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Transition from APAP to CPAP may be a cost-effective health intervention in OSA patients

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ABSTRACT

Objective: Obstructive sleep apnea (OSA) is a common disorder associated with a significant economic burden. Continuous positive airway pressure (CPAP) and auto-titrating positive airway pressure (APAP) are recognized therapeutic options in patients with OSA, although treatment costs are higher with APAP. We conducted a study aimed at evaluating the effectiveness and potential cost savings resulting from the implementation of a protocol guiding the transition to CPAP in OSA patients previously treated with APAP. **Methods:** This prospective study included patients with OSA under APAP who were followed up at the Sleep Medicine outpatient clinic of a tertiary referral hospital between January 2019 and January 2021. Treatment was switched to CPAP in patients who met the following criteria: satisfactory adaptation and adherence to APAP, residual apnea-hypopnea index (AHI) of < 5/hour, and no relevant air leaks. APAP and CPAP outcomes were compared and an estimate of the savings obtained by the transition from APAP to CPAP was calculated. **Results:** Ninety-three patients were included in the study. APAP and CPAP were both effective in correcting obstructive events and improving daytime sleepiness. No significant differences were found regarding treatment adherence and tolerance between both PAP modalities. The selection of fixed-pressure CPAP through 90th or 95th percentile APAP pressure proved to be effective and an alternative strategy to titration polysomnography. At the end of this two-year study, the transition from APAP to CPAP enabled savings of at least 10,353€. **Conclusion:** The transition from APAP to CPAP may be an effective, well-tolerated, safe, and cost-saving strategy in patients with OSA.

Keywords: Obstructive sleep apnea (OSA); continuous positive airway pressure (CPAP); auto-titrating positive airway pressure (APAP); health care costs

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder that affects 9% to 38% of the overall population.[1] The reported prevalence of OSA has escalated concerningly over time, in part due to the increasing number of obese patients, in whom the prevalence exceeds 30%.[2] OSA is an emerging major health problem since it is a recognized, independent risk factor for cardiovascular, metabolic, and psychiatric disorders.[3,4] High disease burden is also related to excessive daytime sleepiness, impaired quality of life, workplace and motor vehicle accidents, losses in productivity, and health care costs.[5,6]

Positive airway pressure (PAP) is the treatment of choice for OSA and may be delivered through continuous positive airway pressure (CPAP) or auto-titrating positive airway pressure (APAP).[7] CPAP delivers constant positive pressure to the upper airway during sleep, preventing its collapse.[8,9] On the other hand, APAP delivers variable pressure depending on changes in airflow resistance, which may vary according to several factors, including the stage of sleep, body position, and the degree of nasal congestion.[10,11] The effects of treatment seem similar between CPAP and APAP and, for that reason, the therapeutic choice often relies on other factors, such as patient preference, specific reasons for non-compliance, and direct and indirect costs.[12,13]

Titration polysomnography (PSG), performed in sleep laboratories, is the gold standard approach to determine optimal PAP levels but is associated with high costs and long waiting lists.[7] Previous studies have shown that the 90th or 95th percentile pressure level obtained through APAP tracking system registration has a good correlation with the PAP levels obtained through titration PSG; this approach is more cost-effective compared to manual laboratory titration.[14,15] In patients treated with APAP, after identifying the most suitable fixed pressure that corrects respiratory events through the 90th or 95th percentile, it is possible to modify treatment to CPAP using that specified level of pressure.

In the Portuguese National Health System, the initial prescription of CPAP or APAP is conducted in Sleep Medicine Centers by pulmonologists, who ensure the diagnostic work-up and therapeutic decision of patients with OSA. Following medical prescription, home respiratory care companies then provide the CPAP or APAP device, and the treatment is entirely

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paid for by the National Health System. Although both are effective in treating OSA, CPAP and APAP have different costs, which are higher with APAP. In Portugal, the contractual prices agreed between the National Health System and home respiratory care companies are 1.0399€/day with CPAP and 1.2079€/day with APAP.[16] In addition, for patients who choose to buy their own PAP machine, the cost of the APAP device is typically higher than that of CPAP. On the other hand, for OSA patients with health insurance, many companies may not approve APAP coverage due to its higher cost when compared to CPAP.

