

# Impact of Airway Humidification Strategy in Mechanically Ventilated COVID-19 Patients

Carole-Anne Lavoie-Bérard, Jean-Claude Lefebvre, Pierre-Alexandre Bouchard, Mathieu Simon, and François Lellouche

**BACKGROUND:** Humidification of inspiratory gases is mandatory in all mechanically ventilated patients in ICUs, either with heated humidifiers (HHs) or with heat and moisture exchangers (HMEs). In patients with COVID-19, the choice of the humidification device may have relevant impact on patients' management as demonstrated in recent studies. We reported data from 2 ICUs using either HME or HH. **METHODS:** Data from patients with COVID-19 requiring invasive mechanical ventilation during the first wave in 2 ICUs in Québec City were reviewed. In one ICU, HMEs were used, whereas heated-wire HHs were used in the other ICU. We compared ventilator settings and arterial blood gases at day one after adjustment of ventilator settings. Episodes of endotracheal tube occlusions (ETOs) or sub-occlusions and a strategy to limit the risk of under-humidification were reported. On a bench test, we measured humidity with psychrometry with HH at different ambient temperature and evaluated the relation with heater plate temperature. **RESULTS:** We reported data from 20 subjects positive for SARS-Cov-2, including 6 in the ICU using HME and 14 in the ICU using HH. In the HME group,  $P_{aCO_2}$  was higher (48 vs 42 mm Hg) despite higher minute ventilation (171 vs 145 mL/kg/min predicted body weight [PBW]). We also reported 3 ETOs occurring in the ICU using HH. The hygrometric bench study reported a strong correlation between heater plate temperatures of the HH and humidity delivered. After implementation of measures to avoid under-humidification, including heater plate temperature monitoring, no more ETOs occurred. **CONCLUSIONS:** The choice of the humidification device used in subjects with COVID-19 had a relevant impact on ventilation efficiency (increased  $CO_2$  removal with lower dead space) and on complications related to low humidity, including ETOs that may be present with heated-wire HHs when used with high ambient temperatures. *Key words:* heated humidification; heat and moisture exchanger; dead space;  $CO_2$ ; COVID-19; endotracheal tube occlusion. [Respir Care 2022;67(2):157–166. © 2022 Daedalus Enterprises]

## Introduction

Questions related to gas humidification during mechanical ventilation are mainly related to (1) the humidification performances and endotracheal tube (ETT) total or partial occlusions associated with under-humidification and (2) the impact of humidification devices' dead space on  $CO_2$  removal.<sup>1</sup>

These 2 issues are relevant in patients with COVID-19 requiring invasive mechanical ventilation.<sup>2,3</sup> Recent studies have shown high rates of endotracheal tube occlusions (ETOs) in patients with COVID-19, occurring with heat and moisture exchangers (HMEs) as well as with heated humidifiers (HHs).<sup>3-9</sup> Authors have evoked specific conditions related to COVID-19 pathophysiology leading to particularly viscous

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Supplementary material related to this paper is available at <http://rc.rcjournal.com/>.

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The authors have disclosed no conflicts of interest.

DOI: 10.4187/respcare.09314

secretions, prolonged mechanical ventilation, and reduced frequency for suctioning, but humidification performances are not discussed. The other component that differentiates

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HME and HH is the impact of the dead space during lung-protective ventilation.<sup>10</sup> Patients with COVID-19 requiring invasive mechanical ventilation most frequently meet ARDS criteria.<sup>11,12</sup> Although pathophysiology may differ from usual ARDS, those patients benefit from lung-protective ventilation.<sup>12-16</sup> We recently demonstrated that with low tidal volumes and high breathing frequencies the instrumental dead space may have an important influence on ventilation efficiency (ie, CO<sub>2</sub> removal).<sup>10</sup> The inspiratory gas humidification system recommended with such ventilator settings is the HH to minimize dead space impact and improve CO<sub>2</sub> clearance.<sup>17</sup> However, in the COVID-19 population, the choice of humidification system is still unclear because HME and HH have each advantages and drawbacks.<sup>18</sup> Indeed, the use of HME filters may seem preferable at first glance with regard to its filtering properties in the pandemic context. However, this strategy is associated with frequent changes of HMEs, potential changes of ETT,<sup>3-5,7</sup> and potentially switch to HH circuits due to respiratory acidosis, which puts health care workers at risk of viral contamination.<sup>18,19</sup> Consequently, the initial choice of the circuit and humidification should not be neglected in this population. We report here the experience of 2 centers using different humidification strategies for mechanically ventilated patients with COVID-19. We discussed these 2 issues related to humidification: the risk of under-humidification and the impact on alveolar ventilation and compared with recent data published in the literature.

