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Official publication of the American College of Chest Physicians



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Chest 1999;116:403-408
DOI 10.1378/chest.116.2.403

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<http://chestjournal.org/cgi/content/abstract/116/2/403>

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Effects of Humidification on Nasal Symptoms and Compliance in Sleep Apnea Patients Using Continuous Positive Airway Pressure*

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Study objectives: To evaluate the effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure (CPAP).

Design: A randomized, crossover design was employed.

Setting: The study was conducted at two suburban community-based hospital sleep laboratories.

Patients: Data were collected on 38 obstructive sleep apnea patients (mean age, 44.1 years) in whom CPAP was a novel treatment.

Interventions: The interventions were heated humidity, cold passover humidity, and a washout period without humidity.

Measurements and results: Patients were titrated with heated humidity or cold passover humidity in the laboratory and subsequently initiated on humidity. Objective compliance, self-report of factors affecting CPAP use, satisfaction with CPAP, feeling upon awakening, and daytime sleepiness were assessed at the completion of each 3-week treatment period and a 2-week washout period. Outcome measures were assessed with one-way analysis of variance followed by Scheffe *post hoc* comparisons. Significant main effects were observed for compliance ($F_{2,37} = 5.2$; $p = 0.008$), satisfaction with CPAP ($F_{2,37} = 4.5$; $p = 0.01$), and feeling refreshed on awakening ($F_{2,37} = 4.4$; $p = 0.02$). A significant decrease in daytime sleepiness was observed between baseline and each of the conditions ($F_{3,37} = 55.5$; $p < 0.0001$), but Epworth sleepiness scale scores did not differ between conditions (all p values > 0.56). CPAP use with heated humidity (5.52 ± 2.1 h/night) was greater than CPAP use without humidity (4.93 ± 2.2 h/night; $p = 0.008$). Compliance differences were not observed between CPAP use with cold passover humidity and CPAP use without humidity. Patients were more satisfied with CPAP when it was used with heated or cold passover humidity ($p \leq 0.05$). However, only heated humidity resulted in feeling more refreshed on awakening ($p < 0.05$). No significant differences were observed among the three groups on the global adverse side effect score ($F_{2,37} = 2.5$; $p = 0.09$). Specific side effects such as dry mouth or throat and dry nose were reported less frequently when CPAP was used with heated humidity compared to CPAP use without humidity ($p < 0.001$).

Conclusions: Compliance with CPAP is enhanced when heated humidification is employed. This is likely due to a reduction in side effects associated with upper airway symptoms and a more refreshed feeling upon awakening. Compliance gains may be realized sooner if patients are started with heated humidity at CPAP initiation. (CHEST 1999; 116:403-408)

Key words: compliance; continuous positive airway pressure; humidity; nasal symptoms; obstructive sleep apnea

Abbreviations: ABMC = Alexian Brothers Medical Center; BMI = body mass index; CDH = Central DuPage Hospital; CPAP = continuous positive airway pressure; ESS = Epworth sleepiness scale; OSA = obstructive sleep apnea; RDI = respiratory disturbance index

Obstructive sleep apnea (OSA) affects 4% of men and 2% of women, and if left untreated is associated with significant mortality.^{1,2} Continuous

positive airway pressure (CPAP) has become the treatment of choice for OSA. Despite its efficacy, compliance is poor. As few as 25% of patients on CPAP use the device > 4 h/night, and the self-reports of patients overestimate the actual use of the device.³⁻⁵ Complaints related to noncompliance include feelings of claustrophobia³ and perceived lack of benefit.⁶ One study⁷ reported that patients with more severe OSA showed greater daily use. Others, however, have reported no differences between compliant and noncompliant patients on the frequency of adverse reactions during therapy or initial disease severity.⁸

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This research was supported by a grant from Fisher & Paykel Healthcare. Sullivan V Elite RTC machines and SCAN 2.01 compliance software were provided by ResMed Corporation.

Manuscript received October 26, 1998; revision accepted March 2, 1999.

