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Ventilator-associated Pneumonia or Endotracheal Tube-associated Pneumonia?

An Approach to the Pathogenesis and Preventive Strategies Emphasizing the Importance of Endotracheal Tube

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Ventilator-associated pneumonia is the most common nosocomial infection in the intensive care unit, and it is associated with prolonged hospitalization, increased health care costs, and high attributable mortality. During the past several decades, numerous studies focused on the crucial role of the endotracheal tube (ETT) in the pathogenesis of ventilator-associated pneumonia. Tracheal intubation thwarts the cough reflex, compromises mucocilliary clearance, injures the tracheal epithelial surface, provides a direct conduit for rapid access of bacteria from upper into the lower respiratory tract, and allows the formation of biofilm on the ETT surface. The combination of these factors puts the mechanically ventilated patient at great jeopardy of developing ventilator-associated pneumonia. Many preventive strategies have arisen from this understanding: control of intracuff pressure, aspiration of subglottic secretions, decontamination of subglottic area, use of antiseptic impregnated ETTs, and elimination or prevention of the ETT biofilm formation. The authors review the role of ETT management for the prevention of the ventilator-associated pneumonia.

VENTILATOR-ASSOCIATED pneumonia (VAP) is defined as nosocomial pneumonia occurring in a patient after 48 h of mechanical ventilation *via* an endotracheal or tracheostomy tube. It is commonly classified as either early onset (occurring within 96 h of start of mechanical ventilation) or late onset (occurring more than 96 h after start of mechanical ventilation). VAP occurs in 9–27% of all intubated patients.[1] In mechanically ventilated patients, the incidence increases with duration of ventilation. The risk of VAP is highest early in the course of hospital stay, and it is estimated to be 3% per day during the first 5 days of ventilation, 2% per day during days 5 to 10 of ventilation, and 1% per day after this.[2] Despite numerous original studies, reviews, and meta-analyses on pathogenesis and prevention strategies of VAP, controversies remain on these issues. This review describes current concepts and highlights the findings of recently published studies concerning the pathogenesis of VAP in relation to endotracheal tube (ETT). This may have important implications in several preventive strategies against this type of pneumonia.

We conducted a review of English language citations published in PubMed and SCOPUS without time limits until March 2008 using combinations of the following terms: *pneumonia, ventilator-associated pneumonia, nosocomial pneumonia, ventilator, tracheal intubation, endotracheal tube, cuff, subglottic secretions, subglottic secretions drainage, subglottic secretion aspiration,* and *prevention*. We searched the titles and the abstracts and retrieved the full-text articles that seemed relevant.

The search and the review of databases was independently performed by two reviewers, and the identified publications were classified as randomized controlled trials, observational studies, reviews and meta-analyses, and case reports and series. We used the GRADE system for grading strength of recommendations and quality of evidence of reviewed publications (table 1).[3]

Tracheal Intubation

In the critically ill, tracheal intubation is performed usually as an emergency procedure to protect airway from aspiration in unconscious patients, facilitate application of mechanical ventilation, or clear airway's secretions in patients with inability to adequately handle copious secretions. However, emergency intubation did not preclude the rapid (within 24 h) colonization of the tracheal mucosa with endogenous flora in previously healthy patients with head trauma and has been identified as an independent risk factor for developing early onset VAP.[4–6] In these patients, aspiration due to loss of

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Table 1. Grading Recommendations (GRADE)

Grade of Recommendation/Description	Methodological Quality of Supporting Evidence	Implications
1A: Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B: Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C: Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
2A: Weak recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B: Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C: Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

GRADE is the system for grading strength of recommendations and quality of evidence from Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, Raskob G, Lewis SZ, Schünemann H: Grading strength of recommendations and quality of evidence in clinical guidelines: Report from an American College of Chest Physicians Task Force. Chest 2006; 129:174–81,[3] modified with permission.

