New Issues and Controversies in the Prevention of Ventilator-associated Pneumonia

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In the past 2 years, American, Canadian, and European scientific societies have published their new evidence-based guidelines for ventilator-associated pneumonia (VAP) prevention. However, these guidelines did not review some potentially useful strategies, such as the use of an endotracheal tube with an ultrathin cuff membrane, an endotracheal tube with a low-volume/low-pressure cuff, a device for continuous monitoring of the endotracheal tube cuff pressure, a device to remove biofilm from the inner site of the endotracheal tube, and saline instillation before tracheal suctioning. Only a few guidelines analyze the time of tracheostomy, and so no firm recommendations can be made regarding its importance. In addition, the guidelines diverge on the use of heat and moisture exchangers or heated humidifiers and on the use of an endotracheal tube coated with antimicrobial agents. The current review focuses on issues of VAP prevention for which there is no clear recommendation, the use of which is controversial. A review of the literature suggests that the use of an endotracheal tube with an ultrathin and tapered-shape cuff membrane and coated in antimicrobial agents may reduce the risk of VAP. These features offer an attractive way to optimize the VAP prevention capacity of endotracheal tubes with a lumen for subglottic secretion drainage. We believe that early tracheostomy should be considered, based on the length reduction of mechanical ventilation and intensive care unit stay, reduction of mortality, and on patient comfort, although early tracheostomy has not yet been shown to favorably impact the incidence of VAP. We believed that heat and moisture exchangers should be considered based on the benefits in terms of cost savings. More research is necessary to clarify the role of continuous cuff pressure monitoring, removal of biofilm formation, and the practice of saline instillation before tracheal suctioning. Only a few guidelines analyze the time of tracheostomy, and therefore no firm recommendations can be made regarding its importance. In addition, the guidelines diverge on the use of heat and moisture exchangers (HME) or heated humidifiers (HHs) and on the use of an endotracheal tube coated with antimicrobial agents. Other recent studies of VAP prevention did not include these measures (18, 19). Therefore, the current review focuses on issues of VAP prevention for which there is no clear recommendation in the currently available guidelines, or the use of which is controversial (13–16). The criteria used to make our recommendations were the following: we define measures as “recommended” if the benefit is supported by a randomized controlled trial (RCT) or metaanalysis, and there are no reservations about the benefit, harms, or costs; we define measures as “worth considering” if the benefit is supported by studies other than an RCT or metaanalysis, or if there are minor uncertainties about the benefit, harms, or costs; in the case of major uncertainties about the benefit, harms, or costs, we define the measure as “more research needed.”

MEASURES NOT REVIEWED IN THE GUIDELINES

Endotracheal Tube with an Ultrathin Cuff Membrane

Subglottic secretions may accumulate above the endotracheal cuff and descend along the folds of the cuff wall to the lower respiratory tract and subsequently cause VAP. Different preventive strategies have been proposed to avoid microaspiration of subglottic secretions, such as removing these secretions by means of an endotracheal tube with subglottic secretion drainage (SSD). The metaanalysis published by Dezfulian and colleagues (20) included 896 patients from 5 studies. Patients intubated with a tube with SSD had a lower risk for VAP (relative risk, 0.51; 95% confidence interval [CI], 0.37–0.71), mainly due to the reduction in early-onset pneumonia (relative risk, 0.38; 95% CI, 0.16–0.88). One key point in the metaanalysis is that four of the five studies recruited patients expected to
require more than 72 hours of mechanical ventilation. After the metaanalysis, a study published by Bouza and colleagues in 2008 (21) randomized 714 cardiac surgery patients to receive mechanical ventilation with SSD or a conventional tube. There were no significant differences in VAP incidence between intubated patients with or without SSD (3.6 vs. 5.3%; \( P = 0.2 \)). However, in patients who had received mechanical ventilation for more than 48 hours, the group with SSD presented a lower VAP incidence (26.7 vs. 47.5%; \( P = 0.04 \)), a shorter length of intensive care unit (ICU) stay (median, 7 vs. 16.5 d; \( P = 0.01 \)), and reduced hospital antibiotic use (€1,206.00 vs. €1,877.00; \( P < 0.001 \)).