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As many as 65% of patients using CPAP report significant side effects such as nasal congestion, dry nose or throat, and discomfort associated with cold air.^{3,6,8-10} Epistaxis occurs less frequently, but can be severe.¹¹ Chronic nasal congestion may compromise a patient's ability to successfully utilize CPAP.¹² Upper airway symptoms are caused by mouth leaks that produce high unidirectional airflow over nasal and oral mucosa. Simulation of a mouth leak in persons breathing with CPAP while awake produces a subjective feeling of mouth and nose dryness, nasal congestion, and an increase in nasal resistance.¹³ Heated humidity, but not cold passover humidity, greatly attenuates the magnitude and duration of the increases in nasal airway resistance. Other investigators have reported increases in nasal mucosal blood flux in patients simulating a mouth leak while using CPAP.¹⁴ Heated humidity prevents the increase in mucosal blood flux, suggesting that the cooling or drying effect of the airflow is responsible for the change. These studies were conducted in normal subjects while awake, but it is reasonable to assume that a similar mechanism may operate in apneic patients while asleep.

Humidity is employed to alleviate dryness and congestion in OSA patients. Two types of humidity are commonly employed: cold passover humidity and heated humidity. Little is known about the effects of these types of humidity on compliance with CPAP or nasal symptoms in sleep apnea patients. One study¹⁰ reported no differences in side effects between patients who used humidity compared to those who did not use humidity. However, no information was given regarding the type of humidity or the criteria used to determine which patients received humidity; therefore, definitive conclusions could not be made. This study evaluates the effects of heated and cold passover humidification on nasal symptoms and compliance with CPAP.

MATERIALS AND METHODS

Subjects

Eligible patients were between 18 and 75 years old, had an OSA diagnosis (respiratory disturbance index [RDI] ≥ 10), and had not received CPAP treatment previously. Comorbid medical or psychological conditions were considered to be exclusion criteria only if the condition interfered with the patient's ability to successfully utilize CPAP. Exclusion criteria included wake resting pulse oximetric saturation $< 90\%$, evidence of upper airway tract infection or flu-like symptoms at the time of titration, hospitalization 3 months prior to study initiation, elective surgery scheduled before the conclusion of the study, or prior surgical intervention for OSA. Participants were not eligible if they required bilevel positive airway pressure ventilation, a full face mask, or supplemental oxygen.

At the time of the initial polysomnogram, patients gave con-

sent. The participants agreed to use CPAP for the duration of the 8-week study and to provide feedback on nasal symptoms and satisfaction with the humidifier. The patients were not informed that the study was designed to assess compliance, but they were debriefed at the conclusion of the study regarding compliance monitoring. Institutional review board approval was obtained from both sites; the consent forms were identical.

Questionnaires

The patients completed a questionnaire assessing chronic nasal symptoms prior to the start of polysomnography. The patients were asked to indicate in the affirmative or negative whether they experienced the following symptoms on a regular basis: dry nose, runny nose, postnasal drip, nasal congestion, nose bleeds, reduced sense of smell, sinus infections, dry throat, sore throat, hoarse voice, cough, or allergies. The patients also completed the Epworth sleepiness scale (ESS). Following the CPAP titration, a modified post-sleep questionnaire was administered. The patients were asked about nasal symptoms they experienced during the titration, and they were asked to indicate (as not at all, somewhat, or a lot) whether they experienced congested nose, dry nose, dry mouth or throat, air leaks from the mask, or skin irritation.

At each assessment interval, the patients completed the ESS and the CPAP questionnaire. The patients were asked to rate adverse side effects in the following terms: (1) not a problem (a slight problem, but it did not interfere with using CPAP); (2) a moderate problem (sometimes I could not use CPAP); or (3) a major problem (I often could not use CPAP). Factors that were considered included the following: pressure from mask or straps; air leaks from the mask; machine noise; cold face or nose; claustrophobia; dry mouth or throat; congested nose; dry nose; nose bleeds; headache; difficulty breathing; chest discomfort; mask coming off the face; and skin irritation. At the end of each treatment period and washout period, the patients were asked to indicate on a 100-mm Likert scale how satisfied they were with CPAP during that time period and how refreshed they felt upon awakening.

