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Title page

Impact of controlled heated breathing tube humidifier on sleep quality under CPAP therapy in a cool sleeping environment.

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Abstract:

There are conflicting data on the effect of adding a heated humidifier to nasal continuous positive airway pressure (CPAP) therapy for patients with obstructive sleep apnea syndrome (OSAS). The effects of heated humidification on sleep quality and treatment side effects for patients who prefer a cold bedroom environment have not been studied.

A randomized, controlled crossover trial involving 19 patients with a first-ever diagnosis of OSAS measured the effect of conventional heated humidification added to CPAP compared to a controlled heated breathing tube humidifier (ThermoSmart®) on sleep quality.

During the night in the sleep laboratory at a mean room temperature of 14 ºC, less condensation formed with the controlled heated breathing tube humidifier (1.9 ml versus 35.3 ml, (p=0.0001)) in the delivery system, the TST, S3/4 and REM sleep phases were significantly longer and the overall side effect score was lower than with conventional heated humidification.

Patients on CPAP desiring a cool bedroom temperature could benefit from controlled heated breathing tube humidification technology (with inputs from ambient temperature, set pressure and flow).

Key words: continuous positive airway pressure, heated humidification, obstructive sleep apnea, side effects.

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Introduction: Continuous positive airway pressure (CPAP) is the preferred treatment for obstructive sleep apnea syndrome (OSAS). However, more than 60% of patients complain of symptoms in the nose and pharynx (1, 2, 3). One option for reducing

such side effects is the additional use of a heated humidifier. However, few data are currently available on the effectiveness of this measure, and the indications for its use have not been adequately defined (4, 5, 6, 7, 8, 9). In addition, the humidification systems available today consist only of a heating plate and water chamber and a control setting which changes the temperature of the heater plate to raise or lower the humidity output from the chamber. These conventional humidifiers are limited in the level of humidity that can be delivered to the patient due to the ambient room temperature. Cool room temperatures can affect the delivery of humidity to the patient by cooling the temperature of the air travelling within the delivery tube, thereby reducing the maximum level of moisture the air can hold. The result is an accumulation of water in the breathing tube, or condensation, and consequentially, a level of humidity delivered to the patient's mask that is lower than desired. During the winter months, many patients who require a heated humidifier to counter nasal/oral or pharyngeal problems complain of condensation forming in the tube of the CPAP device – a problem that has so far not been investigated systematically. It is conceivable that the condensation reduces effective CPAP pressure due to the reduction of the CPAP delivery tube's effective lumen (10).

A new CPAP device (ThermoSmart®, Fisher & Paykel Healthcare, Auckland, New Zealand) incorporating new controlled heated breathing tube humidifier technology comprises of an integrated humidifier consisting of a heater plate and water chamber in addition to a heated breathing tube. The internal algorithm of the humidifier takes into consideration a number of inputs such as set pressure, ambient temperature and flow, and using these inputs adjusts the power to the heated breathing tube in order to maintain the individually adjustable heat and humidity all the way from the chamber output to the patient's mask.

The aim of this study was to compare the effectiveness of CPAP with conventional heated humidification with that of a controlled heated breathing tube humidifier at a cool ambient temperature of below 20 ºC.

