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ORIGINAL ARTICLE

Titration with automatic continuous positive airway pressure in obstructive sleep apnea

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KEYWORDS

Obstructive sleep apnea;
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Abstract

Background and objective: Autotitrating positive airway pressure (APAP) is an accepted titration method to determine the optimal positive airway pressure (PAP), for the treatment of obstructive sleep apnea (OSA). The required duration of APAP monitoring to determine a fixed continuous positive airway pressure level still remains to be established. We aimed to evaluate the variation in PAP level, delivered by APAP devices, at different periods of treatment, to determine the APAP treatment duration required to reach an effective and stable PAP level.

Methods: A cross-sectional study of 62 patients newly diagnosed with OSA were evaluated after 3 months of APAP therapy. APAP data corresponding to the first day (D1), first week (W1), seventh week (W7) and twelfth week (W12) under APAP therapy was collected. For the analysis of the pressure behaviour, the difference of P95th pressure level between W12 and W7 (P W12–W7), W12 and W1 (P W12–W1) and W12 and D1 (P W12–D1) was calculated.

Results: There was a high correlation in P95th pressure level between D1 and W12 ($r=0.771$; $p>0.0001$), W1 and W12 ($r=0.817$; $p>0.0001$), and W7 and W12 ($r=0.926$; $p>0.0001$). This correlation progressively increased with APAP use. A significance difference was found in concordance between P W12–W7 and P W12–D1 ($p=0.046$) within the pressure range ± 2 cmH₂O. However there was no significant difference in concordance between P W12–W7 and P W12–W1.

Conclusions: One week of APAP therapy seems sufficient to determine an effective and stable PAP level, within the pressure range ± 2 cmH₂O.

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a common disorder affecting at least 2%–4% of adult population.¹ Continuous positive airway pressure (CPAP) is considered the treatment of choice of OSAS. There are several methods used to determine the pressure level for CPAP therapy, namely, a full-night manual titration in a sleep laboratory, a split-night diagnostic titration and certain autotitrating positive airway pressure (APAP) devices. A full-night manual titration in a sleep laboratory is considered the best,¹ as it allows direct observation for conducting pressure selection, being able to adjust the fit of the mask, eliminating leaks and helping the patient adapt to CPAP.^{1,2} However, there are some limitations associated with this practice; the costs and time involved in repeat polysomnography (PSG) due to incomplete titrations, laboratory versus home environment and limited “one-night” sampling.^{2,3} APAP devices are able to detect the airflow and pressure in the circuit, as well as the occurrence of respiratory events. It is possible to determine the appropriate pressure through the data obtained from APAP tracking systems registration, with similar adherence and outcomes, and it is more cost-effective, compared to manual laboratory CPAP titration.^{2,4} Many clinicians prescribe CPAP based on automatic titration rather than manual titration. However, the required duration of APAP monitoring to determine a fixed CPAP level still remains to be established.^{2,5}

The aim of this study was to evaluate the variation in positive airway pressure (PAP) level of APAP devices at different periods of treatment, up until 12 weeks, in CPAP-naïve patients with obstructive sleep apnea (OSA), in order to determine the APAP treatment time required to reach an effective and stable PAP level.

Methods

Subjects and study design

We carried out a cross-sectional study that included consecutive adult patients with newly diagnosed OSA followed in the Sleep Medicine Centre – Centro Hospitalar e Universitário de Coimbra, during a two-month period, from March 2014. Recruited patients initiated APAP therapy and were evaluated in consultation with a sleep physician at 3 months. Information concerning gender, age, initial body mass index (BMI), neck circumference (NC), initial and follow-up Epworth Sleepiness Scale (ESS) score, apnea–hypopnea index (AHI) and APAP data (downloaded during the clinical consult) was collected.

