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Discomfort associated with underhumidified high-flow oxygen therapy in critically ill patients

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Abstract *Objective:* To measure (1) the discomfort in non-intubated patients under high-flow oxygen therapy (HFOT) humidified with bubble (BH) or heated humidifiers (HH), and (2) the hygrometric properties of oxygen with a BH and an HH. *Design and setting:* This was a randomized cross-over study in critically ill patients during a 3-day period. The humidification device used at days 1 and 3 was changed for the other at day 2. (2) It was also an experimental bench study using the psychrometric method with five randomized flows (3, 6, 9, 12 and 15 l/min) and different humidification techniques. *Methods:* Discomfort, particularly dryness of the mouth and throat, was measured for two humidification conditions (BH and HH) using a 0–10 numerical rating scale (NRS) by patients requiring HFOT with a face mask at a flow ≥5 l/min, in a double-blinded condition. *Results:* (1) In this clinical study, 30 patients treated by HFOT at a median flow of 7.8 l/min (5.1–10.9) were included. The global incidence of moderate (NRS = 4–6) and severe discomfort (NRS = 7–10) was 25 and 29%, respectively. The median intensities of both mouth and throat dryness were significantly lower with the HH than with the BH [7.8 (5.0–9.4) vs. 5.0 (3.1–7.0), $P = 0.001$ and 5.8 (2.3–8.5) vs. 4.3 (2.0–5.0), $P = 0.005$, respectively]. (2) In the bench study, the mean absolute humidity measured at an ambient temperature of 26°C with the HH was two times greater than with the BH (30 ± 1 vs. 16 ± 2 mg/l, $P < 0.05$) regardless of the flow rate. *Conclusions:* Compared to bubble humidifiers, the use of a heated-humidifier in patients with high-flow oxygen therapy is associated with a decrease of dryness symptoms mediated by increased humidity delivered to the patient.

Keywords Respiratory insufficiency · Oxygen inhalation therapy · Mouth dryness · Pain · Intensive care equipment and supplies

Introduction

Oxygen therapy has long been a common treatment for patients who suffer from an organ dysfunction and are hospitalized in an Intensive Care Unit (ICU) [1, 2]. Non-intubated critically ill patients are often treated by high flow oxygen therapy (HFOT) above 4 l/min using a face mask [3]. The face mask is used in the place of nasal cannula in part because patients with acute respiratory failure (ARF) breath preferentially through an open mouth rather than the nose [3]. Given that oxygen delivered to the patient is dry, clinical practice guidelines [3] recommend humidifying the oxygen when above 4 l/min in the ICU setting, because the humidification function of the nasal mucosa can be insufficient at high oxygen flow rates and/or the critically ill patient with ARF often breathes through the mouth. Breathing dry oxygen could provoke dryness of the mouth, nose, throat and respiratory tract, resulting in discomfort and pain that are frequent and multi-factorial in the ICU setting [4–7]. Breathing dry air by the nose may also lead to the alteration of the mucociliary transport system [8] and cause an increase of airway resistance [9] in healthy subjects. However, there are no recommendations concerning the type of humidification device to use.

Although HFOT is commonly practiced in the ICU, there is a paucity of studies on the humidification of HFOT for this population of patients. The studies that have compared bubble humidifiers (BH) with no humidification were performed in stable patients hospitalized outside the ICU and treated with oxygen flow rates $\leq$5 l/min delivered by a nasal cannula [10–12]. Moreover, to our knowledge, no study has compared BH with heated humidifiers (HH), for which temperature and humidity outputs are expected to be much higher than that of BH.

The objectives of this clinical and bench study were (1) to compare, as a surrogate parameter of humidification, symptoms associated with the dryness of the airway mucosa in critically ill patients treated by HFOT with a face mask using two types of humidification devices: a BH and an HH; (2) to compare the hygrometric properties (temperature, relative and absolute humidity) of the oxygen delivered to the patient at different flows, without humidification and with humidification generated by a BH or a HH.

