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Efficacy of heat and moisture exchangers in preventing ventilator-associated pneumonia: meta-analysis of randomized controlled trials

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Abstract *Objective:* Several randomized controlled trials (RCT) have examined the effect of antibacterial humidification strategies, particularly the replacement of heated humidifiers (HH) by heat and moisture exchangers (HME), in preventing ventilator-associated pneumonia (VAP). The present meta-analysis reviews these RCTs. *Methods:* RCTs were identified by searching the Medline and Cochrane Central Register of Controlled Trials databases from 1990 to 2003. We included RCTs using HMEs in the treatment group and HHs in the control group and reporting the incidence of pneumonia as a study outcome. Two investigators independently abstracted key data on design, population, intervention and outcome of the studies. *Results:* Between 1990 and 2003 eight RCTs met the inclusion criteria of this analysis. Pooling the results from these studies revealed a reduction in the relative

risk of VAP in the HME group (0.7), particularly in MV with a duration of at least 7 days (five RCTs, relative risk 0.57). *Conclusions:* This meta-analysis found a significant reduction in the incidence of VAP in patients humidified with HMEs during MV, particularly in patients ventilated for 7 days or longer. This finding is limited by the exclusion of patients at high risk for airway occlusion from some of the studies. Moreover, contraindications (tenacious secretions, airway obstructive disease, hypothermia) and technical issues of HMEs must be considered. Further RCTs are necessary to examine the wider applicability of HMEs and their extended use.

Keywords Ventilation · Pneumonia · Infection · Humidification · Ventilator-associated pneumonia · Heat and moisture exchanger

Introduction

Nosocomial infections are a major problem in intensive care medicine. Ventilator-associated pneumonia (VAP) is the most important nosocomial infection in intensive care units, accounting for 9 cases/1000 ventilation-days or about 30,000 cases annually in Germany [1]. VAP, defined as pneumonia occurring 48 h after endotracheal intubation and initiation of mechanical ventilation (MV), leads to an attributable mortality rate of up to 30%, lengthening of hospital stay and increased costs [2]. Various causes lie behind the higher risk of pneu-

monia in ventilated patients: (a) During MV pathogens originating from the patients own oropharyngeal or gastrointestinal flora colonize the upper airways and can be aspirated or enter the lung by pooling and leakage of contaminated secretions around the endotracheal tube cuff. (b) Endotracheal intubation causes local trauma and bypasses the normal heat and moisture exchange of inspired gases, leading to inflammation, dry airway epithelia, and epithelial damage within 48 h. (c) MV with dried medical gases worsens the situation in relation to the degree of humidification and heating of inspired gas [3, 4, 5, 6]. Thus MV compromises the de-

fense mechanisms that usually protect the lung from infection.

Humidification of the inspired gas has been shown to prevent these complications. However, active humidification with heated-water humidifiers (HHs) may act as a source of infection by itself as it leads to condensate formation with often high levels of tubing colonization [3]. To decrease condensation and moisture accumulation passive humidifiers are used in place of conventional heated-water humidifiers. These devices collect heat and moisture from the patient's expirations and return it during inspiration. Therefore they are called heat and moisture exchangers (HME). Some HMEs are treated with hygroscopic salts to increase humidification capacity, some have additional bacterial filtering properties, and some combine these different characteristics.

With the exception of patients suffering from hemoptysis, tenacious secretions, increased airway resistance or hypothermia, HMEs are attractive alternatives to heated-water humidification systems because of their passive operation, their lower workload and their lower costs [7]. A number of studies have been undertaken to compare the efficacy of HMEs and conventional heated water humidification systems in terms of humidifying ventilation gases and preventing VAP. Until now there have been eight randomized controlled studies (RCTs) assessing the efficacy of HMEs in reducing bacterial growth and prevention of VAP as outcomes [8, 9, 10, 11, 12, 13, 14, 15]. Slightly lower VAP rates were observed in seven studies, and a significant difference was observed in one study [12], suggesting that HMEs are not only equal to heated water humidifiers but could even lower VAP rates. Recent improvements in the performance characteristics of HMEs prolong the time between HME changes up to 7 days [14], which additionally decreases the need of septic handling, workload and costs. Therefore we performed a meta-analysis to update the results of Cook et al. [16] with regard of effectiveness of HMEs in reducing infectious complications, and to provide some more evidence to this still unresolved question.

