Long-Term Therapy with Continuous Positive Airway Pressure in Obstructive Sleep Apnea: Adherence, Side Effects and Predictors of Withdrawal – A ‘Real-Life’ Study

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Key Words

Continuous positive airway pressure · Obstructive sleep apnea · Adherence · Compliance · Side effects

Abstract

Background: Long-term adherence to positive airway pressure (PAP) treatment is essential in patients with obstructive sleep apnea syndrome (OSAS). **Objectives:** The aim of the present study was to analyze treatment adherence under real-life conditions and factors associated with discontinuation of PAP therapy. **Methods:** Patients newly diagnosed with OSAS and started on PAP therapy were contacted by telephone after a minimum of 1 year. Side effects, quality of life, subjective treatment adherence and Epworth Sleepiness Scale (ESS) scores were assessed. Objective treatment adherence was calculated by reading the built-in run time counter of the PAP device. Anthropometric parameters, level of education, apnea-hypopnea index (AHI), ESS score and the type of PAP therapy prescribed at the time of the first stay in the sleep lab were collected retrospectively. **Results:**

Median follow-up was 13 months (range 7–18 months). Of 303 patients (69 female, 234 male) available for this study, 191 patients (63%) still used the PAP device regularly (‘users’), while 83 (27.4%) had definitively discontinued PAP treatment (‘nonusers’). In the nonusers group, 29 patients (34.9%) discontinued PAP treatment within the first 3 months. In the users group, subjective PAP usage was 6.6 ± 1.5 h/night and objective adherence was 4.7 ± 2.3 h/night. Objective nightly use of PAP treatment correlated significantly with baseline AHI ($r = 0.13$, $p = 0.041$) but not with sex, age, body mass index, ESS score or education level. Patients with a low AHI and ESS score and patients without a coexisting medical condition or with more than two comorbidities tended to discontinue PAP therapy more frequently. **Conclusions:** PAP treatment adherence has to be optimized in OSAS patients. When initiating PAP therapy, clinicians have to focus on those patients at risk for discontinuing treatment. Education sessions and closer follow-up are possible strategies to improve treatment adherence and to avoid treatment discontinuation.

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Introduction

Positive airway pressure (PAP) is the treatment of choice in moderate to severe obstructive sleep apnea syndrome (OSAS). In several studies, normalization of sleep architecture, reduction of daytime sleepiness, improvement in mood and quality of life, reduction of motor vehicle crashes and a decrease in cardiovascular events have been demonstrated [1, 2]. In addition, there are sufficient data to conclude that in severe OSAS, PAP therapy is associated with improved survival [3]. These positive treatment effects depend substantially on the adherence of the patient to the therapy. Patients with average daily PAP use of less than 1 h had significantly lower survival than those patients with an average of 1–6 h and those with an average use of more than 6 h [4].

Although the correlation between adherence and treatment effects is well known and every effort is made to improve daily usage of PAP, in clinical studies, 29–83% of patients were nonadherent, and in the adherent patients, nightly use varied between 3.5 and 6.5 h/night [5–13]. The reasons for nonadherence or poor acceptance are still not fully understood. Side effects are the most frequently reported reason for discontinuing PAP therapy; however, in prospective clinical studies, side effects were not identified as a significant predictor for PAP treatment adherence [14, 15]. Other authors focused on health belief model constructs and identified lower outcome expectancies of treatment and lower functional limitations prior to therapy as the most important factors to explain adherence to PAP [16]. Most of the studies dealing with treatment adherence have been prospective; therefore, a bias towards better adherence cannot be excluded. In a prospective study, the situation, i.e. frequent contact with the sleep lab, telephone calls and questionnaires, among other things, certainly does not reflect real-life conditions, where treatment adherence and side effects are not monitored.

Consequently, this study was not designed prospectively but aimed at investigating the 'true' long-term PAP adherence and the reasons for discontinuing therapy in a large group of OSAS patients.

