep time between different sleep stages was transformed with an arcsin function and expressed as a percentage. Statistical significance was inferred for p-values < 0.05.

Results

Six patients from the conventional CPAP group and six patients from the auto-CPAP group were classified as having sleep stage- and body position-dependent obstructive breathing abnormalities. The sleep stage- and body position-dependence could not be characterized in 15 patients who did not change body position or whose sleep architecture did not include REM sleep during baseline sleep recording. These subjects were therefore excluded from the comparison between sleep stages/body position-dependent and independent patients. Analysis was done with 33 subjects, 16 undergoing conventional CPAP and 17 auto-CPAP therapy. There was no difference in the subject characteristics between the 48 patients recruited for the study, the 40 who participated in the previously published papers and the 33 in whom the body position- and sleep stage-dependency was definable. In the subjects of the auto-CPAP group who had sleep stage- and body position-dependent breathing disorders, the upper and lower pressure limits were set at +2/-4 cmH_2O in three patients and at +3/-4 cmH_2O in the other three.

Patients of the two treatment groups (constant and auto-CPAP) had identical age, body mass index, apnoea/hypopnoea and sleep fragmentation indices, and *P*eff values (tables 1 and 2). Subjective and objective baseline assessment of diurnal sleepiness and *P*eff level were similar in these two groups (table 2). No difference was found in these variables between patients with or without sleep stage/body position-dependent breathing abnormalities in each treatment group.

Body weight and neck circumference did not change during the treatment course. Sleep architecture and breathing characteristics and diurnal somnolence improved in each treatment group whatever the sleep stage- body position-dependent or independent status (table 2). At the end of the treatment period, patients treated with fixed CPAP who had dependent breathing abnormalities demonstrated more daytime sleepiness compared to the other patients of this treatment group and to those of the auto-CPAP group, as suggested by the higher Epworth sleepiness score ($p = 0.08$) and lower ability to stay awake ($p = 0.02$) (table 2). Similarly, diurnal sleepiness improved in dependent and independent patients of the auto-CPAP treatment group. In the auto-CPAP group, the percentage of positive pressure-time that was spent below *P*eff during home CPAP trial was significantly greater in the dependent group than in the independent group ($p = 0.009$).

The machine running time was similar in the fixed and auto-CPAP treatment groups. However, the positive pressure-time and the effective pressure time

Table 2. – Characteristics of patients with and without sleep stage- and body position-dependence of nocturnal breathing disorders in each treatment group

	Conventional CPAP therapy		Auto-CPAP therapy	
	Dependent	Independent	Dependent	Independent
Subjects n	6	10	6	11
*P*eff cmH_2O	9.2±2.0	10.7±3.3	9.5±2.0	10.6±3.7
AHI $events \cdot h^{-1}$				
Baseline	39.0±10.9	54.1±15.2	46.7±24.2	47.9±27.1
Control	3.9±3.0	3.7±4.6	2.0±1.6	3.3±1.8
Ar I $events \cdot h^{-1}$				
Baseline	34.0±7.8	52.0±21.1	48.1±10.9	42.6±19.9
Control	10.8±4.8	9.5±4.7	10.2±6.8	11.3±3.9
ESS				
Baseline	16.8±5.2	15.8±4.9	15.1±2.3	14.3±5.6
Control	9.7±6.7	7.5±3.9	8.0±3.3	6.3±3.4
MWT				
Baseline	16.1±11.5	15.2±11.4	11.1±5.6	18.6±8.7
Control	22.1±13.0+	27.0±10.8	28.1±11.6	26.1±9.2
% PPT < *P*eff			54.7±7.3*	41.1±8.1

Data are presented as mean±SD. *P*eff: effective pressure; AHI: apnoea/hypopnoea index; Ar I: arousal index; MWT: Maintenance of Wakefulness test; CPAP: continuous positive airway pressure; % PPT < *P*eff: the percentage of the time during which a pressure is delivered to a patient, that is less than the effective pressure level. *: $p < 0.05$.

index were significantly less in the fixed CPAP group than in the auto-CPAP group ($p=0.006$). The machine running time, positive pressure-time (fig. 1a), and effective pressure-time index (fig. 1b) were smaller in patients of the fixed CPAP with dependent breathing disorders with than in the other groups. This difference did not reach significance for the first two variables but was significant for the third one ($p=0.02$).

The above mentioned differences in treatment efficiency between patients with dependent breathing disorders treated with fixed CPAP and patients of the other groups were not observed if sleep stage- or body position-dependency were considered alone.

No difference was found in VI between sleep stage/body position dependent and independent patients for the overall treatment period (5.9 ± 2.2 and 5.3 ± 2.6, respectively, $p=0.12$). This index was found to significantly decrease with time in the dependent patients while it remained unchanged in the independent group (fig. 2).