Methods

Study selection

A computerized Medline literature search of articles from 1990 to 2003 was performed using the key words "heat and moisture exchanger," "humidifier," and "pneumonia." Randomized studies were identified using the key words "controlled trial," "clinical trial," and "random." Truncation was used to identify a range of similar terms. The reference lists of the retrieved articles were reviewed for additional studies, as were review articles on the subject. An additional search using the key words "heat and moisture exchanger," "humidifier," and "pneumonia" was performed using the Cochrane Central Register of Controlled Trials. Inclusion criteria for the meta-analysis were the following: (a) RCTs using HMEs in the treatment group and heated water humidifiers in the control

group, (b) reporting of pneumonia definitions and of the incidence of pneumonia as a study outcome, and (c) published in article form. Each study was reviewed for sample size, patient population, randomization, type of HMEs used, use of HME or ventilator circuit exchange, VAP definitions, VAP incidence in treatment and control groups, efficacy rate of study and control humidifying device in the prevention of VAP and duration of MV. Due to the kind of ventilation device examined, blinding had to be left out of consideration. Data were extracted independently by two reviewers (A.K., T.E.) with a structured form and checked for accuracy by a third reviewer (P.G.). Differences were resolved by consensus.

Study characteristics

The initial Medline search yielded 197 articles. Use of the key words "controlled trial," "clinical trial," and "random" revealed 14 articles, 6 of which were RCTs comparing HMEs vs. HHs in respect to VAP as outcome [9, 10, 12, 13, 14, 15]. Reviewing of the reference lists of the retrieved studies and review articles [2, 3, 7, 17, 18, 19, 20, 21, 22] on the topic "VAP" there emerged another two studies [8, 11]. The additional search using the Cochrane Central Register of Controlled Trials revealed no further RCTs. Four of the studies were included in the previous systematic review by Cook et al. [8, 9, 10, 12]. One study [23] analyzed by Cook et al. [16] was excluded as VAP is not reported as an outcome in the article published by the authors of the study. Studies which examined the duration of HME use [24, 25, 26, 27], different kinds of HMEs [24, 28, 29], or the additional use of bacterial filters [30], only, were excluded from the analysis.

All selected studies report "randomly assigned" allocation as minimum requirement for inclusion, a detailed description of randomization procedures is given in three studies [11, 12, 14], only. Calculations of statistical power and sample sizes is given in four studies [12, 13, 14, 15]. In some of the studies, patients suffering from obstructive airway diseases [13], thick or bloody secretions [11, 13, 14] or hypothermia [11] were excluded a priori. Homogeneity between the study groups with respect to disease severity scores is stated in seven of the eight studies [9, 10, 11, 12, 13, 14, 15]. All included studies report homogeneity between the study groups with respect to age, gender, mean duration of MV, and indication for MV. In one study neurological diseases are the more common admission diagnoses in the HME group [15] (26% vs. 14.2% in the HH group, $p=0.032$).

HMEs and HHs are from different manufacturers. Frequency of HME and ventilator circuit changes range from daily [8, 9, 10, 11, 12, 13] to weekly [14] changes of HMEs and from changes every 48 h [8, 13] to no changes [10] of ventilator circuits. These and further characteristics such as study populations, cointerventions, general preventive measures, duration of MV, and disease severity scores are summarized in Table 1.

Data analysis

The outcomes were weighted by the inverse variance; 95% confidence intervals were presented. Heterogeneity tests were calculated for all analyses. As all tests of heterogeneity showed $p>0.1$, the fixed effect model was used to derive the summary estimate using Mantel-Haenzel methods as implemented in STATA 7. A correlation coefficient was calculated to evaluate the correlation between duration of MV and relative risk (RR).