Materials and methods

Detailed methods are provided in the electronic supplementary material (ESM).

Clinical study

Population

All consecutive patients hospitalized in our medical–surgical ICU from August 2006 to March 2007 were included in the study if they required oxygen therapy delivered by a face mask at a flow rate $\geq$5 l/min to maintain an oxygen saturation, measured by pulse oximetry, at $\geq$92%. Exclusion criteria were the presence of delirium leading to difficulty for the patient to rate his/her pain or discomfort using an adapted clinical tool (see below). The presence of delirium was checked daily using the Confusion Assessment Method for the ICU (CAM-ICU) [13, 14] and the Richmond Agitation Sedation Scale (RASS) [15, 16] (see ESM).

The local scientific and ethics committee of Comité d'Organisation et de Gestion de l'Anesthésie Réanimation du Centre Hospitalier Universitaire de Montpellier (COGAR) approved the design of the study, and written consent was waived.

Material

Oxygen flow was adjusted with a flow meter and then humidified with the bubble humidier (BH) or the heated humidifier (HH) before being delivered to the face mask (see ESM) (Fig. 1).

Study design

Patients were randomized and blinded for the type of humidification, according to the initial day of HFOT: humidification with an HH during the even days and humidification with a BH the odd days. This prospective cross-over study was performed for at least 2 days, 3 if possible (Fig. 2).

Evaluated parameters

After each study day (24 h of humidification with either device), and after a period of 2 h without non-invasive ventilation (NIV), aerosol therapy or oral care, the clinical parameters of discomfort were assessed by a blinded observer asking the patient to rate his/her discomfort symptoms using an enlarged ICU-adapted numerical rating scale (NRS) from 0 (no discomfort) to 10 (maximum imaginable discomfort) [7, 17, 18]. The discomfort symptoms were determined for the dryness of the delivered oxygen (dryness of the mouth, throat, nose, difficulty to swallow and throat pain) and for its warmth (facial heat sensation). We also evaluated a total dryness score that

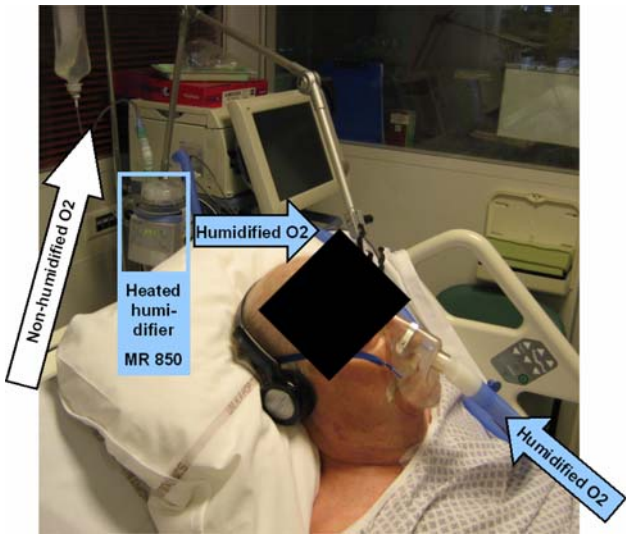

Fig. 1 Humidification of oxygen with a heated humidifier. This figure shows the heated humidification of oxygen with the MR850 heated humidifier and its heated wire circuit (HH) (MR850; Fisher & Paykel Healthcare, Panmure, New Zealand). The MR850 HH is composed of a single-patient humidification chamber and a 22-mm diameter circuit with heated wire. The heated wire was set to maintain proximal temperature (near mask inlet) at 34°C, and the chamber temperature was set at 31°C, as recommended by the manufacturer for HFOT with a face mask. The HH was filled with sterile water and placed between the oxygen source delivered by an oxygen flow meter connected to the wall of the room and the face mask. The HH could be easily applied to our patients because it was already in place, mounted on the ventilator for humidification of the gas delivered during invasive and non-invasive mechanical ventilation, when this was required. All the ventilators in our ICU were equipped with an HH. For the present patient, the ventilator was off, and the HH was used separately