Diagnosis of OSA was obtained with a level 3 sleep study device (Alice PDx, Embletta X100, Nox T3 or Stardust II) at the patient’s home with unattended recording. The following morning sleep studies were manually scored by an experienced sleep technician according to the criteria of the American Academy of Sleep Medicine,⁶ and APAP therapy was immediately prescribed by a sleep physician if criteria for treatment were present, namely: AHI \geq 30 events per hour; AHI \geq 15 events per hour with associated symptoms or cardiovascular comorbidities and AHI = 5–15 events per hour

with significant and intolerable symptoms not explained by other factors.¹

Patients were excluded if any of the following criteria were present: previous use of PAP device, previous pharyngeal OSA surgery, chronic nasal obstruction, hypoventilation disorders, a predominance of central events, malignancy, cognitive disability and incomplete medical data.

APAP and adherence data

The APAP devices were S8 AutoSpirit II™ and S9 AutoSet™ (Resmed, North Ryde, Australia), with nose and face masks optimized for the facial structure and comfort of the patient. Devices were chosen randomly. Heated humidifiers were prescribed when necessary, only after the beginning of treatment. APAP data collected included: air leaks at 95th percentile (P95th), air pressure delivered (P95th), residual AHI and adherence data from the first day (D1), the first week (W1), the seventh week (W7) and twelfth week (W12) under APAP therapy. The titration pressure level assumed to be effective in treating the majority of events was defined as the 95th percentile pressure level, which means that subjects spent 95% of the recording time below this pressure. For the analysis of the pressure behaviour, the difference of the P95th pressure level between W12 and W7 (P W12–W7), W12 and W1 (P W12–W1) and W12 and D1 (P W12–D1) were calculated.

Adherence data included percentage of days of APAP use, percentage of days of APAP use of more than 4 h and median of hours of use per days of use. Only adherent patients (use >4 h/night 70% of the nights)^{7,8} with a leak lower than 0.3 L/s and an AHI < 5 /h at the last evaluation were considered for the pressure behaviour analysis.

Initial analysis compared the sample characteristics and therapy parameters between the two groups, according to the device used, in order to exclude any significant bias, as both detect flow limitation but are driven by different therapy algorithms. Secondly, an analysis of the whole sample was performed.

Analysis

Continuous variables were expressed as mean \pm standard deviation. Frequency and percentage were used for categorical data. The ANOVA test was used for comparison of means in paired samples. Pearson’s correlation coefficient was used to evaluate the relation between P95th pressure level at W12 and the other periods. The Kendall test was used to analyze the concordance between PW12–W7 and PW12–W1 and between PW12–W7 and PW12–D1, within the pressure range of ± 2 cmH₂O (as during a split-night CPAP titration study, the American Academy of Sleep Medicine recommends an increase by 2 or 2.5 cmH₂O with an interval no shorter than 5 min to eliminate obstructive respiratory events, rather than an increase by at least 1 cmH₂O, given the shorter CPAP titration duration).⁹ Results were considered significant at a *p* level of less than 0.05. Statistical analysis was performed with Statistical Package for the Social Sciences (SPSS) version 22.0.

Table 1 Clinical characteristics and adherence data of APAP therapy of study population, group 1 and group 2.

	Study population (n=62)	Group 1 (n=37)	Group 2 (n=25)	p value (group 1 vs. group 2)
Age mean, years	63 ± 12	65.1 ± 10.2	60.3 ± 14.3	0.114
Gender (male/female)	62 (53/9)	34/3	19/5	0.081
BMI mean, kg/m ²	32.28 ± 5.27	31.7 ± 4.9	33.1 ± 5.8	0.304
Neck circumference, mean cm	43.2 ± 4	43 ± 4.2	43.4 ± 3.7	0.82
ESS score (at the diagnosis)	13 ± 6	13.7 ± 5.4	12.8 ± 6	0.551
AHI/h (at the diagnosis)	40.2 ± 22.76	44.5 ± 20.81	33.8 ± 24.43	0.071
ESS score at W12	7 ± 4.1	7.5 ± 3.9	7.2 ± 5	0.772
Residual AHI/h				
D1	5.3 ± 6	4.9 ± 4.2	5.9 ± 8	0.522
W1	4.1 ± 3.8	4.1 ± 3.3	4.1 ± 4.5	0.999
W7	3.2 ± 2.7	3.6 ± 2.8	2.6 ± 2.4	0.151
W12	3 ± 2.5	3.3 ± 2.5	2.5 ± 2.5	0.182
Leak, L/s				
D1	12.9 ± 7.5	13.6 ± 7.5	12.43 ± 7.4	0.187
W1	12.7 ± 7.2	13.26 ± 7.2	12 ± 7.2	0.210
W7	12.8 ± 7.8	13.25 ± 7.8	12.14 ± 7.9	0.140
W12	13.7 ± 8.1	14.29 ± 8.1	13 ± 8.2	0.167
Percentage of nights use >4h	97 ± 3.8	97.4 ± 3.8	96.5 ± 3.8	0.382
Median use, h/night	6.9 ± 0.9	7.1 ± 0.95	6.9 ± 0.85	0.182

