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Role of different nocturnal monitorings in the evaluation of CPAP titration by autoCPAP devices

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Summary The aim of the study was to assess how the analysis of different signals recorded during application of automatic continuous positive airway pressure (autoCPAP) devices improves the evaluation of pressure titration in patients with obstructive sleep apnea syndrome (OSAS) naive to treatment. Seventy-two patients underwent nocturnal polysomnography during autoCPAP (Autoset T, ResMed, Sydney, Australia) application. Progressively more complex combinations of signals were analysed in consecutive steps. According to the analysis of oxyhemoglobin saturation (SaO_2) alone, a fixed CPAP level suitable for treatment could not be identified in 3 subjects. When analysis of posture was added, titration was considered unsatisfactory in 1 more subject, due to a short time spent supine. Further, addition of flow and respiratory movements led to consider titration unsatisfactory in 1 more subject. Analysis of all polysomnographic signals demonstrated a not fully reliable titration in 9 subjects: 1 with short sleep duration, 2 without REM sleep, 4 with a short sleep time spent supine, and 3 subjects (already identified by SaO_2) with insufficient correction of respiratory disorders even when a relatively high CPAP was administered. Mask leaks did not hamper titration. CPAP titration by automatic devices alone results in imperfect titration in $>10\%$ subjects naive to ventilatory treatment. Only polysomnographic recording ensures titration reliability in all patients. Further research is needed to identify simple and economic methods to reliably start the CPAP treatment.

Introduction

It is still recommended to titrate continuous positive airway pressure (CPAP) before prescribing it as a long-term treatment for obstructive sleep

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apnea syndrome (OSAS). According to official statements, CPAP titration must be performed during polysomnography, while a technician adjusts the pressure delivered so as to identify pressure levels preventing upper airway obstruction during sleep.[1] However, the most appropriate criteria for identification of such levels are still uncertain, as it is not clear which respiratory and electroencephalographic parameters correlate best with clinical improvement.[2] Besides, optimal pressure, whatever the criterion to define it, may change over time,[3] although this is not a rule.[4] Therefore, some recent studies proposed to recommend the pressure level for therapy based on subjective criteria, like adherence to treatment and improvement in sleepiness.[5,6] This approach still needs to be validated: in fact, almost all studies comparing titrated vs. sham CPAP showed a similar compliance to both methods;[7] besides, even sham CPAP use may be associated to some improvement in subjective sleepiness, despite no improvement in objective somnolence measured by Multiple Wakefulness Test.[8] Thus, CPAP titration during polysomnography before starting home treatment is not exempt from criticism but, as long as other methods are not proven superior, it is still the standard procedure.

For a reliable CPAP titration, polysomnographic studies must fulfil some criteria: monitoring should last at least three hours in subjects whose apnea/hypopnea index (AHI) is >40, or even more in subjects with milder disease;[9,10] some REM sleep should be recorded, since this sleep stage is sometimes associated with higher pressure requirements;[11–13] some sleep time should be spent in the supine posture, as sleeping supine often requires higher CPAP levels.[12–14] This procedure is complex and expensive; easier methods for CPAP titration could reduce costs and waiting lists. The use of simplified monitorings[15,16] or of automatically adjusting CPAP machines (autoCPAPs) has been proposed for that purpose. The evidence to use simplified monitorings for CPAP titration is still insufficient.[17]

Properties of autoCPAP devices could be theoretically exploited to reduce the work of technicians attending titration studies, allowing them to perform more titrations than usual at the same time,[18] or to perform titrations by means of simplified procedures.[19] Analysis of the variable pressure levels automatically delivered during the night by these devices could give indications about the optimal pressure level for home treatment by machines delivering constant CPAP. Some studies investigated reliability of pressure data recorded during several nights by unattended autoCPAP machines, without any associated monitoring, either in patients naive to CPAP[20] or adequately trained:[21] although this procedure was successful in most patients, a variable success rate was reported, due to imperfect identification of optimal pressure[20–22] or to the inability of some patients to correctly wear nasal mask.[21,23] Studies where autoCPAP was applied for titration purposes during single-night polysomnographic monitorings pointed out a common need of technician interventions.[24,25] Nothing is known about the usefulness of simplified nocturnal monitorings during autoCPAP application. Due to this paucity of data, a committee of the American Academy of Sleep Medicine (AASM) has recently recommended to use validated autoCPAP devices for CPAP titration only during attended polysomnographic studies.[17]

In this study, we performed attended polysomnography for CPAP titration during application of an autoCPAP device (Autoset T) in OSAS patients naive to ventilatory treatment, candidate to home CPAP. Then, we evaluated the titration studies taking into account step-by-step an increasing number of the recorded signals. Our aim was to verify how the information given by the analysis of different signals recorded during autoCPAP application improves the reliability of CPAP titration by automatic devices in such patients.

