## ORIGINAL

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## Water content of delivered gases during non-invasive ventilation in healthy subjects

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Abstract Introduction: No clear recommendation exists concerning humidification during non-invasive ventilation (NIV) and high flow CPAP, and few hygrometric data are available. Methods: We measured hygrometry during NIV delivered to healthy subjects with different humidification strategies: heated humidifier (HH), heat and moisture exchanger, (HME) or no humidification (NoH). For each strategy, a turbine and an ICU ventilator were used with different FiO<sub>2</sub> settings, with and without leaks. During CPAP, two different HH and NoH were tested. Inspired gases hygrometry was measured, and comfort was assessed. On a bench, we also assessed the impact of ambient air temperature, ventilator Humidification · Psychrometry temperature and minute ventilation on HH performances (with NIV settings). Results: During NIV, with

NoH, gas humidity was very low when an ICU ventilator was used  $(5 \text{ mgH}_2\text{O/l})$ , but equivalent to ambient air hygrometry with a turbine ventilator at minimal FiO<sub>2</sub> (13 mgH<sub>2</sub>O/l). HME and HH had comparable performances (25-30 mgH<sub>2</sub>O/l), but HME's effectiveness was reduced with leaks (15 mgH<sub>2</sub>O/l). HH performances were reduced by elevated ambient air and ventilator output temperatures. During CPAP, dry gases (5 mgH<sub>2</sub>O/l) were less tolerated than humidified gases. Gases humidified at 15 or  $30 \text{ mgH}_2\text{O/l}$  were equally tolerated. Conclusion: This study provides data on the level of humidity delivered with different humidification strategies during NIV and CPAP. HH and HME provide gas with the highest water content. Comfort data suggest that levels above 15 mgH<sub>2</sub>O/l are well tolerated. In favorable conditions, HH and HMEs are capable of providing such values, even in the presence of leaks.

Keywords Mechanical ventilation · Non-invasive ventilation · Heated humidifiers . Heat and moisture exchangers .

## Introduction

To date, there is no clear recommendation concerning the type or degree of humidification to be provided during non-invasive ventilation (NIV) or continuous positive airway pressure (CPAP) used for acute respiratory failure [1–3]. The last international consensus conference on NIV did not address this issue owing to a lack of data [1]. Hygrometric measurements are not available during NIV [4], and available data during CPAP concern mainly patients ventilated for obstructive sleep apnea [5, 6]. The use of dry gases during nasal CPAP in healthy subjects has been shown to induce a large increase in nasal resistances [7]. Also, it has been suggested that poor humidification may be associated with an increased risk of difficult endotracheal intubation in case of NIV failure [8].

The studies carried out in intubated patients with various systems of humidification are not transposable to NIV. Non-humidified inspired gases are very dry when an ICU ventilator is used, but upper airways are not bypassed during NIV, contrary to the intubated patient. Also, patients are frequently mouth breathers during NIV, and it was demonstrated that gas humidification is less effective in this situation in comparison with nasal breathing [9, 10]. In addition, ventilatory flows are higher during NIV than spontaneous breathing [11, 12]. Oral dryness appears as one of the most frequently reported complications during NIV [13], and a case of upper airway obstruction related to inadequate humidification of gases has been described during prolonged NIV [14]. Also, many patients concerned by NIV may have bronchial hyperresponsiveness [15, 16]. In addition, the impact of leaks on the performances of humidification systems during NIV is not known. Last, a strong influence of ventilator and ambient air temperature on the performance of heated wire heated humidifiers (HH) has been described during invasive ventilation [17], but has not been reported for NIV settings.

The purpose of this study was to measure the absolute humidity of inspired gases during NIV and CPAP delivered with different humidification strategies in three steps, using psychrometric measurements [14]. We first designed a bench study to assess the impact of external temperature on heated humidifiers (HH). Then two series of experiments were conducted in healthy subjects, concerning NIV and CPAP.

# Method (additional details are provided in an electronic supplement material)

The study was conducted in three phases: an in vitro bench evaluation of HH performances with NIV settings, and two sets of in vivo measurements in healthy subjects

during NIV and CPAP. The protocol was approved by the Ethics Committee of the Société de Réanimation de Langue Française.