Data are presented as mean values ± standard deviation. Group 1 – device S8 AutoSpirit II™; group 2 – device S9 AutoSet™; BMI body mass index; ESS Epworth Sleepiness Scale, AHI apnea–hypopnea index. D1 first day under APAP; W1 first week under APAP; W7 seventh week under APAP; W12 twelfth week under APAP therapy.

Results

Out of a total 110 patients with OSA and APAP therapy, 62 were included, according to the selection criteria. Of the 62 patients, 38 (61.2%) received S8 AutoSpirit II™ (group 1) and 24 (38.7%) received S9 AutoSet™ (group 2). Descriptive summary statistics, outcome and APAP adherence did not differ between groups, in accordance with the device used (Table 1). Relatively to the OSA severity, 12 (19.4%) patients had a mild OSA, 17 (27.4%) a moderate and 33 (53.2%) a severe OSA. There was no significant weight change during follow-up (data not shown).

The APAP devices were programmed with a mean lower and upper pressure set to 5.8 ± 1.13 cmH₂O and 14.2 ± 1.1 cmH₂O, respectively. There were no differences in the objective compliance of APAP therapy or leak levels between groups. When assessing the effectiveness of the treatment, there were no differences between groups. Both mentioned an improvement in the daytime sleepiness, estimated with ESS. The mean residual AHI was ≤ 5 /h after APAP therapy initiation, without differences between groups (Table 1). The apnea–hypopnea index reached normal levels at W12 in 54 patients, with a mean value 2.23 ± 1.1 /h in these patients (data not shown).

As there were no differences in general features, objective compliance and effectiveness of treatment in both device groups, the analysis of pressure behaviour was performed considering the study population, but only including the patients with a residual AHI < 5 /h at the last evaluation (n=54). No significant differences were found between the mean values of air pressure delivered at P95th at the four periods (Table 2).

The concordance rates, within the range ± 2 cmH₂O, between the P95th pressure level at W12 and D1, W12 and W1, W12 and W7 were 92.6%, 94.4% and 100%, respectively (Table 3). Within this range, a significance difference was found in concordance between P W12–W7 and P W12–D1 ($p=0.046$; Table 4), however there was no significant difference in concordance between P W12–W7 and P W12–W1.

Discussion

In this study, we analyzed the variation in PAP level of APAP devices at four different periods of treatment, up until 12 weeks, in a CPAP-naïve population with OSA. We compared, correlated and evaluated the concordance in pressure levels between these periods.

There was no significant difference in concordance between the difference of P95th pressure level at the 12th week and at the 7th week and between the difference of P95th pressure level at the 12th week and the first week of treatment, within the pressure range ± 2 cmH₂O. A significance difference was found in concordance between the difference of P95th pressure level at the 12th week and at the 7th week and between the difference of P95th pressure level at the 12th week and the first day of treatment. This result suggests that one week of APAP therapy is sufficient to determine a therapeutic CPAP level requirement.

Literature concerning the scope of this study is limited; nonetheless many clinicians prescribe fixed CPAP based on APAP monitoring. Currently, there are devices in the market designed to obtain this measure automatically, changing the APAP mode to CPAP mode after a period of time. Furthermore, in some settings and countries, the use of CPAP over

Table 2 Comparison of P95th pressure levels reached at the four periods.