Patients and methods

Consecutive subjects referred for suspected OSAS, after evaluation of clinical history, underwent a nocturnal monitoring, consisting either of standard polysomnography or of portable cardiorespiratory monitoring. On these recordings, AHI was calculated as (number of apneas+hypopneas)/hour of measured, or estimated, total sleep time (TST). OSAS was diagnosed according to AASM recommendations.[26] One hundred OSAS patients with an AHI >20 were found, who were considered candidates to ventilatory treatment. They tried CPAP during daytime both to test their ability to tolerate its application and to verify mask fitting. Eighty-one subjects accepted ventilatory treatment, and to undergo nocturnal polysomnography for pressure titration. After the exclusion of 6 patients with moderate to severe COPD, 75 subjects, 60 male and 15 female, were asked to participate to this study. All of them gave their consent. No subject showed significant central apneas or had congestive heart failure. No patient had used CPAP at night before. Characteristics of the enrolled subjects are shown in Table 1.

Table 1 Baseline characteristics of the subjects.

	Age (yr)	BMI (kg/m^2)	AHI (no/hour of TST)	Awake SaO_2 (%)	Lowest SaO_2 (%)
Mean $\pm$ SD	54.3 $\pm$ 11.7	36.2 $\pm$ 6.4	61.7 $\pm$ 20.5	95.2 $\pm$ 1.6	64.9 $\pm$ 13.9

Definitions of abbreviations: BMI=body mass index; AHI=apnea/hypopnea index; SaO_2=oxyhemoglobin saturation; TST=total sleep time.

Polysomnography was performed by a computerised system (PS-2 Compumedics, Abbottsford, Australia). CPAP titration was performed by means of an autoCPAP machine (AutoSet T, ResMed, Sydney, Australia) that modifies the pressure it administers after the automatic flow detection by in-built pneumotachograph; inspiratory airflow limitation is the main trigger for pressure augmentations. Pressure at the nasal mask was continuously recorded. Patients were recommended to lie supine for at least part of the night. A technician was allowed to intervene only if called by patients who asked to reapply nasal mask after having pulled it off. The protocol was approved by the local scientific committee.

Recordings with time in bed (TIB) $>$ 3 h (if baseline AHI was $>$ 40) or $>$ 4 h (in milder cases) were analysed.[9,10] Sleep was manually scored.[27] Sleep efficiency was calculated as TST/TIB $\times$ 100. Arousal index was calculated as number of arousals and awakenings[28] per hour of TST. Oxygen desaturation index (ODI), defined as the number of oxyhemoglobin saturation (SaO_2) falls $>$ 3%/hour of TIB, was automatically calculated by the polysomnographic system. Apneas and hypopneas were manually scored. Apneas were defined as lack of airflow (detected by thermistors) for at least 10 s, and distinguished in central, mixed and obstructive. Hypopneas were defined as discernible reductions in thoraco-abdominal movements or in airflow $\geqslant$ 10 s followed by either a SaO_2 fall $>$ 3% or an arousal.[26] Total number of apneas and hypopneas per hour of TIB (AHI_{TIB}) and of TST (AHI_{TST}) were calculated. AHI values were also calculated excluding central apneas from the total number of events.

Data recorded and automatically elaborated by the machine were retrieved (ResMed Autoscan 3.12). They included: mean nocturnal CPAP level, mean nocturnal air leak, CPAP level and air leak not exceeded for 95% of the night (95th centile CPAP and 95th centile leak, respectively); apneas and hypopneas (detected by its in-built pneumotachograph) per hour of TIB (AHI_{auto}). Apneas, but not hypopneas, are shown on the report of the device by a symbol allowing us to identify pressure and leak levels at their occurrence.

The 95th centile CPAP was considered as the pressure level suggested by the autoCPAP device for the patient's treatment by means of fixed level CPAP machines. Reliability of titration was assessed in four consecutive steps, taking into account pressure levels administered by the device in association with: (1) oxygen desaturations alone, evaluated on the SaO_2 signal; (2) oxygen desaturations and time spent supine, evaluated on SaO_2 and posture signals, like in "less than full" respiratory monitorings;[29] (3) disordered breathing events and time spent supine, evaluated on signals of SaO_2, posture, airflow, and respiratory movements, like in "full" respiratory monitorings;[29] and (4) respiratory and sleep characteristics, evaluated on all polysomnographic signals. At each step, it was evaluated if respiratory disorders were apparently corrected in the high range of pressure levels administered by the autoCPAP. TST $<$ 3 h, absence of REM sleep, or time spent supine $<$ 1 h were considered indicative of inadequate conditions for a satisfactory CPAP titration, whatever the behaviour of respiratory signals. Analysis of all polysomnographic signals (step 4) was taken as the gold standard for assessment of the acceptability of the titration. Evaluations were always performed in the same order, so that scorers were blinded to the successive, but not to the previous evaluation.