RCTs = randomized controlled trials.

consciousness, more than tracheal intubation *per se*, seems also to be an independent risk factor for early onset VAP.[7,8]

The presence of an ETT impairs mucocilliary clearance and disrupts the cough reflex, thus promoting the accumulation of tracheobronchial secretions and increasing the risk of pneumonia.[9,10] Moreover, the insertion of an ETT often produces injury and probably implantation of exogenous and endogenous bacterial inoculum in the tracheal mucosa.[11] In a case control study performed by Torres *et al.*, after adjusting for age and sex, reintubation was the only significant factor related to the development of VAP.[12] In another prospective observational multicenter study including 750 mechanically ventilated patients, accidental extubation and reintubation after weaning increased the risk of nosocomial pneumonia.[13]

Subglottic Space Secretions

Cuffed ETTs are designed to seal the trachea to carry out positive pressure ventilation and prevent aspiration of fluid and pharyngeal contents into the lower airways. During critical illness, especially in intubated critically ill patients, the oral flora shifts dramatically to a predominance of aerobic Gram-negative bacilli and *Staphylococcus aureus*.[14–16] The stomach and sinuses have been suggested as potential reservoirs for certain bacteria colonizing the oropharynx and trachea, but their importance remains controversial.[17,18] The accumulation of contaminated secretions from oropharynx or gastrointestinal tract in the subglottic space is a crucial event in the pathogenesis of VAP. Several studies have shown that these pooled secretions above inflated ETT cuff may be a source of microaspiration and that it is a leading cause of tracheobronchial colonization and VAP.[19–24] On the basis of the above-mentioned observations, an important preventive strategy should focus on blocking up the leakage of subglottic secretions around the cuff (between ETT and tracheal mucosa), drainage of secretions from subglottic space, and decontamination of the subglottic secretions.

Blocking the Leakage of Subglottic Secretions

Control of Intracuff Pressure or/and a Specifically Designed Cuff? Sealing of ETT often requires that intracuff pressure (Pc) to exceed the safety margin of about 25–30 cm H_2O. The low-volume, high-pressure cuffs required a Pc of more than 60 cm H_2O to achieve a meaningful seal and frequently induced tracheal injury after prolonged use.[25,26] Consequently, ETT with high-volume low-pressure (HVLP) cuffs that can achieve clinical seals at pressures below 30 cm H_2O were introduced. When fully inflated, the HVLP cuff has diameter of 1.5–2 times the diameter of the average adult trachea.[26] When an HVLP cuff is inflated in a trachea to achieve a clinical seal, the excess material folds over itself, developing channels. Subglottic secretions accumulated above the ETT cuff may descend along these channels within the folds of the cuff wall to the lower respiratory tract. This progression is easier with HVLP than with low-volume, high-pressure cuffs, and the risk of VAP increases accordingly.[27–29]

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It was found that when the tracheal pressure was lower than the height of fluid in the column above the HVLP cuff, a rapid leakage of fluid occurred from above the cuff into the trachea during all modes of ventilation.[29,30] Blunt *et al.* found that lubrication of HVLP cuffs with a water-soluble gel reduced the incidence of pulmonary aspiration.[31]

Rello *et al.* were the first to analyze the effects of Pc on the development of VAP. They demonstrated that persistent Pc $<$ 20 cm H_2O within the first 8 days of intubation was a factor independently associated with the development of VAP (relative risk, 4.23; 95% CI, 1.12 to 15.92).[10] Ferre *et al.* developed and validated a device for automatically and continuously ensuring adequate Pc.[32] The efficacy of this device to optimize Pc and to prevent VAP was assessed by Valencia *et al.* in a randomized controlled clinical study.[33] Continuous, automatic regulation of the endotracheal tube cuff was effective in maintaining appropriate inflation (Pc $>$ 20 cm H_2O) compared with routine care. However, no difference in the incidence of VAP was found between the two groups of patients.

During the past years, a new type of HVLP ETT with a polyurethane cuff has been introduced with an ultra-thin cuff membrane (thickness, 7 μm) designed to prevent the formation of folds, thus preventing fluid and air leakage.[24,34] A recent randomized clinical trial found that the use of this type of HVLP ETT, equipped with a lumen for subglottic secretion drainage, was found to reduce the incidence of early- and late-onset VAP when compared with a conventional ETT tube with polyvinyl cuff and without subglottic secretion drainage.[35] One obvious limitation of this study was the inability to discriminate the independent influence of subglottic secretion drainage and polyurethane cuff in the incidence of VAP. In a more recent prospective, single-blinded, randomized study, polyurethane cuffed endotracheal tubes reduced the frequency of early postoperative pneumonia in cardiac surgical patients. Unfortunately the final diagnosis of pneumonia in this study was based on clinical criteria, and microbial etiology was documented only in 15 cases.[36]

Although there is scarce evidence about the exact role Pc in prevention of VAP, ethical issues in performing a clinical trial in intubated critically ill patients with low cuff pressure result in a general recommendation that the intracuff pressure be persistently maintained at 20–30 cm H_2O.[11,36] (GRADE 1C).