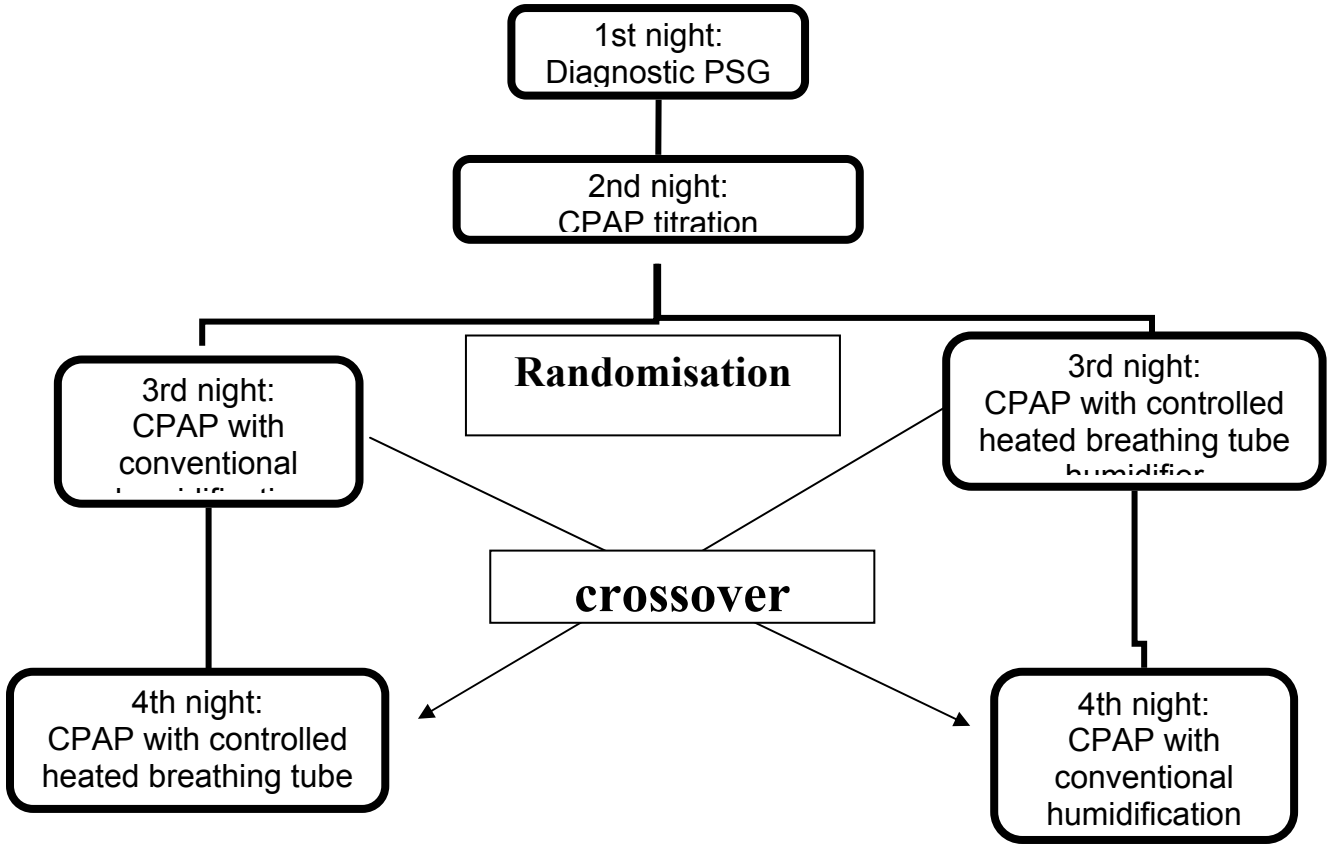
In addition to sleep quality, the incidence and amount of condensation forming in the system overnight were measured during polysomnography (PSG).

Method:

During the winter season from January to March 2005, all patients referred to the sleep laboratory with suspected OSAS were asked to fill in a questionnaire about their usual sleeping habits. Patients who preferred a bedroom temperature of less than 20 ºC or who habitually slept with a window open were invited to participate in the study. The study was approved by the internal review board of the clinic. Patients were fully informed about the study aims and the need to give their written consent, and 19 patients (14 males, 5 females), mean age 55 (+/- 10.4) years, mean BMI 33 kg/m² (+/- 6.3) agreed to be enrolled. All patients underwent PSG. Patients were investigated during the winter months, and only on days with an outside temperature of less than 15 ºC, so that unheated rooms had a temperature of less than 18 ºC. One inclusion criterion was an Apnea Hypopnea Index (AHI) of more than 20/h. Exclusion criteria were: more than 5 central apnea episodes per hour of sleep, an acute infection, decompensated cardiac insufficiency (NYHA level 3 or 4), acute pulmonary embolism, an acute coronary syndrome and severe malignant illness. Patients with signs of respiratory insufficiency were also excluded.