Polysomnography

The sleep studies commenced at the patient's usual bedtime and concluded after the patient's time in bed was approximately 7 h. Standard polysomnography was performed at two suburban community hospitals using commercially available equipment (Central DuPage Hospital [CDH]; Sandman 2.4; Nellcor Puritan Bennett; Pleasanton, CA; and Alexian Brothers Medical Center [ABMC]; model 4412P; Nihon-Kohden; Tokyo, Japan or model 4100 Somnostar; SensorMedics; Yorba Linda, CA). Similar montages were used at both CDH and ABMC: left and right electro-oculography, surface EEG (electrode locations C4-A1, FZ-A2 [CDH only], and O2-A1), submental electromyography, ECG, anterior tibial electromyography, sonogram, nasal/oral airflow via thermistor, thoracic effort, and abdominal effort. Oxyhemoglobin saturation was recorded via pulse oximetry (model 504; Criticare; Waukesha, WI [for CDH]; and Biox 3740; Ohmeda; Louisville, CO [for ABMC]). Desaturations were defined as a drop in oxyhemoglobin saturation of $\geq 4\%$.

Sleep staging was determined according to Rechtschaffen and Kales.¹⁵ An obstructive apnea was defined as cessation of airflow (airflow tracing between 0% and 20% of baseline) for ≥ 10 s, accompanied by an arousal or desaturation. A hypopnea was defined as above, except that airflow tracing was between 20% and 75% of baseline. In both cases, evidence of continued thoracic and/or abdominal effort was required. Arousals were

defined as a 3-s change in EEG, as represented by a frequency shift. Spontaneous arousals were defined by exclusion; they were not associated with a respiratory event or linked to a leg movement, position change, or other gross body movement.

Study Design

A randomized, crossover design was employed. The patients were assigned to either heated humidity or cold passover humidity for the laboratory titration. The patients assigned to heated humidity were titrated with an appropriate humidifier (HC100; Fisher & Paykel Healthcare; Auckland, New Zealand). The patients assigned to cold passover humidity were titrated with an appropriate humidifier (Oasis; Respironics; Murrysville, PA). Each patient underwent either an all-night CPAP titration following a full night of diagnostic study or a split-night study protocol. CPAP was initiated during a split-night study if the RDI was > 30 and oxyhemoglobin desaturation $\geq 4\%$ occurred consistently in association with the sleep breathing events. Titration protocols were identical at both sites. Pressure increases were performed manually: 2 cm for obstructive apneas, and 1 cm for obstructive hypopneas, snores, desaturations, and arousals. All patients were titrated using a nasal mask (Sullivan Mirage; ResMed; San Diego, CA). Effective pressure was attained when evidence of apneas, hypopneas, snoring, hypoxemia, and arousals were ameliorated. CPAP was prescribed after the polysomnogram was reviewed.

All patients were set up with a CPAP machine (Sullivan V Elite Real Time Clock; ResMed) and a Sullivan Mirage nasal mask. The patients were given detailed instructions on the use and care of the CPAP machine, mask, humidifier, and related equipment. For the duration of the study, patients were instructed to maintain a constant temperature in their bedrooms during sleep. When possible, the patients were instructed to maintain a constant humidity in the bedroom; for example, if a room or home humidifier was normally used, the patients were instructed to continue its use. The addition of this type of humidity during the study was discouraged. When the patients were given the heated humidified air, the dial was set at 4. The patients were told not to change this setting if they felt comfortable. If water droplets formed in the mask, patients were instructed to decrease the setting by 0.5 U until the condensation no longer appeared. These are the same instructions used by the health-care company (Health Management; Barrington, IL) for all patients set up on CPAP with heated humidity. Specific to this study, information about side effects was not given, and the patients were not told that the humidifier could be operated without heat. For the first 3 weeks, the participants used the same humidity as in the titration study. This was followed by a 2-week washout period in which no humidity was used. The participants then switched to the alternate humidity for the final 3 weeks. There were three office visits, one at the end of each active treatment period, and one at the end of the washout period. At each office visit, the ESS and CPAP questionnaires were completed.

At each visit, the patients were told that a pressure check was required as part of the study protocol. While the patients completed the questionnaires, compliance data were downloaded from the CPAP machine using compliance software (SCAN 2.01; ResMed). The actual use per 24-h period was recorded; a pressure transducer recorded use only when the patient was breathing with the mask in place. At the first follow-up office visit, the humidifier was taken from the patient and he or she was instructed to use CPAP without humidity. At the second office visit, the alternate humidifier was given to the patient with detailed instructions for its use. At the final office visit, the patient was asked which type of humidifier he or she preferred, and the patient was maintained on this type of humidity.