Bench evaluation of HH performances with NIV settings

A bench evaluation of heated humidifiers set in NIV mode was conducted to assess the impact of temperature on HH performances. Briefly, we previously reported that, because of the regulation system of HH, the higher the temperature at the inlet of the HH was, the lower the water content of the gas delivered to the patient [17]. This assessment was repeated here with specific NIV settings on the HH as recommended by the manufacturers. Inspired gas hygrometry was measured with the ventilator and airway circuit connected to a test lung under the following conditions:

- Two ambient air temperatures were tested: normal, 22–24°C, and high, 28–30°C.
- Two ventilators delivering gas at two different temperatures were used: moderate (close to 30°C, Evita 4) and high output temperature (close to 40°C, T-Bird) [17]. Wall medical gases contain around 3–5 mgH<sub>2</sub>O/l (personal data).
- Two levels of minute ventilation: low (10 l/min) and high (21 l/min).
- The following heated wire heated humidifiers were tested: Aerodyne Ultratherm (Kendall), MR 730 (Fisher&Paykel) and MR 850 (Fisher&Paykel) with compensation algorithm activated. The compensation algorithm allows an automatic increase of the humidification chamber temperature when the heater plate does not deliver enough energy to humidify gases as calculated by the system. The following settings were used (humidity chamber temperature/Y-piece temperature): MR 730: 31/34°C, 34/34°C, MR 850 «NIV position» with compensation, Aerodyne 31/33°C, 33/33°C.
- Several other conditions were tested (no humidification, use of a long dry line).

Three psychrometric measurements were obtained for each condition at steady state after 3 h [18]. Room temperature was maintained constant.

In total, 28 conditions were tested, in addition to the measurements of ambient air (n = 45) and inspired gas without humidification (n = 24).

Healthy subjects ventilated during NIV

Twelve healthy subjects were ventilated with NIV using a bucco-nasal mask in the following conditions (Fig. 1):



- Three types of humidifications: heated humidifier (HH) set on "NIV" position (MR 850 used without compensation system), heat and moisture exchanger (Hygrobac<sup>®</sup>, Tyco Healthcare) (HME) or no humidification (NoH).
- Three types of ventilation using an intensive care unit (ICU) ventilator or a turbine ventilator at two FiO<sub>2</sub><sup>2</sup>
  - an ICU ventilator (PB 840, Tyco Healthcare) with FiO<sub>2</sub> set at 21% using wall dry medical gases
  - a turbine ventilator (T-Bird) with  $FiO_2$  set at 21%, i.e., with gas taken from ambient air (12–15 mgH<sub>2</sub>O/l)
  - a turbine ventilator (T-Bird) set at 50% of FiO<sub>2</sub>, i.e., with a mixture of medical gases and ambient air (8–10 mgH<sub>2</sub>O/l).

Each subject took part in the study over 3 different days, 1 day for each ventilator. The order of the studied ventilators and of the type of humidification were randomized.

- Each experiment was conducted with no or minimal leakage and in the presence of 50% of leaks.
- Last, experiments were repeated during normal minute ventilation and a period of 5 min of hyperventilation around 20 l/min.

For each period, hygrometric measurements of inspired gases were performed after 15 min of ventilation using the psychrometric method [18].

In total, 21 conditions were tested.

Healthy subjects during CPAP

Six healthy subjects were given high flow CPAP (90– 150 l/min) (Vital Signs) with different humidification strategies. Each period lasted 10 min with a "wash-out" period of 5 min between the different ventilation periods. Three humidification strategies were assessed: no humidification (NoH), HH with HC 100, a HH without heated wire, proposed for home ventilation set at maximal intensity and HH with MR 850 set on "NIV" position with activated compensation system. The subjects were blinded for the humidification device used. At the end of each period, hygrometric measurements of inspired gases were performed, and comfort related to mucosal dryness was assessed on a 0 (extreme mucosal dryness) to 10 (no mucosal dryness) visual scale. Comfort was assessed before humidity measurements.

## Statistics

Results are expressed as mean  $\pm$  standard deviation. Analysis of variance was first performed with Friedman test, and two-by-two comparisons were obtained by Wilcoxon signed ranks test. A value of P < 0.05 was considered significant.

## Results

Bench evaluation of HH performances with NIV settings

When using a turbine ventilator set at 21% of FiO<sub>2</sub> without humidification, hygrometry of inspired gases was

equivalent to ambient air hygrometry, but was very low when using an ICU or a turbine ventilator set at 100% of FiO<sub>2</sub> (wall medical gases only). As previously described for settings used during invasive mechanical ventilation [17], performances of heated wire HH were strongly influenced by ambient air temperature, output ventilator temperature and minute ventilation, as shown in Table 1. High ambient air and high ventilation output temperatures strongly reduced HH performances. In the worst conditions (high temperature and high output ventilator temperature), HH did not increase water content in comparison with the humidity delivered without a humidification system with a turbine ventilator. Aerodyne had slightly better performances than MR 730 in all conditions (P < 0.001). MR 850 with compensation activated had the best performances when compared with Aerodyne and MR 730 with recommended settings (31°C at the humidity chamber) (P < 0.001) (Table 1 and Fig. E2).