Study design: The degree of daytime sleepiness was established by means of the Epworth Sleepiness Scale (ESS) and a continuous attention test. All patients underwent a standardized CPAP training programme comprising of group session instruction and practical CPAP training of at least 4 hours per day at a pressure of 5 cm H_2O. Nasal and full face masks from different manufacturers were fitted with extreme care. On the night following diagnostic PSG, CPAP titration was performed with CPAP pressure increased from 6 cm H_2O to up to 12 cm H_2O in increments of 1 cm H_2O. The lowest CPAP pressure, at which AHI was < 5/h, snoring was eliminated and respiratory arousals were normalized, was taken to be the effective therapy pressure. (For flow chart study design see **figure 1**.)

Figure 1: Flow chart study protocol



On the following 2 nights in the sleep laboratory, the patients underwent treatment with the SleepStyle™ 600 CPAP device with ThermoSmart® (HC 602 – software version 1.04 Fisher & Paykel Healthcare) with heated breathing tube on setting 7, heater plate on setting 3 (recommended default settings by manufacturer) in treatment arm 1, and the SleepStyle™ 600 CPAP device with ThermoSmart® Humidification switched off but with an external conventional humidifier attached to the CPAP (HC100, Fisher & Paykel Healthcare) with heater plate on setting 3 (commonly recommended default setting by manufacturer) in treatment arm 2, both at their respective titrated pressure, in randomized order. Standard PSGs were performed on both nights. Each morning, following the PSG, the patients were asked to complete a subjective questionnaire to record their sleep experience and side effects.

The delivery tube system connecting the device to the patient was set up in a defined manner for each of the condensation measurements. Three tubing systems were prepared for each patient. If the patient was disturbed and woken up by water in the tubing system, the entire tubing system was replaced. Before the start of treatment, and in the morning after completion of the measurements, all breathing tubes were weighed and the differences in weight recorded. The water in the humidifier was also weighed immediately before treatment, and again in the morning.

All measurements were made during the winter months from January to April. The room in the sleep laboratory was not heated, and ventilation was achieved by opening the window to simulate the home environment. For the measured data to be included in the study, the room temperature had to be less than 18 ºC. The room temperature was measured electronically and the signal fed into the PSG recordings.

Polysomnography: Respiratory effort was measured by recording the patients' abdominal and thoracic movements by means of induction plethysmography. In addition, snoring sounds were recorded by means of a laryngeal microphone (Alice®

Respironics, USA) and oxygen saturation by means of a pulsoximeter (Nonin™, USA). In diagnostic polysomnography, respiratory flow was measured by nasal prongs and a flow-pressure monitor (Heinen und Lowenstein, Germany). During CPAP therapy, a pressure signal from the mask was recorded and fed into the PSG. The following additional parameters were recorded: electroencephalogram C4A1 or C3A2, submental and pretibial electromyogram, and electrocardiogram. The PSG recordings were evaluated by an experienced physician. The sleep stages and arousals were categorized in accordance with the Rechtschaffen and Kales criteria (11) and the recommendations of the American Sleep Disorders Association (12). Arousals were classified as respiratory if they occurred at the beginning of, or within 2 secs of an apnea or hypopnea. If the flow signal was reduced by more than 50% vis-à-vis the initial signal, for more than 10 secs, the episode was classified as hypopnea; if the amplitude of the flow signal was less than 20% of the initial value, the episode was classified as apnea. PSG was carried out using the Alice® system (Respironics, USA).

Questionnaire: The patients' subjective experiences and side effects with each humidification treatment arm were recorded in the morning after the treatment nights using a questionnaire. The questionnaire was developed internally and used in a different study (13). The questionnaire consisted of 13 items, each scored on a 5-point Likert scale ranging from 0 = very good to 5 = very poor.

Sleepiness: The subjective sleepiness was evaluated by using the Epworth sleepiness scale.

Statistics: The Wilcoxon test was used to identify possible significant differences between PSG results of the different study groups, condensation levels (data from the sleep laboratory), subjective side effects (results of the questionnaire after the first and second night and after the home treatment phase), and compliance data (home treatment).