Patients and Methods

All patients who were newly diagnosed with OSAS and started PAP therapy in the sleep lab of the Bethanien Hospital Solingen between 1/5/2004 and 1/5/2005 were included in the study. The sleep lab of the Bethanien Hospital Solingen is part of a university-based center for sleep medicine and respiratory care. In this

sleep lab, the standard in-hospital procedure for newly diagnosed OSAS patients is to perform an attended baseline polysomnography followed by 2 titration nights. Patients are then discharged from hospital with their PAP device and interfaces. Follow-up visits are not routinely carried out with the exception of patients remarking side effects or having problems with their devices. Those patients are provided with an in-hospital control polysomnography for 1 night.

All patients were contacted by telephone after a minimum of 1 year of PAP treatment. They were asked about treatment comfort and side effects using an analog scale ranking from –5 to +5. In addition, subjective adherence and Epworth Sleepiness Scale (ESS) scores were assessed. Objective treatment adherence was calculated by reading the built-in run time counter of the PAP device and dividing it by the number of days since discharge from the sleep lab. The reading procedure was performed either by the home care provider or by the sleep lab study nurse. If PAP treatment was discontinued, the reasons for discontinuation were requested.

Anthropometric parameters, level of education, apnea-hypopnea index (AHI), ESS score and the type of PAP therapy prescribed at the time of the first stay in the sleep lab were collected retrospectively. Coexisting diseases as documented in the patient file were collected and classified as belonging to one of the following subgroups: cardiovascular diseases, pulmonary disorders, metabolic diseases, neurologic/psychiatric disorders and other diseases.

Written informed consent was obtained from all participants prior to inclusion. The study was approved by the ethics committee of the University Witten/Herdecke.

Statistical Analysis

Numeric variables were expressed as means $\pm$ standard deviation. The χ^2 test was used for percentage values. Calculations for significant differences between different patient groups were carried out using Student's *t* test. Pearson's correlation coefficient *r* was computed between adherence and age, sex, body mass index (BMI), ESS score and AHI. Differences between adherent and nonadherent patients were calculated using univariate analysis of variance. Data analysis was performed in SPSS for Windows, version 11.5 (SPSS Inc., Chicago, Ill., USA).

Results

A total of 303 patients (69 female, 234 male) with OSAS were available for this study. After a median follow-up of 13 months (range 7–18 months), 191 patients (63%) still used the PAP device regularly ('users'), while 83 (27.4%) had discontinued PAP treatment ('nonusers'). Twenty-nine patients (9.6%) were lost to follow-up or refused to give any information about their treatment adherence (fig. 1). Of the users group, 146 patients (76.4%) had at least 1 control polysomnography during the study period, while 45 patients (33.6%) had no follow-up visits. In the nonusers group, no patient had a follow-up visit to the sleep lab.

Fig. 1. Overview of adherence in the whole patient group.

Table 1. Anthropometric variables, baseline data and education level in the different patient groups

	All patients (n = 303)	Users (n = 191)	Nonusers (n = 83)	Unknown (n = 29)
Male, %	77.2	79.6	72.3	75.9
Age, years	58.2 ± 12.4	58.8 ± 12.4	57.8 ± 12.3	55.7 ± 12.4
BMI	31.6 ± 5.7	31.7 ± 5.9	30.8 ± 5.1	33.3 ± 5.9
AHI	33.2 ± 24.8	35.5 ± 25.3	28.0 ± 23.4	33.0 ± 23.7
ESS score				
Before therapy	9.2 ± 4.8	9.5 ± 4.8	8.4 ± 4.5	9.0 ± 5.9
After therapy	5.1 ± 4.3	5.1 ± 4.2	5.3 ± 4.6	–
Level of education				
Graduate	11.2%	8.9%	15.7%	13.8%
White collar	36.3%	37.2%	36.1%	31.0%
Blue collar	35.6%	35.6%	36.1%	34.5%
No education	11.6%	12.0%	9.6%	13.8%
Unknown	5.3%	6.3%	2.4%	6.9%

Table 2. Anthropometric variables and baseline data of male and female patients in the different groups

