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5-Years APAP adherence in OSA patients — Do first impressions matter?

Mafalda van Zeller [a,*], Milton Severo [b,c], Ana Cristina Santos [b,c], Marta Drummond [a,d]

[a] Department of Pulmonology, Centro Hospitalar de São João, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal
[b] Department of Clinical Epidemiology, Predictive Medicine and Public Health, University of Porto Medical School, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal
[c] Institute of Public Health, University of Porto, Rua das Taipas n° 135, 4050-600 Porto, Portugal
[d] Faculty of Medicine, University of Porto, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal

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Summary
Background: Although continuous positive airway pressure (CPAP) is effective in treating obstructive sleep apnoea (OSA), inadequate adherence remains a major cause of treatment failure. This study aimed to determine long term adherence to auto adjusting-CPAP (APAP) and its influencing factors including the role of initial compliance.
Methods: Eighty-eight male patients with newly diagnosed moderate/severe OSA were included. After initiation of APAP treatment, patients had periodic follow-up appointments at 2 weeks, 6 months and then annually for at least 5 years. Patient's compliance to therapy was assessed in each appointment and predictors to treatment abandonment and poor compliance were evaluated.
Results: The studied population had a mean age of 53.8 years and mean apnoea–hypopnoea index of 52.71/h.

The mean time of follow-up was 5.2 (±1.6) years, during that time 22 (25%) patients abandoned APAP, those who maintained treatment had good compliance to it since 94% of them used it more than 4 h/day for at least 70% of days.

A significant negative association was found between age, % of days and mean time of APAP use on 12th day and 6th month and the risk of abandoning. APAP use lower than 33% and 57% of days at 12th day and 6th month, respectively had high specificity (~100%) to detect treatment abandonment.

* Corresponding author.
E-mail addresses: vanzeller.mafalda@gmail.com, mafalda_vanzeller@hotmail.com (M. van Zeller).

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Conclusions: the majority of patients adheres to long term APAP treatment and has good compliance after 5-years of follow-up. Age and initial compliance (% days of use and mean hour/day) have the ability to predict future adherence, as soon as 12 days and 6 months after initiation.

Introduction

Obstructive sleep apnoea (OSA) is a disorder characterized by recurrent episodes of partial or complete obstruction of the upper airways during sleep, associated with increasing respiratory efforts, intermittent arterial oxygen desaturation and sleep disruption [1]. It is a prevalent disease, 4—5% in the general population [2], and is associated with increased cardiovascular risk and mortality, increased risk of traffic accidents and increased use of health care resources [1,3].

Continuous positive airway pressure (CPAP) therapy for OSA was first proposed by Sullivan et al. [4] in 1981 and since then extensive works confirmed its efficiency in the long term treatment [5]. A number of studies have examined outcomes relate to CPAP use and have observed a dose effect of CPAP therapy in improving symptoms, daytime sleepiness and quality of life [6—8].

Inadequate adherence remains a major cause of treatment failure [9,10], and when adherence is defined as greater than 4 h of nightly use, 46—83% of patients have been reported to be non-adherent [11].

Since treatment adherence is widely recognized as a critical problem in the OSA treatment in short and even more so in the long term [12], it is important to determine factors that could help predict treatment compliance since it would enable the creation of mechanisms aiming at improving the long term effectiveness of such treatment. Although various attempts have been made to predict and identify factors which predict short and long term compliance, the available data is diverse and conflicting [13—16]. Also, studies have suggested that early therapy adherence might be of help identifying those who abandon/discontinue or have poor compliance to treatment [17,18]. Nevertheless prospective long-term studies, particularly using auto-adjusting CPAP (APAP) are still lacking.

This prospective study aimed to determine the long-term adherence and compliance to APAP treatment in consecutive patients with moderate and severe OSA and to evaluate the impact of initial adherence and compliance on long-term patients.

Material and methods

Study subjects

Eighty-eight male patients, referred to the Sleep-Disordered Breathing Clinic, with newly diagnosed moderate/severe OSA (apnoea—hypopnoea index (AHI) $>$ 20/h), confirmed by domiciliary sleep study, were included in the study.