More clinical studies are needed to demonstrate the value of HVLP ETT with ultra-thin cuff of polyurethane in prevention of VAP.

Aspiration of Subglottic Secretions. Removal of contaminated oropharyngeal secretions pooled above the ETT cuff through suction of the subglottic area with intermittent or continuous aspiration of subglottic secretions may reduce the risk for aspiration and VAP. Aspiration of subglottic secretions requires the use of specially designed ETTs containing a separate dorsal lumen that opens into the subglottic space (Hi-Lo Evac tube; Mallinckrodt, Athlon, Ireland).

Five randomized controlled trials have examined the effectiveness of aspiration of subglottic secretions.[20,22,23,37,38] Four trials found a statistically significant decrease in the incidence of VAP.[20,22,23,38] All five trials reported a significant delay in the time to development of VAP. Regarding the effect of aspiration of subglottic secretions on the subglottic space and trachea colonization, only one study reported that this procedure attained a lower increase in the rate of contamination. Nevertheless, aspiration of subglottic secretions does not seem to have any effect on mortality, the duration of mechanical ventilation, or intensive care unit or hospital stay.[22,23,37] A recent meta-analysis evaluated 896 patients from the above-mentioned five studies.[24] In the patients who had some form of aspiration of subglottic secretions, the VAP risk reduction was found to be about 50% (summary risk ratio, 0.51; 95% CI, 0.37–0.71), primarily through reducing pneumonia within the first 5 to 7 days after intubation. This meta-analysis concluded that there is a benefit of continuous aspiration of subglottic secretions to reducing VAP, despite the diversity of research variables among the continuous aspiration of subglottic secretions trials. Thus, the use of an ETT with continuous aspiration of subglottic secretions should be recommended in patients expected to require more than 72 h of mechanical ventilation.[39]

Rello *et al.* were the first to report a failure to aspirate subglottic secretions using the Evac ETT with an incidence of 34% (28 of 83 patients) and considered the above mechanism as a risk factor for VAP development. Investigating this dysfunction visually using a flexible bronchoscope, we attributed it to blockage of the subglottic suction port by suctioned tracheal mucosa.[11,40] Moreover, in an animal study, Berra *et al.* found that aspiration of subglottic secretions can cause severe tracheal injury in an area immediately adjacent to the subglottic suction port.[41] In this context, when failure of aspiration of subglottic secretion occurs, stopping the subglottic suction appears a logical maneuver to prevent tracheal damage.

The efficacy of aspiration of subglottic secretions can be influenced by many factors, such as the viscosity of secretions, intermittent *versus* continuous aspiration, presence or absence of swallow, patient position, and position of the Hi-Lo Evac tube in the airway; however, there are no clinical data regarding the impact of these factors in the incidence of VAP.[42]

Although the application of drainage of subglottic secretions (Hi-Lo Evac tube and suction equipment) is associated with an increase of nursing costs, the overall reduction of the incidence of VAP incidence could result in substantial cost savings.[43]

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Proper application of the drainage of subglottic secretions is a safe method that reduces the incidence of VAP, especially in patients expected to require more than 72 h of mechanical ventilation[38] (GRADE 1A). Further studies are required to discriminate the impact of continuous aspiration of subglottic secretions in the incidence of VAP produced by nonfermenting Gram-negative bacilli (*i.e., Pseudomonas aeruginosa*) given the different pattern of airway colonization by these micro-organisms.[44]

