Safety of Combined Heat and Moisture Exchanger Filters in Long-term Mechanical Ventilation*

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Study objective: To evaluate the safety of a combined heat and moisture exchanger filter (HMEF) for the conditioning of inspired gas in long-term mechanical ventilation (MV).

Design: Randomized controlled trial.

Setting: Medical ICU in a large teaching hospital.

Patients: One hundred fifteen consecutive patients who required ≥48 h of MV.

Interventions: Patients were randomized at intubation time (day 1) to receive inspired gas conditioned either by a water-bath humidifier heated at 32°C (HWBH) or by an HMEF (Hygroster; DAR; Mirandola, Italy).

Measurements and main results: The two study groups were comparable in terms of primary pathologic condition at the time of hospital admission, disease severity as measured by the Simplified Acute Physiology Score, and ICU mortality. They did not differ with respect to ventilator days per patient (mean±SD: HMEF, 7.6±6.5; HWBH, 7.8±5.8), incidence of endotracheal tube obstruction (HMEF, 0/59; HWBH, 1/56), and incidence of hypothermic episodes (HMEF, five; HWBH, two). In 41 patients receiving MV for ≥5 days, the morphologic integrity of respiratory epithelium was evaluated on day 1 and day 5, using a cytologic examination of tracheal aspirate smears. The state of ciliated epithelium was scored on a scale from 0 (poorest integrity) to 1,200 (maximum integrity), according to a well-described method. In both patient groups, the scores slightly but significantly decreased from day 1 to day 5 (mean±SD: HWBH, from 787±104 to 745±58; HMEF, from 913±79 to 739±62; p<0.01 for both groups); there were no statistically significant differences between groups.

Conclusions: These data indicate acceptable safety of HMEFs of the type used in the present study for long-term mechanical ventilation. (CHEST 1997; 111:686-91)

Key words: airway humidification; heat and moisture exchanger; intensive care; mechanical ventilation

Abbreviations: ETT=endotracheal tube; HMEF=heat and moisture exchanger filter; HWBH=heated water-bath humidifiers; SAPS=simplified acute physiology score

During mechanical ventilation with an endotracheal tube (ETT) in place, the air conditioning functions of the nose and upper airways are bypassed. To ensure adequate water content and temperature of the gas reaching the trachea, these functions must be taken over by an external device.1-3 For that purpose, it has been common for decades to use heated water-bath humidifiers (HWBH), which are external active sources of heat and water. A more recent solution is the combined heat and moisture exchanger filter (HMEF), which passively retains the heat and humidity, leaving the trachea during expiration, and recycles it during the next inspiration. HMEFs are designed to combine this air conditioning function with bacterial filtration. They have several possible advantages over HWBHs: ease of ventilatory circuit management, reduced cost,4-5 and avoidance of potential complications associated with HWBHs, such as airways burns6 and overhydration of the respiratory tract.5,7

However, while a properly set HWBH guarantees physiologic gas temperature and moisture at the tracheal level, this is not always true of HMEFs, the performances of which depend on a host of factors, including device type, external temperature, tidalvolume, and possible leaks around the ETT cuff.8,9 Therefore, when using HMEFs, inappropriate con-

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ditioning of the inspired gas may be a concern, especially in the case of long-term mechanical ventilation. Potential risks include hypothermia and shivering induced by respiratory heat loss,\textsuperscript{10} impaired mucociliary function,\textsuperscript{11} structural damage to the respiratory epithelium,\textsuperscript{12} and obstruction of Airways or ETT by thickened secretions.\textsuperscript{13-15}

Relatively few clinical data are available on the actual safety of HMEFs when employed for long-term mechanical ventilation. Some studies appear to substantiate the concerns expressed above,\textsuperscript{13-15} but were conducted using HMEFs made of purely hydrophobic material. Although highly effective as antibacterial filters, these are presently known to have less than ideal performances as heat and moisture exchangers.\textsuperscript{8,16-18} By contrast, the more recently marketed HMEFs, in which the air conditioning function is taken over by a hygroscopic membrane, are able to maintain the temperature and water content of inspired gas at levels closer to those achieved with an HWBH.\textsuperscript{8,16-18} To our knowledge, safety data relevant to the long-term use of these newer devices in mechanically ventilated patients are limited to the very recent and carefully designed work by Dreyfuss and associates;\textsuperscript{5} these authors recorded various clinical end points and found no adverse effect associated with the HMEF.