Exclusion criteria were established previously: neoplastic diseases, active infectious diseases, FEV_1/FVC $<$ 70, hypercapnia ($PCO_2 \geq$ 55 mmHg), and the absence of national health system. Also, this study was restricted to male gender, due to the distribution of OSA in the patient population [2].

The study was approved by the Ethics Committee and all patients gave written informed consent to participate.

Study design

This is a prospective observational study.

After initiation of APAP treatment, patients had periodic follow-up appointments at 2 weeks, 6 months and then annually for at least 5 years. Patient's compliance to therapy was assessed using the home ventilator's memory card data in each appointment and predictors to treatment abandonment and poor compliance were evaluated.

Adherence refers to treatment maintenance trough time and compliance to the daily use evaluated using the percentage of days of use and mean time/day.

Methods

An overnight sleep study was performed using a five channel recording device (AlphaScreen®, Vyasis). This device produces a computerized recording of variations in oronasal airflow (measured by nasal cannula and thermistor), abdominal and thoracic respiratory efforts, roncopathy, body position, wrist actimetry, pulse rate, and arterial oxygen saturation (measured by finger pulse oximetry). The device estimates the total sleep time from the wrist actimetry registry, eliminating those periods with high activity. It automatically calculates the number of apnoeas plus hypopneas per hour of estimated sleep time and it also provides information of desaturations $>$4% per hour of estimated sleep time and the cumulative percentages of sleep time under 90% oxygen saturation.

In all cases, sleep technicians carried out a manual analysis of the recordings, by counting apnoea and hypopnoea episodes according to guidelines [19], dividing the total number of these episodes by sleep time in hours, thus obtaining manual AHI.

Following diagnosis, OSA physiology, symptoms and consequences were explained to patients as well as the advantages and possible complications of APAP treatment. This was performed by the same Respiratory Physician in all cases.

All patients were prescribed APAP (REMstar™ Auto, Respironics Inc., Murrysville, PA, USA) therapy with a mean minimum pressure of 4 cm H_2O and a mean maximum pressure of 17 cm H_2O.

In Portugal, APAP treatment costs which include delivery and technical maintenance by domiciliary respiratory care givers companies, is completely covered by the Portuguese national health system, therefore treatment was provided with no additional cost to patients.

Periodic follow-up were conducted at approximately 2 weeks (12 days), 6 months and then annually post-treatment initiation with evaluation of the clinical symptoms and APAP compliance variables (number of hours per night, percentage of total days of APAP usage), pressure on 90% nighttime (P90) and residual apnoea–hypopnoea index (AHI) were assessed analysing data from the memory card of the ventilator.

Compliance to therapy was classified as very good if patients used APAP more than 90% of days and more than 6 h/night, good if they used between 70 and 90% of days and more than 4 h/night, and poor if the use was below 70% of days and/or less than 4 h/night. Those patients who did not renewed their APAP prescriptions although they kept treatment indication were classified as abandoning treatment.

During the medical appointments, whenever necessary heated humidification was added, nasal corticosteroids prescribed and masks were changed according to patient's preference or to control excessive leak in order to improve efficacy, comfort and compliance.

The need to maintained APAP treatment and compliance encouragement was reassured in all visits.

Analysis

Descriptive statistics were generated for the study sample using means and standard deviation (SD) for quantitative variables and proportions for categorical variables.

Poisson generalized linear models were used, with the default natural log link and offset in the variable natural log follow-up time (t) to estimate incidence rate ratio of abandoning treatment.

The area under the ROC curve (AUC) was estimated to assess the discrimination ability of several variables. If the AUC was less than 0.6 it was consider to have insufficient discrimination ability, if it was between 0.6 and 0.8 it was regarded as acceptable and if higher than 0.8 excellent [20]. The significant level was fixed at 0.05.

Statistical analyses were performed using the software R 2.12.1.

Results

Overall studied population characteristics at baseline are presented in Table 1.

The total mean time of follow-up was 5.2 (1.6) years, during which 22 patients (25%) abandoned APAP therapy within 3.4 (1.5) years. The 66 (75%) patients who remained under treatment were follow for a mean time of 5.7 (1.1) years.

The 5-years compliance of patients who maintained treatment was very good in 77.3%, good in 16.7% and poor in 6.1% of patients. Regarding the risk of poor compliance, only the poor initial compliance at 12th days and 6th month was associated with it.

