

Persistence of Upper-Airway Symptoms During CPAP Compromises Adherence at 1 Year

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BACKGROUND: The most common adverse effects of CPAP are related to the upper airways. We evaluated upper-airway symptoms before and after a CPAP trial as well as their effect on CPAP adherence. We also evaluated the effect of humidification added to CPAP therapy on upper-airway symptoms. **METHODS:** We followed for 1 y 536 subjects with obstructive sleep apnea scheduled consecutively for CPAP initiation. Subjects completed visual analog questionnaires on nasal stuffiness, rhinorrhea, and mouth dryness (0 = no symptoms, 100 = severe symptoms). **RESULTS:** Before CPAP initiation, mean nasal stuffiness score was 29.6 ± 24.9 , rhinorrhea score was 16.0 ± 21.7 , and mouth dryness score was 43.8 ± 33.1 . In subjects who quit CPAP treatment before the 1-y follow-up, the increase in rhinorrhea score during CPAP initiation was significant, 5.3 (95% CI 0.5–9.5, $P = .02$), and in those using CPAP at 1 y, nasal stuffiness score and mouth dryness score decreased significantly during initiation, -5.1 (95% CI -7.9 to -2.4 , $P < .001$) and -21.2 (-25.5 to -17.4 , $P < .001$). Mouth dryness score decreased significantly with CPAP regardless of humidification: change with humidification, -18.1 (95% CI -22.1 to -14.3), $P < .001$; change without, -10.5 (95% CI -16.9 to -4.1), $P = .002$. Humidification also prevented the aggravation of rhinorrhea (change, -0.4 [95% CI -2.6 to 1.9], $P = .75$) and alleviated nasal stuffiness (change -5.3 [95% CI -7.8 to -2.6], $P < .001$) with CPAP, whereas its absence induced a significant rise in symptom scores: change in rhinorrhea, 11.5 (95% CI 7.1 – 16.7), $P < .001$; change in nasal stuffiness, 8.5 (95% CI 3.9 – 13.5 , $P < .001$). **CONCLUSIONS:** The severity of upper-airway symptoms before CPAP does not predict CPAP use at 1 y, whereas CPAP non-users at 1 y had smaller or no alleviation in symptom scores during initiation compared with those who continued CPAP treatment. *Key words:* CPAP; humidification; nasal stuffiness; mouth dryness; obstructive sleep apnea; upper-airway symptoms. [Respir Care 2016;61(5):652–657. © 2016 Daedalus Enterprises]

Introduction

CPAP is the standard treatment for obstructive sleep apnea (OSA).^{1,2} CPAP effectively reduces snoring, apneas and hypopneas, thereby improving sleep quality and reducing daytime sleepiness as well as other symptoms.^{1–3} Adverse effects of CPAP treatment are mild and often

related to the upper airways.^{4,5} Nevertheless, these adverse effects can cause patients discomfort and even lead to treatment cessation.^{6,7} Previously, upper-airway complaints, especially rhinorrhea and sneezing, were assumed to increase during CPAP treatment.⁶ Recently, however, we evaluated the nasal symptoms of 385 subjects before CPAP initiation and 2 months after and found that upper-airway symptoms related to dry mucosa seemed to decrease during CPAP treatment.⁸ In that previous study,

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subjects received no humidification devices, whereas symptomatic subjects received topical medication (steroids and saline). Several studies have shown that heated humidification can effectively reduce upper-airway symptoms during CPAP treatment,⁹⁻¹² but the effect of humidification on CPAP adherence remained unclear. Some studies have shown that objectively measured adherence increases with humidification,^{10,13} whereas other studies have shown that adding humidification to the treatment fails to improve CPAP adherence despite a reduction in upper-airway symptoms.¹²⁻¹⁴

One could speculate that the early addition of humidification alleviates patients' symptoms and may ameliorate long-term CPAP adherence. In this study, we added a humidification device for all of our symptomatic subjects. The aim of this study was to evaluate upper-airway symptoms before and after a CPAP trial as well as their effects on CPAP adherence by following the subjects for 1 y. We also aimed to describe the effect of adding humidification to CPAP therapy on upper-airway symptoms.