The present study had the following objectives: (1) to confirm the clinical safety of HMEFs for prolonged mechanical ventilation (ie, >48 h), and (2) to provide additional information regarding the integrity of tracheobronchial epithelium in such conditions.

**Materials and Methods**

**Study Design**

This study took place during an 18-month period in the medical ICU of a large teaching hospital. Advantage was taken of a recent institutional decision to introduce HMEFs into the daily practice of respiratory care in this ICU, so that approval by the local ethical committee was not sought. During the study period, each patient with an indication for mechanical ventilation was considered for inclusion at the time of intubation or at ICU admission if already intubated. Subjects who were hypothermic (central or rectal temperature <36°C), or who had been intubated for 12 h before ICU admission were excluded.

Eligible patients were randomized to inhale air conditioned with either an HWBH (HWBH group) or an HMEF (HMEF group). The same conditioning method was strictly maintained throughout the time while receiving mechanical ventilatory assistance, unless crossover from HMEF to HWBH was deemed necessary by the clinical staff. Crossover in the opposite direction was prohibited. Only patients who continued to receive ventilatory assistance for at least 48 h were retained for analysis.

**Respiratory Equipment and Care**

Intubation was performed via the orotracheal route, with tubes of 7.5 or 8 mm outer diameter. Three brands of ventilators were used: Servo 900e (Siemens-Elema; Solna, Sweden), MA-2 (Puritan-Bennett; Carlsbad, Calif), and Vedar (Hamilton Medical; Rüthis, Switzerland). In the HWBH group, the inspired air was water saturated to achieve a temperature of 32°C at the Y-connector of ventilator tubing, using a standard device (Fisher Paykel; Auckland, New Zealand, or Puritan-Bennett). In the HMEF group, unconditioned gas was passed through a recently marketed HMEF (Hygroster; DAR, Mirandola, Italy) inserted between the ETT and the Y-connector. The HMEF consisted of a hygroscopic membrane for heat and moisture exchange (cellulose, patient's side of the device), and of a hydrophobic pleated membrane for bacterial filtration (fiberglass, ventilator side). In critically ill ventilated patients, the average temperature and humidity outputs of this device were previously documented at 30 mg H₂O per liter of inspired air and 32°C, respectively.\textsuperscript{6} The advertised dead space added to the circuit by the HMEF we used (Hygroster) is 95 mL.

Ventilator tubings were changed every 48 h in the HWBH group, and at weekly intervals in the HMEF group. Respiratory therapy was performed by trained staff every 4 h or more if clinically indicated.

**Clinical Data Collection and End Points**

Demographic data, primary pathologic condition on admission, ICU mortality, the simplified acute physiology score (SAPS),\textsuperscript{19} and finally each of the following clinical end points were recorded: (1) days receiving mechanical ventilatory assistance; (2) days in the ICU; (3) airway obstruction by a mucous plug, as established by a bronchoscopy performed for clinical reasons; (4) HMEF obstruction (defined as the necessity to change the HMEF because of either an accumulation of thick secretions or an increase in inflation pressure not explained by a change in ventilator settings); (5) ETT obstruction (inability to pass down the ETT a suction catheter of outer diameter 4 mm); and (6) occurrence of hypothermia (two or more consecutive body temperature readings below 36°C).

