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Effect of heat and moisture exchangers on the prevention of ventilator-associated pneumonia in critically ill patients

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Abstract

Ventilator-associated pneumonia (VAP) remains one of the major causes of infection in the intensive care unit (ICU) and is associated with the length of hospital stay, duration of mechanical ventilation, and use of broad-spectrum antibiotics. We compared the frequency of VAP 10 months prior to (pre-intervention group) and 13 months after (post-intervention group) initiation of the use of a heat and moisture exchanger (HME) filter. This is a study with prospective before-and-after design performed in the ICU in a tertiary university hospital. Three hundred and fourteen patients were admitted to the ICU under mechanical ventilation, 168 of whom were included in group HH (heated humidifier) and 146 in group HME. The frequency of VAP per 1000 ventilator-days was similar for both the HH and HME groups (18.7 *vs* 17.4, respectively; P = 0.97). Duration of mechanical ventilation (11 *vs* 12 days, respectively; P = 0.48) and length of ICU stay (11 *vs* 12 days, respectively; P = 0.39) did not differ between the HH and HME groups. The chance of developing VAP was higher in patients with a longer ICU stay and longer duration of mechanical ventilation. This finding was similar when adjusted for the use of HME. The use of HME in intensive care did not reduce the incidence of VAP, the duration of mechanical ventilation, or the length of stay in the ICU in the study population.

Key words: Heat and moisture exchanger; Ventilator-associated pneumonia; Quality improvement; Nosocomial infection; Critically ill patients

Introduction

Hospital-acquired pneumonia remains as one of the main causes of infection in the intensive care unit (ICU) (1,2) and is associated with the length of hospital stay (1,3), duration of mechanical ventilation, and use of broad-spectrum antibiotics. This condition results in increased hospital costs (1,2,4-6) and patient mortality (3,6). This type of pneumonia occurs more frequently in patients who have been on mechanical ventilation for more than 48 h, characterizing the ventilator-associated pneumonia (VAP). The mortality due to VAP varies between 24 and 50%, reaching 76% in high-risk situations (7). Diagnosis is based on the appearance of a new or progressive pulmonary infiltrate accompanied by fever, leukocytosis, and purulent sputum (8).

The natural mechanisms of inspired air humidification and heating are suppressed during mechanical ventilation. Induced air heating and humidification can be achieved actively by using heated humidifiers (HH), or passively, by means of heat and moisture exchangers (HME). Aspiration of the condensed water that is formed in the ventilator circuit as a consequence of air heating and humidification is one of the causes of VAP. The bacteria colonizing the patients themselves can proliferate in the condensate and return to the airways and lungs by inhalation of this contaminated material. Therefore, it is possible that the use of HME could contribute to preventing the onset of VAP with a positive impact on the reduction of the incidence of VAP. Various

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controlled and randomized clinical studies have compared HME and HH with respect to the occurrence of VAP (9-12). However, data on their real benefit regarding VAP prevention remain inconclusive.

Data collected in our institution (1999-2009) have revealed an incidence of VAP per 1000 ventilator-days of 18.7 (Menegueti MG, Bellissimo-Rodrigues F, unpublished data). This high incidence has prompted the search for a type of intervention that could improve control of this infection. In this context, the aim of this study was to evaluate the impact of HME on the likelihood of critically ill patients developing VAP. The duration of mechanical ventilation, length of ICU stay, occurrence of adverse events, and overall mortality in the ICU were also investigated.

Material and Methods

This was a prospective study performed in the ICU of a tertiary care hospital associated with a public medical school and university. It is a 9-bed adult ICU that delivers intensive care to highly complex medical and surgical patients. All the patients admitted to the ICU with an expected length of stay greater than 48 h were considered eligible for the study. The present study was approved by the Research Ethics Committee of Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (Protocol No. 7076/2010). Written informed consent was obtained from all patients or from an appropriate surrogate when the patient was unable to provide the consent. This investigation consisted of a before-and-after study comparing the chance of acquiring VAP 10 months prior to (pre-intervention group) and 13 months (post-intervention group) after initiation of the use of an HME filter.

Study population

The study was conducted on 314 patients admitted to the ICU under mechanical ventilation, 168 of whom were included in group HH and 146 in group HME. Demographic and clinical data were collected from the medical records and physical examination of the patients. Organ dysfunction was assessed by Acute Physiology and Chronic Health Evaluation (APACHE) II score (13). All patients aged >18 years submitted to mechanical ventilation and admitted to the ICU between January 2009 and November 2010 were invited for inclusion in the study and were examined on a daily basis.