Selective Decontamination of Subglottic Space

Selective digestive decontamination (SDD) is a preventive technique against hospital-acquired infections aimed at selectively eliminating aerobic Gram-negative bacilli and yeast from the mouth and stomach by local administration of nonabsorbable antimicrobial agents combined during the first 3–4 days with a parenteral antibiotic to prevent early infections.[45,46] Despite numerous randomized controlled clinical trials and large meta-analyses clearly indicating a decrease in the rate of VAP and mortality (especially in surgical and trauma patients), the routine use of SDD has not become common in clinical practice.[47–50] The explanation of this paradox arises from the relative complexity of the technique, the constant threat of increased emerging antimicrobial resistance and the unknown cost efficacy ratio.[39] Decontamination of oropharyngeal secretions with chlorhexidine also appears to be an effective measure to prevent VAP.[51] However, a recent meta-analysis that included 1202 patients reported that the use of oral decontamination with chlorhexidine did not significantly decrease either the incidence of VAP or the mortality rate.[52]

Independent of the actual source of the pathogenic bacteria leading to VAP (exogenous or endogenous), the subglottic space represents the "anteroom" for microaspiration of contaminated secretions in to lower respiratory tract. Thus, the selective decontamination of the subglottic space could be an attractive idea for reducing the incidence of VAP in mechanically ventilated patients. This hypothesis was tested in a randomized controlled clinical study in 79 consecutive multiple trauma patients on mechanical ventilation using the suction lumen of Evac ETT for continuous infusion of antibiotic solution in the subglottic space (fig. 1).[53] A significantly lower incidence in both tracheal colonization and VAP was found, without, however, a significant difference in patients' outcome. (GRADE 1B).

Endotracheal Tube Biofilm Formation

Another important aspect of the contribution of the ETT in the pathogenesis of VAP is that it serves as a reservoir for microorganisms by providing them a surface to adhere. In other words, it allows the microorganisms to form *a biofilm.* According to Costerton *et al.*, a biofilm is "a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface."[54] All varieties of biomedical implants and transcutaneous devices are prone for bacterial colonization and biofilm formation. A biofilm is a permanent source of infection and provides protection to the microorganisms from antibiotics by accretion of this protective glycocalyx.[55] Thus, in biofilms, microbial resistance seems to depend on multicellular strategies entirely different from the now familiar plasmids, transposons, and mutations that confer innate resistance to individual microorganisms.[56]

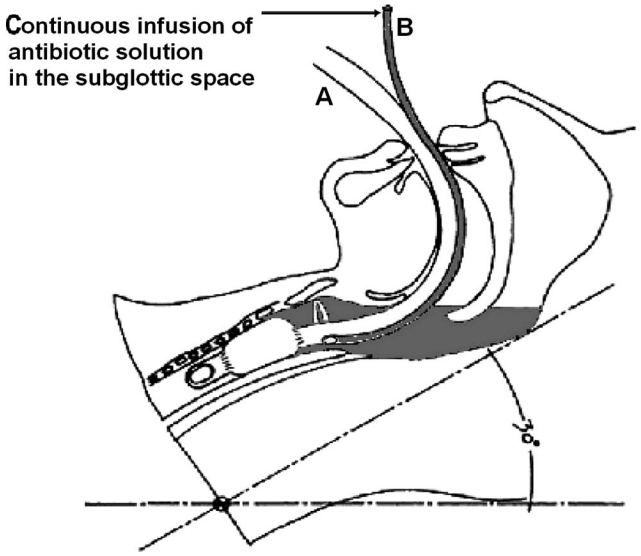

Fig. 1. Selective decontamination of subglottic space. (*A*) Hi-Lo Evac tube (Mallinckrodt, Athlon, Ireland). (*B*) Suction lumen.

Biofilm forms on the ETT very quickly after intubation and appears to be a significant source of bacterial inoculation of the lungs.[57–59] Aggregates of ETT biofilm can be easily detached by suction catheter and disseminated towards the lower respiratory tract by shear forces imparted by the ventilator inspiratory gas flow.[60,61] Feldman *et al.*, studied ETT colonization in mechanically ventilated patients and found that all airway access tubes had secretions lining the interior of the distal third of the tube that formed a biofilm.[60] They noted that the sequence of colonization in patients undergoing mechanical ventilation was the oropharynx (36 h), stomach (36–60 h), lower respiratory tract (60–84 h), and, thereafter, the ETT (60–96 h). Adair *et al.*, in an observational study investigated the relationship between ETT biofilm and VAP[60] and they observed that 70% of patients with VAP had identical pathogens isolated from both ETT biofilm and tracheal secretions.