### Methods

We conducted a retrospective observational study including all intubated patients in the 2 designated COVID-19 centers for adults in Québec City between March 23, 2020, and June 6, 2020. A waiver of consent was obtained from institutions.

In one center, HHs (MR850, Fisher & Paykel, Auckland, New Zealand) were used to reduce instrumental dead space. In the other center, HME (Hygrobac S, Medtronic, Minneapolis, Minnesota) was the first-line humidification strategy for its filtering characteristics.

We collected information about demographics, set and measured respiratory parameters, total dead space, and arterial blood gases after intubation and after initial modifications of the ventilator settings. We also collected need for humidification system changes and clinical outcomes, including ETOs and subocclusions. Total dead space was calculated by the addition of ETT volume (related to the diameter), HME volume (45 mL, when present), connectors

### QUICK LOOK

#### Current knowledge

Proper humidification of gas delivered to patients during mechanical ventilation is mandatory. Heat and moisture exchangers (HMEs) or heated humidifiers (HHs) may be used, with different performances in humidification and different mechanical properties (resistance and dead space).

#### What this paper contributes to our knowledge

During mechanical ventilation of patients with ARDS due to COVID-19, the choice of the humidification strategy had a relevant impact on ventilation efficiency (reduced CO<sub>2</sub> clearance due to increased dead space with HMEs) and endotracheal tube obstructions with HHs. Specific strategies to avoid under-humidification were effective.

(CO<sub>2</sub> sensor: 5 mL; closed suction system: 9 mL), and estimated physiologic dead space (~ 1.1 mL/kg PBW).<sup>10</sup>

### Bench Study

We conducted a bench study aiming to determine the relation between the heater plate temperature and the absolute humidity delivered by the heated-wire HH used in our institution. Different settings were studied; we concomitantly recorded the heater plate temperature of the HH and measured the inspiratory absolute humidity with the psychrometric method as previously described.<sup>20</sup>

Based on these data, we implemented several measures to prevent under-humidification related to HH dysfunction:

1. Activation of the compensation algorithm on HH devices<sup>20</sup> or increase of the humidification chamber temperature when under-humidification was suspected or when heater plate temperature was below 62°C (Video E1, supplementary material, Figure E1 electronic supplement, see related supplemental materials at <http://rc.rcjournal.com/>),
2. Monitoring of the heater plate temperature. This monitoring became part of the regular checks of the respiratory therapists of the ICU. The recommendation was to adjust humidifiers settings when heater plate temperature was below 62°C (Video E2, supplementary material, see related supplemental materials at <http://rc.rcjournal.com/>), and
3. Installation of a new air conditioning system compatible with the negative-pressure rooms.

### Results

Twenty-six patients with confirmed COVID-19 were admitted in the participating ICUs during the

# AIRWAY HUMIDIFICATION IN VENTILATED SUBJECTS WITH COVID-19

Table 1. Demographic Characteristics, Respiratory Parameters, Arterial Blood Gases, and Outcomes of the Subjects With Heated Humidifier and Heat and Moisture Exchanger

	HH Group <i>n</i> = 14	HME Group <i>n</i> = 6	<i>P</i> ‡
Demographic characteristics			
Age, y	60.4 ± 15.5	60.3 ± 11.8	.99
Male gender, <i>n</i> (%)	10 (71%)	4 (67%)	> .99
Height	171 ± 11	169 ± 7	.70
BMI, kg/m <sup>2</sup>	26.9 ± 3.4	31.3 ± 6.7	.14
Respiratory parameters*			
Frequency, breaths/min	24.6 ± 4.3	24.7 ± 5.9	.99
V <sub>T</sub> , mL	384 ± 52	440 ± 54	.04
Minute ventilation, L/min	9.5 ± 2.1	10.7 ± 1.8	.24
V <sub>T</sub> , mL/kg PBW	5.9 ± 0.7	6.9 ± 0.8	.01
Minute ventilation, mL/kg/min PBW	145 ± 28	171 ± 48	.14
PEEP, cm H <sub>2</sub> O	12.8 ± 2.7	10.3 ± 1.5	.05
Intrinsic PEEP, cm H <sub>2</sub> O	1.1 ± 0.7	1.5 ± 0.8	.29
F <sub>IO<sub>2</sub></sub>	0.57 ± 0.17	0.56 ± 0.15	.87
Driving pressure, cm H <sub>2</sub> O	9.9 ± 2.9	10.8 ± 3.7	.54
C <sub>RS</sub> , mL/cm H <sub>2</sub> O	41.6 ± 11.6	45.5 ± 18.2	.56
Dynamic mechanical power,† J/min	23.0 ± 6.4	30.0 ± 9.6	.07
V <sub>D</sub> , mL	102 ± 14	147 ± 11	< .001
V <sub>D</sub> /V <sub>T</sub> , %	26.7 ± 2.8	33.7 ± 2.9	< .001
Ventilatory ratio	1.61 ± 0.45	2.19 ± 0.60	.03
Arterial blood gases*			
Arterial pH	7.35 ± 0.07	7.35 ± 0.02	.87
P <sub>aCO<sub>2</sub></sub> , mm Hg	42.3 ± 7.4	48.0 ± 4.9	.10
P <sub>aO<sub>2</sub></sub> , mm Hg	81.1 ± 12.5	86.5 ± 11.7	.37
P <sub>aO<sub>2</sub></sub> /F <sub>IO<sub>2</sub></sub>	152 ± 45	165 ± 48	.56
HCO <sub>3</sub> <sup>-</sup> , mm Hg	22.7 ± 2.6	25.5 ± 3.1	.05
Outcomes data			
Duration of ventilation, d	14.1 ± 13.2	20.5 ± 8.3	.29
ICU length of stay, d	19.4 ± 13.6	21.5 ± 7.3	.73
Died, <i>n</i>	3	3	.30