Healthy subjects during NIV

Twelve different healthy subjects took part in each set of measurements. All subjects completed the whole study. Average temperature and hygrometry of ambient air were identical for the various ventilators under test. Average temperature in ambient air was  $23.6 \pm 1.2^{\circ}$ C, relative humidity was  $54.8 \pm 8.6\%$ , and absolute humidity was  $11.7 \pm 2.2 \text{ mgH}_2$ O/l.

With HH, the mean absolute humidity of delivered gas was of  $29.4 \pm 1.9 \text{ mgH}_2\text{O/l}$  without leaks and  $27.7 \pm 2.7 \text{ mgH}_2\text{O/l}$  with leaks (P = 0.02). Mean temperature of inspired gases was  $30.6 \pm 0.8^{\circ}\text{C}$  with no influence of leaks. The ventilator used had little influence on performances (Figs. 2, 3). Without leaks, the gas delivered with HME had a mean level of absolute humidity of  $28.3 \pm 2.1 \text{ mgH}_2\text{O/l}$ , which was equivalent to HH, whatever the ventilator used (Figs. 2, 3). Mean temperature of inspired gases was  $29.5 \pm 1.3^{\circ}\text{C}$  without

#### Table 1 Bench study

		Normal ambient temperature (22–24°C) $11.7 \pm 2.0$ $11.4 \pm 3.2$		High ambient temperature (28–30°C) $13.7 \pm 2.2$ $13.6 \pm 2.5$		
Ambient air $(n = 45)$ No humidification $(n = 24)$						
T-Bird 21%						
T-Bird 100%		$3.5 \pm 1.4$		$3.5 \pm 0.7$		
EVITA 4		$3.7 \pm 1.8$		$3.2 \pm 0.1$		
Heated humidifiers	Settings	10 l/min	20 l/min	10 l/min	20 l/min	Absolute Humidity theoretically delivered
T-BIRD 21%FiO <sub>2</sub>						
Aerodyne	31/33	$24.8 \pm 1.2$	$20.2 \pm 1.6$	$18.3 \pm 0.3$	$18.0 \pm 1.6$	32.1
	34/34	$30.2 \pm 2.7$	$24.9 \pm 1.6$	$23.5 \pm 0.2$	$21.2 \pm 0.4$	37.7
MR 730	31/34	$23.8 \pm 1.6$	$20.2 \pm 3.8$	$16.5 \pm 1.2$	$13.8 \pm 1.0$	32.1
	34/34	$27.7 \pm 1.5$	$26.0 \pm 1.1$	$23.7 \pm 2.0$	$19.4 \pm 3.8$	37.7
T-BIRD 100%FiO <sub>2</sub>						
Aerodyne	31/33	$20.5 \pm 0.7$	$15.5 \pm 0.6$	$13.9 \pm 2.9$	$11.8 \pm 0.3$	32.1
	34/34	$27.5 \pm 2.9$	$20.3 \pm 1.0$	$17.2 \pm 0.6$	$14.4 \pm 0.2$	37.7
MR 730	31/34	$17.2 \pm 1.7$	$13.6 \pm 0.2$	$11.8 \pm 0.6$	$8.7 \pm 0.3$	32.1
	34/34	$23.4 \pm 0.3$	$23.0 \pm 2.9$	$19.8 \pm 6.5$	$13.7 \pm 2.7$	37.7
MR 850	"NIV"	$28.1 \pm 0.7$	$23.5 \pm 3.4$	$20.2 \pm 0.3$	$16.0 \pm 0.8$	32.1
EVITA 4 100%FiO <sub>2</sub>						
Aerodyne	31/33	$25.9 \pm 2.0$	$22.4 \pm 3.2$	$17.8 \pm 1.0$	$13.4 \pm 1.0$	32.1
	34/34	$30.1 \pm 2.7$	$28.3 \pm 0.4$	$22.6 \pm 2.8$	$17.7 \pm 1.4$	37.7
MR 730	31/34	$22.4 \pm 4.4$	$19.8 \pm 3.5$	$13.0 \pm 0.9$	$9.5 \pm 0.7$	32.1
	34/34	$28.7 \pm 1.1$	$22.3 \pm 3.2$	$18.0 \pm 1.5$	$14.5 \pm 0.4$	37.7
MR 850	"NIV"	$24.1 \pm 1.9$	$24.3 \pm 0.4$	$20.8 \pm 1.4$	$19.1 \pm 0.7$	32.1