Table 1 RCTs characteristics (*APACHE* Acute Physiology and Chronic Health Evaluation, *ETS* endotracheal secretion, *ICU* intensive care unit, *ISS* Injury Severity Score, *NR* not reported, *SAPS* Simplified Acute Physiology Score, *SUP* stress ulcer prophylaxis)

Source	Population	Intervention	Cointervention	General preventive measures	Exclusions after randomization	Duration of ventilation	Disease severity scores
Martin et al. [8]	ICU patients, ventilation >24 h	Daily change of HME (hygroscopic) vs. HH	Circuit changes every 48 h, water traps in both groups	Gloves, mask, cap; sterile suction tube, water and syringes; suctioning at nurse discretion (reevaluated twice daily); physiotherapy twice a day Suctioning every 2 h (“sterile technique”) after saline instillation	NR	9.7±10 d in HME group, 13.5±10 d in HH group	NR
Roustan et al. [9]	General ICU patients (≥35 kg)	Daily change of HME (hygroscopic) vs. HH	No circuit changes (daily decontamination), water traps in HH group only	Sterile irrigation water	NR	10.9±14.5 d in HME group, 8.2±11.9d in HH group	SAPS: 11.5±4.9 in HME group, 11.5±4.8 in HH group
Dreyfuss et al. [10]	Medical ICU patients, ventilation >48 h	Daily change of HME (hygroscopic) vs. HH	No circuit changes, water traps in HH group emptied at least every 4 h		17 patients in HME group and 16 in HH group due to ventilation <72 h, all patients developing pneumonia within first 48 h	10±8.6 d in HME group, 12.5±14.2 d in HH group	SAPS: 16±4.9 in HME group, 16.4±5.3 in HH group
Branson et al. [11]	Medical and surgical ICU patients, ventilation >24 h	Daily change of HME (hygroscopic) vs. HH	Weekly circuit changes	Suctioning when needed: open system, single use-catheters, sterile technique	group ventilated >5 days or developing thick ETS	4.5±3.9 d in HME group, 4.1±3.2 d in HH group	SAPS: 9±3 in HME group, 8±4 in HH group
Kirton et al. [12]	Trauma ICU patients	Daily change of HME (hygroscopic) vs. HH	Weekly circuit changes	Closed system suction catheters changed every 3 d, same nutrition protocol and SUP	6 patients in HME group developing contraindications for HME use	20.4±15.3 d in HME group, 16.3±13.7 d in HH group	ISS: 22±10 in HME group, 20±10 in HH group
Boots et al. [13]	General ICU patients, ventilation >48 h	Daily change of HME (combined) with (a) circuit changes every 48 h or (b) every 96 h vs. HH with circuit changes every 48 h	See left	Suctioning at nurse discretion, gloved hands, saline instillation for physiotherapy only	Patients ventilated <48 h	(a) 5.2 (2–58.5) d and (b) 7.6 d (4–40) in HME groups, 6.3 d (2–37.3) in HH group	APACHE II: 19±2 in (a)+(b) HME groups, 18±2 in HH group
Kollef et al. [14]	Medical and surgical ICU patients (≥17 ys.)	Weekly change of HME (hygroscopic) vs. HH	No circuit changes, water traps in both groups (for significant condensate formation only)	Respiratory therapists examination every 2 h, suctioning at least every 8 h	9 patients who were enrolled twice, 3 patients who were already ventilated on admission	4.67±5.8 d in HME group, 3.7±4.1 d in HH group, switching from HME to HH after 7 days	APACHE II: 17±6.9 in HME group, 18.2±6.3 in HH group
Memish et al. [15]	Medical and surgical ICU patients (adult)	HME (hygroscopic) vs. HH	NR	NR	Patients ventilated <48 h, patients discontinuing HME	8.5±10.5 d in HME group, 10.1±9.3 d in HH group	APACHE II: 20.8±9.4 in HME group, 20.6±8.1 in HH group