\*After initial adjustment of respiratory parameters.

†Mechanical power was calculated with the following formula  $MP = 0.098 \times \text{frequency} \times V_T \times (\text{peak pressure} - [0.5 \times \text{Driving pressure}])$ .<sup>41</sup>

‡Nominal variables were expressed with frequencies and percentage (%) and were analyzed using Fisher exact test. Continuous variables were analyzed using 1-way ANOVA.

HH = heated humidifier

HME = heat and moisture exchanger

BMI = body mass index

PBW = predicted body weight

study period, among which 20 were intubated and included in the analysis. In total, HH was used in 14 subjects and HME in 6. Fourteen were male; mean age was 60 ± 14 y; mean initial P<sub>aO<sub>2</sub></sub>/F<sub>IO<sub>2</sub></sub> ratio was 156 ± 45 mm Hg; all patients had P<sub>aO<sub>2</sub></sub>/F<sub>IO<sub>2</sub></sub> ratio below 300 mm Hg (Table 1).

### Impact of Humidification Strategy on Minute Ventilation and CO<sub>2</sub> Clearance

The total calculated dead space in the HME group was 147 ± 11 mL and 102 ± 14 mL in the HH group. In the HME group, P<sub>aCO<sub>2</sub></sub> was higher (48.0 vs 42.3 mm Hg),

despite higher tidal volumes and minute ventilation (171 vs 145 mL/kg/min PBW). Ventilatory ratio was consequently higher with HME. Driving pressure and mechanical power were also higher in the HME group (Table 1).

During the course of the hospitalization, HME was replaced by HH in 3 subjects (50%) to increase alveolar ventilation because of acidosis associated with high plateau pressure, and frequent HME changes every 48–72 h were required in the HME group.

We found 11 studies recently published<sup>15,16,21-23,25,26,28,29,31</sup> reporting respiratory parameters and arterial blood gases in mechanically ventilated subjects with COVID-19 to

Table 2. Breathing Frequency, Tidal Volume, Minute Ventilation, Arterial Blood Gases, and Estimated Dead Space Ventilation in Patients With COVID-19 in 12 Studies Describing the Respiratory Mechanics of This Population