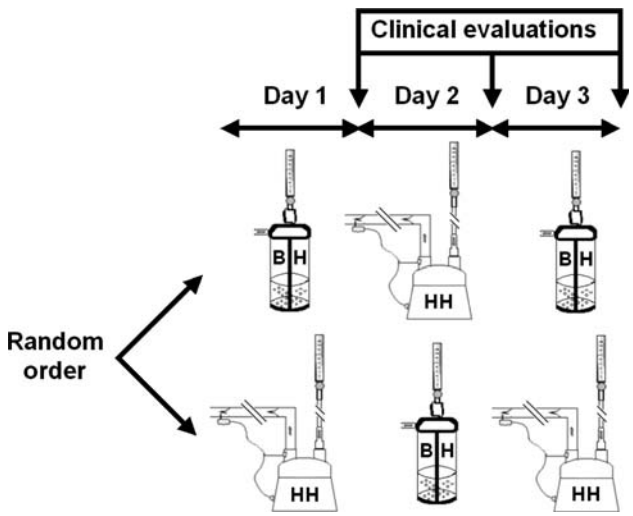

Fig. 2 Design of the clinical study *BH* bubble humidifier; *HH* heated humidifier

pooled all five dryness symptoms. The last day of the study, the patient was asked to rate his or her preference for the humidification device used, with respect to the humidification of the upper airway mucosa and the warmth of the mask, using a 5-point verbal scale: $+2$ = much better than the other device, $+1$ = better, 0 = no preference, -1 = worse and -2 = much worse. Finally, the level of vapor condensation on the inner side of the face mask was recorded each day by the blinded observer as either present or absent. Oxymetry, respiratory rate and tidal volume were measured each day using a Wright flow meter (see ESM).

Demographics including severity of illness on ICU admission and data pertaining to therapies that could be associated with dryness of the airway mucosa were collected.

Bench study

This study was performed in our ICU in June 2007. The temperature, the relative and the absolute humidity of oxygen delivered with the two humidification devices, as well as without humidification, were measured using the psychrometric method, which is the most commonly employed technique [19, 20] (see ESM).

The measurement of hygrometric properties of oxygen delivered at five incremental flow rates (3–6–9–12–15 l/min), non-humidified or humidified by BH or HH, were randomized (15 conditions in all). The absolute humidity was calculated using the temperatures recorded for each of the conditions so as to reflect the hygrometric properties of the oxygen that was delivered to the patient.

Statistical analysis

Qualitative data are expressed as number of events (%) and continuous data as mean ± SD or as median and inter-quartile range when they were not normally distributed. For clinical data, values obtained at day 1 and day 3 were pooled together and then compared with those observed at day 2 using the Wilcoxon's rank test. Mann–Whitney's U test was used to evaluate non-paired measurements. Categorical variables were analyzed using the chi-square test. For the bench study, measurements were pooled together and compared with the Wilcoxon's rank test. We considered a P value <0.05 to be statistically significant (see ESM).

Results

Clinical study

Among the 61 patients eligible during the period of the study, 26 were not analyzed: delirium ($n = 14$), no need