Results

Incidence of VAP

The number of patients, pneumonia definitions, pneumonia rates, RRs and 95% CIs of the RCTs included in this meta-analysis are given in Table 2. Taken together there were 693 patients in the intervention groups and 675 patients in the control groups of the eight trials. Pooling the results from these eight RCTs reveals a significant reduction in the RR of VAP in the HME group (0.69, CI 95% 0.51–0.94; Fig. 1). The value obtained from an overall test of homogeneity ($\chi^2=5.86$, d.f.=7, $p=0.56$) shows no evidence of heterogeneity. Two subanalyses were performed. Subanalysis A examined the effect of the duration of MV on pneumonia rates: In RCTs with a MV duration of 7 days or longer [8, 9, 10, 12, 15] the RR was 0.57 (CI 95% 0.38–0.83; Fig. 1B). In those with a MV duration of less than 7 days [11, 13, 14] the RR was 0.99 (CI 95% 0.59–1.62). The correlation between duration of MV and RR is confirmed by the correlation coefficient of -0.83 (CI 95% -0.97 to -0.31). Due to the different pneumonia definitions used in these RCTs subanalysis B examined the effect of microbiologically confirmed diagnosis of VAP on pneumonia rates. In RCTs with clinical diagnosis of VAP [9, 12, 14, 15] the RR was 0.64 (CI 95% 0.44–0.92), while in those using a microbiologically

confirmed diagnosis of pneumonia [8, 10, 11, 13] the RR was 0.83 (CI 95% 0.49–1.42).

Discussion

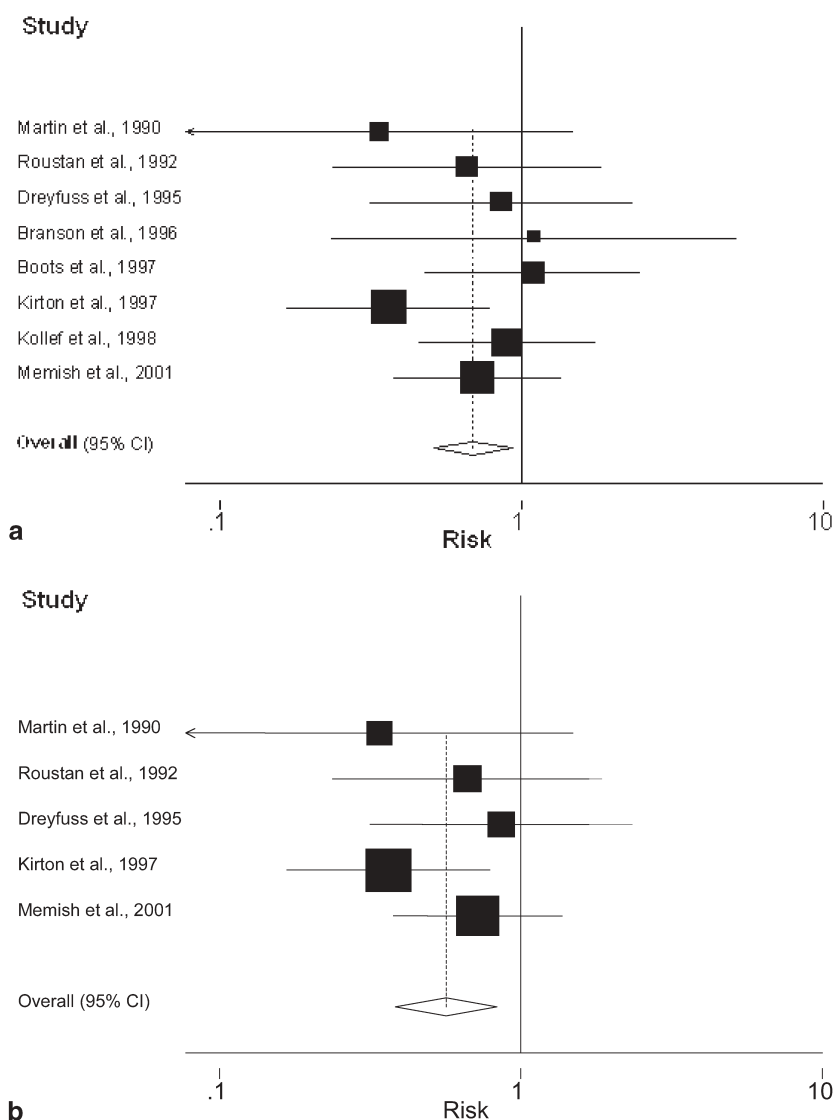
Pneumonia occurs at a rate of 1–3% per day of MV and thus is the most common nosocomial infection among ICU patients [31]. A multitude of studies have therefore been performed to investigate different prevention strategies, leading to guidelines published by the American Thoracic Society [32] and those of the Centers for Disease Control [6]. Even in the latest update, however, of the “Guidelines for preventing health-care-associated pneumonia” of the Centers for Disease Control and the Healthcare Infection Control Practices Advisory Committee in 2003 includes practices for which no recommendations are given, as sufficient evidence or consensus about efficacy is lacking.