Study	Subjects With COVID-19, N	V <sub>T</sub> (mL/kg PBW)	Frequency (breaths/min)	Minute Ventilation (mL/kg/min PBW)	Arterial pH	PaCO <sub>2</sub> (mm Hg)	HH/HME	Catheter Mount	Other Connectors (mL)	Estimated Mean Dead Space Ventilation <sup>a</sup> (L/min)
Diehl et al <sup>25</sup>	22	6.0	33	198	7.19	55	HME (51 mL)	Yes (38 mL)	MS: 10 CS: 5	194 × 33 = 6.4
Grieco et al <sup>26</sup>	30	6.4	28	179	7.35	43	HME (93 mL)	No	CO <sub>2</sub> : 10	188 × 28 = 5.3
Haudebourg et al <sup>23</sup>	30	6.0	28	168	7.36	44	HME (51 mL)	Yes (20 mL)	CS: 5	193 × 28 = 5.4
Beloncle et al <sup>22</sup>	25	6.0	28	168	—	41	HME (35 mL)	No	CS: 10	145 × 28 = 4.1
Barbeta et al <sup>21</sup>	50	6.8	22	150	7.31	47	HME > HH (50 mL)	Yes (20 mL)	CS: 5	166 × 22 = 3.7
Ferrando et al <sup>31</sup>	742	6.9	24	166		45	NA	NA	NA	
Grasselli et al <sup>29</sup>	297	7.0	20	140	7.38	46	NA	NA	NA	
Cavayas et al <sup>32</sup>	43	7.5	20	150	7.38	44	NA	NA	NA	
Laverdure et al <sup>28</sup>	36	6.1	25	152	NA	NA	NA	NA	NA	
REVA et al <sup>15</sup>	4,244	6.1	24.9	152	7.41	40	NA	NA	NA	
Botta et al <sup>16</sup>	497	6.4	21	136	7.36	46	81% HH			
HME	95	6.5	23	146	7.35	46	HME	NA	NA	
HH	402	6.4	21	134	7.36	45	HH	NA	NA	
Lavoie-Bérard study										
HME	6	6.9	25	171	7.35	48	HME (45 mL)	No	CO <sub>2</sub> : 10 CS: 5	147 × 25 = 3.7
HH	14	5.9	25	145	7.35	42	HH	No	CS: 5	102 × 25 = 2.5

Median or mean values are reported. Authors were contacted to specify the amount of instrumental dead space applied (humidification device, catheter mount, CO<sub>2</sub> cuvette, closed-suction connectors, and other connectors). The volume of the endotracheal tube (~ 15 mL) and the physiological dead space related to airways (accounting for 1.1 mL/kg PBW for intrathoracic anatomic dead space ~ 75 mL) were added, whereas the alveolar dead space was not counted. We could not get this information for several studies that are, consequently, not presented here.  
HH = heated humidifier  
HME = heat and moisture exchanger  
MS = metabolic sensor  
CS = closed-suctioning connector  
CO<sub>2</sub>: = CO<sub>2</sub> sensor