Data are reported as mean $\pm$ SD only when normally distributed, or as median (range). Correlations between variables were assessed by linear regression analysis. Mann–Whitney test was applied for comparisons between groups of patients. A $P < 0.05$ was considered significant.

Results

Three subjects requested to interrupt the study after $<$ 3 h. All the following results are relevant to the remaining 72 subjects.

Data calculated before EEG assessment are shown in Table 2.

Analysis of oximetry (step 1) revealed a satisfactory correction of SaO_2 behaviour in most cases. Ten subjects showed an ODI $>$ 10. As in 7 of them

Table 2 Data from polysomnography with autoCPAP before EEG assessment.

	Lowest SaO_2 (%)	ODI (no/hour)	TIB supine (min)	AHI_{TIB} (no/hour)	Non-c. AHI_{TIB} (no/hour)
median	89.0	3.2	339.5	4.4	3.6
range	59–95	0.0–45.7	39–496	0.0–49.5	0.0–47.7

Definitions of abbreviations: ODI=oxygen desaturation index, automatically calculated per hour of time in bed; TIB=time in bed; AHI_{TIB}=apnea/hypopnea index, manually calculated per hour of time in bed; non-c.=non-central.

oxygen desaturations were mostly confined to periods when a relatively low pressure was administered, at this step titration was considered unsatisfactory in 3 subjects.

Analysis of posture showed that 1 subject had remained supine for <1 h. Combined analysis of oximetry and posture (step 2) led to consider titration unsatisfactory in 4 cases.

Analysis of flow and respiratory movements revealed an $AHI_{TIB}>10$ in 12 subjects, while, if central apneas were excluded, it was >10 in 10 subjects. As in 6 of them hypopneas and obstructive apneas were mostly confined to periods with relatively low pressures administration, correction of respiratory disorders could be considered insufficient in 4 subjects: three of them had already been identified by SaO_2 analysis, while the last one had not, because most of her apneas were associated to very mild oxygen desaturations. Therefore, the combined analysis of all respiratory signals and of posture (step 3) led to consider titration unsatisfactory in 5 cases.

Polysomnography data calculated after EEG assessment are shown in Table 3.

TST was <3 h in only 1 subject, while REM sleep was not recorded in 2 subjects. TST supine was <1 h in 4 subjects (one of them without REM sleep). Altogether sleep or posture were inadequate for a fully reliable titration in 6 subjects. In the remaining 66 subjects, AHI_{TST} was >10 in 13 subjects, but, if central apneas were excluded, in only 10 subjects. In 6 of the latter subjects titration was considered satisfactory because hypopneas and obstructive apneas were mostly confined to periods of relatively low pressure administration; in 1 patient because obstructive events only appeared during alternating wake and stage 1 NREM sleep in the initial three hours of the recording, whereas they disappeared in the final four hours, when a stable sleep was recorded. Therefore, analysis of all polysomnographic signals (step 4) demonstrated that titration was imperfect or unsatisfactory in 9 subjects, and acceptable in 63 subjects.

Number of titrations that were correctly evaluated by means of each analysis are shown in Table 4.

Data retrieved and elaborated by the autoCPAP device are shown in Table 5. AHI_{auto} was significantly correlated ($P<0.001$) to ODI ($r^2=0.28$), AHI_{TIB}, both including and not including central apneas ($r^2=0.50$ and 0.38, respectively), and to AHI_{TST} ($r^2=0.56$ and 0.46, with and without central apneas, respectively). The 95th centile leak exceeded 0.4 l/s in 18 subjects. It was significantly, but weakly, correlated to AHI_{auto} ($r^2=0.08$, $P=0.019$), and to ODI ($r^2=0.07$, $P=0.03$), but not to manually calculated AHI values or to arousal index. Mean mask leak was not correlated with any variable relevant to respiratory disorders rate.

Mask was reapplied by the technician during the night after complete removal in 7 subjects.