Table 1 Sample characteristics at baseline.

Variable	$n = 88$
	Mean (SD)
Age (years)	53.8 (11.5)
BMI (kg/m2)	33.23 (5.0)
ESS	12.15 (5.3)
AHI (events/h)	52.71 (20.6)
	n (%)
Smoking habits	
Non-smokers	30 (36.1)
Former smokers	37 (44.6)
Current smokers	16 (19.3)
Hypertension	26 (30.2)
Stroke	16 (18.6)
Acute myocardial infarction	8 (9.4)
Angina	2 (2.3)
Cardiac arrhythmia	2 (2.3)
Employment status	
Employed	43 (56.6)
Unemployed	8 (10.5)
Retired	25 (32.9)
Marital status	
Married/Living as a couple	54 (68.4)
Living alone (single/divorced/widowed)	25 (31.6)

BMI – body mass index, ESS – Epworth sleepiness scale, AHI – apnoea–hypopnoea index.

The incidence rate ratio of patient's characteristics, disease severity and initial compliance (12th days and 6th months) for abandoning APAP treatment are presented on Table 2. Patients with poor compliance at 12 days and 6 months had an increased risk of abandoning treatment 5.8 (95%CI: 2.11–15.95) and 14.5 (4.14–51.02) times higher than those with very good compliance, respectively.

A significant negative association was observed between risk of abandoning APAP treatment and age [0.96 (95%CI: 0.93–0.99)]. Regarding 12th day compliance, the risk of abandonment was lower with increase % of days usage [0.63 (95%CI: 0.52–0.75)] and mean time [0.65 (95%CI: 0.51–0.82)] of APAP use. Similar results were observed for the 6th month compliance (Table 2).

The authors found no relation between initial ESS score and 5-years APAP abandonment risk nor with disease severity represented as AHI. Neither smoking habits nor the presence of comorbidities, employment or marital status were associated with long term (5-years) APAP adherence.

Regarding initial compliance (% days of use and mean time/night) on 12th day and 6th month and age influence on abandoning treatment we noticed that the ROC AUC ranged from 0.693 (% days at 12th day compliance) to 0.865 (% days at 6 months) (Table 3), revealing acceptable to excellent discrimination ability between those who abandoned treatment and those who did not.

We found that patients who used APAP less than 83.3% and 95.4% of days and less than 5.93 and 5.55 mean hours/day at 12th day and 6th month, respectively, were at higher risk of abandoning therapy. In fact, the use of APAP lower than 33% and 57% of days at 12th day and 6th month,

Table 2 Five years risk of abandoning APAP treatment.

Variable	RR	95%CI
Age	0.96	0.93—0.99
BMI	1.005	0.926—1.091
ESS initial	0.98	0.91—1.06
AHI	0.997	0.997—1.018
Smoking habits		
Non-smokers	1	
Former smokers	0.47	0.15—1.44
Current smokers	1.83	0.67—5.06
Any medical comorbidity		
Absent	1	
Present	1.05	0.43—2.59
Employment status		
Unemployed	1	
Employed	0.72	0.2—2.54
Retired	0.39	0.09—1.75
Marital status		
Married/living as a couple	0.68	0.28—1.66
Living alone (single/ divorced/widowed)	1	
12th Day compliance		
Very good	1	
Good	1.71	0.55—5.29
Poor	5.80	2.11—15.95
Mean hours/day	0.65	0.51—0.82
% Days/10% of days	0.63	0.52—0.75
6th Month compliance		
Very good	1	
Good	3.64	0.91—14.56
Poor	14.54	4.14—51.02
Mean hours/day	0.59	0.48—0.74
% Days/10% of days	0.70	0.62—0.79

BMI — body mass index, ESS — Epworth sleepiness scale, AHI — apnoea—hypopnoea index.

Table 3 Likelihood ratio and predictive values of 12th day and 6th month compliance and age to predict treatment abandonment.