for HFOT ($n = 10$) and intubation for mechanical ventilation ($n = 2$) less than 48 h after inclusion. Five patients were missing because of occasional peak work loads. In all, 30 patients were included for analysis. Eleven patients were not evaluated after day 2 because HFOT was not needed at day 3 ($n = 8$), intubation ($n = 2$) and a refusal to change the humidification device (heated humidifier) because of improved discomfort symptoms ($n = 1$). In all, for each of the six symptoms, 40 evaluations were performed with an HH and 39 evaluations with a BH. The median room temperature and relative humidity were 24°C (23–26) and 34% (32–41), respectively. Patient characteristics are shown in Table 1. Among the 17 patients treated by non-invasive ventilation (NIV), only 5 patients required NIV for a total duration of more than 6 h per day, 2 of which were intubated. Throughout the duration of the study, there was no significant difference between the median oxygen flow delivered with HH and BH [7.0 (5.1–10.8) vs. 7.0 (5.0–11.5) l/min], nor was there for the median minute ventilation [9.6 (7.0–12.1) vs. 10.3 (7.3–12.3) l/min]. For all the dryness symptoms and throughout the study period, the cumulative incidences of no discomfort (NRS score = 0), light discomfort (NRS score = 1–3), moderate discomfort (NRS = 4–6) and severe discomfort (NRS = 7–10) were respectively 24, 13, 27 and 37% when a BH was used, and 33, 20, 26 and 22% when an HH was used ($P < 0.01$). The median intensity of total dryness score was significantly lower with a HH than with a BH [3.1 (1.7–4.8) vs. 4.8 (2.0–6.4), $P < 0.01$]. The decrease of discomfort was more important for the mouth and throat dryness (Fig. 3). No significant difference in facial heat sensation was observed between the two humidification devices (Fig. 3). Upon the last day of the study, patient preference was significantly higher for HH than BH with respect to humidification of the upper airway mucosa [1.0 (0.0–1.3) vs. 0.0 (–1.0–0.3), $P = 0.02$, respectively], whereas no significant difference was observed regarding the warmth of the mask [0.0 (0.0–1.3) vs. 0.0 (–1.0–0.0), $P = 0.17$]. The presence of vapor condensation on the inner side of the face mask was observed in 18% of the evaluations when a BH was used, compared to 90% with an HH ($P < 0.001$).

In attempt to show an interaction between the oxygen flow rate and dryness symptoms, the 12 patients with a

Table 1 Characteristics of the 30 patients included in the study

Age (years)	58 (48–71)
Sex (F/M)	5/25
Type of admission, *n* (%)	
Medical	9 (30)
Surgical	21 (70)
SAPS II	35 (24–47)
SOFA	5 (2–8)
Mechanical ventilation before inclusion, *n* (%)	24 (80)
Duration of mechanical ventilation (h)	8 (1–24)
Time between admission to ICU and inclusion (h)	24 (8–50)
Oxygen flow at inclusion time (l/min)	8 (5–11)
Oxymetry (%)	98 (95–99)
Respiratory rate (b/min)	24 (18–28)
Tidal volume (ml)	350 (300–525)
Minute ventilation (l/min)	10 (6–11)
Medical prescriptions, *n* (%)	
At least one drug associated with mouth dryness	19 (63)
At least two drugs associated with mouth dryness	13 (47)
Naso-gastric catheter	19 (63)
Non-invasive ventilation	17 (57)
Aerosol therapy	17 (57)

Continuous data are expressed in median (25–75 percentiles)
SAPS II simplified acute physiological score II [34]; *SOFA* sequential organ failure assessment score [35]