In general, the patients were able to use each humidifier for the duration of the treatment period. Daily logs were not maintained, but patients were queried about CPAP use during each treatment period. When patients did not use CPAP because of travel, these days were excluded from analysis. No more than 3 days during a treatment period had to be excluded in any patient. The patients who attempted to use CPAP each night, but had difficulties maintaining use throughout the night, were included in analyses, provided that the mean daily use was > 1 h for at least one of the treatment periods.

Statistical Analysis

Values are given as mean \pm SD. Comparisons among the two treatment conditions and the washout period were conducted using one-way analysis of variance. Significant main effects were followed with Scheffe *post hoc* comparisons. Unless otherwise indicated, statistical significance required $p \leq 0.05$ (two-tailed).

RESULTS

Patient Characteristics

Forty-seven patients were enrolled in the study. Nine patients were unable to complete the protocol. Two patients were dropped from the study at the time of CPAP titration. One patient titrated with cold passover humidity exhibited persistent central apneas, and one patient titrated with heated humidity exhibited poor sleep efficiency and a significant degree of sleep discontinuity. Definitive pressure settings could not be obtained for either patient. One patient receiving cold passover humidity developed a severe headache during the second day of the study. This patient was subsequently prescribed heated humidity. One patient developed a severe dry nose and epistaxis on the second day of the washout period. He was immediately reinitiated on heated humidity, with complete resolution of the epistaxis. One patient removed the gasket in his cold passover humidifier after 3 days of use. He was unable to replace it after washing, and he did not contact anyone for a replacement. One patient was lost to follow-up. Two patients were excluded from analyses because average daily use was < 1 h/night during both treatment periods.

Thirty-eight patients completed the 8-week protocol. Seventeen patients had full-night CPAP titrations, and 21 patients had split-night studies. Twenty-two patients were randomized to heated humidity, and the remaining 16 received cold passover humidity. There were no differences between randomized groups in age, gender, study type, body mass index (BMI), RDI or CPAP pressure (all p values ≥ 0.07). These data are presented in Table 1. No differences were noted in age, gender, study type, BMI, RDI, or CPAP pressure between the two sleep laboratories (all p values ≥ 0.37).

Table 1—Demographic and Polysomnography Variables for 38 Patients Randomized to Heated or Cold Passover Humidity*

Variable	Heat (n = 22)	Cold (n = 16)	Total (n = 38)
Gender			
Male	17	13	30†
Female	5	3	8†
Study type			
Full night	10	7	17†
Split night	12	9	21†
Age, yr	44.9 ± 10.5	43.1 ± 11.9	44.1 ± 11
BMI, kg/m ²	37.5 ± 7.2	37.7 ± 9.8	37.6 ± 8.3
RDI, events/h	44.8 ± 29.5	67.0 ± 44.8	54.2 ± 37.9
CPAP pressure, cm H ₂ O	9.5 ± 2.7	9.5 ± 2.9	9.5 ± 2.7

*Data are expressed as No. or mean ± SD.

† χ^2 analysis.

Nasal Symptoms

Prior to CPAP titration, patients were asked to indicate in the affirmative or negative whether they experienced symptoms related to nasal pathology on a chronic basis. All symptoms except epistaxis were experienced by at least 20% of patients on a chronic basis. These results are shown in Table 2.

Preference

At the conclusion of the study, the patients were maintained on the humidifier of their choice. Twenty-nine of 38 patients (76%) preferred the heated humidifier to the cold passover humidifier. The number of preexisting nasal symptoms did not predict humidifier choice (independent sample *t* test, *p* = 0.68). The patients who chose heated humidity reported 4.0 ± 2.9 chronic nasal symptoms, whereas those who preferred cold passover humidity reported 3.6 ± 3.4 chronic nasal symptoms. Two patients who chose heated over cold passover humidity

Table 2—Chronic Nasal Symptoms in Sleep Apnea Patients Prior to Treatment With CPAP

Symptom	Percent
Dry nose	39
Runny nose	26
Postnasal drip	34
Nasal congestion	61
Epistaxis	3
Reduced sense of smell	29
Sinus infections	24
Dry throat	58
Sore throat	21
Hoarse voice	29
Cough	34
Allergies	34

actually preferred using CPAP without humidity. These patients were told they could use CPAP without humidity, but they were encouraged to use the heated humidifier. Several patients with an established choice requested to keep both humidifiers. For ease of transport, some patients requested to keep the cold passover humidifier to use only when traveling. Two patients who chose the cold passover humidifier requested to keep the heated humidifier when they were told it could be used with or without heat.