The question whether HMEs are efficient in reducing the incidence of VAP is such an unresolved issue. In 1998 Cook et al. [16] performed a systematic review to compare the effect of different airway management strategies on VAP rates. They reviewed five trials comparing HMEs vs. HHs with respect to the incidence of VAP [8, 9, 10, 12]. Despite the fact that only one study reported a significant result and appropriate sample size [12], they concluded that the use of HMEs is associated with lower

Table 2 Incidence of VAP (CFU colony forming units, CXR: chest radiography ETS endotracheal secretion, PSB protected specimen brush, T temperature, WBC white blood cell count)

Source	Number of patients		Pneumonia rates		Pneumonia definition	RR (95% CI)
	Intervention group	Control group	Intervention group	Control group		
Martin et al. [8]	31	42	6% (2)	19% (8)	Suggestive CXR film and purulent sputum and ETS potential pathogen	0.34 (0.08–1.49)
Roustan et al. [9]	51	61	10% (5)	15% (9)	New or progressive infiltrate and fever and leukocytosis and purulent ETS	0.66 (0.24–1.86)
Dreyfuss et al. [10]	61	70	10% (6)	11 (8)	New and persistent infiltrate and purulent ETS and positive PSB culture $>10^3$ cfu/ml or same organism found in blood culture and ETS without other infection	0.86 (0.32–2.34)
Branson et al. [11]	49	54	6% (3)	6% (3)	Purulent sputum and ETS potential pathogen and $T>38^\circ\text{C}$ and new infiltrate	1.1 (0.23–5.21)
Kirton et al. [12]	140	140	6% (8)	16% (22)	New or progressive infiltrate and change in sputum purulence or positive ETS culture >72 h after intubation	0.36 (0.17–0.79)
Boots et al. [13]	75	41	19% (14)	17% (7)	New infiltrate and $T>39^\circ\text{C}$ or $<36^\circ\text{C}$ and $\text{WBC} <4 \times 10^9/\text{l}$ or $>11 \times 10^9/\text{l}$ and ETS cultures positive for potential pathogen and increased sputum production/purulent sputum, occurring after 48 h of ventilation	1.09 (0.48–2.49)
Kollef et al. [14]	163	147	9% (15)	10% (15)	New or progressive infiltrate and two of the following: $T>38.3^\circ\text{C}$; $\text{WBC} >10 \times 10^9/\text{l}$; purulent ETS	0.90 (0.46–1.78)
Memish et al. [15]	123	120	11% (14)	16% (19)	CDC criteria and one of the following: purulent sputum; positive blood culture; positive ETS culture; positive antibody titer; histopathological evidence	0.72 (0.38–1.37)

Fig. 1 a Analysis of VAP in all RCTs comparing HHs with HMEs. **b** Analysis of VAP in RCTs comparing HHs with HMEs over 7 days or more of MV. *Diamond* Summary relative risk and 95% confidence interval. *Size of squares* is inversely proportional to the variance of the studies



VAP rates. More recently a systematic review has tried to identify the most effective method of humidification in ventilated ICU patients with regard to the incidences of tracheal tube occlusion and VAP [17]. Only two prospective randomized trials met the rather restrictive inclusion criteria [12, 14], mostly due to unclear randomization procedures and missing power calculations, a limitation recognized by the author. Therefore no data synthesis was performed, but both included supported HME as reducing the incidence of VAP.

The present meta-analysis included the RCTs analyzed by Cook et al. plus two subsequently published RCTs on the effect of HMEs on the development of pneumonia [14, 15] and two further RCTs [11, 13] not included by Cook et al. All of the studies included here used pneumonia definitions comparable to the CDC definition of nosocomial pneumonia. Despite the differences in hu-

midification systems the included studies reported no differences in general preventive measures and airway management between the study groups. All included studies reported homogeneity between the study groups with respect to age, gender, mean duration of MV, and indication for MV. Homogeneity between the study groups with respect to disease severity scores is noted in seven of the eight studies [9, 10, 11, 12, 13, 14, 15].