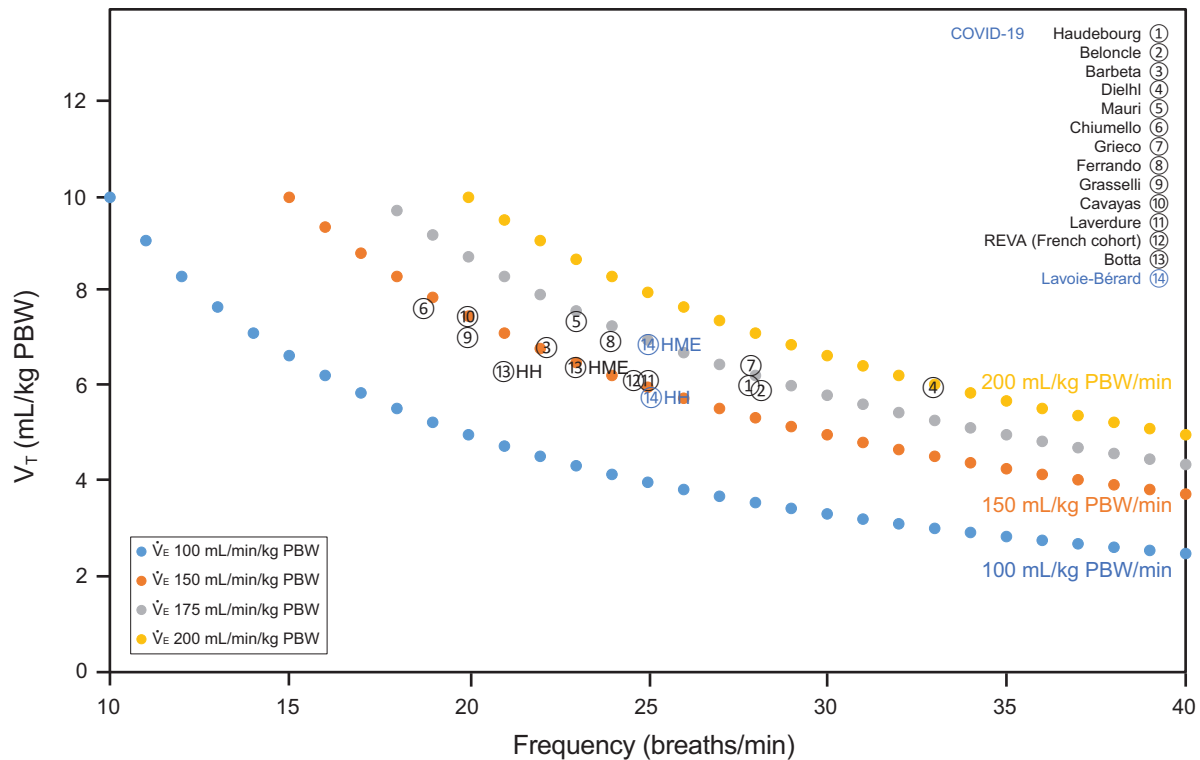


Fig. 1. Representation of the initial ventilatory needs (tidal volume in mL/kg PBW and breathing frequencies) in subjects with COVID-19. Data from studies providing these settings are displayed<sup>15,16,21-29,31-34</sup>. In these studies, most subjects required at least 150 mL/kg/min PBW of minute ventilation and up to 198 mL/kg/min PBW when high instrumental dead space was utilized.<sup>25</sup> In 2 studies providing data for subjects managed with HH and subjects managed with HME, the minute ventilation required was higher with HME; however,  $P_{aCO_2}$  was also higher due to increased instrumental dead space. PBW = predicted body weight;  $\dot{V}_E$  = minute ventilation.

compare with our data (Table 2, Fig. 1). Minute ventilation went from 134 to 198 mL/kg/min PBW but most frequently  $> 150$  mL/kg/min PBW. In one study, data for HH and HME were available.<sup>33,34</sup> Similarly, mean minute ventilation was higher with HME in comparison with HH (146 vs 134 mL/kg/min), but mean  $P_{aCO_2}$  was also higher (46 vs 45 mm Hg) (Table 2).

### Impact of Humidification Strategy on Endotracheal Tube Occlusions

Three events of partial or complete ETOs requiring urgent bronchoscopy ( $n = 1$ ) and/or tube exchange ( $n = 2$ ) occurred, associated with episodes of desaturation. None of the subjects who developed ETT obstruction had COPD, 2 had asthma, and all had severe ARDS. Abundant and tenacious secretions were noted a few days before ETT obstruction. Those events occurred between 6–15 days following intubation (mean  $12.0 \pm 4.6$  d). They occurred only in the ICU where HHs were used and while high ambient temperatures ( $> 28^\circ\text{C}$ ) were recorded, and no more events happened after implementation of safety measures to avoid under-humidification, including better control of ambient temperature, monitoring of heater plate temperature, and

activation of the compensation algorithm of the HH (Fig. 2).

### Bench Study

Results for the relation between the humidity delivered and the heater plate temperature are shown on Figure 3. There is a positive correlation between temperature of the plate and absolute humidity ( $R^2 = 0.9425$ ,  $P < .001$  when data of all ambient temperature are pooled).

### Discussion

In our cohort, we found that in the HME group  $P_{aCO_2}$  was higher despite higher minute ventilation in intubated subjects with COVID-19, explained by increased dead-space ventilation and decreased alveolar ventilation. Ventilation efficiency and  $CO_2$  clearance were increased with minimized instrumental dead space in the HH group. We also report a worrying number of ETOs occurring in the unit using HH. This complication reflecting poor humidification was found in several centers recently.<sup>3-8</sup> We report a bench study showing a strong correlation between heater plate temperature of the HH with humidity delivered.

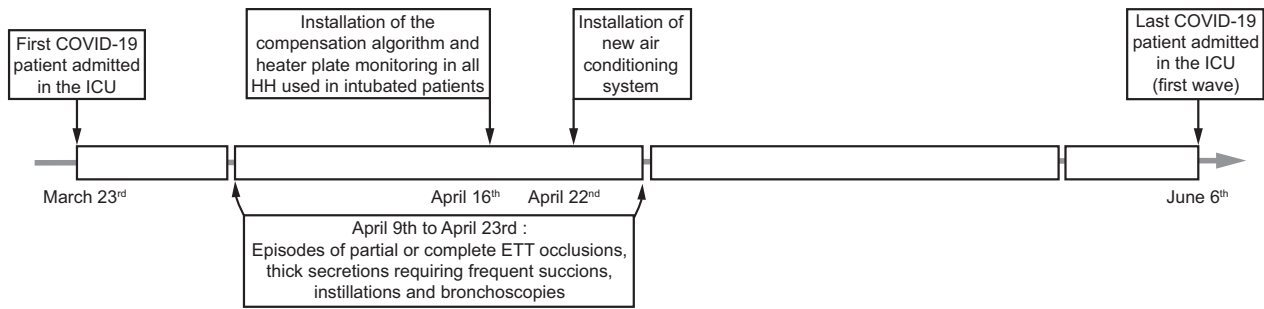


Fig. 2. Timeline of the under-humidification events and safety measures leading to the complete disappearance of the problem in the unit that used heated humidifiers (HHs) as its first-line humidification strategy. While utilizing a HH, it is important to be aware of the caveat associated with high ambient temperatures. Utilization of an efficient air conditioning system to reduce ambient temperature below 25°C, activation of the compensation algorithm of the HH, and monitoring of the heater plate temperature may reduce the risk of this life-threatening complication related to under-humidification with HH. HH = heated humidifier, ETT = endotracheal tube.