Power analysis: Based on previous experience of patients and examination results, a reduction of sleep quality was expected when condensation formed in the tube. As a consequence, the parameter wake time after sleep onset (WASO) was chosen as the primary parameter indicative of sleep quality. A difference of 20 min of the time after

sleep onset (WASO) was decided to be clinically relevant. Based on the results of the previous examination, a standard deviation of 20 min was expected. This is why in a one-sided test the study group comprises 17 patients. $P<0.05$ was regarded as being significant.

Randomization: The study was randomized via blinded envelope prior to the beginning of the study.

Results:

After undergoing history taking, a physical examination and diagnostic PSG, 19 patients gave their written consent to participate in the study. Their median age was 55 (SD +/- 10.4) years, median BMI 33 (SD +/- 6.3) kg/m^2, and median AHI 53 (SD+/- 27.6), minimal oxygen saturation 76% (SD +/-12.4) and median ESS was 11 (SD +/- 5.0). According to the randomization list, 10 patients were treated with the conventional humidification first; the other 9 with the controlled heated breathing tube humidifier.

Room temperature: The mean nocturnal room temperature, monitored electronically, was 14.2 ºC (SD +/- 1.8) when the conventional humidification was used and 13.8 ºC (SD +/- 1.8) in the nights when the controlled heated breathing tube humidification technology was applied. The difference was not significant. The individual data of room temperature, in each night are shown in **table 1**.

Table 1:
Condensate in the breathing system, mean room temperature and absolute humidification. Data during the night using the conventional humidifier and the controlled heated breathing tube humidifier.

Patient no.	Pressure [cm H_2O]	Mean room temperature [°C]		Water in mask/tube [ml]		Absolute humidification* [ml]	
		Conventional humidifier	Controlled heated breathing tube humidifier	Conventional humidifier	Controlled heated breathing tube humidifier	Conventional humidifier	Controlled heated breathing tube humidifier
1	7	17.3	11.9	34	0	145	229
2	8	15.6	14.0	34	2	131	136
3	8	14.6	11.6	16	0	130	143
4	12	13.6	14.0	63	2	222	158
5	9	10.8	13.6	29	2	143	92
6	7	15.3	13.6	54	1	76	119
7	7	12.6	12.9	36	5	114	154
8	10	16.2	16.6	26	2	151	149
9	10	14.6	16.0	40	2	145	229
10	7	11.7	11.1	69	2	103	138
11	8	11.0	10.9	27	0	120	137
12	7	15.4	12.2	13	2	178	170
13	7	13.2	14.7	49	2	123	134
14	7	14.1	14.2	22	3	153	85
15	7	13.0	12.0	37	4	113	140
16	7	16.3	15.5	35	1	142	116
17	9	15.1	15.0	7	2	159	203
18	9	13.7	16.1	33	3	125	200
19	7	15.3	15.7	46	2	116	158
mean	**8.1**	**14.2**	**13.8**	**35.3**	**1.9**	**136.3**	**152.1**
±SD	**1.4**	**1.8**	**1.8**	**16.0**	**1.3**	**30.9**	**40.0**
p		**0.52**		**0.0001**		**0.12**	

Absolute humidification* = difference of water in the heating chamber between evening and morning
minus water in the mask/tube system

The ambient relative humidity was not measured. However air conditioning and central heating were switched off. Temperature and ambient relative humidity were adjusted by means of natural ventilation.

Delivery system: An average of 2.4 (SD +/- 0.8) mask/tube systems were used during treatment with conventional humidification, while treatment with controlled heated breathing tube humidification technology required only 1.1 mask/tube systems (SD +/- 0.2). The difference was statistically significant (p=0.0003).

Condensation: Measurement of the weight of the delivery systems prior to, and on the morning after, therapy, reflecting the amount of condensation formed in the tubing, revealed an average volume for all 19 patients of 35.3 ml (SD +/- 16.0) under treatment with conventional humidification, and 1.9 ml (SD +/- 1.3) with controlled heated breathing tube humidification technology. The difference between the two therapy modes was significant (p=0.001). The individual measurements of condensation in the tubing as well as the difference between the humidifier's quantity of water for the evening and following morning can be seen in **table 1**.