**Cytologic Examination of Endotracheal Aspirate**

The integrity of tracheobronchial ciliated epithelium was evaluated from the cytologic examination of endotracheal aspirate obtained 30 s following the slow instillation of 10 mL isotonic saline solution into the ETT, as described by Chalon et al.\textsuperscript{20} Briefly, smears were immediately prepared and sprayed with a fixative (Merckofix; Merck; Dietikon, Switzerland), and later stained according to Papanicolaou. Throughout the study, microscopic examination was carried out by the same trained member of laboratory staff, who was blinded to the patient's group. Recognizable respiratory epithelial cells were graded for morphologic integrity on a six-point scale, one point being assigned for the normal appearance of each of the following characteristics: 1, cilia; 2, end plate; 3, color of cytoplasm; 4, cell shape and cytoplasm texture; 5, nuclear size; and 6, nuclear shape and texture. The grades of 200 epithelial cells were added to obtain a final score with a maximum possible value of 1,200 (indicating maximum cytologic integrity) and a minimal value of 0 (indicating maximum damage). In anesthetized patients undergoing surgery, the score calculated in this fashion is known to deteriorate markedly following a few hours of ventilation with dry air.\textsuperscript{20} Within the first 24 h following randomization (day 1), all patients included in the study had smears prepared from two separate
samples obtained at least 4 h apart. Smears were similarly obtained in duplicate on day 5 in all patients still intubated at that time. Cytologic evaluation was restricted to this latter subgroup.

**Data Analysis**

The clinical end points recorded in all patients who continued to receive mechanical ventilatory assistance for at least 48 h were compared between the two study groups, using a two-tailed Student's t test for independent samples or a χ² test, as appropriate. In the subgroup of subjects who continued to receive mechanical ventilatory assistance for at least 5 days, the cytologic scores were statistically evaluated with analysis of variance for repeated measures. All analyses were performed on an intention-to-treat basis, as usually recommended;²¹ ie, the patients who crossed over from an HMEF to an HWBH remained assigned to their original group. The alpha level of all tests was set at 0.05. Results are expressed as the mean±SD.

**RESULTS**

Two hundred thirty-seven consecutive patients were randomized; 115 continued to receive mechanical ventilatory assistance for at least 48 h, 59 in the HMEF group and 56 in the HWBH group.

The two groups were comparable in terms of gender ratio, primary abnormality, and severity of illness as determined from the SAPS score (Table 1, left). On the average, patients in the HWBH group were slightly older than those in the HMEF group (p<0.02). There were six crossovers from HMEF to HWBH, four motivated by the occurrence of moderate hypothermia and two by the need to minimize dead space (see below).

Sixty-three patients continued to receive mechanical ventilatory assistance for ≥5 days. In 41 of these, cytologic evaluation was possible on both day 1 and day 5 as detailed below. Within this latter subset, no patient crossed over from HMEF to HBWH, and there were, again, no statistical differences, but for age, between the two groups (Table 1, right).

**Clinical End Points**

In the 115 patients who continued to receive mechanical ventilatory assistance for ≥48 h the method of inspired air conditioning had no discernible effect on the chosen end points (Table 2). In particular, the use of an HMEF did not prolong the time spent receiving mechanical ventilatory assistance and was not associated with any obstruction of the ETT, while one occurred in the HWBH group.

There were two instances of HMEF obstruction. Both occurred on day 1, in one patient because of particularly sticky secretions, and in the other because the HMEF had been fortuitously installed backwards (by staff unfamiliar with the device, who used additional tubing for adaptation), leading to excessive water accumulation on the patient side of the device. On both occasions, the problem was detected promptly and did not recur following replacement of the HMEF.

Of the seven hypothermic episodes observed in the whole study, six (four in the HMEF and two in the HWBH group) were moderate (body temperature remaining above 35°C) and four (three in the HMEF and one in the HWBH group) were largely explained by a concomitant factor, either continuous venovenous hemodiafiltration or massive blood transfusion. In the HMEF group, the four moderate episodes were rapidly corrected upon crossing over to an HWBH temporarily heated above 32°C. The only severe episode (32°C) occurred in an HMEF patient during massive blood transfusion, but did not last more than a few hours; this particular patient fortuitously was not crossed over to an HWBH.