In this study, we aimed to evaluate the effectiveness and potential cost savings resulting from the transition from APAP to CPAP in patients with OSA followed up in a Sleep Medicine outpatient clinic of a tertiary referral hospital in northern Portugal.

METHODS

Study Design and Data Collection

The present prospective, single-center study included adult patients with previously diagnosed OSA, treated with APAP, who were followed up at the Sleep Medicine outpatient clinic of the Vila Nova de Gaia/Espinho Hospital Center, in Portugal, between January 2019 and January 2021. Data collection and analysis were conducted in February 2021.

All patients were evaluated by a pulmonologist with expertise in sleep medicine. After an initial and variable period of treatment with APAP, the patients were switched to CPAP treatment. The transition of the treatment from APAP to CPAP was carried out in patients who met the following criteria: satisfactory adaptation to APAP, good adherence to treatment (use for > 4 hours/night in at least 70% of the nights), residual apnea-hypopnea index (AHI) of < 5/hour, and no relevant air leaks (leak in the 95th percentile < 25L/min). Informed consent was obtained from all patients, and the study protocol was approved by the ethics committee of the Vila Nova de Gaia/Espinho Hospital Center.

The PAP devices were chosen by the home respiratory care companies, providing they were suitable for medical prescription (S9 AutoSet™ or AirSense 10 AutoSet™ from ResMed, or SystemOne™ or DreamStation™ from Philips Respironics). Treatment was started with a nasal interface; if the patient complained of discomfort or intolerance or required better air leak control, treatment was changed to an oronasal interface. Humidifiers and heated circuits were prescribed both with APAP or CPAP when needed for patient comfort.

Patients were excluded if any of the following criteria were present: poor adaptation or compliance to APAP treatment, hypoventilation disorders, a predominance of central events, cognitive disability, and incomplete medical data.

The number of hours that the PAP device was used per night, the percentage of nights the PAP device was used for more than 4 hours, residual AHI, and air leak were established through machine-recorded compliance data. Regarding APAP, data was collected in the three months prior to CPAP transition. CPAP data was collected after three months of treatment.

Definitions

The diagnosis of OSA was obtained with PSG conducted in the hospital (level 1) or on an outpatient basis (level 2) or by home cardiorespiratory polygraphy (level 3). Sleep studies were manually scored by an experienced sleep technician according to the criteria of the American Academy of Sleep Medicine.[17] The diagnosis was established based on the criteria of the third edition of the International Classification of Sleep Disorders,[18] and OSA severity was defined as mild for AHI of ≥ 5/hour and < 15/hour, moderate for AHI of ≥ 15/hour and ≤ 30/hour, and severe if AHI > 30/hour. Positional OSA was defined as a total AHI of ≥ 5/hour, with a > 50% reduction in the AHI between the supine and nonsupine positions. Rapid eye movement (REM) sleep-related OSA was defined as the occurrence of obstructive apneas and hypopneas predominantly or exclusively during REM sleep in patients who underwent PSG.

Statistical Analysis

A descriptive analysis was performed. Normality was tested using the Shapiro-Wilk test. Continuous variables were described using mean and standard deviation or median and interquartile range (IQR). Categorical variables were expressed as frequencies (n) and percentages (%). For the analyses of repeated measurements in a single sample, Wilcoxon's signed-rank test was applied for continuous variables, and McNemar's test was performed for categorical variables. All statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS)® program (Chicago, Illinois, USA), version 22.0. The level of statistical significance was set at $p < 0.05$.