Another preventive strategy to avoid the progression of subglottic secretions into the lower respiratory tract is to avoid channel formation within the folds of the endotracheal cuff. When fully inflated, conventional high-volume/low-pressure (HVLP) cuffs have diameters 1.5–2 times that of the average adult trachea. When HVLP cuffs are inflated in a trachea to achieve a clinical seal, the excess material folds over itself, developing channels. Subglottic secretions accumulated above the endotracheal cuff may descend along the folds of the cuff wall to the lower respiratory tract, causing VAP. Recently, HVLP cuffs of ultrathin membrane (thickness of 7 \( \mu \)m, compared with >50 \( \mu \)m of the conventional polyvinylchloride membrane cuff) have been designed to prevent the formation of folds in the cuff, and thus prevent fluid and air leakage. In a study by Dullenkopf and colleagues (22), the in vitro fluid leakage past the tube cuff was compared in conventional HVLP cuffs of polyvinyl from different manufacturers and in HVLP cuffs made of an ultrathin polyurethane membrane. A vertical polyvinylchloride trachea model with an internal diameter of 20 mm was intubated, and cuffs were inflated from 10 to 60 cm H2O. Colored water (5 ml) was added to the top of the cuff. At pressures up to 60 cm H2O, fluid leakage past tube cuffs occurred within 5 minutes in all conventional cuffs. In the ultrathin polyurethane cuff, fluid leakage was not observed at pressures of 20 cm H2O. Besides, computed tomography was performed after bathing the cuffs in contrast medium and inserting them into the polyvinylchloride trachea model at pressures of 20 cm H2O. Due to folds, all conventional HVLP endotracheal tubes showed additional contrast enhancement within the cuff area. In another study by Dullenkopf and colleagues (23), 50 patients were randomized to receive endotracheal intubation with a conventional HVLP cuff of polyvinylchloride from different manufacturers versus an HVLP cuff of ultrathin polyurethane membrane. Cuff pressure to prevent air leakage at a standardized ventilator setting (peak inspiratory pressure, 20 cm H2O; positive end-expiratory pressure, 5 cm H2O; and respiratory rate, 15 breaths/min) was assessed by auscultation of audible sounds in the mouth. The HVLP ultrathin polyurethane cuff required significantly lower sealing pressures (9.5 [8–12] cm H2O) than the other brands (19.1 [8–42] cm H2O). In the study by Poelaert and colleagues (24), 134 patients undergoing cardiac surgery were randomized to receive an endotracheal tube with either an ultrathin polyurethane cuff or a conventional polyvinylchloride cuff. The group with the ultrathin cuff presented a lower incidence of early postoperative pneumonia. Multivariate regression analysis demonstrated that the use of an ultrathin polyurethane cuff was protective against early VAP (odds ratio, 0.31; 95% CI, 0.13–0.77; \( P = 0.01 \)). However, Poelaert and colleagues’ study was performed in a small population of patients undergoing cardiac surgery who may not be representative of other types of patients at risk for VAP. Furthermore, the polyurethane cuff used in that study also had a tapered shape. The benefit of this shape is that, at least on one place in the trachea, the inflated cuff fits the trachea perfectly; at this site, there are no folds, and so leakage and microaspiration may be reduced. Therefore, it is still uncertain whether the polyurethane cuff or the tapered shape, or both, are responsible for the favorable results.