	Cut-off	Sens	Spec	PPV	NPV	ROC AUC
12th Day compliance						
Mean	5.93	72.7	78.2	44.2	88.2	0.734[b]
hours/day	2.25	9.1	100.0	100.0	76.7	
% Days/10%	83.3	45.5	97.0	83.3	84.2	0.693
of days	33.3	9.1	100.0	100.0	76.7	
6th Month compliance						
Mean	5.55	72.7	77.3	51.6	89.5	0.815[a]
hours/day	2.50	27.3	100.0	100.0	80.4	
% Days/10%	95.4	95.5	65.2	47.7	97.7	0.865[a]
of days	57.0	31.8	100.0	100.0	81.5	
Age	49	59.1	77.3	46.4	85.0	0.70[b]

[a] Excellent discrimination ability.
[b] Acceptable discrimination ability.

respectively, had high specificity (~100%) to detect treatment abandonment.

Discussion

The full benefit of many effective medications will only be achieved if patients adhere to prescribed treatment regimens [21].

Among patients with chronic illnesses, approximately 50% do not take medications as prescribed [22]. Hippocrates' exhortation to the physician to "not only be prepared for what is right himself, but also to make the patient… cooperate" has consistently failed over the years [23]. It seems that adherence to therapy may vary across different pathologies and that chronic conditions present particular difficulties for medication adherence and persistence [24].

Regarding respiratory diseases, compliance rates of 48—67% have been reported for inhaled therapy in Asthma and COPD [25,26] and similar values have been indicated for long term oxygen therapy (50—65%) [27] and nebulizers in COPD (50—57%) [28].

McArdle et al. [29] reported that 68% of patients continued treatment after five years, but long-term adherence to both CPAP and particularly APAP is scarce in the literature and very heterogeneous since different criteria have been used to define it. The most widely used definition of nPAP adherence is a minimum of 4 h/day for at least 70% of days [30,31].

In our study 75% of patients maintained treatment after 5-years of follow-up and the majority of patients who maintained treatment had very good (77.3%) or good (16.7%) compliance — 94% of patients used it more than 4 h/day for at least 70% of days [32]. Previous studies performed in Portugal reported distinct patterns of adherence and compliance. A study reported that 15.6% of patients had discontinued treatment and only 54% of patients were classified as compliant within the first year of follow-up [33]. Different results were presented by Soares Pires et al.34 in which 27.7% patients dropped out within the first 6 months of therapy, but those who kept the APAP device had a median use of 88.3% of days and 6.02 h/night at 6 months of follow-up.

Interventions to improve treatment compliance had been analysed and technical aspects had been evaluated as well [35,36]. Autotitration and other new therapeutic modalities have been associated with improvements in patient comfort [37]. However, most authors have reported similar adherence rates for APAP and fixed CPAP [35].

Various factors that are likely to influence adherence have been evaluated, including age [38], gender, socioeconomic factors [39], and disease and symptoms severity [29,40,41].

It is important to determine factors that could help to predict compliance to treatment since it would enable the creation of mechanisms aiming at improving long term effectiveness of such treatment or supporting the decision to suspend it. This is particularly important at a time of financial austerity affecting healthcare services in Portugal and worldwide.

Interestingly, we found that age and particularly components of initial compliance (% days of use and mean time/day), as soon as 12 days have the ability to predict future levels of adherence and the risk to abandon treatment.

Predicting long term CPAP compliance based on initial demographic, clinical and polysomnographic data is difficult [42].

Previous studies have showed that data obtained after a 2-week trial can predict compliance at one year [43], and has been stressed that initial compliance might be a predictor of long term adherence/treatment continuance [18]. Also, recently, Ghosh [17] proposed a simple prediction equation that uses data after a two week CPAP trial to identify long-term poor compliance.

Our study, being prospective and with a higher time of follow-up (5-years), reinforces this information, highlighting the importance of initial adherence as soon as 12 days.

This is hugely relevant since it suggests that the main focus should be on the first appointment after diagnosis and that probably explaining OSA physiology, symptoms and consequences as well as the advantages and possible complications of APAP treatment is determinant and should be done as soon as possible.

This study also raises an ethical and economic question since in Portugal patients have no additional costs with APAP treatment which is totally supported by the National Health Care System. We found that APAP use lower than 33% and 57% of days at 12th day and 6th month, respectively, had high specificity (~100%) to detect treatment abandonment and is in fact lower than the adherence goals usually used for treatment efficacy — should we insist longer to convince patients to be more compliant and to adhere?