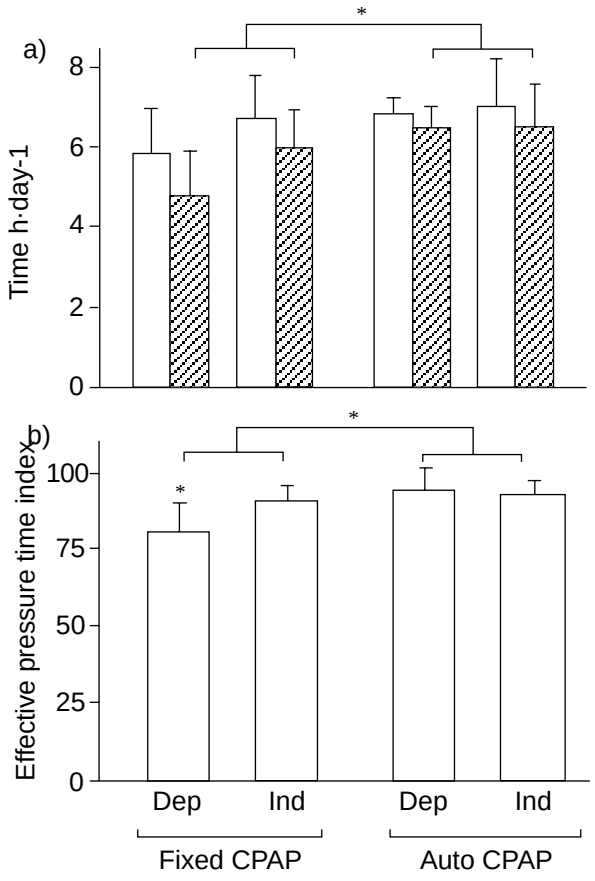

Fig. 1. – Mean $\pm$ SD values of a) the machine running time (□) and positive pressure time (▨), and b) and effective pressure time index in each treatment group, depending on their sleep stage/body position-dependency. The effective pressure time index is defined as the ratio of the number of hours a pressure is delivered to the number of hours the machine is turned on. The parameters measuring treatment duration tended to be lower in dependent patients treated with fixed continuous positive airway pressure (CPAP) but these differences did not reach significance. The effective pressure index was significantly lower in this group compared to others. *: significant difference ($p<0.05$) between indicated groups.

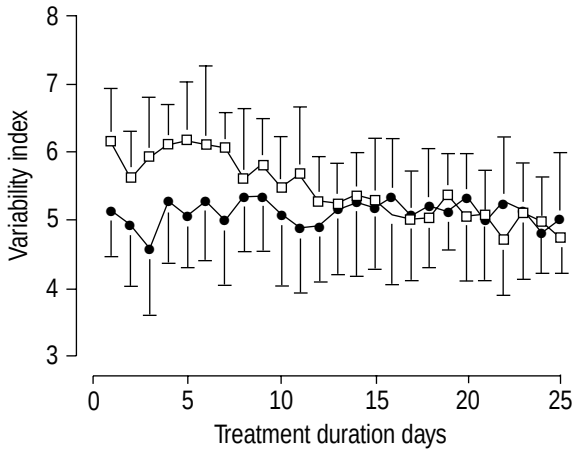

Fig. 2. – Mean $\pm$ SD values of the variability index measured day-by-day in patients of the auto-CPAP group, with (□) and without (●) sleep stage- and body position-dependence of nocturnal breathing abnormalities. This index tended to decrease with time. No significant difference was found in the changes in VI with time between the two groups.

Discussion

To the authors' knowledge, this is the first study to look at the influence of body position- and sleep stage-dependence of obstructive breathing abnormalities and CPAP mode on CPAP efficiency.

The criteria that were used to define body position-dependence is the same as that previously used by SHEPARD and coworkers [20, 21]. Interestingly, these authors found that, in a retrospective study of 100 patients, 43% of patients with body position-dependent nocturnal breathing disorders also had a sleep stage-dependence according to the criteria that were used in the present study; therefore, the prevalence of sleep stage- and body position-dependence in their study population was 21%, which is very close to that observed in the present study in those patients where this dependency could be analysed (25%).

The present results suggest that CPAP compliance and the benefits of treatment on neuropsychological variables are improved with auto-CPAP therapy in patients with sleep stage- and/or body position-dependent nocturnal breathing disorders, compared to fixed CPAP. This is of primary importance when objective compliance to CPAP therapy is poor; only 46% of patients treated with fixed CPAP apparatus use it at least 4 $h\cdot day^{-1}$ [22]. According to the prevalence of body position- and sleep stage-dependence that were observed in the present study, auto-CPAP therapy may be more effective than conventional CPAP treatment in 25% of obstructive sleep apnoea (OSA) patients. On the other hand, the present results suggest that in patients with no such body position- and sleep stage-dependence, auto-CPAP therapy may not bring additional benefits compared to fixed CPAP. Therefore, auto-CPAP therapy may have

specific indications in a subset of OSA patients, but is obviously not more effective than conventional CPAP in the majority of sleep apnoea patients. These parameters should be taken into account in any clinical trial comparing auto-CPAP and conventional CPAP efficiencies.

Body position and sleep stage have been shown to significantly influence the positive pressure level that abolishes obstructive breathing abnormalities [1, 2]. The present authors are aware that several other factors also contribute to determine the positive pressure needs, and potentially, the changes in positive pressure requirements within the night, and from one night to another [3–5]. This can account for the important scatter in VI that was found in both groups (fig. 2). However, it is particularly interesting to note that the behaviour of this index with time, differed between the groups with different sleep stage- and/or body position-dependence status, with the VI decreasing with time in patients with dependent breathing abnormalities. Several factors can contribute to the decrease in VI over time such as the greater stability in body position during CPAP therapy [23] and the improvement in upper airway shape and/or dimension [24]. Several other factors may obviously be involved that remain to be investigated.

The observation that VI progressively decreases in dependent patients, to become similar to that of the independent group within 3 weeks of treatment, suggests that the benefits of auto-CPAP machines may be limited during the first weeks of treatment. Further studies should be conducted to analyse if VI values, and its changes during the course of CPAP therapy, may bring additional information on auto-CPAP behaviour, independently of the sleep stages- and or body position-dependent and independent status.

It is concluded that patients with body position- and/or sleep stage-dependency of nocturnal breathing disturbances, may benefit more from auto-continuous positive airway pressure therapy than from fixed continuous positive airway pressure, at least during the initial course of their treatment. Long-term prospective, randomized trials are needed to determine if additional factors can help to identify patients whose compliance and clinical response would be enhanced by using auto-continuous positive airway pressure devices and to investigate if positive pressure variations may be helpful in identifying them.

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