Another preventive strategy to avoid the progression of subglottic secretions into the lower respiratory tract is the use of an endotracheal tube incorporating these two potential benefits: the ultrathin membrane cuff and SSD. In a randomized study of 280 patients, which compared the incidence of VAP between patients intubated with an endotracheal tube incorporating SSD and an ultrathin polyurethane membrane and patients with a conventional endotracheal tube with polyvinylchloride cuff (25), the tube incorporating the two potential advantages was associated with a lower incidence of global VAP (11/140 [7.9%] vs. 31/140 [22.1%]; hazard ratio, 3.3; 95% CI, 1.66–6.67; \( P = 0.001 \)), early-onset VAP (5/140 [3.6%] vs. 15/140 [10.7%]; hazard ratio, 3.3; 95% CI, 1.19–9.09; \( P = 0.02 \)), and late-onset VAP (6/63 [9.5%] vs. 16/60 [26.7%]; hazard ratio, 3.5; 95% CI, 1.34–9.01; \( P = 0.01 \)). The main contribution of that study is that an endotracheal tube with ultrathin polyurethane cuff and SSD could prevent early as well as late-onset VAP, whereas the metaanalysis by Dezfulian and colleagues (20) concluded that SSD reduces the risk of early-onset, but not late-onset, VAP. Unfortunately, the ultrathin cuff was combined with subglottic drainage, and so the direct influence of the ultrathin cuff could not be assessed.

Based on the available studies, it is not clear whether these devices reduce time on the ventilator, cost of care, and days on antibiotics. Therefore, the utility of these devices can be questioned, especially as they have not been subject to large RCTs. Thus, the use of an endotracheal tube with SSD can be defined as “recommended,” whereas the incorporation of an ultrathin membrane cuff and tapered-shape cuff could be defined as “worth considering.”

**Device for Continuous Monitoring of Endotracheal Tube Cuff Pressure**

Another preventive strategy for avoiding the progression of subglottic secretions into the lower respiratory tract is to maintain optimal cuff pressure. The pressure of the cuff should be sufficiently high to seal the lower airways and to avoid leakage of oropharyngeal debris into the lower respiratory tract. In a study by Rello and colleagues (26), a trend toward a higher risk of VAP was found among patients with persistent intracuff pressures below 20 cm H2O (relative risk, 2.57; 95% CI, 0.78–8.03). Among intubated patients not receiving antibiotics, persistent intracuff pressure below 20 cm H2O was independently associated with the risk of VAP (relative risk, 4.23, 95% CI, 1.12–15.92). Moreover, the cuff pressure should be maintained under 30 cm H2O to prevent tracheal injury (27, 28).

In the study by Valencia and colleagues (29), 142 patients were randomized to receive either mechanical ventilation with continuous regulation of the cuff pressure with an automatic device (which continuously displays the levels of cuff pressure in real time) or routine care of the cuff pressure with a manual manometer. In the latter group, cuff pressure was checked every 8 hours or in case of audible leakage. Cuff pressure less than 20 cm H2O was less frequently observed in the automatic device group than in control subjects (45.3 vs. 0.7% determinations; \( P < 0.001 \)). However, there were no differences between the groups in the rate of VAP with clinical criteria, VAP with microbiological confirmation, ICU mortality, hospital mortality, and length of ICU or hospital stay. Thus, the intracuff pressure should be maintained between 20 and 30 cm H2O. Although cuff pressure was better controlled with the automatic device, there is insufficient evidence to make a definitive recommendation regarding its use.
**Endotracheal Tube with SSD, Low-Volume/Low-Pressure, and Constant-Pressure Inflation Cuff**

Another endotracheal tube has been proposed for reducing the incidence of VAP (Lotrach; Venner Capital, Singapore), which incorporates the following features to avoid the progression of subglottic secretions into the lower respiratory tract: SSD; a low-volume/low-pressure cuff; and a device to maintain pressure cuff inflation constant. As mentioned previously here, when the conventional HVLP cuffs are inflated within the trachea, the excess material folds over itself and creates channels, and the subglottic secretions accumulated above the endotracheal cuff may descend along the folds to the lower respiratory tract, causing VAP. The low-volume/low-pressure cuff (made of high-compliance silicone) offers the advantage over the conventional HVLP cuff of producing fewer folds. Young and colleagues (30) found that this endotracheal tube reduced pulmonary aspiration in bench-top models and in anesthetized and critically ill patients compared with a conventional tube. However, no data about VAP were reported. Thus, it is not possible to make a definitive recommendation regarding the use of this kind of endotracheal tube in the prevention of VAP.