Absolute humidity (in  $mgH_2O/l$ ) of ambient air and of delivered inspired gases without humidification and with different heated humidifiers at different settings. MR850 was evaluated in «NIV» position with automated compensation activated (software 560). In the "settings" column, temperature at humidification chamber and temperature at Y-piece are given: 31/34 is usually recommended for NIV, corresponding to  $31^{\circ}C$  at the chamber and  $34^{\circ}C$  at the Ypiece. Three hygrometric measurements were performed for each condition. In addition, 45 measurement for ambient air and 24 for inspired gas with no humidification were performed. Absolute humidity theoretically delivered corresponds to the humidity of a satured gas at the temperature of the set humidity chamber (31°C with 100% of relative humidity = 32.1 mgH<sub>2</sub>O/l and 34°C with 100% of relative humidity = 37.7 mgH<sub>2</sub>O/l). The ventilators used have a low ventilator output temperature (close to 30°C, Evita 4; Dräger Medical) or high ventilator output temperature (close to 40°C, T-Bird) [17] 39.7% of their effectiveness, with a drop of the mean absolute humidity to  $17.1 \pm 2.8 \text{ mgH}_2\text{O/l}$  (P < 0.01) HME's performances in case of leaks.

When no humidification was used, the ventilator significantly influenced the inspired gas humidity,

leaks and 25.6  $\pm$  1.3°C in the presence of leaks with varying from 5.5  $\pm$  1.1 (with ICU ventilator) to 13.0  $\pm$ HME (P < 0.001). In the presence of leaks, HME lost 1.6 mgH<sub>2</sub>O/l (with a turbine ventilator at 21% of FiO<sub>2</sub>) (P < 0.001). Mean temperature of inspired gases varied from  $25.2 \pm 1.9$  with ICU ventilators to  $25.5 \pm 2.1$  °C (Figs. 2, 3). The ventilator had also little impact on with a turbine ventilator. With the ICU ventilator, leaks had only little influence on these performances  $(5.5 \pm 1.1 \text{ with no leaks vs. } 4.6 \pm 0.9 \text{ mgH}_2\text{O/l in case}$ of leaks) (Figs. 2, 3). With a turbine at 21% of FiO<sub>2</sub>, the

Fig. 2 Healthy subjects during NIV. Absolute humidity (in mgH<sub>2</sub>O/l) of inspiratory gases during NIV according to the method of humidification, of the type of driving gas [dry (PB840), ambient air (T-Bird 21% of FiO<sub>2</sub>) or intermediate (T-Bird 50% of FiO<sub>2</sub>)] in presence or absence of leaks. Measurements were performed with the psychrometric method. Mean and standard deviations are displayed. HH heated humidifier, HME heat and moisture exchanger, NoH no humidification

Fig. 3 Healthy subjects during NIV. Loss of inspired gas absolute humidity due to leaks with the various methods of gases humidification during NIV.  $\Delta$  Absolute Humidity  $(mgH_2O/l) = Absolute$ Humidity without leaks -Absolute Humidity with leaks



mean absolute humidity of inspiratory gases was  $13.0\pm1.6$  with no leaks and  $12.0\pm1.4$  mgH\_2O/l in case of leaks.

Hyperventilation did not modify the water content of inspired gases with the various strategies of humidification (see ESM, Table E1 and Fig. E1).

## Healthy subjects ventilated during CPAP

Six healthy subjects completed all the study periods. With  $(3.8 \pm 2.3)$  and higher when no humidification, inspired gases humidity was (P < 0.005), similar with HC1  $5.1 \pm 0.3 \text{ mgH}_2\text{O/I}$  with FiO<sub>2</sub> set at 50%. With the HC  $6.1 \pm 2.2$  (P = 0.16) (Fig. 4).

100 set at the maximal intensity position, inspired gases humidity was  $15.1 \pm 1.6 \text{ mgH}_2\text{O/l}$ , and with the MR 850 set on the NIV position, inspired gases humidity was  $27.7 \pm 2.7 \text{ mgH}_2\text{O/l}$  with FiO<sub>2</sub> set at 50%. Hygrometric results are displayed in Fig. 4. The FiO<sub>2</sub> level had only minor influence on humidity results or comfort assessment (Fig. 4). The CPAP level (5 or 7.5 cmH<sub>2</sub>O) did not influence humidity results or comfort assessment (data not shown). Comfort assessed on a 0–10 visual scale was significantly lower when no humidification was used ( $3.8 \pm 2.3$ ) and higher when a humidifier was used (P < 0.005), similar with HC100,  $6.5 \pm 2.1$  and MR850,  $6.1 \pm 2.2$  (P = 0.16) (Fig. 4).