### Table 1—Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>HMEF * ≥48 h</th>
<th>HWBH</th>
<th>HMEF ≥5 d¹</th>
<th>HWBH</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>59</td>
<td>56</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Age, yr, mean±SD</td>
<td>52.6±15.3²</td>
<td>59.5±13.2</td>
<td>53.3±15.1¹</td>
<td>58.2±16.8</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>45/14</td>
<td>41/15</td>
<td>18/3</td>
<td>13/7</td>
</tr>
<tr>
<td>SAPS, mean±SD</td>
<td>12.9±5.1</td>
<td>12.8±5.0</td>
<td>12.4±4.8</td>
<td>14.2±5.9</td>
</tr>
<tr>
<td>Death in the ICU, No. (%)</td>
<td>17 (29)</td>
<td>19 (34)</td>
<td>9 (43)</td>
<td>8 (40)</td>
</tr>
<tr>
<td>Primary abnormality on hospital admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>17</td>
<td>22</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>23</td>
<td>23</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Neurologic</td>
<td>9</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Intoxication</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>9</td>
<td>4</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

*MV=mechanical ventilation.

¹And cytologic evaluation possible on both day 1 and day 5.

²p<0.02 compared with HWBH.
In two patients receiving controlled hypoventilation for severe ARDS, with tidal volumes between 400 and 500 mL, removal of the HMEF and the consequent reduction of external dead space induced a dramatic decrease in $\text{PaCO}_2$ (from 88 to 51 mm Hg in one instance, and from 125 to 83 mm Hg in the other).

Cytologic Examination of Endotracheal Aspirate

Sixty-three patients were receiving mechanical ventilation for $\geq 5$ days (33 in the HMEF group, and 30 in the HWBH group) (Fig 1). Smears were unreadable for lack of recognizable ciliated cells on either day 1 or day 5 in 22 patients (13 in the HMEF and nine in the HWBH group). In the remaining 41 patients (20 in the HMEF group, and 21 in the HWBH group), the scores slightly but significantly decreased from day 1 to day 5 (from $787\pm104$ to $745\pm88$ in the HWBH group and from $813\pm79$ to $739\pm62$ in the HMEF group; p<0.01 for both groups). There was no statistically significant difference between groups, in the absolute scores on day 1 or day 5 or in the amount of decrease from day 1 to day 5.

**Figure 1.** Time course of cytologic scores in patients who continued to receive mechanical ventilation for $\geq 5$ days and received inspired gas conditioned either by an HWBH (n=20) or by an HMEF (n=21). Data indicated as mean±SD. Asterisk=p<0.01 day 5 vs day 1. NS=not statistically significant.

### Table 2—Clinical Outcome*

<table>
<thead>
<tr>
<th></th>
<th>HMEF</th>
<th>HWBH</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>59</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Days in ICU</td>
<td>$11.1\pm7.7$</td>
<td>$13.8\pm13$</td>
<td>NS</td>
</tr>
<tr>
<td>Days of MV</td>
<td>$7.6\pm6.5$</td>
<td>$7.8\pm5.8$</td>
<td>NS</td>
</tr>
<tr>
<td>Tube obstruction</td>
<td>0</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>HMEF obstruction (%)</td>
<td>2 (0.3)</td>
<td>—</td>
<td>NS</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>5</td>
<td>2</td>
<td>NS</td>
</tr>
</tbody>
</table>

*MV=mechanical ventilation; NS=not significant.

**DISCUSSION**

The safety of heat and moisture exchangers for long-term use in mechanical ventilation has not been well defined. Concern is legitimate, considering that these devices may not condition inspired air quite as well as HWBHs do,\textsuperscript{18} and have indeed been associated with an increased incidence of ETT obstruction.\textsuperscript{13–15} One controlled trial of HMEF vs HWBH was even discontinued following one death related to this latter complication in one patient using an HMEF.\textsuperscript{14} A common denominator to all these studies was the use of purely hydrophobic devices, which in terms of heat and moisture transfer are clearly inferior to HMEFs equipped with a hygroscopic membrane.\textsuperscript{8,16–18} The latter reach a performance slightly below that of an HWBH heated at $32^\circ\text{C}$.\textsuperscript{18}

The clinical safety of HMEFs for long-term mechanical ventilation in the ICU has received little attention. Indeed, to our knowledge, there is only one relevant study. Dreyfuss and associates\textsuperscript{9} examined ICU patients who continued receiving mechanical ventilation for >48 h, using a design similar to ours and the same brand of HMEF. Clinical indicators of humidifying efficiency, such as the number of tracheal instillations per day and the number of patients developing atelectasis, were not influenced by the method of inspired gas conditioning. ETT obstruction was observed in only one of 61 patients who used an HMEF. Our study is entirely consistent with these results (Table 2).