Mean of P95th pressure level (cmH ₂ O)	Study population (n = 54)	p value
P95th D1	11.27 ± 1.53	0.407
P95th W1	11.12 ± 1.53	
P95th W7	11.32 ± 1.66	
P95th W12	11.18 ± 1.62	

P95th 95 percentile. There was a high correlation in P95th pressure level between D1 and W12 ($r=0.771$; $p>0.0001$), W1 and W12 ($r=0.817$; $p>0.0001$), and W7 and W12 ($r=0.926$; $p>0.0001$). This correlation progressively increased with APAP use.

Table 3 Concordance in effective pressure levels.

	Concordance with P95th pressure level at W12 (n)		
	D1	W1	W7
Concordance in the range ± 2 cmH ₂ O	92.6% (50)	94.4% (51)	100% (54)

P95th 95 percentile.

Table 4 Comparison of effective level pressure concordance.

	Concordance between P W12–W7 and P W12–W1 (n)	p value	Concordance between P W12–W7 and P W12–D1 (n)	p value
Concordance in the range ± 2 cmH ₂ O	94.4% (51)	0.083	92.6% (50)	0.046^a

PW12–W7 difference between the P95th pressure at W12 and W7; PW12–W1 difference between the P95th pressure at W12 and W1; P W12–D1 difference between the P95th pressure at W12 and D1.

^a Statistically significant result.

APAP is more frequent for different reasons—cost, comfort, efficacy, etc. However, the EPAP chosen for the CPAP mode is frequently performed using the automatic algorithm of APAP devices and not with an overnight PSG, due to the greater cost and difficult laboratory access. Therefore, knowledge about the time needed for an APAP device to establish an effective and stable fixed EPAP is extremely important in order not to extend the period with the APAP device in a meaningless way nor to curtail the period before an effective EPAP measure is obtained.

Various studies analyzed the pressure behaviour with APAP therapy, in patients with OSA. However, to the best of our knowledge, an APAP monitoring with the aim of determining stabilization of the pressure level has not been performed. Choi¹⁰ compared 2 weeks of auto-adjusted titration and titration using a predictive equation with full night standard titration, with no significant difference in concordance between auto-adjusting titration and titration using an equation compared to manual titration, within the range ± 1 cmH₂O. Damiani et al.⁵ analyzed the titration effectiveness of two APAP devices, during one night with each device (two consecutive nights), with agreement between the median pressure level, confirmed with portable monitoring in laboratory and with fixed CPAP at the APAP recommended pressures (third and fourth nights). Bachour et al.¹¹ tried to find the optimal APAP trial duration; patients received APAP during a 5-day trial at home. No difference was found in the pressure variability index between the 5 days. Luo et al.¹² reported that CPAP from automatic titration (3–5 nights) was

significantly higher than the pressure obtained from manual titration. Although these studies have different aims, some results may be compared to our findings. It is worth noting the short duration of home unattended titration (1 night to 2 weeks) which does not provide sufficient time to obtain significant differences in therapeutic pressure level. A delayed effect of CPAP has been described.¹³ Series¹⁴ quantified the changes in the required level two weeks after a sleep study and after 2, 8 and 20 months of CPAP therapy. The effective CPAP level progressively decreased with time, with significant differences between the first three evaluations. This delayed effect of CPAP could be attributed to an improvement in upper airway morphology,¹⁵ and/or to the correction of sleep fragmentation.¹⁶ The required pressure to eliminate obstructive respiratory events varies over a night depending on factors like alcohol, hypnotic agent use, body position, nasal obstruction and sleep state.^{2,17} Additionally, pressure requirements may vary over time due to weight change, different medical condition and resolution of upper airway oedema caused by repetitive apnea.^{18,19}

Based on these statements, our study considered a longer period of APAP therapy, compared to previous studies. Additionally, three evaluation periods corresponded to the mean pressure values of three separate weeks (W1, W7 and W12), allowing an average pressure over the course of the night, for seven consecutive nights in three different weeks. As far as we know, there is no literature about the required duration of APAP monitoring required to prescribe a fixed pressure, and our study, after a follow-up of 12 weeks,

showed that one week of APAP therapy seems sufficient to determine an effective and stable fixed pressure level.

A limitation of this study is the relatively small sample size.

Conclusion

In conclusion, one week of APAP therapy seems sufficient to determine an effective and stable PAP level, within the pressure range ± 2 cmH₂O. Future studies, with a larger number of patients, are necessary to corroborate these findings.