	All patients (n = 303)	Users (n = 191)	Nonusers (n = 83)	Unknown (n = 29)
<i>Males</i>	(n = 234)	(n = 152)	(n = 60)	(n = 22)
Age, years	57.5 ± 12.0	58.1 ± 12.0	57.4 ± 12.3	53.9 ± 12.5
BMI	31.5 ± 5.4	31.4 ± 5.6	31.5 ± 4.8 ^a	32.6 ± 5.3
AHI	34.4 ± 24.9 ^b	35.7 ± 25.5	32.4 ± 24.8 ^c	31.5 ± 21.2
ESS score before therapy	9.3 ± 4.8	9.6 ± 4.8	8.2 ± 4.6	10.3 ± 5.0
<i>Females</i>	(n = 69)	(n = 39)	(n = 23)	(n = 7)
Age, years	60.5 ± 13.3	61.2 ± 13.9	59.0 ± 12.5	61.3 ± 14.1
BMI	31.9 ± 6.7	33.0 ± 5.6 ^a	28.9 ± 5.6	35.6 ± 7.4 ^a
AHI	29.1 ± 24.1	35.0 ± 25.0 ^c	16.4 ± 13.9	37.6 ± 31.7 ^c
ESS score before therapy	8.7 ± 4.9	9.2 ± 4.8	8.9 ± 4.3	5.4 ± 6.9

^a p < 0.05 versus BMI of female nonusers; ^b p < 0.05 versus AHI of all female patients; ^c p < 0.05 versus AHI of female nonusers.

The majority of patients were treated with conventional fixed continuous PAP (CPAP; 88.8%), while 5.9% had automatic CPAP, 3.3% bilevel PAP and 2% adaptive servoventilation. In the users group, subjective adherence reported by the patients was 6.6 ± 1.5 h/night, and objective PAP use measured by the clock counter was 4.7 ± 2.3 h/night. There was no significant difference between patients who had a follow-up visit and patients who did not have a follow-up visit with regard to their reported adherence (6.7 ± 1.3 vs. 6.4 ± 1.9 h/night, respectively) or their objective adherence (4.7 ± 2.2 vs. 4.9 ± 2.6 h/night, respectively).

Table 1 summarizes the anthropometric parameters, baseline AHI, ESS score before and after PAP treatment and the level of education in the whole study group and separately in the users and nonusers groups. Nonusers had a lower AHI and a lower ESS score at baseline than users, but this was not statistically significant. In addition, in the nonusers group, there was a tendency to have a graduate education.

In contrast, the baseline AHI in the female nonusers was the lowest AHI of all subgroups and was statistically significantly lower than in the female users (table 2). The AHI in the female nonusers was also significantly lower

Table 3. Comorbidities in the different patient groups

	All patients (n = 303)	Users (n = 191)	Nonusers (n = 83)	Unknown (n = 29)
Diseases per patient	1.4 ± 1.0	1.3 ± 0.9	1.4 ± 1.1	1.7 ± 1.1
0 diseases, %	20.8	18.8	26.5	17.2
1 disease, %	35.3	40.3	26.5	27.6
2 diseases, %	29.7	30.9	30.1	20.7
>2 diseases, %	14.2	9.9	16.9	34.5

Coexisting diseases were included as documented in the patients' files.

Table 4. Univariate analysis of correlation between nightly PAP adherence (hours of nightly use) and clinical and polysomnographic parameters

	r	P
Sex	-0.04	0.276
Age	0.08	0.141
BMI	-0.02	0.405
AHI	0.13	0.041
ESS score	-0.09	0.117

Table 5. Odds ratios between clinical and polysomnographic variables and treatment discontinuation

	OR	95% CI
Female gender	1.49	0.82–2.71
AHI ≤20	1.98	1.17–3.36
ESS score <10	2.15	1.24–3.74
Age <50 years	1.21	0.73–2.05
BMI <30	1.22	0.73–2.05

OR = Odds ratio; CI = confidence interval.

than in the male nonusers, while there was no significant difference in the AHI between male users and nonusers. In addition, female nonusers had a statistically significantly lower BMI than female users. Again, there was no significant difference in the BMI between male users and nonusers (table 2).