A predictor of treatment abandonment and poor compliance should be collected early on in the process, nevertheless, we also analyse the impact of 6-months compliance in long term adherence since we have a long period of follow-up and that possible interventions to enhance adherence are developed within the first weeks and months. We thought that a 6-month evaluation could be considered as a "last chance performance" for patients especially since in Portugal, the treatment is supported by the National Health System, and prescriptions have to be revalidated by a respiratory physician every 3-month, corresponding the 6-months evaluation to a second prescription renewal. If it is legitimate to give patients a second opportunity at 3-months evaluation, considering the results found in this study it would not be correct to do so at 6-months (second prescription renewal) regarding costs and potential benefits.

It has been stressed in the literature [44,45] that education plays an important role in adherence—informed patients tend to be motivated patients. The use of educational sessions for patients seems to have good results [34] although the durability of different strategies to enhance adherence is still under debate [12]. In a previous study referring to the impact of a group education session on APAP compared to patients who had not had it, we found increased adherence to APAP at 6 months [36]. Nevertheless, when the same patients were reevaluated the significant impact of the educational session vanished at 12th months of follow-up.

In the present study, no educational sessions were made as described in the Methods section, as the authors thought this would be a way of assessing adherence without further intervention, information was given about disease and its treatment to patients during each appointment. Nevertheless, patients with 12th day poor compliance might be selected for early intervention and afterwards, according to its impact, it could be decided if it was worthy to maintain treatment. Such strategy would require further studies.

We found a high incidence of patients with past medical history including stroke (18.6%) and acute myocardial infarction (9.4%). Previous studies reported that during a seven-year follow-up period, cardiovascular disease was present in 36.7 percent of patients with obstructive sleep apnea [46]. Also, other study including OSA patients noted a previous medical history of myocardial infarction in 8.1 percent and stroke in 7.1 percent [47].

Over the last decade, epidemiologic and clinical research has consistently supported the association of OSA with increased cardiovascular morbidity and mortality. Such evidence prompted the American Heart Association to issue a scientific statement describing the need to recognize OSA as an important target for therapy in reducing cardiovascular risk [48].

As potential limitations of this study, the authors refer the fact that the OSA diagnosis was based on a domiciliary sleep study instead of attended polysomnography. Nevertheless, both have been previously compared, showing that the first one is a viable, accurate, satisfactory, useful and cost effective way of diagnosing OSA [49]. Also, the study design aimed to obtain an homogeneous sample of patients, having all patients, regardless their symptoms or comorbilities, undoubtful indication for nPAP therapy. Furthermore these consecutive patients were all diagnosed and followed by the same physician, avoiding inter-individual bias. Male patients were enrolled since OSA prevalence is higher in this group [2] so it would be more efficient to include a significant number of patients to get results. Moreover, the inclusion of both gender patients is an important aspect when discussing treatment adherence and could be seen as a limitation of this study. It is a downfall since other studies have showed conflicting evidence regarding of gender in long term compliance [16,38,50].

Also our strategy for APAP initiation relied on the use of initial pressures chosen empirically based in our center previous experience which might be argued. The choose of interfaces and decision to prescribe medication for nasal symptoms was performed in a patient-to-patient basis, without any specific protocol but intended to satisfy the patient resulting in a very practical and clinical approach.

Initial symptom evaluation performed using ESS was not related to long term compliance neither to treatment abandonment. The authors did not evaluate the 12-day change in sleepiness scale since the initial treatment period (12 days) was considered very short and possibly not enough to achieve ESS scores to draw.

On the other hand we believe that the adherence criteria used, classifying compliance in three distinct groups (very good, good and poor) was beneficial since more recent findings [8,51] point out that adherence goals usually used (>4 h per day for at least 70% of days) may be outdated and this will allow future comparisons within studies.

In this study, a reasonable proportion of patients (75%) adhered to 5-years APAP treatment and had very good to

good compliance. Age and initial compliance (% days of use and mean hour/day) have the ability to predict future adherence and the probability of treatment abandonment, as soon as 12 days and 6 months after initiation. First impressions seem to last.

Conflict of interest

None.

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