RESULTS

Study population

In a total of 209 patients with OSA undergoing APAP therapy, 93 were included based on the selection criteria. The reasons underlying participant exclusion from the study were: poor APAP compliance (n = 81), residual AHI of > 5/h under APAP therapy (n = 19), associated hypoventilation disorders (n = 11), and significantly incomplete medical records (n = 5). Most patients were male (76.3%), and the median age was 61 [51 - 67] years. A significant prevalence of cardiovascular disease was observed, namely arterial hypertension (66.7%), obesity (52.7%), dyslipidemia (41.9%), and heart failure (26.9%). Most patients (78.5%) had moderate or severe OSA, with a median AHI of 25.1/hour [16.9 - 41.0]. The

demographic and clinical characteristics of the patients are summarized in Table 1.

PAP outcomes

After starting treatment with APAP, the median time until CPAP transition was 18 [8 - 36] months. The median APAP minimum and maximum pressures were 6 [5 - 6] cmH_20 and 12 [12 - 14] cmH_20, respectively. APAP was effective in eliminating sleep respiratory events, resulting in a median residual AHI of 1.7/hour [0.9 - 2.8]. Although patients presented good adherence to APAP (median use of 7 hours/night and use for > 4 hours/night in 93% of the cases), 61.3% exhibited side effects related to therapy, namely mucosa dryness (49.5%), nasal congestion (11.8%), feeling of air leak (7.5%), cold feeling (5.4%), and facial pain (5.4%). Mucosa dryness and cold feeling were solved with humidifiers and heated circuits, respectively, in all patients who reported these side effects.

In 97.8% of the patients, optimal pressure determination for CPAP treatment was conducted based on the 90th or 95th percentile pressure level identified in the last APAP therapy report. In 2.2% of the patients, the determination of CPAP pressure was based on titration PSG, performed in the sleep laboratory. The median initial CPAP pressure was 10 [9 - 11] cmH_20. Pressure adjustment was required in 16.1% of the patients due to intolerance to high pressure (33.3%), controlled residual AHI, enabling pressure reduction (26.7%), high air leak (20%), and uncontrolled residual AHI, requiring pressure increase (20%). The median final CPAP pressure was 9 [8 - 11] cmH_20.

The comparison between APAP and CPAP therapy is shown in Table 2. Both were equally effective in improving daytime sleepiness, a hallmark symptom of OSA, as indicated by the Epworth Sleepiness Scale (ESS). The percentage of patients with at least one side effect was statistically lower with CPAP than with APAP (32.6% *vs*. 60.9%; $p < 0.001$); they included mucosa dryness (20.4%), feeling of air leak (8.6%), nasal congestion (n = 6; 6.5%), feeling of high pressure (3.2%), and aerophagia (1.1%). It is noteworthy that CPAP was statistically superior to APAP in controlling the residual AHI (1.4/h *vs*. 1.7/h; $p = 0.033$), although both therapies were effective.

Table 1. Demographic and clinical characteristics of the patients.

Baseline characteristics	Study population (n = 93)
Age, years	61 [51-67]
Male	71 (76.3)
BMI, kg/m^2	30.2 [26.6-33.9]
Neck circumference, cm	42.6±3.66
Mallampati score	
I	10 (10.8)
II	7 (7.5)
III	20 (21.5)
IV	18 (19.4)
N/A	38 (40.9)
Comorbidities	
Obesity	49 (52.7)
Arterial hypertension	62 (66.7)
Diabetes mellitus	21 (22.6)
Dyslipidemia	39 (41.9)
Atrial fibrillation	8 (8.6)
Heart failure	25 (26.9)
History of stroke	5 (5.4)
Baseline ESS score	11.5 [6-15]
Sleep study	
Level 1	35 (37.6)
Level 2	16 (17.2)
Level 3	42 (45.2)
OSA Severity	
Mild	20 (21.5)
Moderate	36 (38.7)
Severe	37 (39.8)
AHI, n/hour	25.1 [16.9-41]
T90, min	18 [4-62]
Positional OSA	15 (16.1)
REM-related OSA (n=51)*	6 (11.8)

Data are presented as n (%) or mean ± SD or median [interquartile range]; N/A – not available. *Only patients who underwent a level 1 or 2 sleep study. AHI: apnea-hypopnea index; BMI: body mass index; OSA: obstructive sleep apnea; REM: Rapid eye movement; T90: total sleep time spent with arterial oxygen saturation < 90%.