At least 1 coexisting disease was present in 79.2% of the OSAS patients, with a mean of 1.4 ± 1.0 diseases per patient. Cardiovascular diseases (39.2%), pulmonary dis-

orders (16.1%), metabolic diseases (14.5%) and neurologic/psychiatric disorders (3.1%) were the most frequent comorbidities. Comparing the number of diseases per patient, there were more patients without a coexisting medical condition in the nonusers than in the users group (26.5 vs. 18.8%, respectively) and also more patients with more than 2 comorbidities (16.9 vs. 9.9%, respectively; table 3).

In a univariate analysis, objective nightly use of PAP treatment in the users group correlated significantly with baseline AHI ($r = 0.13$, $p = 0.041$) but not with sex, age, BMI or ESS score (table 4).

As shown in table 5, the odds of discontinuing treatment in the first year was twice as high in patients with an AHI ≤20 (odds ratio 1.98, 95% confidence interval 1.17–3.36) and more than twice as high in patients with an ESS score <10 (odds ratio 2.15, 95% confidence interval 1.24–3.74).

All patients in the nonusers group were asked about the time of treatment discontinuation and the reasons for stopping treatment. A total of 29 patients (34.9% of nonusers) discontinued PAP treatment within the first 3 months, 50 patients (60.2%) within the first 6 months and 64 patients (77.1%) within the first 12 months. Only 7 patients (8.4%) discontinued PAP treatment after 1 year. In 12 patients (14.5%), the time of discontinuation was unknown. Most of the patients who stopped PAP treatment complained about side effects of the interface (24.1%), such as leakage or skin irritation, and about discomfort with the device (13.3%). Other reasons for treatment discontinuation were claustrophobia (12.1%), rhinitis (6%) and insomnia (4.8%). A total of 17% of the patients stopped treatment because they did not have any symptoms before starting PAP therapy and therefore they did not feel better using the device.

Discussion

One of the most interesting aspects of this study is the fact that it is a real-life study reflecting 'true' PAP treatment adherence and discontinuation in a large group of OSAS patients. When patients were discharged from hospital, neither the patient nor the physician was aware of the fact that 1 year later treatment continuation and adherence would be explored. In this context, a dropout rate of 27% was found, while 63% of the patients were still definitely on PAP treatment, with a mean nightly use of 4.7 h. The percentage of our patients still using PAP after 1 year is smaller than previously reported in prospective

studies with rates of 76–89% of patients still using their PAP machine after a follow-up of 9–15 months [17–20]. On the other hand, our result is close to the data from McArdle et al. [8], who designed a study closer to the ‘real-life’ conditions of our study and observed continued CPAP usage after 5 years in 68% of their patients. The objective average nightly use of 4.7 h in our patients who continued treatment is also slightly below previously reported rates of use ranging from 4.7 to 5.7 h per night [11, 17, 21, 22]. One limitation of our study is that PAP usage was only calculated by dividing the built-in clock time total by the number of days since discharge from hospital. Therefore, it is possible that patients did not use their machine every night or there was a great variability in the number of hours of use each night. That may partly explain the difference of about 2 h between objectively measured and subjectively reported adherence, but this phenomenon was already described in earlier studies [7, 23].

Most of our patients who discontinued PAP treatment stopped therapy within the first 6 months, which emphasizes that the pattern of adherence is established early and that attempts to reduce the dropout rate have to focus on the first weeks of treatment [24]. Treatment side effects and problems with the interface or the device were the most frequently reported reasons for rejecting the PAP device. However, 17% of the patients stopped treatment because, despite a high AHI, they did not have any symptoms before starting PAP therapy and therefore experienced no subjective benefit from the treatment. Taken together with our observation that 12% of the patients reported claustrophobia, these results accentuate the role of psychological rather than biomedical factors in accepting long-term therapy with a PAP device. Perceptions of risk, outcome expectancies of therapy and functional limitations in daily life are important early predictors of continued use of CPAP and should be addressed in behavioral strategies to improve adherence [25].