Among the three patients with unsatisfactory CPAP titration due to incomplete correction of respiratory disorders, one was an obese woman (BMI 48.2 kg/m^2) without airway obstruction at spirometry, but who had recently recovered from an episode of respiratory failure; her respiratory disorders during autoCPAP application were mostly represented by hypopneas during REM sleep; following a new polysomnographic evaluation, she was later recommended bilevel ventilation. The second patient was a morbidly obese man (BMI 46.6 kg/m^2) with mild airway obstruction (FEV_1 88% of predicted value, FEV_1/VC 64.6%); in this patient the autoCPAP did not prevent a moderately high number of apneas and hypopneas, although AHI and oxygen desaturations improved markedly with respect to the baseline study; he refused immediate polysomnographic re-evaluation, and was recommended a CPAP 2 cm H_2O higher than indicated by the autoCPAP machine. The last subject, who experienced highly desaturating obstructive apneas throughout most of his sleep time, did not show peculiar characteristics during autoCPAP application; he later received polysomnographic manual CPAP titration and was recommended a pressure level 4 cm H_2O higher than the one indicated by the autoCPAP. The 95th centile leaks in the three patients were, respectively, 0.44, 0.40 and 0.38 l/s.

Among the six subjects with inadequate sleep or posture, three accepted to repeat polysomnography:

Table 3 Data obtained by full assessment of the polysomnographic studies with autoCPAP.

	TIB (min)	TST (min)	Sleep eff.%	Stage 1 (min)	Stage 2 (min)	Stage3–4 (min)	StageREM (min)	Arousal index (no/hour)	TST supine (min)	AHI_{TST} (no/hour)	Non-c. AHI_{TST} (no/hour)
median	423.5	349.8	85.6	26.0	195.3	43.0	65.0	15.2	252.5	4.7	4.2
range	225–515	170–440	38–98	5–87	64–304	0–165	0–168	5.2–58.7	3–438	0.0–57.4	0–55.4

Definitions of abbreviations: TIB=time in bed; TST=total sleep time; sleep eff.=sleep efficiency; AHI_{TST}=a pnea/hypopnea index, manually calculated per hour of total sleep time; non-c.=non-central.

Table 4 Titrations correctly evaluated by each analysis.

Polysomnographic signals analysed	Correctly evaluated titrations	
	No	%
None	63	87.5
SaO_2	66	91.7
SaO_2+posture	67	93.0
SaO_2+posture+airflow+ respiratory movements	66	91.7

the newly titrated CPAP differed from the previously obtained 95th centile CPAP by between +1 and −1 cm H_2O. On average, subjective somnolence was less in these six subjects than in the other 66 patients ($P<0.05$), but there was a large overlap between groups (Epworth scores 6.5, range 1–23, vs. 13.3, range 1–24).

Discussion

Use of unattended autoCPAP, without any simultaneous monitoring, has been proposed as a possible method for identification of optimal fixed pressure for treatment of OSAS subjects as an alternative to manual CPAP titration during polysomnography. The 90th or the 95th centile pressure level administered during the night by these machines is considered indicative of the optimal pressure.[24,25] In this study, in 87.5% cases, pressure levels alone delivered by an autoCPAP machine during a single-night in OSAS patients naive to ventilatory treatment was able to provide reliable indications about pressure level that could be administered by fixed CPAP ventilators to prevent sleep respiratory disorders. Respiratory and posture signals allowed us to recognise some cases of unsatisfactory titration, improving the effectiveness of the auto-titration procedure; there were only minor differences among analyses based on different combinations of such signals. Some cases of unsatisfactory titration were due to inadequate sleep, and could be identified only by full polysomnography analysis.

Correction of respiratory disorders was unsatisfactory in 3 of the 72 patients studied here. It is possible that pulmonary disease contributed to the unsatisfactory autoCPAP performance in two of these subjects, while the reason for the failure in the third one remained obscure. It is noteworthy that in two of these subjects the prescribed

Table 5 Data retrieved and automatically elaborated by the Autoset T device.

	Mean CPAP (cm H_2O)	95th centile CPAP (cm H_2O)	Mean air leak (l/s)	95th centile leak (l/s)	AHI_{auto} (no/hour)
Median	9.4	11.2	0.02	0.28	12.9
Range	5.8–12.6	7.6–15.4	0.0–0.48	0.0–0.96	1.3–52.5

95th centile CPAP=CPAP level not exceeded for 95% of the time in bed; 95th centile leak=air leak not exceeded for 95% of the time in bed.

treatment modality differed substantially from the one that would have been prescribed following analysis of autoCPAP levels alone. We looked if titration failure in these patients could be due to excessive air leaks. For Autoset devices, it is recommended not to exceed air leaks of 0.4 l/s, as, beyond that point, the machines may not correctly identify respiratory disorders and may not work properly. The 95th centile leaks in the three patients were within acceptable limits, or exceeded them only very slightly. In many patients of this study, the 95th centile air leak exceeded the 0.4 l/s threshold, but that did not result in inadequate correction of respiratory disorders for the titration purposes. Therefore, titration failures could never be attributed to lack of intervention by a technician. In this study the intervention of the technician was critically important only in seven patients who had completely removed the mask.