**Device to Remove Biofilm Formation**

Another preventive strategy that has been proposed to reduce the risk of VAP is to remove the biofilm formation on the inner side of the endotracheal tube. Conventionally, the endotracheal tube is cleaned via a small and flexible suction catheter, which is inserted into the tube and manipulated to remove lodged mucus. However, this may not remove all secretions. A device with a balloon (Mucus Shaver; National Institutes of Health, Bethesda, MD) was designed to remove the biofilm. The device is introduced through the tube until its tip reaches just beyond the end of the tube, when the balloon is inflated sufficiently to force the two shaving rings firmly against the wall of the tube. Thereafter, the device is gently retrieved during a period of 3–5 seconds to remove the remaining accumulated mucus from the lumen of the tube.

In the study by Kolobow and colleagues (31), eight sheep were mechanically ventilated for 72 hours (in two sheep, routine suctioning of the tube was performed every 6 h in a conventional manner, or as needed; in six sheep, the Mucus Shaver was used after routine suctioning). The mean peak inspiratory pressure during the course of the study was lower in the study group than in control subjects (18.7 ± 1.39 vs. 21.4 ± 1.91 cm H₂O). After extubation, scanning electron microscopy of the internal lumen of the tube was used to evaluate biofilm formation; none was found in the experimental group, but, in the control group, the biofilm formation was extensive. In the study by Berra and colleagues (32), 12 sheep were intubated with an endotracheal tube coated with silver-sulfadiazine and mechanically ventilated for 72 hours (in five sheep, routine suctioning of the tube was performed every 6 h in a conventional manner or as needed; in seven sheep, after routine suctioning, the Mucus Shaver was used). After extubation, in the control group, the tube always showed heavy colonization and biofilm formation (median debris thickness, 380 μm; range, 270–550 μm). In the study group, however, only three tubes were colonized. Although these results seem promising, no data regarding VAP prevention are currently available. Thus, it is not possible to make a definitive recommendation regarding its use.

**Saline Instillation before Tracheal Suctioning**

Routine saline instillation before tracheal suctioning is a controversial issue. This practice may increase the incidence of VAP, because it dislodges more viable bacterial colonies from the endotracheal tube than the insertion of a suctioning catheter without previous saline instillation (33), and this dislodgement may lead to contamination of the lower airways. Besides, saline instillation before tracheal suctioning may contribute to the occurrence of hypoxemia (34).

On the other hand, saline instillation before tracheal suctioning may decrease VAP incidence, because it increases the amount of thick secretions removed, stimulates coughing, which may bring secretions to the trachea for subsequent suctioning, and may decrease the biofilm in the endotracheal tube. In the study published by Caruso and colleagues (35), 262 patients were randomized to receive either isotonic saline instillation before tracheal suctioning or no treatment. In the saline group, fewer patients experienced microbiologically proven VAP (23.5 vs. 10.8%; patients; P = 0.008) and microbiologically proven VAP per 1,000 days of mechanical ventilation (21.2 vs. 9.6%; P < 0.01). No significant differences were found in the incidence of endotracheal tube obstruction, pulmonary and lobar atelectasis, and mortality, or between the duration of mechanical ventilation and ICU stay. In the light of the potential problems associated with saline instillation, this one study is not considered sufficient to recommend its routine use. In specific situations (e.g., patients with thick and difficult to drain secretions), saline instillation may be a temporary option.