The HME hygroscopic filter device (Humid Vent® Filter Compact, Gibeck, Germany) was used for all the patients undergoing mechanical ventilation and admitted to the ICU, provided that there was no contraindication. The device was changed every 24 h according to manufacturer recommendations and the hospital guidelines for infection control. Patients were excluded from the study if they presented abundant thick secretion with or without blood, pulmonary hyperinflation, bulky bronchopleural fistula, body temperature lower than 32°C, minute volume >10 L/min, low respiratory muscle reserve, or significant impairment of the respiratory mechanics due to severe obstruction of the airways or acute respiratory distress syndrome and bronchospasm.

The HH was an MR410 Respiratory Humidifier (Fisher & Paykel Healthcare Ltd., New Zealand). The ventilators consisted of microprocessed equipment (Savina or Evita XL, Drägermedical, USA, or Bird 8400, Tri-Bird Prod. Co., USA) operating in the mode consistent with the patient's underlying disease.

Identical measures for VAP prevention were established for both patient groups: no routine change of ventilator circuits, a semirecumbent body position, continuous enteral nutrition, oral wash with 2% clorhexidine (14,15), respiratory physiotherapy, no verification of residual gastric volume, and no aspiration of subglottic secretions.

Daily visits were performed by the ICU staff accompanied by a member of the local committee for hospital infection control, with the purpose of establishing the VAP diagnosis and searching for any adverse events caused by hypercapnia and/or endotracheal tube obstruction by secretion. These procedures applied for VAP prevention as well as the antibiotics policy were under the responsibility of the same ICU staff and the hospital infection control members for both groups of patients. The diagnosis of pneumonia was based on the criteria of the Centers for Disease Control and Prevention (16). Pneumonia was considered to be VAP when it was diagnosed after 48 h of mechanical ventilation. Based on the time of onset of pneumonia, VAP can be further categorized into early (occurring within the first 4 days of mechanical ventilation) and late (occurring after day 4). Etiologically, late VAP is more frequently due to multidrug-resistant pathogens and has a poorer prognosis than early VAP. In general, risk factors are the same (9).

The primary end point was to compare the VAP rate between the two groups. Secondary outcomes included duration of mechanical ventilation, length of ICU stay, occurrence of adverse events, and ICU overall mortality.

Statistical analysis

From 1999 to 2009, the VAP rate at the study ICU was 18.7 episodes per 1000 ventilator-days (Menegueti MG, Belissimo-Rodrigues F, unpublished data). In order to achieve the sufficient power to detect a 60% reduction in VAP incidence, with $\alpha = 5\%$ and $\beta = 20\%$, the calculated sample size was 125 patients in each group. Considering the possible patient's drop out during the study, the sample size was increased to 168 in the HH group and to 146 in the HME group. Statistical analyses were performed using the SAS 9.2 program (SAS Institute Inc., SAS/STAT® User's Guide, Version 9.2, USA: SAS Institute Inc., 2008). Data are reported as median and range and were compared by the Mann-Whitney U-test. A P value lower than 0.05 was considered to be significant. A *post hoc* subgroup analysis

was conducted by adjusting multiple logistic regression models with VAP as the dependent variable and age, gender, comorbidities, length of ICU stay, and duration of mechanical ventilation as independent variables.

Results

Of the 325 patients initially included, 11 (3.4%) were ultimately excluded because the study protocol was not followed correctly (5 patients in the HH group and 6 in the HME group).

Overall, 314 patients participated in this investigation. They were divided into two groups, namely group HH (N = 168), which included patients that utilized HH, and group HME (N = 146), which consisted of patients that used HME.

Analysis of the clinical characteristics of the patients revealed that both groups had similar distribution in terms of age, gender, comorbidity, medical conditions that led to ICU admission, and APACHE II score, as summarized in Table 1. Respiratory failure, risk factors for developing VAP, and circulatory shock were also similar for the two groups.

During the study, 56 VAP events were diagnosed, 29 in the HH group (15 early VAP events) and 27 in the HME group (18 early VAP events). There were no reductions in VAP rates when groups HH and HME were compared. Moreover, the incidence of VAP per 1000 ventilator-days was similar in the HH and HME groups (18.7 *vs* 17.4; P = 0.97). There were no significant reductions in the incidence of VAP (either early or late VAP episodes) in the patients included in the HME group.

Most VAP episodes diagnosed [(43/56 (77%)] were confirmed microbiologically, including 21 episodes in the HH group and 23 in the HME group. The microorganisms isolated are listed in Table 2.

Table 1. Demographic and clinical characteristics of the patients in the HH and HME groups.