The summary result from these eight studies indicates a significant reduction in the RR of VAP in the HME group (0.7, CI 95% 0.5–0.94), which is even more pronounced in a subanalysis including the five studies with a duration of at least 7 days of MV [8, 9, 10, 12, 15] (0.57, CI 95% 0.38–0.83). Both results are due mainly to the study by Kirton et al. [12] (RR 0.41, 95% CI 0.2–0.86), which also noted the longest duration of MV (20.4±15.3 days in HME group, 16.3±13.7 days in HH group).

It is usual to distinguish early-onset VAP, which occurs during the first 4 days of MV, from late-onset VAP, which develops after 5 or more days of MV [3], each accounting for 50% of cases [18]. In general, risk factors are the same. Patient-related risk factors are increased age, chronic lung disease, acute respiratory distress syndrome, polytrauma, burns, and neurosurgery. Risk factors related to airway management are duration of ventilation, reintubation, frequent circuit changes, low intracuff pressure, and tracheostomy. Other risk factors are enteral nutrition, supine positioning, histamine 2 receptor antagonists, and aspiration [18, 33]. In addition to duration of MV, the main differences between early- and late-onset VAP are a poorer prognosis in late-onset VAP and different causative micro-organisms: Early-onset VAP is mostly due to the common respiratory tract or oropharyngeal flora and methicillin-susceptible *Staphylococcus aureus* whereas late-onset VAP is often due to multiresistant organisms such as methicillin-resistant *S. aureus* or aerobic Gram-negative bacteria such as *Pseudomonas aeruginosa* [3, 18], the latter originating in 50% from endogenous sources and in 50% from cross contamination [34].

Only four of the studies included in this meta-analysis used microbiologically confirmed diagnosis of VAP [8, 10, 11, 13], only two of which reported the causative organisms for VAP [10, 15]. Although the exact pathogenesis of VAP remains unclear in most of the RCTs included in the present analysis, this is no major limitation. The higher incidence of VAP in RCTs using microbiologically confirmed diagnosis is not significant; the lower incidence of VAP in RCTs relying on clinical diagnosis is affected by the statistical weight of these studies [12, 14, 15].

Circuit colonization was examined in three of the included RCTs [8, 10, 13], all of which reporting a significant reduction in colonization in the HME group. Therefore the significant benefit of HMEs revealed by this analysis could be explained by minimizing the need for septic manipulations of the airway/circuit as well as by minimizing circuit condensate. Ventilator circuits are rapidly colonized with bacteria, and the condensate within these circuits can have very high bacterial counts [20]. Aspiration of circuit condensate may play a role in the development of VAP [10], in particular in long-term ventilated patients.

The aim of the present meta-analysis was to examine the efficacy of HMEs in preventing VAP; therefore other aspects of the use of these devices such as dead space, resistive load, and potential for airway occlusion were not considered. Indeed, trials using earlier models of HMEs [8, 9] reported an increased incidence of airway occlusion, which caused some of the authors [11, 13, 14] to exclude patients at high risk for airway occlusion, for example, asthma and hemoptysis, from the studies. In contrast, trials using HMEs with enhanced intrinsic hu-

midifying performance resulted in no difference in the incidence of airway occlusion [12, 28]. Moreover, the use of HMEs in combination with a “booster,” a new device improving the heat and water preservation of ventilatory gases, has been reported [35].

However, since only few RCTs have investigated the effect of newer HMEs on airway occlusion, these must be used with caution in patients with copious or thick secretions, poor respiratory muscle reserve, or severe airway obstructive disease [22]. In addition, they should be removed and replaced by HHs in patients with acute respiratory distress syndrome [36]. The use of HMEs may decrease not only the incidence of VAP in patients eligible for these devices but also the associated workload and costs. Branson et al. [37] calculated that the use of an HME instead of an HH would result in cost savings of US \$15.80/day. Kollef et al. [14] examined an extended-use of HMEs for up to 7 days and observed no significant differences for hospital mortality, duration of MV, or length of stay in the hospital or the ICU compared to humidification via an HH. Due to the longer changing intervals they calculated cost savings of \$41.441/year at their hospital. Their results are limited by a mean duration of ventilation of 4.2 days in the intervention group; therefore only 21 of 147 HMEs were used for the whole of the 7 days. Interestingly, there are further studies describing the extended use of HMEs without complications [24, 25, 26, 27], thereby supporting the results of Kollef et al.