Sub-analysis including patients with positional or REM-related OSA revealed no statistically significant differences between APAP and CPAP outcomes, except in the subgroup of patients with positional OSA, in which the number of hours of therapy per night was greater with CPAP than with APAP (7.5h *vs*. 6.7h; *p = 0.046*). It should also be noted that in patients with positional OSA, residual AHI tended to be higher in those treated with CPAP than with APAP (6.8/h *vs*. 2.3h; *p = 0.374*).

After switching treatment to CPAP, most (91.4%) patients maintained good tolerance. However, in 8.6% of the patients, CPAP was poorly tolerated, mostly because of mucosa dryness (50%) and feeling of nasal obstruction (25%). The treatment needed to be switched again to APAP in 5.4% of the patients due to the occurrence of side effects, and in one patient with OSA and chronic obstructive pulmonary disease (COPD) overlap syndrome, the treatment was changed to bilevel positive airway pressure (BPAP) on account of persistent daytime hypercapnia, despite controlled residual AHI.

Among all patients, 33.3% were discharged to Primary Health Care since they had good adherence and tolerance to CPAP, with clinical benefit and corrected nocturnal respiratory events. None of these patients were referred to the Sleep Medicine Center again during the follow-up period of this study. Loss of follow-up was observed in five (5.4%) patients.

The mean time between the beginning of CPAP treatment and the end of the study was 22.8 ± 7.7 months. Based on the contractual costs of PAP therapy in Portugal, the transition from APAP to CPAP enabled a mean savings of 119 ± 39.11€ per patient and, at the end of this two-year study, including 87 patients who remained under CPAP treatment, an amount of 10,353.84€ was saved.

DISCUSSION

In the present study, both PAP modalities were effective, allowing the correction of nocturnal obstructive events and the improvement of subjective sleepiness, as measured by the ESS. Indeed, CPAP was statistically superior to APAP in the correction of residual AHI. Still, the clinical meaning of this finding is probably irrelevant, as both therapies enabled to achieve a residual AHI of < 5/hour. Our results are in line with previous studies documenting that both APAP and CPAP are similar in their ability to eliminate respiratory events and improve daytime OSA-related symptoms.[12,13]

Patients showed good tolerance to APAP and CPAP, although side effects tended to be less frequent with the latter. It is noteworthy, however, that the occurrence of fewer side effects with CPAP might be explained by the fact that they could have been previously identified and corrected during the initial treatment with APAP. With both PAP modalities, side effects were mainly minor and reversible. Unlike previous studies revealing that APAP was better tolerated and more effective than CPAP in increasing patient compliance, we found no differences between both therapies regarding treatment tolerance and adherence.[19,20]

In daily clinical practice, the pressure chosen for CPAP is frequently selected using the automatic algorithm of APAP devices.[12,13,21] Here, the choice of CPAP pressure was based on the 90th or 95th percentile APAP pressure in most cases; this strategy proved effective since CPAP pressure readjustment was needed in only 16.1% of the patients and in none

Table 2. PAP treatment outcomes.