CPAP pressure: The arithmetic mean of the pressure measured at the mask with heated humidification was 0.3 cm H_2O (SD ± 0.1) lower than the set CPAP pressure. The mean with the heated humidification controlled by the heated breathing was 0.3 cm H_2O lower at the mask than the set CPAP pressure.

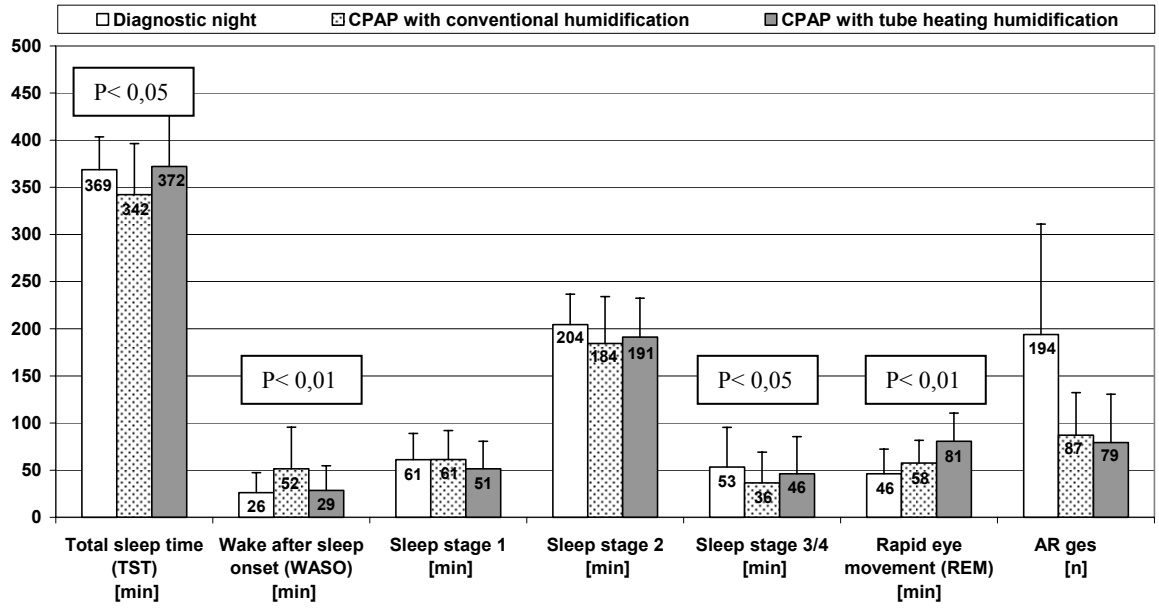
The difference between both forms of therapy was not significant.

The PSG data, diagnostic and under respiratory humidification treatment, with conventional humidification and controlled heated breathing tube humidification technology are presented in **table 2 and figure 2**.

Table 2: PSG data

	Diagnostic night			CPAP with conventional humidification			CPAP with tube heating humidification			statistical data: comparison of both treatments
	n	**mean**	SD	n	**mean**	SD	n	**mean**	SD	
Sleep Eff [%]	19	**89**	7	19	**80**	9	19	**85**	7	**0,0269**
WASO [% SPT]	19	**7**	5	19	**13**	10	19	**7**	6	**0,0079**
S1 [%]	19	**17**	7	19	**19**	10	19	**14**	8	**0,0050**
S2 [%]	19	**56**	9	19	**53**	10	19	**51**	9	NS
S3/4 [%]	19	**14**	11	19	**11**	9	19	**13**	11	NS
REM [%]	19	**12**	7	19	**17**	6	19	**21**	6	**0,0141**
AR INDEX [n/h TST]	19	**32**	21	19	**15**	8	19	**13**	9	NS
central Apnea [n]	19	**6**	14	19	**4**	8	19	**4**	7	NS
obstructive Apnea [n]	19	**132**	125	19	**0**	0	19	**2**	5	NS
mixed Apnea [n]	19	**24**	61	19	**0**	1	19	**3**	10	NS
Hypopnea [n]	19	**162**	94	19	**31**	19	19	**39**	34	NS
total AHI	19	**53**	28	19	**6**	3	19	**8**	8	NS
SaO2 minimal [%]	19	**76**	12	19	**90**	3	19	**89**	3	NS