Compliance

A significant main effect for compliance was observed ($F_{2,37} = 5.2$; *p* = 0.008). Compliance was higher for CPAP use with heated humidity (5.52 ± 2.1 h) compared to CPAP use without humidity (4.93 ± 2.2 h; *p* = 0.008), but no difference was observed between CPAP use with cold passover humidity and CPAP without humidity, or between heated and cold passover humidity (*p* values > 0.14). Duration of use ranged from 1.0 to 9.1 h/night on heated humidity, 0.8 to 8.0 h/night on cold passover humidity, and 0.8 to 8.6 h/night during the washout period.

Symptom Improvement

The overall satisfaction with CPAP and feeling refreshed on awakening were assessed with a 100-mm Likert scale. Significant main effects were observed for overall satisfaction with CPAP ($F_{2,37} = 4.5$; *p* = 0.01) and feeling refreshed on awakening ($F_{2,37} = 4.4$; *p* = 0.02). Heated humidity and cold passover humidity were associated with greater satisfaction (*p* ≤ 0.05). Heated humidity, but not cold passover humidity, was associated with feeling more refreshed on awakening (*p* = 0.005). A significant decrease in daytime sleepiness was observed between baseline and each of the conditions ($F_{3,37} = 55.5$; *p* < 0.0001), but ESS scores did not differ between conditions (all *p* values > 0.56).

Adverse Side Effects

At the conclusion of each treatment period and washout period, adverse side effects were assessed and a global score was calculated. No significant differences were observed among the three groups ($F_{2,37} = 2.5$; *p* = 0.09). Item analysis comparisons were conducted to determine which individual side effects differed between CPAP use with heated humidity and CPAP use without humidity, because this may account for the compliance difference. To control for multiple pairwise comparisons, the *p* value was set at 0.01. Patients reported that dry

mouth or throat and dry nose interfered to a greater degree when CPAP was used without humidity compared to CPAP use with heated humidity ($p < 0.001$). These side effects were not different between cold passover humidity and no humidity (p values > 0.35). Differences in compliance, symptom improvement, and adverse side effects between CPAP use with heated humidity, CPAP use with cold passover humidity, and CPAP use without humidity are presented in Table 3.

DISCUSSION

CPAP use with heated humidity, but not cold passover humidity, resulted in greater usage when compared to CPAP use without humidity. Specific side effects that compromised CPAP use, such as dry mouth or throat and dry nose, were experienced to a lesser degree during heated humidification, when compared to CPAP use with cold passover humidity or CPAP use without humidity. The patients were more satisfied with CPAP when it was used with either heated or cold passover humidity. However, the patients awoke feeling more refreshed when CPAP was used with heated humidity. This suggests that the increased compliance with heated humidity was a result of fewer adverse side effects, specifically dry mouth or throat, dry nose, and feeling more refreshed on awakening.

Sixty percent of patients in this sample reported chronic nasal congestion prior to initiating CPAP therapy. Nasal symptoms are common in patients with OSA, and nasal obstruction is a risk factor for sleep apnea.¹⁶ Nasal congestion due to allergy promotes sleep-disordered breathing in normal sub-

jects, and it is associated with an increased risk for moderate to severe OSA.^{16,17} Furthermore, chronic nasal symptoms predispose OSA patients to mouth breathing. This normally has few consequences, but the use of CPAP exacerbates mouth leaks, causing high unidirectional airflow across the nasal and oral mucosa. The flow of cold air through the nose dries the mucosa and increases nasal airway resistance.¹⁸ This also stimulates local nerves and leads to the release of inflammatory mediator cells.¹⁹ Mouth leaks in normal subjects reproduce symptoms experienced by patients using CPAP, leading to increased nasal airway resistance and nasal mucosal blood flow.^{13,14} The results of this study suggest that heated humidifiers can prevent these changes in OSA patients and that the humidity output of cold passover humidifiers is insufficient to prevent mucosal drying.