Overall patients (n = 93)	APAP	CPAP	p-value
Residual AHI, n/hour	1.7 [0.9-2.8]	1.4 [0.6-2.2]	0.033*
Use > 4 hours, % of nights	93.3 [86.7-98]	93 [83.6-98.9]	0.370
Mean use, hours/night	7 [6-8]	7 [6-8]	0.121
Side effects	56 (60.9)	30 (32.6)	<0.001*
ESS post-PAP	3 [3-5]	3 [3-4]	0.625
Positional OSA (n=15)	APAP	CPAP	p-value
Residual AHI, n/hour	2.3 [1.4-3.5]	6.8 [6-8]	0.374
Use > 4 hours, % of nights	92.4 [85-98.9]	89 [84.4-98]	0.092
Mean use, hours/night	6.65 [5-7.5]	7.5 [6.5-8]	0.046*
Side effects	8 (57.1)	4 (28.6)	0.219
ESS post-PAP	3 [3-6]	4 [4-5]	0.630
REM-related OSA (n=51)	APAP	CPAP	p-value
Residual AHI, n/hour	2.25 [1.6-2.8]	1.9 [0.8-2.8]	0.344
Use > 4 hours, % of nights	93.05 [84.5-98.9]	91.5 [73.3-96.1]	0.225
Mean use, hours/night	7.25 [6.5-7.75]	7.5 [6.25-8.25]	0.854
Side effects	3 (50)	1 (16.7)	0.625
ESS post-PAP	4 [3-6]	4 [4-6]	0.633

Data are presented as n (%) or median [interquartile range]; *p-value <0.05. AHI: apnea-hypopnea index; APAP: auto-titrating positive airway pressure; CPAP: continuous positive airway pressure; ESS: Epworth Sleepiness Scale; OSA: obstructive sleep apnea; PAP: Positive airway pressure; REM: Rapid eye movement.

of them was overnight PSG necessary, a relevant finding given the costs and difficult access to the sleep laboratory. The possibility of defining CPAP optimal pressures through APAP device-recorded data is a window of opportunity for the use of telemedicine in OSA patients. In fact, there are devices on the market designed to automatically measure the ideal PAP level, switching remotely from the APAP mode to CPAP mode after a period of time.[22] This available resource may not only improve the follow-up of patients with OSA but also enable telehealth instead of conventional face-to-face clinical visits, which may be a valuable alternative in the era of the Coronavirus Disease 2019 (COVID-19) pandemic. At the same time, regardless of the pandemic context, telehealth and telemonitoring remain useful tools since patients with OSA are typically a working population, and, for that reason, this alternative to conventional visits allows them to save time and resources and avoid absences from work.

At the end of the study, the median final CPAP pressure was lower than the initial pressure. This might be explained by the fact that the most frequent reasons for pressure readjustment were intolerance to high pressure and controlled residual AHI, allowing pressure reduction. In addition, a delayed effect of CPAP has also been previously described.[23] The effective CPAP level may progressively decrease with time, which can be attributed to an improvement in upper airway morphology and/or the correction of sleep fragmentation, which we can speculate that may also have contributed to a lower median final CPAP pressure in our study.[24,25,26]

It has been previously demonstrated that only one week of APAP therapy seems sufficient to determine an effective and stable PAP level within the pressure range of ± 2 cmH_20.[21] However, in the current study, we verified a longer time from the beginning of APAP until the transition to CPAP (18 [8 - 36] months). This finding may be explained by the fact that some patients were already under treatment with APAP for a long time, and the transition to CPAP was only conducted because of patient inclusion in this study. This finding may somehow suggest that doctors are not fully aware of the effectiveness, safety, and cost savings of the transition from APAP to CPAP in their daily clinical practice.

It is well known that the required level of pressure to eliminate obstructive respiratory events varies overnight depending on several factors, such as body position, sleep state, nasal obstruction, and the use of alcohol and hypnotic agents.[10,11,14] APAP could be a more attractive PAP modality if such pressure requirement variability were resolved. Nonetheless, in this study, we found that the benefits of the transition from APAP to CPAP remained, even in the subgroup of patients with positional OSA and REM-related OSA. However, patients with positional OSA under CPAP treatment presented a median residual AHI of 6.8/hour, slightly above the desired value (< 5/hour). It is important to note that a small number of patients was included in the subgroup of positional OSA and that there was no statistically significant difference between APAP and CPAP with regard to residual AHI. Nevertheless, this data may suggest that patients with positional OSA may not be good candidates for switching from APAP to CPAP. Additionally, in this study, REM-related OSA was probably underdiagnosed, given that in 45.2% of the patients, PSG was not performed.