Methods

Subjects

We followed for 1 y 536 consecutive OSA subjects starting their CPAP treatment at the Sleep Unit at the Helsinki University Central Hospital, a tertiary sleep apnea referral hospital, between May 2010 and December 2012. The subjects were admitted to our sleep unit for CPAP initiation. All subjects had previously undergone an American Academy of Sleep Medicine type III (Embletta, EMBLA, ResMed, San Diego, California) sleep study showing an apnea and hypopnea index of $>5/h$ and suffered from daytime sleepiness.

All subjects had received information about CPAP therapy from a physician specializing in sleep medicine and agreed to be scheduled for a few days' CPAP trial. Subjects underwent CPAP initiation at home or at the hospital. At home, titrations were performed for a mean period of 4 ± 2 nights with the ResMed Autoset CPAP device (ResMed, San Diego, California) as described earlier.¹⁵ We set the pressure between 4 cm H₂O and a maximum of 20 cm H₂O, and a ResLink (ResMed, San Diego, California) device with a pulse oximeter was attached to the device to monitor oxygen saturation during the CPAP trial. For subjects with reduced mobility or restricted learning ability, CPAP initiation was done at the sleep unit with the Autoset CPAP device. The cardiorespiratory sleep study device Embla N7000 (ResMed, San Diego, California) served to monitor the subjects at the Sleep Unit during automatic titration. Subjects were offered all types of CPAP

QUICK LOOK

Current knowledge

The most common CPAP adverse effects are related to the upper airways, and can cause patient discomfort and even lead to treatment cessation.

What this paper contributes to our knowledge

Subjects had frequent upper-airway symptoms prior to CPAP treatment, and the severity of symptoms before CPAP initiation did not predict long-term CPAP use. Mouth dryness decreased significantly with CPAP treatment regardless of humidification. The addition of heated humidification reversed the tendency of nasal stuffiness and rhinorrhea to worsen with CPAP treatment. We also showed that CPAP non-users at 1 y had no alleviation or a smaller alleviation in symptom scores during initiation compared with those who continued CPAP treatment at the 1-y follow-up.

interfaces before starting CPAP and later when needed. Masks were adjusted individually to be accepted by the subject, to achieve maximum comfort, and to ensure the absence of air leak. No mask switching occurred during the few days' CPAP trial. Moreover, we considered a trial successful if a subject was willing to continue CPAP treatment at home. After a successful trial, a 3-month and a 1-y follow-up visit were scheduled. The Research and Ethics Committee at our hospital approved the study protocol (38/2011, M101060027).

Three outcome variables related to the upper-airway symptoms were measured in this study. We used a subjective questionnaire method graded from no symptoms to severe symptoms. The subjects completed our routine self-reported visual analog questionnaire (0 = no symptoms, 100 = severe symptoms) inquiring about their morning nose stuffiness, morning mouth and throat dryness, and morning rhinorrhea (see the supplementary materials at <http://www.rcjournal.com>) before and after a few nights' CPAP trial. To all subjects who had used nasal decongestants during the CPAP trial, we assigned a nasal stuffiness score of 100.

The subjects were not randomly designated for humidification, but a sleep nurse was instructed to add heated humidification to the treatment during the CPAP trial if the subject reported any upper-airway symptoms that disturbed his or her daily life or if the subject regularly used nasal steroids. Humidification was later administered if a subject's upper-airway symptoms worsened with CPAP initiation.

Table 1. Characteristics of All Subjects and According to Decongestant Use

Characteristics	All (N = 536)	Decongestant	
		Users (n = 35)	Non-users (n = 501)
Age, y	55 ± 12	52 ± 10	56 ± 12
Body mass index, kg/m ²	32 ± 7	30 ± 7	32 ± 7
Apnea-hypopnea index	33 ± 22	39 ± 26	33 ± 21
Oxygen desaturation (4%) index	29 ± 22	33 ± 25	29 ± 22
S _{pO₂} , %	93 ± 4	92 ± 4	93 ± 3
Epworth Sleepiness Scale	9 ± 3	9 ± 5	9 ± 4

Data are shown as mean ± SD.