Conclusion

Taken together the findings of the present meta-analysis reveal a significant reduction in the incidence of VAP in patients humidified with HMEs during MV, particularly among patients ventilated for at least 7 days. The applicability of this finding is limited by the a priori exclusion of patients at high risk for airway occlusion from some of the studies, by the different cointerventions performed, and by the different brands of HMEs used in the trials. To overcome these limitations further RCTs are necessary. To evaluate the wider applicability of the newer HMEs, their combination with new devices such as boosters [35], and their extended use these studies require: (a) adequate pneumonia definitions, for example, the Centers for Disease Control definition for nosocomial pneumonia, and (b) appropriate sample size and power calculations. For example, given an incidence of VAP of 8% in the control group, as observed by Davis et al. [24], 1,400 patients in the both of intervention and control group would be needed to demonstrate a 30% decrease in VAP rates (at a 95% confidence limit and a statistical power of 80%). This is laborious, but it will improve the evidence of airway management strategies in critically ill patients.

References

1. Gastmeier P, Geffers C, Sohr D, Dettenkofer M, Daschner F, Ruden H (2003) Five years working with the German nosocomial infection surveillance system (Krankenhaus Infektions Surveillance System). *Am J Infect Control* 31:316
2. Kollef MH (1999) The prevention of ventilator-associated pneumonia. *N Engl J Med* 340:627
3. Chastre J, Fagon JY (2002) Ventilator-associated pneumonia. *Am J Respir Crit Care Med* 165:867
4. Craven DE, Steger KA (1995) Epidemiology of nosocomial pneumonia. New perspectives on an old disease. *Chest* 108:1S
5. Branson RD (1998) The effects of inadequate humidity. *Respir Care Clin N Am* 4:199
6. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R (2004) Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep* 53:1
7. Branson RD, Campbell RS (1998) Humidification in the intensive care unit. *Respir Care Clin N Am* 4:305
8. Martin C, Perrin G, Gevaudan MJ, Saux P, Gouin F (1990) Heat and moisture exchangers and vaporizing humidifiers in the intensive care unit. *Chest* 97:144
9. Roustan JP, Kienlen J, Aubas P, Aubas S, du Cailar J (1992) Comparison of hydrophobic heat and moisture exchangers with heated humidifier during prolonged mechanical ventilation. *Intensive Care Med* 18:97
10. Dreyfuss D, Djedaini K, Gros I, Mier L, Le Bourdelles G, Cohen Y, Estagnasie P, Coste F, Boussougant Y (1995) Mechanical ventilation with heated humidifiers or heat and moisture exchangers: effects on patient colonization and incidence of nosocomial pneumonia. *Am J Respir Crit Care Med* 151:986
11. Branson RD, Davis K Jr, Brown R, Rashkin M (1996) Comparison of three humidification techniques during mechanical ventilation: patient selection, cost, and infection considerations. *Respir Care* 41:809
12. Kirton OC, DeHaven B, Morgan J, Morejon O, Civetta J (1997) A prospective, randomized comparison of an in-line heat moisture exchange filter and heated wire humidifiers: rates of ventilator-associated early-onset (community-acquired) or late-onset (hospital-acquired) pneumonia and incidence of endotracheal tube occlusion. *Chest* 112:1055
13. Boots RJ, Howe S, George N, Harris FM, Faoagali J (1997) Clinical utility of hygroscopic heat and moisture exchangers in intensive care patients. *Crit Care Med* 25:1707
14. Kollef MH, Shapiro SD, Boyd V, Silver P, Von Harz B, Trovillion E, Prentice D (1998) A randomized clinical trial comparing an extended-use hygroscopic condenser humidifier with heated-water humidification in mechanically ventilated patients. *Chest* 113:759