**Fig. 4** Healthy subjects during CPAP. Absolute humidity of inspired gases and comfort during high flow CPAP in different conditions: with no humidification (*white bars*), with the heated humidifier HC100 (*grey bars*) and with the heated humidifier MR850 (NIV position) (*black bars*) at two levels of FiO<sub>2</sub>: 21 and 50% for each condition. Mean and standard deviations are displayed

## Discussion

This study is the first to measure hygrometry of delivered gases during NIV with different humidification systems and to assess the influence of leaks, minute ventilation, settings, and ventilator used. The humidification strategies strongly influenced the water content of delivered gases. which ranged from less than  $5 \text{ mgH}_2\text{O/l}$  to nearly 30 mgH<sub>2</sub>O/l (Fig. 2). HMEs lost almost 40% of their humidification efficiency in the presence of leaks (Figs. 2, 3). This study demonstrated good performances of heated wire HH set with NIV parameters when used in favorable conditions, but the bench evaluation demonstrated lower performances in case of high ambient air and output ventilator temperature (Table 1). During CPAP, humidity was low (5 mgH<sub>2</sub>O/l) when no humidification was used and reached  $15-30 \text{ mgH}_2\text{O/l}$  with a non-heated wire-HH used for home ventilation and a recent heated-wire HH, respectively (Fig. 3). Interestingly, gases humidified at either 15 or 30 mgH<sub>2</sub>O/l seemed to be equally tolerated, whereas gases delivered at 5 mgH<sub>2</sub>O/l induced severe discomfort because of mouth dryness (Fig. 4).

## Heated humidifier performances

In this study, in favorable conditions with low ambient air temperature (during NIV with healthy subjects) the heated wire HH (MR 850, Fisher & Paykel) remained efficient whatever the type of ventilator used, the level of leaks and the level of minute ventilation (Fig. 2). With the MR 850 HH, inspiratory gases water content went from 28 to almost 30 mgH<sub>2</sub>O/l (Fig. 2). By contrast, performances were much lower in conditions of high ambient air and high output ventilator temperature (bench study) with several tested heated wire HHs (Table 1). The impact of these factors on heated wire HH had been previously demonstrated with settings adapted to invasively ventilated patients [17]. It was demonstrated that HH performances were inversely correlated with the inlet humidification chamber temperature. The situation with inlet chamber temperature above the set chamber temperature (leading to a reduction of heater plate heating) is frequent during NIV for several reasons. First, chamber temperature is set relatively low during NIV (usually 31°C instead of 37°C for intubated patients) (Fig. E2). Second, turbine ventilators are frequently used for NIV delivery, and it has been shown that these ventilators deliver higher ventilator output temperatures [17]. In the literature, hygrometric evaluation of HHs during NIV exists only for devices without heated wires [6, 19]. In one study, a HH without a heated wire, proposed for home ventilation, was tested [19]. Holland et al. [19] assessed the HC 100 humidifier in vitro and evaluated the impact of ventilatory settings on humidification, and of humidification on delivered pressure in an in vitro study

reproducing NIV conditions with leaks. In these experimental conditions HC 100 delivered gas with absolute humidity from 21.3 to 23.6 mgH<sub>2</sub>O/l. Wiest et al. [6] measured gas humidity delivered by two HHs used during CPAP for obstructive sleep apnea, including the HC 100. They found that humidity of inspired gases went from 26.2 to 26.5 mgH<sub>2</sub>O/l with this HH at different CPAP levels. By contrast, in our study (healthy subjects ventilated during high flow CPAP), the HC 100 humidifier provided humidity of only  $15.1 \pm 1.6 \text{ mgH}_2\text{O/l}$ . In the studies of Wiest and Holland [6, 19], turbine ventilators were used, while in our study a high flow CPAP (90 to 150 l/min) was used, which probably explains the hygrometric differences.