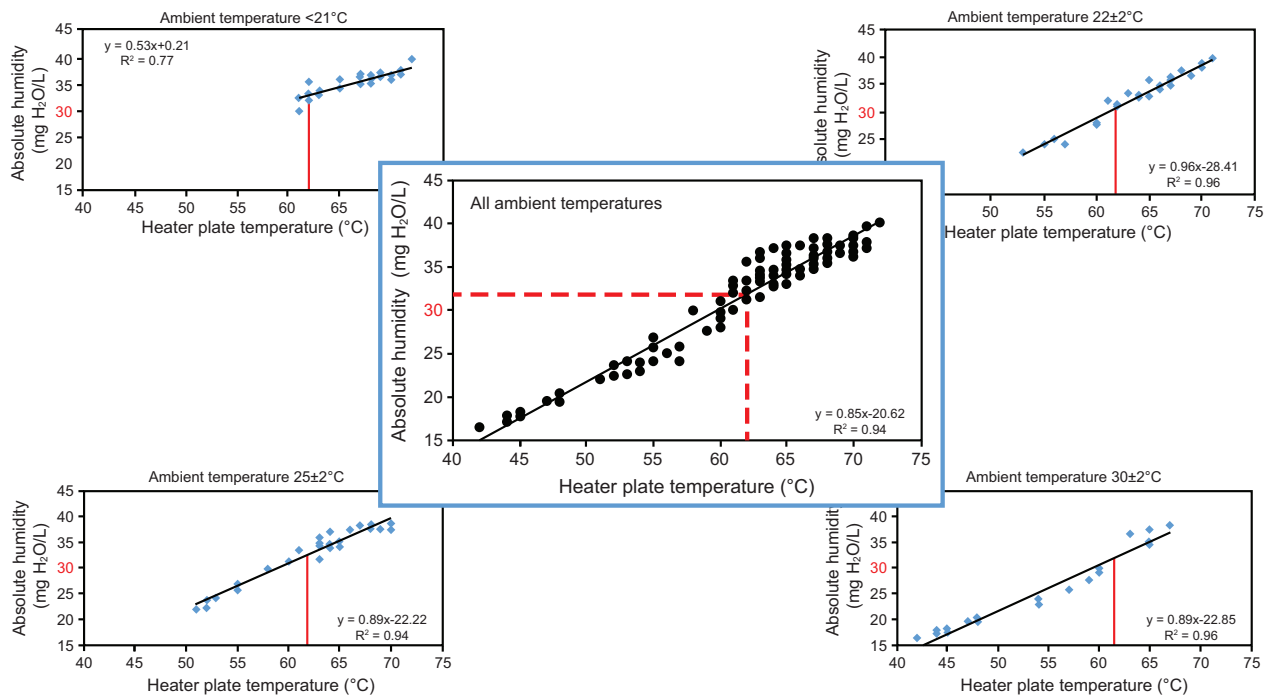


Fig. 3. Relation between the heater plate temperature (in °C) and absolute humidity (mg H<sub>2</sub>O/L) with an MR850 heated-wire heated humidifier. We conducted a bench study including 105 measurements of absolute humidity at steady state (after 1 h of stability) with the psychrometric method,<sup>20</sup> with varying the heater plate temperature. We found a strong correlation between the heater plate temperature and the delivered inspiratory absolute humidity ( $R^2 = 0.9425$ ,  $P < .001$ ). Data for different ambient temperatures (below 21°C, 22 ± 2°C, 25 ± 2°C, and 30 ± 2°C) are displayed, and the central panel shows all data. A heater plate temperature > 62°C ensures a safe humidity delivered whatever the ambient temperature.

After the implementation of measures to avoid under-humidification, including heater plate temperature monitoring, no more ETOs occurred.