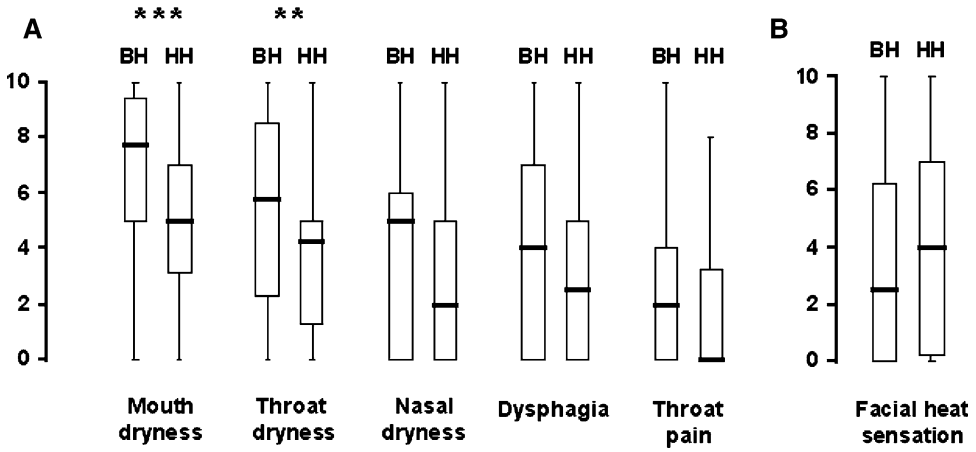

Fig. 3 Intensity of each discomfort symptom evaluated for each of the two humidification devices. This figure shows the intensity of all dryness discomfort symptoms. **a** Decreased with heated humidification compared to the bubble humidifier. The difference was significant only for mouth and throat dryness and trended towards significance for the others (P values ≤0.12). The facial heat sensation (**b**) was not significantly greater with the heated humidifier ($P = 0.20$). Medians are expressed as horizontal bars, 25–75 percentiles as *boxes* and maximal–minimal values as vertical bars. ***$P < 0.001$; **$P < 0.01$

moderate flow (5–6 l/min) were compared with the 9 patients with a high flow (≥10 l/min). No significant differences were shown between these two groups for the median intensity of each of the five dryness symptoms or their totality [4.1 (0.9–7.0) vs. 3.5 (2.5–5.5), $P = 0.96$], nor for the median delta intensity between the two humidification devices tested [0.5 (0.0–3.0) vs. 1.5 (−1.0–3.5), $P = 0.58$]. Moreover, for the 30 analyzed patients, no significant correlation was shown between the oxygen flow rate and the median intensity of dryness symptoms, nor for the median delta intensity between the two humidification devices (all r^2 coefficients <0.047).

Bench study

During the period of the bench study, atmospheric pressure was 755 mmHg, ambient temperature was 26°C, relative humidity was 73%, and absolute humidity was 18 mg/l. Bench study results are shown in Fig. 4. The median temperature measured with the HH was significantly higher than with the BH [34.1 (33.7–34.3) vs. 26.7 (26.4–26.8) °C, $P < 0.05$], as were the median relative humidity [77.6 (77.3–82.4) vs. 60.7 (59.7–66.3) %, $P < 0.05$] and the median absolute humidity [29.7 (24.4–30.6) vs. 15.6 (14.9–16.9) mg/l, $P < 0.05$), irrespective of the flow value. The median relative and absolute humidity levels measured without humidification device at a temperature of 26.7 (26.6–26.9) °C were respectively 17.3% (14.6–19.8) and 4.4 (3.7–5.0) mg/l.