Ethical responsibilities

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and longterm care of obstructive sleep apnea in adults. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2009;5:263–76.
2. Morgenthaler TI, Aurora RN, Brown T, Zak R, Alessi C, Boehlecke B, et al. Practice parameters for the use of autotitrating continuous positive airway pressure devices for titrating pressures and treating adult patients with obstructive sleep apnea syndrome: an update for 2007: Standards of Practice Committee of the AASM. *Sleep*. 2008;31:141–7.
3. Ahmed O, Parthasarathy S. APAP and alternative titration methods. *Sleep Med Clin*. 2010;5:361–8.
4. Kushida CA, Berry RB, Blau A, Crabtree T, Fietze I, Kryger MH, et al. Positive airway pressure initiation: a randomized controlled trial to assess the impact of therapy mode and titration process on efficacy, adherence, and outcomes. *Sleep*. 2011;34:1083–92.
5. Damiani MF, Quaranta VT, Tedeschi E, Drigo R, Ranieri T, Caratù T, et al. Titration effectiveness of two autoadjustable continuous positive airway pressure devices driven by different algorithms in patients with obstructive sleep apnoea. *Respirology*. 2013;18:968–73.
6. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2012;8:597–619.
7. Soares Pires F, Drummond M, Marinho A, Sampaio R, Pinto T, Gonçalves M, et al. Effectiveness of a group education session on adherence with APAP in obstructive sleep apnea – a randomized controlled study. *Sleep Breath*. 2013;17:993–1001.
8. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis*. 1993;147:887–95.
9. Kushida CA, Chediak A, Berry RB, Brown LK, Gozal D, Iber C, et al. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea positive airway pressure titration task force of the American Academy of Sleep Medicine. *J Clin Med*. 2008;4:157–71.
10. Choi JH, Jun YJ, Oh JI, Jung JY, Hwang GH, Kwon SY, et al. Optimal level of continuous positive airway pressure: auto-adjusting titration versus titration with a predictive equation. *Ann Otol Rhinol Laryngol*. 2013;122:339–43.
11. Bachour A1, Virkkala JT, Maasilta PK. AutoCPAP initiation at home: optimal trial duration and cost-effectiveness. *Sleep Med*. 2007;7–8:704–10.
12. Luo J, Xiao S, Qiu Z, Song N, Luo Y. Comparison of manual versus automatic continuous positive airway pressure titration and the development of a predictive equation for therapeutic continuous airway pressure in Chinese patients with obstructive sleep apnoea. *Respirology*. 2013;18:528–33.
13. Leech JA, önal E, Lopata M. Nasal CPAP continues to improve sleep-disordered breathing and daytime oxygenation over long-term follow-up of occlusive sleep apnea syndrome. *Chest*. 1992;102:1651–5.
14. Sériès F, Marc I, Cormier Y, La Forge J. Required levels of nasal continuous positive airway pressure during treatment of obstructive sleep apnoea. *Eur Respir J*. 1994;7:1776–81.
15. Ryan CF, Lowe AA, Li D, Fleetham JA. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after chronic nasal continuous positive airway pressure therapy. *Am Rev Respir Dis*. 1991;144:939–44.
16. Sullivan CE, Issa FG, Berthon-Jones M, Saunders NA. Pathophysiology of sleep apnea. In: Saunders NA, Sullivan CE, editors. *Sleep and breathing*. New York: Dekker; 1984. p. 299–363.
17. Bastos HN, Cardoso AV, Castro AS, Gomes R, Pinto T, Marinho A, et al. Randomised short-term trial of high-span versus low span APAP for treating sleep apnoea. *Sleep Breath*. 2016;20:183–90.
18. Mortimore IL, Kochhar P, Douglas NJ. Effect of chronic continuous positive airway pressure (CPAP) therapy on upper airway size in patients with sleep apnoea/hypopnoea syndrome. *Thorax*. 1996;51:190–2.
19. Collop NA, Block AJ, Hellard D. The effect of nightly nasal CPAP treatment on underlying obstructive sleep apnea and pharyngeal size. *Chest*. 1991;99:855–60.