Heat and moisture exchanger performances

In this study, the HMEs were as effective as the HHs in the absence of leaks. In the presence of leaks, however, which is the usual situation during NIV, HMEs lost 39.7% of their "water reserve" and a great part of their effectiveness (Figs. 2, 3). This behavior has never been demonstrated during NIV, but had previously been described by Tilling and Hayes with an in vitro model of uncuffed tracheal tube, as used in pediatric patients [20]. In Tilling and Hayes' study, the decrease in the humidity output was related to the tidal volume used and to the level of leaks. The experimental setting used in the present study to promote leaks (tube placed between the mask and subjects skin) may have enhanced expiratory leaks. We used a level of leaks of 50% in our study. The mean level of leaks in real life in not known. In physiological studies conducted in patients on NIV for acute respiratory failure, the leaks varied from 27 to 60%, but in most situations stand around 30% [11, 21]. In a less controlled, real-life setting, the mean level of leaks may be higher, around the level chosen in this study. Also, it must be kept in mind that the HME used in this study performs very well [22].

Hygrometry when no humidification is used

With no humidification and the use of a turbine ventilator at 21% of FiO<sub>2</sub>, the gas delivered had a water content of 13.0 ± 1.6 mgH<sub>2</sub>O/l and was little influenced by leaks (Figs. 2, 3). In this situation, the humidity level depends probably upon ambient air humidity. In our study, the ambient air relative humidity was  $54.8 \pm 8.6\%$ , and the absolute humidity was  $11.7 \pm 2.2 \text{ mgH}_2\text{O/l}$ , while air conditioning was not used. In the study by Holland et al. [19], the absolute humidity delivered via a turbine ventilator (BiPAP<sup>®</sup>, Respironics) in the absence of humidification was only  $4.8-5.3 \text{ mgH}_2\text{O/l}$ . This difference from our results is probably related to air-conditioning used in their study. In a study by Wiest et al. [5] conducted in patients during CPAP, the mean absolute humidity of inspiratory gases with no humidification system was 9.9 mgH<sub>2</sub>O/l. The humidity range of the room varied from 5.3 to 16.4 mgH<sub>2</sub>O/l, but it was not specified if air conditioning was used.

In previous studies, only turbine ventilators were tested [5, 19]. However, ICU ventilators are frequently used to deliver NIV. In a recent survey on NIV use conducted in French ICUs, an ICU ventilator was used in 79% of the cases, a turbine ventilator in 12% of the cases and a home device in 5% of the cases [23]. In the present study, with no humidification and an ICU ventilator, the delivered gases were as low as 5 mgH<sub>2</sub>O/l (Fig. 2), which is potentially deleterious, leading to upper airway mucosal dryness, discomfort and a potential risk of increasing bronchial hyperresponsiveness [24]. The absence of humidification during NIV may increase the frequency of difficult intubations in case of NIV failure as recently suggested [8].

## Contribution of this study

These data may be helpful to draw guidelines for humidification during NIV and CPAP in a field where very few data are available. Some insight to design recommendations stem from data on chronically ventilated patients. Among patients treated with CPAP at home, signs of upper airway dryness are reported in up to twothirds of the patients [25–28]. In a study comparing CPAP used with a HH or without humidification, these symptoms were less frequent when a humidification device was used [29]. It was also shown that tolerance and compliance to treatment were better when gases delivered during the CPAP were humidified [25, 27, 29, 30]. In a study by Massie [30], also conducted in patients on CPAP therapy, HHs (HC 100<sup>®</sup>, Fisher & Paykel) or cold passover humidifiers (Oasis<sup>®</sup>, Respironics) were assessed in a cross-over design, and comparisons were also made with the pre-study period, while no humidification was used. With HHs as well as with non-heated humidification, nasal and oral dryness symptoms were reduced, and compliance to CPAP was increased in comparison with the pre-study period. However, most patients preferred heated humidification [30]. The performances of these two devices were evaluated in another study in healthy subjects on CPAP [6]. The cold passover humidifier Oasis<sup>®</sup> delivered inspired gases with a humidity of 16.7 mgH<sub>2</sub>O/l, and the HH HC 100<sup>®</sup> delivered 26.2 mgH<sub>2</sub>O/l [6].

Based on these studies, gases with water content below 10 mgH<sub>2</sub>O/l frequently lead to symptoms of oral dryness and discomfort. As shown in our study, absence of humidification with an ICU ventilator or a turbine

ventilator using FiO<sub>2</sub> higher than 50% both result in less than 10 mgH<sub>2</sub>O/l of water content. Mucosal dryness is reduced with systems providing gases with humidity above 15 mgH<sub>2</sub>O/l [29, 30]. In the absence of recommendations on the optimal level of humidity during NIV and given the specific conditions of this ventilation (high flows, frequent oral breathing, risk of bronchial hyper-responsiveness), it appears reasonable to avoid delivering dry gases containing less than 10 mgH<sub>2</sub>O/l. This can be achieved with both HH and the HME used in our study, even in case of leaks (Fig. 2). Tolerance of inspired gases in the grey zone between 10 and 15 mgH<sub>2</sub>O/l remains hazy. Also, the optimal level to avoid bronchial hyperresponsiveness or to reduce the risk of atelectasis is not known. Humidity provided by a turbine ventilator without humidification and low FiO<sub>2</sub> depends on room air humidification and conditioning.