Figure 2: Comparison of the data of the diagnostic PSG with CPAP and conventional versus tube heating humidification



Heated conventional humidification was associated with significantly shorter TST and significantly reduced sleep efficiency, and a significantly higher proportion of light sleep S1; in addition, the proportions of slow wave and REM sleep were also significantly lower vis-à-vis controlled heated breathing tube humidification technology.

Side effects: The questionnaire data on the patients' side effects in the first two therapy nights are shown in **table 3**.

Table 3:

Questionaire:
Comparison of complaints after the first treatment night

	CPAP with conventional humidification			**CPAP with tube heating humidification**			**Statistical data: comparision of both treatments**
	n	**mean**	**SD**	**n**	**mean**	**SD**	
Question 01	19	**2,5**	1,4	19	**1,5**	1,0	**0,0288**
Question 02	19	**1,5**	1,1	19	**1,7**	1,2	NS
Question 03	19	**1,6**	0,8	19	**1,5**	0,8	NS
Question 04	19	**1,7**	0,9	19	**1,4**	0,7	NS
Question 05	19	**1,4**	0,6	19	**1,3**	0,7	NS
Question 06	19	**2,0**	1,6	19	**1,4**	1,5	NS
Question 07	19	**1,9**	1,7	19	**1,3**	1,6	NS
Question 08	19	**3,4**	1,4	19	**0,3**	0,5	**0,0001**
Question 09	19	**1,5**	1,8	19	**0,7**	0,8	**0,0414**
Question 10	19	**0,8**	1,1	19	**0,8**	1,4	NS
Question 11	19	**0,7**	1,0	19	**0,5**	0,8	NS
Question 12	19	**1,0**	1,1	19	**0,7**	1,1	NS
Question 13	19	**0,6**	0,8	19	**0,5**	0,8	NS
SumScore	19	**20,7**	6,9	19	**13,5**	7,5	**0,0069**

Question 01 How did you sleep last night?
Question 02 How sleepy did you feel today?
Question 03 How would you rate your physical performance today?

Question 04 How would you rate your ability to concentrate?
Question 05 How would you rate your mood today?
Question 06 How would you rate the tempreture of the air?
Question 07 How would you rate the humidity of the air?
Question 08 Were you bothered by pressure changes?
Question 09 Were you bothered by cold sensation on the face?

What side effects did you experience?

Question 10 Dryness of mouth?
Question 11 Eye watering?
Question 12 Sensation of cold on the face?
Question 13 Sensation of pressure in the chest?

Sleepiness: After 3 weeks of treatment, the median ESS was reduced from 10.8 to 6.4 (+/- 2.9) in the conventional humidification group and 6.2 (+/- 3.2) in the controlled heated breathing tube humidification technology group (difference not significant).

Discussion

The results of this study show that in a cool ambient temperature, conventional heated humidification is associated with a considerable amount of condensation in the CPAP mask and tubing system. This can be reliably avoided through the use of an auto-adjusted humidifier with a heated breathing tube. The difference between the two humidification modes with regard to sleep quality and subjective experience was significant. Controlled heated breathing tube humidification technology (ThermoSmart®) with a heated breathing tube significantly reduced light sleep (stage 1 sleep, S1) and time awake after sleep onset (WASO). Conversely, the time spent in deep sleep (sleep stages S3/4), REM sleep, and total sleep time (TST) were significantly increased with controlled heated breathing tube humidification technology. Subjective disturbances with controlled heated breathing tube humidification technology were less frequent.