In our study, PAP adherence in the users group was correlated only with the AHI, while age, sex, BMI and subjective sleepiness had no statistically significant influence on nightly usage of the device. These findings are in correspondence with previous studies describing a positive influence of OSAS severity on subsequent adherence in the majority of patients [1]. Although not addressed in our study, in earlier investigations even the necessary CPAP pressure had no significant effect on PAP usage [26, 27]. However, in contrast to our results, previous authors described self-reported daytime sleepiness, as indicated by a score of greater than 10 on the ESS, to be associated with long-term CPAP use [8]. The reason for this

discrepancy may be that the patients in the present study complained less of sleepiness than in other studies, as indicated by a mean pretherapeutic ESS score of 9.

Because definitively discontinuing treatment is probably more serious for OSAS patients than using the PAP device only a few hours each night, the focus of the present study was not only on treatment adherence in the users group but to a greater extent on patient-related factors associated with a certain probability of stopping therapy within the first months. The data suggest that in patients with an AHI below 20 or an ESS score below 10, the risk of treatment discontinuation is twice that in other patients. In light of this, the question has to be raised whether nonsleepy patients or patients with a low AHI should be treated at all. There are conflicting data about the efficacy of PAP treatment in OSAS patients with mild to moderate disease (AHI 5–30). Some studies found that CPAP did not improve subjective sleepiness or blood pressure in those patients [28, 29], while other studies demonstrated an increase in quality of life [30, 31] or a benefit with regard to cardiovascular outcome [32]. Thus, it remains unclear whether CPAP has utility across outcomes for OSAS patients with this level of disease severity. However, if physicians decide to initiate PAP treatment in those patients, they should devote more time to education and follow-up visits during the first months of therapy to prevent treatment discontinuation. This seems to be true especially for moderately obese women with mild OSAS, because in our study these were the typical characteristics of the patients who stopped PAP treatment.

Another interesting aspect of the present study was the correlation between therapy adherence and comorbidity. As reported previously [33, 34], coexisting diseases were very common in our OSAS patients, with 79% of them being adversely affected by at least 1 comorbidity. Although the mean number of comorbidities was not different in users and nonusers, in the group who discontinued treatment, there were more patients with no coexisting disease and with more than 2 diseases. It can be speculated that otherwise healthy people tend to minimize symptoms and dismiss possible consequences of untreated sleep apnea. On the other hand, patients may be unaware of the strong association between their comorbidities and sleep-disordered breathing and, therefore, do not accept the necessity of treating an ‘additional’ disease like obstructive sleep apnea. This emphasizes the importance of providing patients with detailed information and education, particularly during initiation of PAP therapy [35, 36].

One limitation of the present study is that it specifically reflects the standard procedure in our sleep lab, which may differ from other sleep centers. However, in Germany, many insurance companies do not accept routine follow-up visits for OSAS patients. Therefore, it is general practice in many sleep labs to perform follow-up visits only in patients complaining of treatment problems. In our study, treatment adherence in those patients with problems and a follow-up visit did not differ from that in 'uncomplicated' patients without a follow-up visit, which is an argument for a closer follow-up, at least in those OSAS patients with treatment problems. Another limitation is the fact that only the built-in run time of the device was used to determine PAP usage. This approach was selected because there were some devices without the

possibility to provide more detailed information about the daily usage. However, we suggest that the lack of more precise information does not limit our results, particularly with regard to the statements of the nonusers group.

In conclusion, the present data suggest that in 'real life' – outside of clinical studies – PAP treatment adherence in OSAS patients needs to be enhanced and the dropout rate needs to be reduced. Several factors are associated with the probability of discontinuing PAP therapy, including subjective sleepiness, the severity of the sleep-disordered breathing and the number of comorbidities. Sleep medicine clinicians should consider these factors when initiating PAP therapy in patients with obstructive sleep apnea.

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