Subjective improvement in mood and energy has been reported in CPAP users without nasal symptoms when compared to CPAP users with nasal symptoms.¹² Although compliance data were not reported in the study by Redline et al,¹² it is possible that the improvements in daytime functioning were the result of greater CPAP use by the group without nasal symptoms. In the present study, preexisting nasal symptoms did not predict humidity choice or influence compliance. However, a reduction in nasal symptoms associated with mucosal drying was observed with heated humidity. Although the attenuation of nasal symptoms did not result in lower ESS scores, it is possible that improvements in mood and energy may also have occurred. In the only other study to examine side effects and humidification, Pepin et al¹⁰ reported no difference in adverse side effects between patients who used humidity and those who did not use humidity. The type of humidifier was not reported in their study; patients using CPAP without humidity may have been compared to patients using CPAP with cold passover humidity.

Compliance with CPAP has been reported extensively in the literature and is well recognized to be less than optimal. Despite the recognition that CPAP compliance needs to be improved, few intervention studies have been undertaken. The support and education of CPAP users have been the only interventions reported in the literature. Chervin et al²⁰ performed a randomized clinical trial assessing the effects of education on compliance. The two treatment groups received an additional phone call or printed literature, whereas the control group received only the standard information that was conveyed at the time of evaluation. The groups that received additional information, either verbally or in writing, showed greater compliance compared to the control group. In fact, compliance was greater by 1.3 h/night for the group that received verbal informa-

Table 3—Differences in Outcome Measures Between CPAP Use With Heated Humidity, CPAP Use With Cold Passover Humidity, and CPAP Use Without Humidity*

Outcome Measure	Heated Humidity	Cold Passover Humidity	Without Humidity
Usage, h/night	5.52 ± 2.1†	5.15 ± 1.9	4.93 ± 2.2
Epworth sleepiness scale	6.2 ± 3.8‡	7.2 ± 4.8‡	6.7 ± 3.9‡
Feeling upon awakening	74.0 ± 15.9§	68.9 ± 23.4	62.0 ± 23.4
Satisfaction with CPAP	73.9 ± 19.1§	72.9 ± 22.6	62.3 ± 27.6
Adverse side effects (global score), No.	4.9 ± 3.3	6.2 ± 3.8	6.5 ± 4.9

*Data are expressed as mean ± SD. Measures for feeling upon awakening and satisfaction with CPAP range from 0 (poorest) to 100 (highest possible rating).

† $p = 0.008$ vs without humidity.

‡Results are significantly different from baseline ($p < 0.0001$)

§ $p = 0.02$ vs without humidity.

|| $p = 0.05$ vs without humidity.

tion via telephone, and compliance was increased by 2.7 h/night for the group that received additional written information. Increased compliance has also been demonstrated in a group setting.²¹ The patients who had been on CPAP for varying lengths of time had an average compliance of 5.2 h/night. Following attendance at one CPAP clinic that provided patient support, education, an equipment check, and symptom treatment, subsequent compliance increased to a mean of 6.3 h/night.

This is the first study to demonstrate that CPAP use can be increased by an intervention other than patient education and support. Compliance was improved by 0.59 h/night by the addition of heated humidification (a finding that is lower than the results of previous intervention studies, but still clinically relevant). The optimal amount of CPAP use has yet to be determined, and any increase in use is desirable. Humidification in this study was supplied to all eligible patients starting CPAP, and it was initiated during pressure titration. In clinical practice, humidification is usually reserved for patients who complain of persistent and severe side effects related to upper airway symptoms, and its introduction may be delayed for several weeks or months. Waiting for the development of upper airway symptoms may identify the patients most likely to benefit from humidification, but delaying its introduction may reduce potential benefits on compliance. Indeed, patients who become irregular CPAP users (defined as extreme variability in use averaging < 4 h/night) can be identified by the fourth day of treatment.²²

In summary, this is the first study to systematically examine the effects of humidity on compliance and adverse side effects in OSA patients using CPAP. The results of this study demonstrate that heated humidity increases compliance with CPAP. The difference in compliance may be explained by a reduction in side effects associated with upper airway symptoms and awakening feeling more refreshed after using CPAP with heated humidity. Compliance gains may be realized sooner if patients are started with heated humidity at the initiation of CPAP.

ACKNOWLEDGMENT: The authors wish to thank Lauren Krivis, John Krivis, and Joanna Dvorak of Health Management, Inc., and Janet Webb and Andrea Early of Suburban Lung Associates for their assistance during the study.

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DOI 10.1378/chest.116.2.403

This information is current as of August 19, 2008

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