	HH group (N = 168)	HME group (N = 146)
Characteristics		
Gender (female)	73 (43%)	65 (44%)
Age (mean and range in years)	56 (15-89)	52 (17-87)
APACHE II score (mean and range)	26 (10-47)	27 (10-48)
Death risk (mean and range in %)	56 (6-98)	58 (4-98)
Comorbidity		
Diabetes mellitus	21 (12%)	22 (15%)
Renal failure	35 (21%)	47 (32%)
Coronary disease	34 (20%)	16 (11%)
COPD	15 (9%)	3 (2%)
Infectious diseases	88 (52%)	75 (51%)
Hypertension	52 (31%)	38 (26%)
Malignancy	48 (28%)	34 (23%)
Reason for ICU admission		
Respiratory failure	37 (22%)	25 (17%)
Liver transplantation	9 (5%)	10 (7%)
Major surgery, postoperative	10 (6%)	4 (3%)
Shock	67 (40%)	61 (42%)
Severe sepsis	10 (6%)	18 (12%)
Cardiac arrest	17 (10%)	12 (8%)
Others	18 (11%)	16 (11%)
Risk factor during ICU stay		
Tracheostomy	59 (35%)	59 (40%)
Inhibitors of gastric acid secretion	67 (40%)	61 (42%)

Data are reported as number of patients with percent in parentheses or as otherwise stated. HH = heated humidifier group; HME = heat and moisture exchanger group; COPD = chronic obstructive pulmonary disease.

Table 2. Microorganisms isolated from patients with VAP who received heated humidifiers (HH) or heat and moisture exchangers (HME).

Microorganisms	HH group		HME group	
	Blood culture	Tracheal aspirate or bronchoscopy	Blood culture	Tracheal aspirate or bronchoscopy
Enterococcus faecalis	1	-	-	-
Coagulase-negative *Staphylococcus*	2	-	2	-
Staphylococcus aureus	2	-	1	1
Acinetobacter baumannii	1	7	2	9
Corynebacterium	-	-	1	1
Enterobacter cloacae	1	-	-	-
Klebsiella pneumoniae	-	-	-	1
Pseudomonas aeruginosa	2	6	2	5
Serratia marcescens	-	1	-	-
Stenotrophomonas maltophilia	-	1	-	2
Fungus	-	2	-	1
Total	9	17	8	20

Data are reported as number of positive results. VAP = ventilator-associated pneumonia.

Table 3. Chances of developing VAP in patients who received heated humidifiers (HH) or heat and moisture exchangers (HME).

	VAP	No VAP	OR crude (95%CI)	OR adjusted (95%CI)
HH	29 (9.24)	139 (44.27)	1	1
HME	27 (8.60)	119 (37.90)	1.09 (0.61-1.94)	1.08 (0.57-2.06)

Data are reported as number of VAP cases with percent in parentheses. VAP = ventilator-associated pneumonia. OR crude = comparison between groups. OR adjusted = comparison between groups adjusted for gender, age, chronic diseases, length of stay, and duration of mechanical ventilation.

Table 4. Duration of mechanical ventilation in the study population.

Mechanical ventilation (days)	VAP	No VAP	OR crude (95%CI)	OR adjusted (95%CI)
Up to 10	16 (5.10)	180 (57.32)	1	1
11 to 30	31 (9.87)	67 (21.34)	5.20 (2.68-10.12)	5.21 (2.68-10.14)
31 to 50	6 (1.91)	8 (2.55)	8.43 (2.6-27.33)	8.32 (2.56-27.09)
>50	3 (0.96)	3 (0.96)	11.25 (2.1-60.35)	11.37 (2.11-61.19)

Data are reported as number of VAP cases with percent in parentheses. VAP = ventilator-associated pneumonia. OR crude = comparison between groups. OR adjusted = comparison between groups adjusted for gender, age, chronic diseases and length of stay.

Duration of mechanical ventilation (11 *vs* 12 days; P = 0.48) and length of ICU stay (11 *vs* 12 days; P = 0.39) did not differ between the HH and HME groups. The ICU overall mortality was similar for both groups (55.3 *vs* 55.4%), and the death risk calculated by the APACHE II prognostic index was 56 and 58% for the HH and HME groups, respectively. No adverse event was identified in either group.

The chance of developing VAP did not differ between the study groups, thereby demonstrating the ineffectiveness of HME as a preventive measure, with a crude odds ratio of 1.09 (95%CI = 0.61-1.94). After adjustment for gender, age, comorbidities, duration of mechanical ventilation, and length of stay in the ICU, the likelihood of developing VAP again did not differ between the study groups, with an adjusted odds ratio of 1.08 (95%CI = 0.57-2.06; Table 3).