The hygrometric data presented here must be balanced with other comparisons between HH and HME and the respective advantages and drawbacks of each systems. During NIV, patients may have higher work of breathing and minute ventilation, and a reduced  $CO_2$  elimination with HME in comparison with HH [11, 31], but a recent randomized controlled trial comparing HH and HME showed no difference in patient's outcome [32].

The study was not conducted in patients, and study periods were short in comparison with some real-life settings. NIV sessions last a minimum of 1 h and may be prolonged over several days. Comfort related to gas humidification should also be evaluated in patients during NIV and CPAP with acute respiratory failure for longer periods.

## Conclusions

This study provides new data on the level of humidity delivered to patients with different humidification strategies during NIV and CPAP. We found that HH and HME allow the delivery of gases with the highest water content (25-30 mgH<sub>2</sub>O/l), but HME's efficiency was strongly reduced in the presence of leaks (15 mgH<sub>2</sub>O/l). Heated wire HH performances were strongly reduced with high ambient air and ventilator output temperatures, as previously described with settings for intubated patients [17]. Comfort data suggest that the minimal humidity of inspired gases during NIV should be at or above 15 mgH<sub>2</sub>O/l (with temperatures ranging from 25 to 30°C). HH in favorable conditions and HME even in case of leaks can provide this humidity. These results may be useful to better choose the humidification device during NIV and CPAP and to develop recommendations.

## References

- Evans TW (2001) International Consensus Conferences in Intensive Care Medicine: non-invasive positive pressure ventilation in acute respiratory failure. Organised jointly by the American Thoracic Society, the European Respiratory Society, the European Society of Intensive Care Medicine, and the Societe de Reanimation de Langue Francaise, and approved by the ATS Board of Directors, December 2000. Int Care Med 27:166–178
- Mehta S, Hill NS (2001) Noninvasive ventilation. Am J Respir Crit Care Med 163:540–577
- Ricard JD (2006) Humidification. In: Tobin M (ed) Mechanical ventilation. McGraw-Hill, New York, pp 1109–1120
- Branson RD (2006) Humidification of respired gases during mechanical ventilation: mechanical considerations. Respir Care Clin North Am 12:253–261
- Wiest GH, Foerst J, Fuchs FS, Schmelzer AH, Hahn EG, Ficker JH (2001) In vivo efficacy of two heated humidifiers used during CPAP-therapy for obstructive sleep apnea under various environmental conditions. Sleep 24:435–440
- Wiest GH, Fuchs FS, Brueckl WM, Nusko G, Harsch IA, Hahn EG, Ficker JH (2000) In vivo efficacy of heated and non-heated humidifiers during nasal continuous positive airway pressure (nCPAP)-therapy for obstructive sleep apnoea. Respir Med 94:364–368
- Richards GN, Cistulli PA, Ungar RG, Berthon-Jones M, Sullivan CE (1996) Mouth leak with nasal continuous positive airway pressure increases nasal airway resistance. Am J Respir Crit Care Med 154:182–186
- Esquinas A, Nava S, Scala R, Carrillo A, Díaz G, Artacho R, Pérez M, Zhang X, Povoa P, Vidal G, Chiumello D, Armando P, Suero C, Vassallo J, Meyanci Koksal G (2008) Humidification and difficult endotracheal intubation in failure of NIMV: preliminary results. Am J Respir Crit Care Med 177:A644
- 9. Primiano FP Jr, Montague FW Jr, Saidel GM (1984) Measurement system for respiratory water vapor and temperature dynamics. J Appl Physiol 56:1679–1685
- Sara C, Currie T (1965) Humidification by nebulization. Med J Aust 191:174–179
- Lellouche F, Maggiore SM, Deye N, Taille S, Pigeot J, Harf A, Brochard L (2002) Effect of the humidification device on the work of breathing during noninvasive ventilation. Int Care Med 28:1582–1589