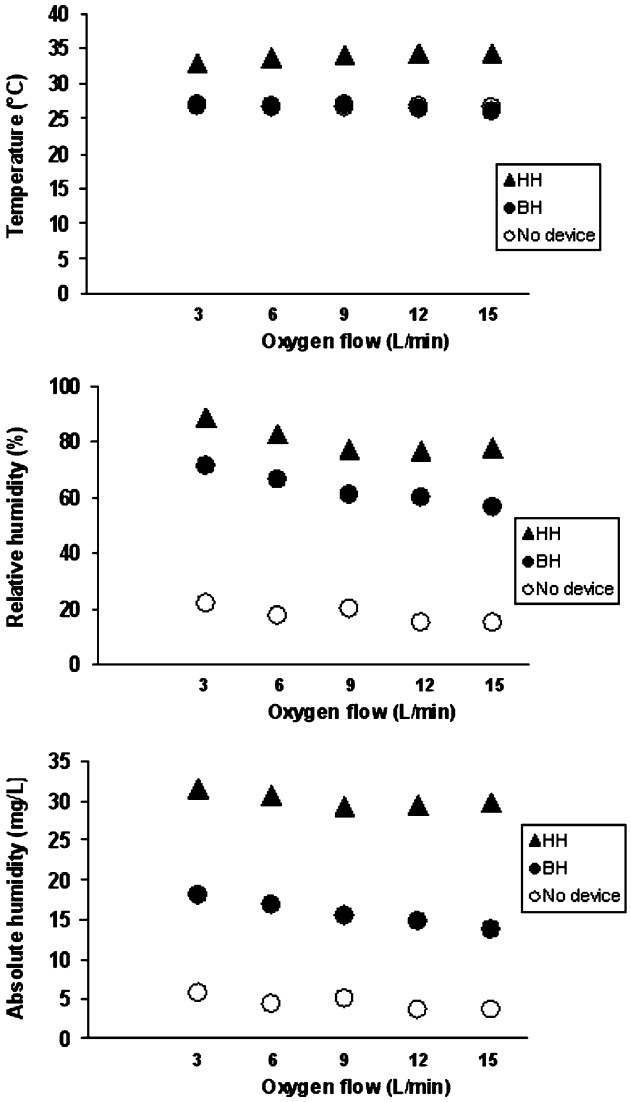

Fig. 4 Hygrometric properties of oxygen delivered at increasing flow rates, without and with a bubble or a heated humidifier, measured with the bench test. This figure shows the hygrometric measurements of the bench study. The median temperature measured with the HH was significantly higher than with the BH [34.1 (33.7–34.3) vs. 26.7 (26.4–26.8) °C], as was the median relative humidity [77.6 (77.3–82.4) vs. 60.7 (59.7–66.3) %] and the median absolute humidity [29.7 (24.4–30.6) vs. 15.6 (14.9–16.9) mg/l], all P values <0.05, Wilcoxon's rank tests. The median relative and absolute humidity levels measured without humidification device at a temperature of 26.7 (26.6–26.9) °C were respectively 17.3 [14.6–19.8] % and 4.4 [3.7–5.0] mg/l. For the two conditions, all the measurements were obtained at constant room air conditions (temperature = 26°C; relative humidity = 73%; absolute humidity = 18 mg/l)

Discussion

The main finding of this study is that high-flow oxygen therapy delivered to non-intubated, critically ill patients is often associated with discomfort and that the level of discomfort is associated with the humidification technique employed. These findings are supported three different ways. First, moderate to severe discomfort was reported in over half the patients, but the discomfort symptoms associated with the dryness of the mouth and throat were significantly lower when an HH was used. The fact that only trends towards lower discomfort with HH were observed for other symptoms, such as nasal dryness, throat pain and difficulty to swallow, could be explained by the high rate of use of a nasal-gastric catheter (63%), mainly in patients recovering from digestive tract surgery. Second, the presence of vapor condensation on the inner side of the face mask was dramatically more frequent when an HH was used compared to a BH. This has been suggested as an index for adequate levels of humidity delivered to the patient. As reported in mechanically ventilated ICU patients, the visual evaluation of vapor condensation could be recommended because this provides a very accurate estimation of the humidifying efficacy of the humidification device when compared to the psychrometric method [21]. Third, the bench test study supports the main findings of the clinical study because the delivered oxygen had higher hygrometric properties when an HH was used

compared to a bubble humidifier. The mean absolute humidity was two times greater with an HH than with a BH.

The reduction of discomfort associated with HFOT in critically ill patients is clinically relevant for several reasons. On one hand, ICU patients frequently report pain and discomfort symptoms [4, 5] whose etiology may be diverse, such as medical history [6], but is often related to care procedures and devices [7]. ICU stressors have been associated with an increased morbidity, explained in part by an increased stress response [18], a worse quality of life [22, 23] and unpleasant memories [24] in survivors. The present study demonstrates that increasing absolute humidity of the gas breathed by critically ill patients requiring HFOT is associated with an improvement of mouth and airway mucosa dryness. Consequently, this could contribute to a better preservation of the mucociliary transport system [8] and reduced airway resistance [9]. This is an important factor in critically ill patients who frequently develop atelectasis and nosocomial infections, such as sinusitis and pneumonia [25]. Regarding the findings of our study, the use of an HH could be considered in critically ill patients treated by HFOT delivered with a face mask because these patients often breath through the mouth and/or the humidification capacity of the nasal mucosa could be insufficient at high flows of oxygen, as reported for patients treated by NIV for acute respiratory failure [26, 27]. In the same way, improved humidification of hospitalized patients' airways could be of interest in order to avoid the sick building syndrome associated with air conditioning, which is often reported by health caregivers [28, 29] and could be particularly important in critically ill patients who commonly have a high minute ventilation and/or breath frequently through the mouth. The absence of correlation between the oxygen flow rate and the dryness symptoms in our study could be explained in part by the fact that some hypoxemic critically ill patients breath predominantly through the mouth, as nasal flow is low or absent. In addition to humidifying the delivered oxygen, an efficient humidifier could improve mucosa dryness by compensating for the dry air conditioned environment of the ICU. Second, the absolute humidity measured by the bench test decreased lightly when the oxygen flow increased (Fig. 4).