Our cytologic data provide additional information on the adequacy of airway humidification achieved with an HMEF in long-term mechanical ventilation. The scoring method used herein has been able to detect morphologic damage to the airway epithelium after as little as 2 h of ventilation with dry gas.\textsuperscript{20} Subsequently,\textsuperscript{12} the same group studied anesthetized patients during approximately 4 h of preoperative ventilation and found clear decreases in cytologic scores when using dry (from 861 to 631; p<0.01) and 60% saturated gas at ambient temperature (from 845 to 757; p<0.01), but not when using fully saturated gas at $32^\circ\text{C}$ (from 880 to 873). In view of these data, it seems reasonable to assume that the damage inflicted on the airway epithelium by several days of exposure to inappropriately conditioned inspired gas would be detected by this method. On day 1, we obtained scores in agreement with the initial values reported in the study cited above. The modest but statistically significant decrease noted in both groups from day 1 to day 5 is probably related to the multiple aggressions inflicted on the lower airway mucosa of intubated patients, in particular tracheal suctioning. We cannot exclude some contribution of inadequate tracheal temperature and humidity to
this progressive reduction in cytologic scores. This is true even in the HWBH group, since there is no consensus in what constitutes optimal conditioning of inspired gas in these conditions. The similar time course of scores in both groups indicates that this contribution, if at all present, is not greater with an HMEF, than with an HWBH. The proportion of patients in whom scores were unavailable because of unreadable smears tended to be higher in the HMEF group, a potential source of bias. This appears not to be a serious concern, since the inability to recognize a sufficient number of epithelial cells was essentially encountered on day 1 in presence of heavily purulent secretions, an event highly likely to bear any relationship to the water content and temperature of inspired gas in the initial hours of mechanical ventilation. In conclusion, 5 days of mechanical ventilation with an HMEF were not associated with any additional damage to the tracheal epithelium beyond that already observed when using an HWBH in similar conditions.

Other features of interest concerning the safety of HMEFs for long-term use in the ICU should be mentioned briefly. Since even HMEFs generate inspired gas temperatures slightly below those obtained with an HWBH heated at 32°C, their use might theoretically favor the occurrence of hypothermia, as reported for purely hydrophobic devices. The study by Dreyfuss and associates provides no information on this point, which hardly seems a concern in view of our data: of the five hypothermic episodes recorded in the HMEF group (Table 2), all were transient, and in only one did body temperature drop below 35°C; in this latter instance, massive blood transfusion was the essential, if not the only, contributor.

The resistance of HMEs to airflow may progressively rise during use, occasionally to values in excess of 10 cm H₂O/L/s. The resulting increase in patient work of breathing may conceivably impede weaning from the ventilator. Although this undesirable effect is not excluded by the present data, it is noteworthy that patients in the HMEF group did not spend more time receiving mechanical ventilatory assistance than those in the HWBH group (Table 2). The same finding is reported in the study by Dreyfuss and associates.

Two final remarks are in order. First, the external dead space added by the HMEF (95 mL in the present study) may occasionally present a problem when using permissive hypercapnia, as happened in two patients of the present study, in whom removal of the device was associated with a marked decrease in PaCO₂. Last, although not addressed by the present study, antibacterial filters are not 100% efficient, at least in practical conditions; therefore, the presence of an HMEF in a ventilator circuit should not lead to relaxing the procedures to actively prevent cross-contamination by airborne pathogens.

In summary, this is the second randomized controlled trial providing information on the comparative safety of an HMEF equipped with a hygroscopic membrane vs the standard HWBH during long-term mechanical ventilation. In contrast with previous reports on purely hydrophobic devices, we confirm that the HMEF investigated in this and another study does not produce a higher incidence of ETT obstruction. We provide original data showing that with 5 days of consistent use, this passive method of heating and humidifying the inspired gas does not inflict morphologic damage to the tracheobronchial epithelium in excess of that already recognizable when using the standard active method. The HMEFs of the type used in the present study appear safe for long-term mechanical ventilation in the ICU.

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