Statistical Analysis

The data are presented as means ± SD or as n (%). The most important outcomes are given with 95% CIs. The comparisons between the groups were made by a *t* test, bootstrapped type *t* test, or chi-square test, when appropriate. The changes within groups were analyzed by applying a bootstrapped type *t* test. The changes of symptom scores between groups were made by bootstrap type analysis of covariance, using baseline measurement as a covariate. The bootstrap method is significantly helpful when the theoretical distribution of the test statistic is unknown or in the case of violation of the assumptions (eg, non-normality). The normality of the variables was tested by using the Shapiro-Wilk *W* test. No adjustment was made for multiple testing. The STATA 14.0 (StataCorp, College Station, Texas) statistical package was used for the analyses.

Results

Altogether, 536 subjects underwent CPAP initiation that lasted a mean of 4 ± 2 d. Subjects' characteristics are described in Table 1. During initiation, 35 subjects (7%) had used a decongestant at least once. We noticed no significant differences between groups of decongestant users and non-users (Table 1). At the 3-month follow-up visit, 455 subjects (85%) continued CPAP treatment, and their average CPAP use was 3.5 ± 2.4 h, and at the 1-y follow-up, 305 subjects (57%) continued CPAP treatment, and their average CPAP use was 4.4 ± 2.3 h. Of users at the 1-y follow-up, 179 (59%) used CPAP for >4 h/d.

Humidification

We initially provided 417 (78%) subjects with heated humidification: another 30 (6%) subjects received humidification later. A total of 16 subjects (3%) refused the

Table 2. CPAP Users at 3-Month and 1-Year Follow-Up Visits According to Humidification Use

CPAP Users	With Humidification (n = 417)	Without Humidification (n = 119)	<i>P</i>
At 3-mo follow-up	355 (85)	100 (84)	.77
At 1-y follow-up	238 (57)	67 (56)	.84

Data are shown as n (%).

Table 3. Upper-Airway Symptoms Before and After CPAP Initiation

Symptoms	Baseline	After Initiation	Change	<i>P</i>
Nasal stuffiness	29.6 ± 24.9	27.4 ± 25.8	-2.3 (-4.6 to 0.2)	.060
Rhinorrhea	16.0 ± 21.7	18.2 ± 24.7	2.2 (0.3-4.4)	.040
Mouth dryness	43.8 ± 33.1	27.4 ± 25.8	-16.5 (-19.8 to -12.9)	<.001

Data are shown as mean ± SD and mean (95% CI).

humidification offered, and 73 subjects (14%) required no humidification at all. There was no difference in CPAP adherence at the 3-month and 1-y follow-up visits between the subject group using CPAP with and without humidification (Table 2).

Upper-Airway Symptoms Before and After CPAP Initiation

Upper-airway symptom severity scores before and after CPAP initiation are presented in Table 3. After CPAP initiation, the mouth dryness score decreased significantly, whereas a modest increase was seen in mean rhinorrhea score (Table 3). There was a significant difference between all symptom severity scores before CPAP initiation according to humidification use versus no humidification use (*P* < .001) (Fig. 1). The changes in severity scores after CPAP initiation are presented in Figure 1. In the humidification group, nasal stuffiness and mouth dryness scores decreased significantly, and in the no-humidification group, mouth dryness decreased, whereas nasal stuffiness and rhinorrhea scores increased significantly (Table 4). The changes in symptom severity scores between humidification and no-humidification group after adjusted prior values were significant for the rhinorrhea score (*P* = .01) and mouth dryness score (*P* = .02).