Contrary to invasive or non-invasive mechanical ventilation [26, 27] and CPAP [30], the impact of the humidification of oxygen has been poorly reported in the literature, especially for hypoxemic critically ill patients [3]. The studies that have compared bubble humidifiers with no humidification device were performed in stable patients, hospitalized outside the ICU and treated with oxygen flow rates $\leq$5 l/min delivered by a nasal cannula [10–12]. The difference of discomfort symptoms between humidification with a bubble humidifier compared to no humidification was small [12] or not significant [10, 11]. In the same way, there are few studies that have reported hygrometric properties of oxygen at very high flow rates. A study has compared four different bubble humidifiers at four different oxygen flow rates varying from 2 to 8 l/min [31]. The results are very similar to ours concerning the hygrometric properties of oxygen when a BH was used. The measured absolute humidity, which decreased as the oxygen flow increased, was between 15 and 20 mg/l [31].

Our study has several limitations. First, the discomfort measurement was subjective. However, the discomfort symptoms have been self-rated by all the patients for both humidification devices, as expected by the cross-over design. The enlarged 0–10 NRS used to measure the discomfort symptoms is the best-adapted clinical tool for the critically ill patient who is often tired [32, 33]. This tool has been shown to have a better validity and reliability for measurement of acute pain than both the visual analogue scale and the verbal scale [17]. Moreover, discomfort symptoms were only evaluated with non-delirious patients.

Second, the clinical impact of the humidification device on atelectasis and nosocomial infections was not evaluated in our study. Before the widespread use of HH can be recommended, including wards and emergency departments after adaptation to these non-ICU settings by manufacturers, the comfort improvements suggested by this study applying heated humidification must be shown to be associated with improvements in patient outcomes and satisfaction to prove its cost effectiveness. As all the mechanical ventilators in our unit were equipped with a heated humidifier, there was no additional nursing work load or additional cost associated with the use of this humidifier compared to another one, such as a bubble humidifier. For the time being, having a device that costs so much more (26 €, net of tax for a heated-wire circuit), but that does not totally alleviate discomfort, is not clinically and economically satisfying and relevant and should be used only in some patients with major dryness symptoms.

Third, the clinical impact of the use of a BH or HH was not compared to no humidification at all, in accordance with practice guidelines [3]. Fourth, the psychrometric method only has been used in a bench test, not clinically. This was because humidity and temperature measurements would have been altered by expired gas. The hygrometric properties measured by the bench test had the same properties of the oxygen that was delivered at the inlet of the face mask. Last, the sample size of analyzed patients was too small to measure the impact of both the humidification device and the medical prescriptions, such as drugs, gastric catheter and/or NIV, on the incidence of discomfort. However, patient evaluations were performed after a period of at least 2 h without a NIV session.

In conclusion, the critically ill patients of our study often reported dryness symptoms with high flow oxygen therapy. Compared to a bubble humidifier, the use of a heated humidifier is associated with a decrease of dryness symptoms. This conclusion is supported by clinical and bench measurements demonstrating increased humidity

delivered to the patient. Active humidification of oxygen therapy can be considered for some patients with excessive dryness symptoms to improve their comfort and decrease the dryness of the airway mucosa. Further studies are needed to measure the clinical impact of these devices on respiratory function and associated outcomes in these critically ill patients, and the cost-effectiveness of a more widespread use.

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