Minute ventilation required by mechanically ventilated subjects in this study was high and consistent with recently published studies conducted in critically ill subjects with COVID-19 managed with protective mechanical ventilation.<sup>15,16,21-32</sup> In this situation, with high breathing frequencies and low set tidal volumes, we found a noteworthy

impact of instrumental dead space on alveolar ventilation (CO<sub>2</sub> elimination) as recently suggested.<sup>10</sup> With HME, minute ventilation was > 150 mL/kg/min PBW, whereas with HH the minute ventilation was 15% lower. Despite reduced minute ventilation, P<sub>a</sub>CO<sub>2</sub> was lower with HH, likely explained by the lower dead-space ventilation allowing a higher alveolar ventilation.<sup>35</sup> Several authors have demonstrated that the dead-space reduction when changing HME for HH leads to a significant reduction of the P<sub>a</sub>CO<sub>2</sub><sup>35-38</sup> or

lower tidal volume when  $P_{aCO_2}$  was kept constant, resulting in decreased plateau pressure and driving pressure in patients with ARDS.<sup>38-39</sup>

In our study, higher mechanical power was found in the HME group in comparison with HH group, more likely related to higher tidal volumes. High mechanical power may be associated with ventilator-induced lung injury (VILI)<sup>40</sup> and increased mortality.<sup>41</sup> Reducing minute ventilation by lowering tidal volume or breathing frequency, thanks to minimized dead space, would reduce mechanical power. Nevertheless, it is not known whether the magnitude of this effect is sufficient to alleviate VILI and improve outcome.

Interestingly, half of the subjects with HME thereafter developed severe acidosis requiring reduction of the dead space by changing the humidification device, a situation at risk of aerosol generation.<sup>19</sup> In addition, many device changes were necessary in the HME group, at least 2 or 3 times every week. The benefits related to reduced handling of the respiratory circuit were added to the benefits related to increased  $CO_2$  removal.

Besides mechanical differences, humidification devices have different humidification performances. There is no evidence demonstrating HH superiority for clinical outcomes<sup>42</sup> in terms of ETO rate or ventilator-acquired pneumonia, but many clinicians believe their humidification performances are superior to HMEs and avoid prolonged utilization of HME.<sup>43,44</sup> This is true only when operating conditions are optimal.<sup>20</sup> In the present study, we reported an unacceptable high rate of ETOs in subjects managed in one of the COVID-19 ICUs where HHs were used. Several studies recently reported similar issues with ETOs or subocclusions with subjects with COVID-19 with rates up to 72%.<sup>3-9</sup> The largest case series reported 12 ETOs in 11 subjects, 7 occurring with HME and 4 with heated-wire HH.<sup>3</sup> The authors discussed the role of the type of secretions in patients with COVID-19, the duration of mechanical ventilation, but not the possibility of under-humidification. Other case series reported high rates of ETO and did not discuss the role of humidification to explain this complication but rather the type of secretions, the reduction of suctioning in this specific situation, and the duration of invasive mechanical ventilation in subjects with COVID-19.<sup>4-9</sup>

ETOs are potentially life threatening, resulting in frequent cardiac arrest,<sup>45</sup> requiring most often urgent ETT exchange that is associated with risk to the patient and the clinician due to viral exposure.<sup>19</sup> Studies have shown that humidification performances of HMEs are very heterogeneous in terms of humidity delivered to patients, increasing the risk of ETOs.<sup>46</sup> A major issue is that some filters are also labeled HME filters, whereas bench evaluation demonstrates very low humidification performances.<sup>46,47</sup> The humidity measured with the psychrometric method is in line with the risk of tube occlusions.<sup>46</sup> With HME delivering  $> 28$  mg  $H_2O/L$  (including the Hygrobac S used in the HME center), measured with

the psychrometric method, the rate of ETO was very low.<sup>46</sup> However, below 25 mg  $H_2O/L$ , it increases a lot.<sup>46</sup>

ETO were also reported with HHs in our study and in other studies.<sup>3,8</sup> With HH turned off, it was not a surprise that ETOs were frequent.<sup>8</sup> Bench analysis demonstrated measured humidity delivered below 10 mg  $H_2O/L$ , which led to major under-humidification.<sup>48</sup> It was demonstrated that performances of heated-wire HHs may be altered by several factors, including ambient temperature and ventilator outlet temperature.<sup>20</sup> One major qualification with HH use is that they lose their performance when ambient temperature rises in the room or are exposed to direct sunlight.<sup>20</sup> In these situations, the heater plate produces less heat to maintain a constant, targeted temperature in the outlet chamber. Consequently, less water vapor is present in the humidification chamber, leading to inspiratory humidity below safe and recommended levels of 30 mg  $H_2O/L$ .<sup>20</sup> In the present study, the temperature in the unit where cases of ETO happened was between 28–30°C following the installation of negative-pressure devices and modification of the air conditioning circuit. Temperature remained high until air conditioning was restarted with modified aeration circuit. In addition, and to avoid this potentially fatal complication, we activated the compensation algorithm for HH that increases inspiratory humidity even in the case of high ambient temperature and implemented systematic monitoring of the heater plate temperature. There was no event related to under-humidification recognized after the implementation of safety measures such as restarting of air conditioning, activation of the compensation algorithm, and monitoring of heater plate temperature. With heater plate temperature  $> 62^\circ C$  with the HH used in this study, adequate inspiratory humidity seemed guaranteed. Of note, the automated compensation algorithm that was shown to partially improve the risk of under-humidification is available with the MR850 and the recent generation of HHs. Other humidifier companies (eg, Teleflex, Hamilton) propose humidifiers with specific settings to avoid under-humidification in nonoptimal situations such as high ambient temperature.