**MEASURES REVIEWED, BUT NOT RECOMMENDED, IN THE GUIDELINES**

**Early Tracheostomy**

Prolonged intubation is associated with laryngeal injury and tracheal stenosis (36–39). Early tracheostomy has been proposed as a way of avoiding these complications when the use of prolonged intubation is anticipated.

Early tracheostomy has reduced the incidence of VAP in some studies, but not in others. The metaanalysis by Griffiths and colleagues (40) included 382 patients from five randomized or quasirandomized controlled studies, which compared early tracheostomy with either late tracheostomy or prolonged endotracheal intubation. Early tracheostomy (within 7 d of invasive mechanical ventilation) did not significantly reduce the risk of VAP (relative risk, 0.90; 95% CI, 0.66–1.21) or mortality (relative risk, 0.79; 95% CI, 0.45–1.39). However, early tracheostomy significantly reduced the duration of mechanical ventilation (mean difference, −8.5 d; 95% CI, −15.3 to −1.7) and length of ICU stay (mean difference, −15.3 d; 95% CI, −24.6 to −6.1).

After this metaanalysis, Blot and colleagues (41) reported the results of a trial in which 125 patients expected to require more than 7 days of mechanical ventilation were randomized to receive either prolonged intubation or early (within 4 d) tracheotomy. No difference was found between the two groups in mortality, VAP incidence, duration of mechanical ventilation, ICU stay, sedation use, or laryngeal or tracheal complications. Greater comfort was the sole benefit afforded by tracheotomy.

The metaanalysis recently published by Durbin and colleagues (42) included 641 patients from seven randomized or quasirandomized controlled studies, which compared early tracheostomy either with late tracheostomy or with prolonged endotracheal intubation. No significant differences were found in the risk of pneumonia or mortality. However, by restricting the analysis to three randomized trials comparing early tracheostomy (performed within the first 5 d) vs. late tracheostomy, a reduction in mortality was found (odds ratio, 0.40; 95% CI, 0.25–0.97) and ICU stay (−10.96 d; 95% CI, −17.42 to −4.38) with early tracheostomy.

The survey by Veenith and colleagues (43) explored the practice of tracheostomy in 228 ICUs in the United Kingdom.
Percutaneous tracheostomy is still preferred to the surgical technique, being performed by 92% of ICUs. The timing of tracheostomy remains variable: in 82% of ICUs, tracheostomy is performed in the first 10 days of mechanical ventilation.

Based on the benefits shown by metaanalyses in terms of reduced length of mechanical ventilation and ICU stay (40) and reduced mortality (42), and on the benefits in patient comfort (41), we define the execution of early tracheostomy as “worth considering” in patients with an anticipated length of mechanical ventilation of more than 7 days. However, early tracheostomy has not yet been shown to favorably impact the incidence of VAP. An important problem is to be able to predict which patients will require prolonged intubation. In the review by Durbin and colleagues (42), an algorithm is suggested for deciding when to perform tracheostomy in critically ill patients. The algorithm included the following situations: upper airway obstruction; neurologic disease with Glasgow coma score of 6 or less; spinal cord injury at or above C4; acute neuromuscular disease with autonomic dysfunction or underlying lung disease; acute respiratory distress syndrome score of 2.5 or greater on Day 7; and patient with burns with substantial full-thickness burns or active infection.

MEASURES RECOMMENDED BY SOME GUIDELINES, BUT NOT BY OTHERS

Endotracheal Tube Coated with Antimicrobial Agents

Biofilm formation has been demonstrated on the inner endotracheal tube surface of patients undergoing mechanical ventilation (44–46). This provides an ideal environment for pathogens to colonize the device. Later, this biofilm can become detached from the endotracheal tube surface of patients undergoing mechanical ventilation or during suctioning or bronchoscopy into the lower respiratory tract, whereas, in the standard group, heavy colonization of the ventilator tubing (104–106 per ml). In the in vitro study, the silver-sulfadiazine–coated endotracheal tube group showed heavy bacterial colonization in the endotracheal tube, ventilator circuit, or lower respiratory tract, whereas, in the standard group, heavy colonization was found in the endotracheal tube (P < 0.01), ventilator tubing (P = 0.03), and lower respiratory tract (P < 0.01).