15. Memish ZA, Oni GA, Djazmati W, Cunningham G, Mah MW (2001) A randomized clinical trial to compare the effects of a heat and moisture exchanger with a heated humidifying system on the occurrence rate of ventilator-associated pneumonia. *Am J Infect Control* 29:301
16. Cook D, De Jonghe B, Brochard L, Brun-Buisson C (1998) Influence of airway management on ventilator-associated pneumonia: evidence from randomized trials. *JAMA* 279:781
17. Bench S (2003) Humidification in the long-term ventilated patient; a systematic review. *Intensive Crit Care Nurs* 19:75
18. Cook D (2000) Ventilator associated pneumonia. *Intensive Care Med* 26:31
19. Hess D (2002) Infection control in the intensive care unit. The role of the ventilator circuit. *Minerva Anesthesiol* 68:356
20. Bowton DL (1999) Nosocomial pneumonia in the ICU-year 2000 and beyond. *Chest* 115:28S
21. Richards G (1998) The role of filtration during humidification. *Respir Care Clin N Am* 4:329
22. Littlewood K, Durbin CG Jr (2001) Evidenced-based airway management. *Respir Care* 46:1392
23. Hurni JM, Feihl F, Lazor R, Leuenberger P, Perret C (1997) Safety of combined heat and moisture exchanger filters in long-term mechanical ventilation. *Chest* 111:686
24. Davis K Jr, Evans SL, Campbell RS, Johannigman JA, Luchette FA, Porembka DT, Branson RD (2000) Prolonged use of heat and moisture exchangers does not affect device efficiency or frequency rate of nosocomial pneumonia. *Crit Care Med* 28:1412
25. Thomachot L, Leone M, Razzouk K, Antonini F, Vialet R, Martin C (2002) Randomized clinical trial of extended use of a hydrophobic condenser humidifier: 1 vs. 7 days. *Crit Care Med* 30:232
26. Thomachot L, Boisson C, Arnaud S, Michelet P, Cambon S, Martin C (2000) Changing heat and moisture exchangers after 96 hours rather than after 24 hours: a clinical and microbiological evaluation. *Crit Care Med* 28:714
27. 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
28. Thomachot L, Viviani X, Arnaud S, Boisson C, Martin CD (1998) Comparing two heat and moisture exchangers, one hydrophobic and one hygroscopic, on humidifying efficacy and the rate of nosocomial pneumonia. *Chest* 114:1383
29. Thomachot L, Vialet R, Arnaud S, Barberon B, Michel-Nguyen A, Martin C (1999) Do the components of heat and moisture exchanger filters affect their humidifying efficacy and the incidence of nosocomial pneumonia? *Crit Care Med* 27:923
30. Lorente L, Lecuona M, Malaga J, Revert C, Mora ML, Sierra A (2003) Bacterial filters in respiratory circuits: an unnecessary cost? *Crit Care Med* 31:2126
31. Ibrahim EH, Ward S, Sherman G, Kollef MH (2000) A comparative analysis of patients with early-onset vs late-onset nosocomial pneumonia in the ICU setting. *Chest* 117:1434
32. American Thoracic Society (1996) Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies. *Am J Respir Crit Care Med* 153:1711
33. Vincent JL, Lobo S, Struelens M (2001) Ventilator associated pneumonia: risk factors and preventive measures. *J Chemother* 13 [Spec no 1]:211
34. Bertrand X, Thouverez M, Talon D, Boillot A, Capellier G, Floriot C, Helias JP (2001) Endemicity, molecular diversity and colonisation routes of *Pseudomonas aeruginosa* in intensive care units. *Intensive Care Med* 27:1263
35. Thomachot L, Viviani X, Boyadjiev I, Vialet R, Martin C (2002) The combination of a heat and moisture exchanger and a Booster: a clinical and bacteriological evaluation over 96 h. *Intensive Care Med* 28:147
36. Prin S, Chergui K, Augarde R, Page B, Jardin F, Vieillard-Baron A (2002) Ability and safety of a heated humidifier to control hypercapnic acidosis in severe ARDS. *Intensive Care Med* 28:1756
37. Branson RD, Davis K Jr, Campbell RS, Johnson DJ, Porembka DT (1993) Humidification in the intensive care unit. Prospective study of a new protocol utilizing heated humidification and a hygroscopic condenser humidifier. *Chest* 104:1800