Upper-Airway Symptoms and CPAP Use at 1 Year

There was no statistical difference in baseline upper-airway symptom scores before CPAP initiation between the subjects who continued CPAP treatment at 1 y (users)

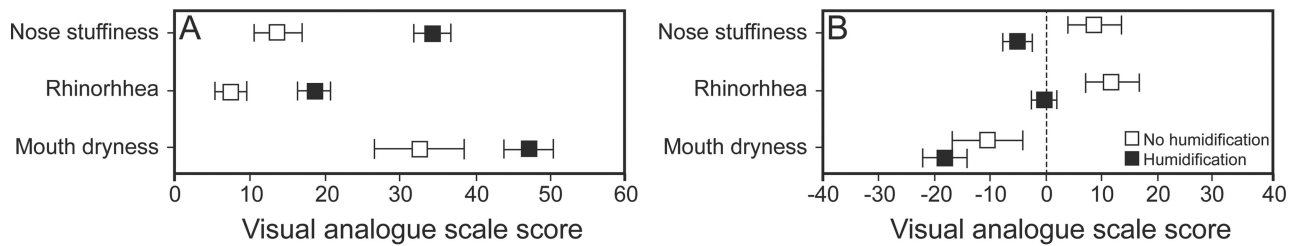


Fig. 1. Upper-airway symptom severity before CPAP (A) and change after CPAP initiation (B) in subjects with and without humidification using a visual analogue scale score: 0 = no symptoms, 100 = severe symptoms. Error bars represent 95% CI.

Table 4. Change in Upper-Airway Symptom Scores Before and After CPAP Initiation

Symptoms	With Humidification		Without Humidification	
	Change	P	Change	P
Nasal stuffiness	-5.3 (-7.8 to -2.6)	<.001	8.5 (3.9-13.5)	<.001
Rhinorrhea	-0.4 (-2.6 to 1.9)	.75	11.5 (7.1-16.7)	<.001
Mouth dryness	-18.1 (-22.1 to -14.3)	<.001	-10.5 (-16.9 to -4.1)	.002

Data are shown as mean (95% CI).

and those who had quit the treatment before the 1-y follow-up visit (non-users) (Fig. 2). In the non-user group, the increase in the rhinorrhea score during CPAP initiation was significant, and in the CPAP user group, the nasal stuffiness score and mouth dryness score decreased significantly (Table 5). The changes in severity scores between humidification and no-humidification group after the adjusted prior value were significant for nasal stuffiness ($P < .001$), mouth dryness ($P < .001$), and rhinorrhea score ($P = .041$).

Discussion

In this prospective follow-up study, we show that the severity of upper-airway symptoms before CPAP does not predict CPAP use at 1 y, whereas CPAP non-users at 1 y had smaller or no alleviation in symptom scores during initiation compared with those who continued CPAP treatment. Mouth dryness decreased during CPAP treatment regardless of the use of humidification. In the no-humidification group, nasal stuffiness and rhinorrhea increased significantly, whereas in the humidification group, nasal stuffiness scores decreased, and rhinorrhea scores showed no change.

Many OSA patients already exhibit upper-airway symptoms before receiving any treatment for OSA.¹⁶ The adverse effects of CPAP therapy are local mainly to the upper airways but may cause patients substantial discomfort,^{5,6,8,17} even leading to treatment cessation. This study confirms one of our previous findings,⁸ that CPAP treat-

ment alleviates mouth dryness in OSA subjects. We may speculate that mouth dryness usually decreases during CPAP treatment because patients no longer need to gasp for air through their mouth at the end of apnea events. However, some patients may develop a unidirectional air leak through the mouth, thereby causing worsening in mouth dryness.^{18,19} Meanwhile, the persistence of mouth dryness with CPAP therapy may also stem from other diseases or from adverse effects of medications,²⁰ or we assume that it may even signal insufficient CPAP pressure levels, causing apneas and hypopneas to persist.

The use of heated humidification with CPAP blocks the tendency of nasal stuffiness to worsen during CPAP treatment. Ryan et al¹² have previously shown that adding humidification to CPAP therapy reduces the frequency of nasal symptoms. We noticed that the severity of nasal symptoms before the CPAP trial has no influence on long-term CPAP use, whereas those subjects who had no alleviation or only small alleviation of nasal symptoms during CPAP initiation quit CPAP treatment more often.