CPAP therapy is the preferred treatment for obstructive sleep apnea syndrome. Unfortunately, however, it often leads to bothersome symptoms in the nose and throat (1, 2, 3). Experimental data (4, 5) have shown that if a mouth leak develops under nasal CPAP treatment, high unidirectional flow occurs in the nose, increasing both the blood supply to the nasal mucosa and nasal airway resistance. This can be avoided with heated humidification. Comparative studies have demonstrated that higher relative and absolute humidity levels are seen at the nose with heated vs. cold humidification, such that any increase in nasal resistance will be less (6, 7). Available data on the practical application of heated humidification differ. A prospective randomized study by Massie (8) involving only patients receiving CPAP therapy for the first time showed an improvement in CPAP compliance under heated humidification, which proved to be superior to cold humidification. Another study found that heated humidification improved compliance in patients who had bothersome nasopharyngeal symptoms under CPAP (9).

In contrast, other studies showed that neither the all-important initial acceptance of CPAP therapy nor the subjective side effects experienced in the first treatment night were improved by heated humidification (14, 15, 16, 17). Many questions about humidification treatment thus remain unanswered, e.g. the level of absolute humidity required for optimal treatment results is not clear, nor is the identification of patients that need humidifier-assisted treatment nor heated breathing tube humidification.

To our knowledge, no studies have thus far been carried out to investigate the impact of heated humidification on sleep quality in a cool ambient environment. Under simulated conditions, Bacon et al. (10) were able to show that condensation in the delivery tube caused the effective CPAP pressure in the mask to vary from 5.6 cm H_2O below the set pressure during the inspiration phase to 3.5 cm H_2O above it during the expiration phase. We found no pressure differences between the mask and the CPAP device. If a patient in our study was disturbed and woken up by the noise associated with condensation, the mask/tube system was replaced so that no pressure reduction could occur. It is therefore possible that if the CPAP set-up was left untouched despite a build-up of condensation, transient variations in mask pressure may have been present and observable on the PSG system. It must be mentioned however that the design of the study might have had an impact on the varying results regarding sleep stages and sleep quality as the change of tubing and mask could have caused a prolonged wake time. However, the change was only made when the patient woke due to water in the tubing. New masks and tubing were ready so that emptying the system would have taken more time than a complete change. Given that both set-ups consisted of a heater plate and water chamber with the only differing component in the treatment arms being the heated breathing tube and algorithm (with inputs from ambient temperature, flow and set pressure), it appears likely that the addition of the heated breathing tube and algorithm allows the prevention of condensation. Currently, we still do not know the optimal level of humidification needed to reduce the side effects of CPAP at the mucosa of the upper airways. For technical reasons, it was not possible to measure the level of humidity in the patients' upper airways. The fact that room temperature was not different in both groups and that a randomized crossover was given from night to night implies that room humidity and other ambient conditions were not different in both groups.

It is essential to note that these results apply only under the conditions as stated. All patients preferred a cool bedroom. These ambient conditions were controlled during measurements in the sleep laboratory. For this reason, our results are only valid for these conditions and results can not be generalized to all ambient temperature conditions. All patients underwent CPAP treatment for the first time, and nasopharyngeal symptoms were not a criterion for inclusion in the study. The humidifier setting was kept constant

during the night in the sleep lab, which is not representative of the home setting where patients might adjust their settings to prevent further condensation once experiencing a build-up of condensation for the first time. Consequentially, when doing so, a patient is sacrificing humidity output and the result of our study is unable to provide any information on what effect this might have on comfort. Further CPAP investigations should examine the question of whether compliance would improve in all patients undergoing such humidifier treatment, or only in patients with severe nasopharyngeal symptoms.

At the present time, there is no difference in cost between the controlled heated breathing tube humidifier investigated in this study and a conventional CPAP device on the German market. We consider the additional energy costs for heating the tube to be negligible. This means that economic considerations do not have to be taken into account in the selection of a CPAP device and form of humidification: medical arguments are the only factors to be taken into consideration.

We suggest that patients requiring heated humidification and desiring a cool bedroom temperature might benefit from the usage of the controlled heated breathing tube humidification technology.

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