On the bench, we found a strong relationship between heater plate temperature and inspired absolute humidity. With heater plate temperature  $> 62^\circ C$ , delivered humidity  $> 30$  mg  $H_2O/L$  seemed guaranteed. The systematic monitoring of the heater plate temperature was implemented in the unit by respiratory therapists, allowing a specific focus on this issue. We believe that this is a valuable monitoring tool to detect and manage under-humidification in units at risk (ie, with high ambient temperature). Unfortunately, the monitoring of condensate at the Y-piece or at the humidification chamber, which informs that the gas is near 100% relative humidity,<sup>49</sup> is less helpful when ambient temperature is high.<sup>20</sup> Indeed, condensation occurs when a sufficient gradient exists between ambient

temperature and the temperature of the gas in the ventilator circuit.

It is important to note that excessive condensate may form in the circuit if the automated or manual humidity compensation functions are enabled, especially in the case of reduced ambient temperature or sudden change in minute ventilation. It is recommended to disable the compensation settings in this situation. However, there is limited risk of excessive heat with such devices as the temperature at the humidification chamber cannot exceed 40°C (with the automated compensation algorithm in the invasive mode). In addition, this mode is activated to compensate for under-humidification; and based on our measurements, the algorithm partially avoided under-humidification (depending on the tested condition, inspiratory humidity was 28–35 mg H<sub>2</sub>O/L), but there was no overheating or over-humidification. The risk of excessive humidification was described with gas at 43–45°C with 100% relative humidity (58 to 64 mg H<sub>2</sub>O/L of absolute humidity).<sup>50</sup>

Our study has certain limitations, notably a small sample size that could limit the generalizability of the results. In addition, the small size of the study sample did not allow definitive conclusions to be drawn on the various effects of humidification devices (impact of dead space and differences in hygrometric performance). Second, the additional dead space was mainly related to the HME itself, and only one type of HME was used. However, the HME used is one of the smallest effective HMEs on the market,<sup>46</sup> so the increase in dead space may be equal or worse with a larger HME or when the catheter mount is used. The severity of the patients may have been different in both groups, and alveolar dead space may explain in part the differences in minute ventilation, but this parameter was not measured in our study.

Even in this small study, we found a high number of ETOs, which highlighted the eminent risk of under-humidification if HH device is not use appropriately. Another limitation is that different centers used different humidification systems. This introduced potential confounding factors on different clinical practices between centers, limiting the comparison between both systems. However, the population studied was similar in the 2 centers, and those centers are in the same city and same affiliated university. Finally, subocclusions were not systematically recorded but are probably more frequent with clinically relevant complications. ETT subocclusions result in increased resistances of the tube,<sup>51</sup> increased work of breathing, potentially aggravating the lung injuries or to delayed weaning.<sup>52,53</sup>

### Conclusions

Our data suggest that the humidification strategy in patients with COVID-19 may have significant impact on

ventilatory efficiency and humidification performances. We also showed that the humidification strategy may have significant impact on risk of ETT obstruction in patients with COVID-19. Minimizing instrumental dead space with HH was associated with significantly increased alveolar ventilation leading to lower P<sub>a</sub>CO<sub>2</sub> despite lower minute ventilation. HH may lead to suboptimal humidification and unacceptable and life-threatening ETOs if ambient temperature is too high. Several safety measures may prevent these potentially serious events.

The ventilation efficiency related to instrumental dead space in addition to the humidification performances and circuit manipulations should be considered when deciding the humidification strategy in this specific population. It is consequently reasonable to use HH first line to avoid circuit changes, while monitoring heater plate temperature and activating humidity compensation algorithm when required to limit risk of potentially life-threatening ETO events.

### ACKNOWLEDGEMENTS

We want to thank Serge Simard MSc, senior biostatistician, for the analysis of the data. Dr Lellouche developed a free application (VentilO) to set the ventilator with protective ventilation and to optimize the settings. The application was funded by Fisher & Paykel.

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