To the best of our knowledge, this is the first study evaluating the effectiveness and potential cost savings with the transition from APAP to CPAP in a population of OSA patients. Assessing the cost-effectiveness of health interventions is an essential guide for public health decision-making in order to better decide the allocation of economic resources. Impressively, in the present study, the implementation of a protocol guiding the transition from APAP to CPAP in a relatively small population of OSA patients allowed savings of nearly 10,350€ in only two years. We believe that our results raise important questions in daily clinical practice, given that OSA is a prevalent chronic disease and PAP is a treatment for life, imputing huge costs to healthcare systems. Furthermore, it should also be noted that, in some countries, after discharge from hospital consultation, Primary Health Care physicians renew chronic PAP prescriptions, but they cannot change them; therefore, awareness regarding the transition from APAP to CPAP must exist at the level of Sleep Medicine Centers. Moreover, if we take the chronicity of PAP therapy, the relatively young age of OSA patients, and the increasing worldwide average life expectancy into account, the savings potential would be even more significant.[27]

Our results encourage the development and implementation of protocols guiding the transition from APAP to CPAP in OSA patients at the level of Sleep Medicine Centers. To this end, appropriate human and technical resources must be allocated, including the use of telehealth.

This study presented some limitations. Among the 209 patients recruited initially, only 93 were included, indicating that we could be facing a selection bias. This fact may limit the generalizability of the conclusions drawn herein since the transition to CPAP was conducted in a very specific population of OSA patients with good compliance, acceptable tolerance, and correction of obstructive events under APAP therapy. Thus, we can speculate that, in OSA patients, APAP - through its ability to automatically adjust the air pressure throughout the night - is a suitable initial therapeutic strategy with the intention of later switching treatment to CPAP, an equally effective but less expensive therapeutic option. On the other hand, although our results demonstrate the potential savings obtained from the transition from APAP to CPAP, a real cost-effectiveness analysis was not carried out. In addition, the potential savings resulting from the selection of the CPAP pressure through the 90^{th} or 95^{th} percentile APAP pressure instead of titration

PSG were not taken into account. Another limitation of this study was the relatively short follow-up of the patients included. In fact, because of this limitation, it may be difficult to ascertain if the fixed pressure defined in the CPAP before hospital discharge will remain suitable throughout the patient's life since weight variations and anatomical changes in the upper airways due to aging may occur. For this reason, after discharge to Primary Health Care, OSA symptoms and the compliance report, namely residual AHI, should be regularly assessed in order to identify the need for a new referral to hospital consultation. Finally, this study has limited generalizability to the overall OSA population since it was conducted in a single Portuguese center, and both treatment costs and OSA patients' management can be significantly different in other settings, namely in other countries. A randomized, single-blind, crossover trial evaluating efficacy, compliance, side effects, and patient satisfaction would allow us to draw more definitive conclusions.

The present study shows that the transition from APAP to CPAP may be an effective, well-tolerated, safe, and cost-saving strategy in patients with OSA. The routine implementation of a systematic and uniform guiding protocol with established criteria for the transition from APAP to CPAP in Sleep Medicine Centers potentially enables relevant savings for healthcare systems while maintaining PAP treatment quality.

AUTHOR CONTRIBUTIONS

AA: study conception and design; materials or referral of patients; data collection/assembly; data analysis and interpretation. ARG: data collection/assembly; data analysis and interpretation. DM, IS, and DF: study conception and design; materials or referral of patients. RM, IF, RM, and CN: materials or referral of patients. All authors: drafting and revision of the manuscript.

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