Our results also showed that there were no differences between groups with respect to duration of mechanical ventilation and length of stay in the ICU after adjustment for HH and HME. As for the number of days that patients were kept under mechanical ventilation, the chances of developing VAP was about five (OR = 5.2; 95%CI = 2.68-10.12), eight (OR = 8.43; 95%CI = 2.6-27.33), and eleven (OR = 11.25; 95%IC = 2.1-60.35) times higher in patients submitted to mechanical ventilation for 11-30, 31-50, and over 50 days compared to individuals who remained under mechanical ventilation for less than 11 days. This result was the same after adjustment for utilization of a filter, as shown in Table 4. Regarding the length of stay in the ICU, the probability of developing VAP was about six (OR = 5.92; 95%CI = 2.99-11.74), eight (OR = 8.38; 95%CI = 2.61-26.94), and twelve (OR = 12.57; 95%CI = 2.32-68.15) times higher for patients staying for 11-30, 31-50, and over 50 days in the ICU compared to those who stayed for less than 11 days. These data were also the same after adjustment for filter utilization.

Discussion

Literature studies have been contradictory in relation to the impact of HME on VAP prevention. A meta-analysis (9) including nine studies and 1378 patients revealed that the use of HME reduces VAP rates particularly in individuals submitted to mechanical ventilation for over 7 days (relative risk = 0.7; 95%CI = 0.50-0.94). However, previous non-randomized investigations that were not included in this meta-analysis had found significantly lower VAP rates with the use of HH compared to HME (17,18). Two other randomized studies reported a nonsignificant difference in VAP rates (10,11), and a randomized investigation including 120 patients described a lower VAP incidence with HH in patients under mechanical ventilation for over 5 days (15.69 *vs* 39.62%; P = 0.006) (19). A later meta-analysis published by Siempos et al. (12), including 13 randomized clinical assays representing 2580 patients, did not detect any differences between HME and HH in terms of VAP incidence, mortality in the ICU, length of stay in the ICU, duration of mechanical ventilation, or episodes of airway obstruction.

Our data indicate that the use of HME was not enough to prevent VAP in ICU patients. This is corroborated by the fact that there were no differences between the study groups for any of the parameters evaluated, including VAP incidence, duration of mechanical ventilation, length of stay in the ICU, and global mortality rate. On the other hand, filter utilization led to optimization of the work of the nursing staff since application of the filter eliminated the need to open the circuit and discard the water that accumulated in the respirator. There was also a fall in the number of technical problems with the respirator sensors, which contributed to reduced expenditure with maintenance services. Regarding HME expenses in our institution, the average daily cost per patient was US$6.48 *vs* US$5.9 for HH and HME, respectively. Despite the lower HME cost, also demonstrated in other studies (10), it is noteworthy that this device is not exempt from risks. The most severe complication is endotracheal tube obstruction by secretion. This is due to diminished moisture production, especially when a larger minute volume is employed, which is common to all commercially available instruments to a higher or lesser extent (17,20). In our case, obstruction of the endotracheal tube with need for re-intubation did not occur, but this is an adverse effect that has been described in other studies (21-28). Another concern is the increase in dead space with hypercapnia and airway resistance, which are mainly dependent on the internal volume of the filter and accumulation of liquids, respectively (29-31). In the present study, there was no record of hypercapnia or increased airway resistance requiring HME withdrawal.

Here, the fact that there was no reduction in the rate of VAP in the presence of HME compared to HH is in agreement with various published randomized investigations (10-12,17-19). A study by Kirton et al. (21) evaluating 280 trauma victims reported a lower VAP incidence for HME. A possible explanation for the fact that our results were different from those of Kirton et al. would be the severity of the patients (APACHE II >25) included herein associated with their several comorbidities. Other aspects that could influence our results refer to the filters employed in the present investigation, which were provided by different suppliers from those of other studies, as well as the frequency of filter exchange and the diagnostic criteria for VAP. Moreover, the studied populations differed between investigations (21). Nevertheless, various clinical studies have demonstrated that longer HME use, from 24-48 h up to 4 or 7 days, is not related to an increased risk of VAP (32-34).

Our results agree with the proposed VAP pathophysiology in the sense that inoculation of bacteria into the lungs is believed to usually occur through the extraluminal source, while it is thought to take place by the intraluminal route only sporadically (35,36).

The present study has some limitations. First, direct assessment of the heating and humidification of the inspired air was not carried out, since we relied on manufacturer specifications. Secondly, VAP was not diagnosed via an invasive procedure for all patients; in some individuals, only clinical and radiological criteria were employed for diagnosis. Finally, our study did not include a randomized trial.

It may be suggested that both HH and HME can be utilized in the ICU, without any significant impact on VAP incidence. Considering hospital costs and lack of contraindications, the use of HME should be considered as an alternative humidification method for patients submitted to mechanical ventilation. Further studies are necessary for clarification of the actual effect of this device on VAP prevention.

Our results have demonstrated that the use of HME in an intensive care unit did not reduce the incidence of VAP, the duration of mechanical ventilation, or the length of stay in the ICU in the study population.

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