In our clinic, we add humidification to CPAP treatment when the patients complain of nasal symptoms, even moderate ones. We also add humidification if the patient uses nasal steroids. This explains the high percentage (77%) of humidification used in our study population. In the no-humidification group, scores for nasal stuffiness and rhinorrhea were significantly higher, whereas with humidification, they remained unchanged. This result calls into question whether all CPAP patients should receive humidification, since it is both bulky and costly. Perhaps such decisions are best made individually. Nevertheless, our results presume that failing to provide humidification to patients with initial nasal symptoms may lead to low CPAP adherence or even CPAP cessation. Subjects with and without humidification were supervised closely for any upper-airway symptoms; therefore, the role of the effect of expectation (Hawthorne effect), if any, would have been a minor one, in the evaluation on upper-airway symptoms in the humidification group.

We acknowledge some limitations of the study. First, we did not randomize the use of humidification. Rather, we administered humidification according to individual

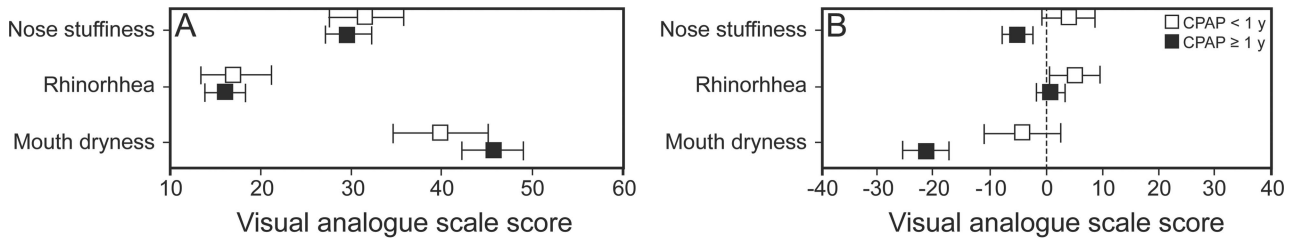


Fig. 2. Upper-airway symptom severity before CPAP (A) and change after CPAP initiation (B) in subjects using CPAP for different lengths of time using a visual analogue scale score: 0 = no symptoms, 100 = severe symptoms. Error bars represent 95% CI.

Table 5. Change in Upper-Airway Symptom Scores in Subjects Not Continuing CPAP Use at 1-Year Follow-Up (Non-Users) and Those Continuing CPAP at 1-Year Follow-Up (Users)

Symptoms	Non-Users		Users	
	Change	P	Change	P
Nasal stuffiness	-5.3 (-7.8 to -2.6)	<.001	8.5 (3.9-13.5)	<.001
Rhinorrhea	-0.4 (-2.6 to 1.9)	.75	11.5 (7.1-16.7)	<.001
Mouth dryness	-18.1 (-22.1 to -14.3)	<.001	-10.5 (-16.9 to -4.1)	.002

Data are shown as mean (95% CI).

symptoms, so we could not confirm the effect of humidification on CPAP adherence. Second, we included decongestant users in the analysis of nasal symptoms, knowing that this may have slightly overestimated our nasal symptom scores. Meanwhile, we presumed that nasal stuffiness disturbed CPAP therapy at least enough to compel the subjects to request medications for it. Third, we recognize myriad other factors and adverse effects that impact adherence, but we believe that these do not change the conclusions for our results because our subjects were consecutive and all received the same instructions and the same CPAP device. Moreover, we have previously shown that the satisfaction rate with the CPAP interface does not affect daily CPAP use.²¹ We do recognize that the CPAP interface may affect the severity of upper-airway symptoms. Effectively, in this study, no mask switching occurred during the CPAP trial, excluding any effects of CPAP interfaces on the modifications of the upper-airway symptoms with CPAP.

Conclusions

Upper-airway symptoms before CPAP initiation show no correlation with CPAP adherence at 1 y. Mouth dryness decreases significantly with CPAP treatment. Moreover, the addition of heated humidification reverses the tendency of nasal stuffiness and rhinorrhea to worsen with CPAP treatment. Finally, we showed that CPAP non-users at 1 y had no alleviation or had smaller alleviation in symptom scores during initiation compared with those who continued CPAP treatment at the 1-y follow-up.

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