Theoretically, information to identify cases of imperfect correction of respiratory disorders could be given by the autoCPAP itself. In fact, other studies validated automatic AHI scoring by the Autoset device.[30–32] In this study, as the detection of respiratory events by the machine and by manual scoring on the polysomnography were based on different signals and criteria, we could not exactly control the accuracy of AHI_{auto}. Nevertheless, the values of AHI_{auto} and AHI_{TST} were significantly correlated, suggesting that AHI_{auto} could probably help to evaluate adequacy of correction of respiratory disorders when no monitoring is performed during the Autoset T device application. However, the report of the machine does not inform us about the precise time and pressure levels administered when hypopneas are detected. Therefore, AHI_{auto} appears more useful to evaluate Autoset T effectiveness when it is applied for treatment. If it is applied for pressure titration, rather than the number and the frequency of respiratory disorders, it is important to know how respiratory disorders are corrected at each administered pressure level. For that reason, usefulness of AHI_{auto} for the assessment of titration reliability has not been evaluated in this study. Such considerations may not apply to other autoCPAP devices, using different softwares packages. SaO_2, evaluated simultaneously with CPAP levels, proved sufficient to identify all cases of unacceptable correction of respiratory disorders. The addition of other respiratory signals did not provide further useful information.

Four cases of imperfect titration were due to insufficient sleep time spent supine. Posture signal alone identified only one of these subjects, as the remaining three remained awake for most of the time they spent supine. In fact, for most subjects supine posture is the most uncomfortable position to sleep, so that longer time is spent awake when supine than when lying on a side. Therefore, a reliable identification of sleep time spent supine requires also the recording of the signal for sleep scoring, like in full polysomnography.

Finally, 3 subjects showed either a short TST or absence of REM sleep. Only signals for sleep scoring, that are included only in polysomnographic monitorings, could identify such cases.

Patients who did not receive fully reliable CPAP titration due to inadequate sleep or posture were on average less sleepy than the other subjects; however, among them one subject had a very high Epworth score. Contrary to the cases of failure due to incomplete respiratory disorder correction, in these patients new titration studies, when performed, always led to prescribe a CPAP level that was very similar to the one that would have been prescribed following just the analysis of pressure levels delivered by the autoCPAP device. In fact, not all patients require a higher pressure in REM sleep,[11,13] and in the supine posture;[13] however, it is unknown how to identify in advance which patients change pressure requirements with sleep state or posture, so a fully reliable CPAP titration still requires REM sleep and some sleep in the supine posture.

One limitation of this study is that partially arbitrary criteria for definition of satisfactory titration had to be adopted, since methods for identification of optimal CPAP are not well standardised, and precise cut-offs are not available. The criteria that were used took into account present knowledge on the importance of sleep

characteristics, posture, and correction of respiratory disorders in CPAP titration.[9–14]

Another limitation of this study is that no manual titration was performed to compare the 95th centile pressure level provided by the autoCPAP with manually determined optimal pressure. Therefore, possible cases of overestimates of optimal pressure by the autoCPAP could not be identified.

Besides, flow limitation episodes were not assessed. The importance of the persistence of few or minor disorders, like a small number of obstructive apneas and hypopneas or flow limitation episodes, during administration of high pressure levels is dubious: it has been demonstrated that such events during administration of the best achievable pressure level in a titration night do not impair the following clinical success of CPAP treatment.[33] Thus we considered only the few cases indicative of unsuccessful titration due to incomplete correction of respiratory disorders when apneas or hypopneas occurred even at the highest pressures delivered.

In conclusion, titration by autoCPAP, performed without any simultaneous monitoring, did not provide fully reliable information about pressure level correcting respiratory disorders during sleep in $>10\%$ of OSAS patients naïve to ventilatory treatment. Recording of respiratory signals and of posture improved recognition of acceptable titrations, but did not totally prevent misinterpretations, due to sporadic occurrence of inadequate sleep. Therefore, these results support the need of polysomnography for a fully reliable CPAP titration, even when it is performed by autoCPAP.[18] This procedure has very high costs that cannot be sustained in every country. We speculate that initial adaptation at home to CPAP application, and subsequent recording of oximetry and posture during autoCPAP application could limit the risk of insufficient sleep during titration. Further research is needed to prove this hypothesis or to identify other simple and economic methods to reliably start CPAP treatment.

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