- 12. L'Her E, Deye N, Lellouche F, Taille S, Demoule A, Fraticelli A, Mancebo J, Brochard L (2005) Physiologic effects of noninvasive ventilation during acute lung injury. Am J Respir Crit Care Med 172:1112–1118
- Hill NS (1997) Complications of noninvasive positive pressure ventilation. Respir Care 42:432–442
- Wood KE, Flaten AL, Backes WJ (2000) Inspissated secretions: a lifethreatening complication of prolonged noninvasive ventilation. Respir Care 45:491–493
- 15. Cabanes LR, Weber SN, Matran R, Regnard J, Richard MO, Degeorges ME, Lockhart A (1989) Bronchial hyperresponsiveness to methacholine in patients with impaired left ventricular function. N Engl J Med 320:1317–1322
- Hospers JJ, Postma DS, Rijcken B, Weiss ST, Schouten JP (2000) Histamine airway hyper-responsiveness and mortality from chronic obstructive pulmonary disease: a cohort study. Lancet 356:1313–1317
- Lellouche L, Taillé S, Maggiore SM, Qader S, L'Her E, Deye N, Brochard L (2004) Influence of ambient air and ventilator output temperature on performances of heated-wire humidifiers. Am J Respir Crit Care Med 170:1073–1079
- Ricard JD, Le Miere E, Markowicz P, Lasry S, Saumon G, Djedaini K, Coste F, Dreyfuss D (2000) Efficiency and safety of mechanical ventilation with a heat and moisture exchanger changed only once a week. Am J Respir Crit Care Med 161:104–109
- Holland AE, Denehy L, Buchan CA, Wilson JW (2007) Efficacy of a heated passover humidifier during noninvasive ventilation: a bench study. Respir Care 52:38–44
- 20. Tilling SE, Hayes B (1987) Heat and moisture exchangers in artificial ventilation: an experimental study of the effect of gas leakage. Br J Anaesth 59:1181–1188
- 21. Fraticelli A, Lellouche F, L'Her E, Taillé S, Mancebo J, Brochard L (2008) Comparison of different interfaces during NIV in patients with acute respiratory failure. Crit Care Med (in press)
- 22. Lellouche F, Taillé S, Lefrançois F, Deye N, Maggiore SM, Jouvet P, Ricard JD, Fumagalli B, Brochard L, Groupe de travail sur les Respirateurs de l'AP-HP (2009) Humidification performances of 48 passive airway humidifiers: comparison with manufacturers' data. Chest 135(2):276– 286

- Demoule A, Girou E, Richard JC, Taille S, Brochard L (2006) Increased use of noninvasive ventilation in French intensive care units. Int Care Med 32:1747–1755
- Cockcroft DW (2001) How best to measure airway responsiveness. Am J Respir Crit Care Med 163:1514–1515
- 25. Martins De Araujo MT, Vieira SB, Vasquez EC, Fleury B (2000) Heated humidification or face mask to prevent upper airway dryness during continuous positive airway pressure therapy. Chest 117:142–147
- 26. Pepin JL, Leger P, Veale D, Langevin B, Robert D, Levy P (1995) Side effects of nasal continuous positive airway pressure in sleep apnea syndrome: study of 193 patients in two French sleep centers. Chest 107:375–381
- Rakotonanahary D, Pelletier-Fleury N, Gagnadoux F, Fleury B (2001) Predictive factors for the need for additional humidification during nasal continuous positive airway pressure therapy. Chest 119:460–465
- Sanders MH, Gruendl CA, Rogers RM (1986) Patient compliance with nasal CPAP therapy for sleep apnea. Chest 90:330–333
- 29. Wiest GH, Lehnert G, Bruck WM, Meyer M, Hahn EG, Ficker JH (1999) A heated humidifier reduces upper airway dryness during continuous positive airway pressure therapy. Respir Med 93:21–26
- 30. Massie CA, Hart RW, Peralez K, Richards GN (1999) Effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure. Chest 116:403–408
- 31. Jaber S, Chanques G, Matecki S, Ramonatxo M, Souche B, Perrigault PF, Eledjam JJ (2002) Comparison of the effects of heat and moisture exchangers and heated humidifiers on ventilation and gas exchange during non-invasive ventilation. Int Care Med 28:1590–1594
- 32. Lellouche F, L'Her E, Abrouk F, Deye N, Rabbat A, Jaber S, Fartoukh M, Conti G, Cracco C, Ricard JD, Mal H, Mentec H, Loisel F, Lacherade JC, Rodriguez P, Brochard L (2006) Impact of the humidification device on intubation rate during NIV: results of a multicenter RCT. Am J Respir Crit Care Med 3:A471