In a series of in vitro and animal models, Rello and colleagues (52) demonstrated lower colonization rates in silver-coated tubes than in conventional endotracheal tubes. In another study by Rello and colleagues (53), 121 patients who required mechanical ventilation for more than 24 hours were randomized to receive either a silver-coated or a conventional endotracheal tube. The use of silver-coated tubes was associated with delayed colonization on the tube and tracheal aspirates, and reduction of maximal bacterial burden of tracheal aspirates compared with the control device. Probably due to the small sample size, this study did not demonstrate any impact on VAP incidence or antibiotic use.

In the randomized North American Silver-Coated Endotracheal Tube (NASCENT) study by Kollef and colleagues (54), a total of 2,003 patients expected to require mechanical ventilation for more than 24 hours were assigned to undergo intubation with either a silver-coated or a conventional tube. The silver-coated endotracheal tube was associated with a lower occurrence rate of microbiologically confirmed VAP (37/766 [4.8%] vs. 56/743 [7.5%]; P = 0.03) and with delayed VAP development (P = 0.005 by generalized Wilcoxon test). A retrospective cohort analysis based on the NASCENT study (55) revealed that, in patients who developed VAP, mortality was lower in patients in the silver-coated tube group than in patients in the control group. However, in patients without VAP, mortality was higher in the silver-coated tube group. In the cost-effectiveness analysis by Shorr and colleagues (56), silver-coated endotracheal tubes were recognized as a preventive measure that yielded potential hospital cost savings. In this analysis, the authors assumed a reduction in the relative risk of VAP in patients intubated for 24 hours from 35.9 to 24%. The savings per case of VAP prevented was $12,840, with an assumed marginal VAP cost of $16,620 and costs of $90.00 for coated and $2.00 for uncoated endotracheal tubes. In multivar-
## Table 1. Recommendations by Current Guidelines, New Evidence, and Our Recommendations

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<td>Lorente and colleagues (25).</td>
<td>Worth considering</td>
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<td>Endotracheal tube with an ultrathin and tapered-shape cuff membrane</td>
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<td>Poelaert and colleagues (24). RCT with 134 cardiac surgery patients. Reduced VAP.</td>
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<td>Valencia and colleagues (29). RCT with 142 patients. Reduced time of cuff pressure lower than 20 cm H2O; but no reduction in VAP.</td>
<td>More research needed</td>
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<td>Endotracheal tube with SSD and LVLP and constant pressure inflation cuff</td>
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<td>Young and colleagues (30). RCT with 54 patients. Reduced aspiration; but, no VAP data were reported.</td>
<td>More research needed</td>
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<td>Tracheostomy: early better than late</td>
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<td>Griffiths and colleagues (40). Metaanalysis with 382 patients. Reduced duration of MV and ICU stay; but no reduction in VAP or mortality.</td>
<td>Worth considering</td>
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<td>Measures recommended by some guidelines but not others—</td>
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<td>Rello and colleagues (55). RCT with 121 patients. Reduced tracheal aspiration colonization; but no reduction in VAP.</td>
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<td>Heat moisture exchanger better than heated humidifier</td>
<td>R Make NR</td>
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<td>Siempos and colleagues (63). Metaanalysis of 2,580 patients. Reduced humidification costs; but no reduction in VAP, mortality, duration of MV, or ICU stay.</td>
<td>Worth considering HMES, based on cost savings.</td>
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**Definition of abbreviations:** BSAC = British Society for Antimicrobial Chemotherapy; CCCS = Canadian Critical Care Society; ETF = European Respiratory Task Force; HMES = heat and moisture exchangers; ICU = intensive care unit; LVLP = low volume/low pressure; MV = mechanical ventilation; NR = no recommendation; R = recommended; RCT = randomized, controlled trial; SHEA/IDSA = Society for Healthcare Epidemiology of America/Infectious Diseases Society of America; SSD = subglottic secretion drainage; em dash = the guideline did not review this issue; VAP = ventilator-associated pneumonia.
Partial pressure (P) sensitivity analyses, the silver-coated endotracheal tubes yielded persistent savings (95% CI, $9,630–$16,356) per case of VAP prevented. With other base-case inputs held constant, the break-even cost for silver-coated endotracheal tubes was $388. These assumptions may not be replicated exactly in other settings, but the use of a silver-coated endotracheal tube is recommended.

**HMEs or HHs**

A metaanalysis published by Kola and colleagues (57), which enrolled 1,578 patients from nine trials, found that the use of HME decreased the rate of VAP (relative risk, 0.7; 95% CI, 0.50–0.94). This metaanalysis, however, did not include the nonrandomized studies by Cohen and colleagues (58) and by Blin and colleagues (59), who found significantly decreased VAP rates with HHs compared with HMEs.

After the metaanalysis of Kola and colleagues, two randomized studies reported a nonsignificant difference in VAP rate (60, 61), and one randomized study reported a lower VAP incidence, with HHs in patients requiring mechanical ventilation for more than 5 days (15.7 vs. 39.6%; \( P = 0.006 \)) (62).

A later metaanalysis published by Siempos and colleagues (63), including 13 randomized controlled trials representing 2,580 patients, found no difference between the HME and the HH group in incidence of VAP, ICU mortality, length of ICU stay, duration of mechanical ventilation, or episodes of airway occlusion. However, HMEs were cheaper than HHs in each of the studies. Based on the benefits in terms of cost savings, we define HMEs as “worth considering” in patients without contraindications for their use, such as hyperthermia, atelectasis, thick secretions, or hemoptysis.

**CONCLUSION**

We believe that the use of an endotracheal tube with an ultrathin and tapered-shape cuff and coated in antimicrobial agents can reduce the risk of VAP. The combination of both these features with SSD offers an attractive way of optimizing VAP prevention.

Furthermore, early tracheostomy should be considered in patients with an anticipated length of mechanical ventilation of more than 7 days, based on the reduction of mechanical ventilation and ICU stay length and mortality, and on patient comfort. However, early tracheostomy has not yet been shown to favorably impact the incidence of VAP. Based on cost savings and in the absence of contraindications, the use of a HME should be considered as a method of providing humidification in patients undergoing mechanical ventilation.

More research is necessary to clarify the value of continuous cuff pressure regulation, removal of biofilm formation, and routine saline instillation before tracheal suctioning.

Because the risk of VAP increases with length of mechanical ventilation, patients with prolonged ventilation are likely to benefit the most from these preventive measures. Although a clinical algorithm has been proposed to spot prolonged ventilator dependency (42), in many circumstances it remains hard to identify patients who will require long-lasting mechanical ventilation. Therefore, one might consider adopting all these VAP prevention measures in every mechanically ventilated, critically ill patient.

Finally, in many of the issues reviewed, some questions remain unanswered. We lack information on cost effectiveness, and have little or no data about impact on mortality, duration of mechanical ventilation, and hospitalization. Furthermore, in some studies, the particular patient selection precludes generalization of the results. Sometimes the sample size of the study appeared to be deficient. In view of these results, further research is necessary to establish definite recommendations about these preventive measures. Table 1 summarizes the recommendations of the current guidelines about these measures to VAP prevention (13–16), new evidence, and our recommendations. In the Canadian Critical Care Society guidelines, a measure was recommended if there were no reservations about endorsing it, and no recommendation was made if evidence regarding an intervention was inadequate, or if there were major uncertainties about the benefits, harms, and costs (14).

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