Despite the findings of the above-mentioned studies, it remains unclear whether ETT biofilm formation is a significant risk of VAP or it simply represents a contamination from exogenous or endogenous sources without any important sequelae.[62,63]

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Prevention of Biofilm Formation

Prevention of ETT biofilm formation can be achieved by three methods: decontamination of ETT by SDD, use of specific antiseptic impregnated ETT, and synchronized mucus aspiration in the distal end of ETT.

Decontamination of ETT. The effect of SDD (tobramycin, polymyxin, and amphotericin B) on ETT biofilm formation in mechanically ventilated patients has been studied by the group of Adair *et al.* in the early nineties.[64,65] SDD was found to eliminate only the colonization by enteric Gram-negative bacteria. No effect was observed in ETT biofilm formed by Gram-positive bacteria and *Pseudomonas* spp. In a more recent observational clinical study, the same authors compare the efficacy of gentamicin nebulized *via* the ETT with that of parenteral cefotaxime or cefuroxime in preventing the formation of ET biofilm.[66] Nebulized gentamicin attained high concentrations in the ET lumen and was more effective in preventing the formation of biofilm than either parenterally administered cephalosporin. (GRADE 2C).

Use of Specific Antiseptic Impregnated ETTs. Silver is a highly effective antibacterial substance used for coating a variety of biomaterials to prevent the formation of biofilm and subsequent infection.[62,67,68] Silver is generally considered to be nontoxic. Its topical use to prevent infection after burn and other injuries is rarely associated with toxicity despite extensive clinical experience.

Olson *et al.* evaluated the influence of silver-coated ETTs on the lung bacterial burden of mechanically ventilated dogs challenged with buccal administration of *Pseudomonas aeruginosa*.[69] They found that silver-coated ETTs had a significantly lower rate of colonization with aerobic bacteria compared to noncoated ETTs. In addition, the colonization of the inner surface of the silver-coated ETTs was significantly delayed compared to the noncoated ETTs. Finally, the silver-coated ETTs were associated with significantly reduced bacterial burden and lung inflammation. In another animal study, a combination of silver-sulfadiazine and chlorhexidine in polyurethane-coated ETT was tested in mechanically ventilated sheep.[70] In the coated ETT group, tracheal colonization was eliminated in seven of eight sheep compared with the control group, in which all eight were heavily colonized. In addition to silver and chlorhexidine impregnated ETTs, another new combination antiseptic, Gendine (combination of gentian violet and chlorhexidine)–impregnated ETTs, has been tested *in vitro* for efficacy and safety.[71] Gendine-coated ETTs were shown to have broad-spectrum activity, prolonged antimicrobial durability, and high efficacy in inhibiting adherence of organisms commonly causing nosocomial pneumonia.

Rello *et al.* recently investigated the use of a novel silver-coated ETT in adult critically ill patients who required mechanical ventilation for more than 24 h.[72] In this ETT, silver ions are microdispersed in a proprietary polymer on both the inner and outer lumens and may migrate to the ETT surface to provide a sustained antimicrobial effect. This prospective, randomized study assessed the feasibility and safety of this type of ETT and tested its effect on bacterial burden in the airways. The silver-coated ETT was found feasible and well-tolerated. It is also associated with reduced bacterial burden in tracheal aspirates and delayed colonization of the tube and in the tracheal aspirate. Interestingly, an *in vitro* study demonstrated that the effectiveness of antiseptic-impregnated ETTs in preventing the growth of bacterial pathogens associated with VAP may vary with different organisms.[73] In the previously mentioned study of Rello *et al.*, the silver-coated ETT group experienced less *Enterobacteriaceae* spp. but more, although nonsignificantly, *P. aeruginosa* colonization of the trachea.

Antiseptic impregnated ETTs may reduce airway colonization by bacterial pathogens associated with VAP, but more studies are needed to determine whether these findings will translate to a decreased incidence of VAP. (GRADE 2B).

Synchronized Mucus Aspiration in the Distal End of ETT. A modified ETT that allows automatic aspiration of all mucus as it reaches the immediate vicinity of the ETT has been recently introduced: the Mucus Slurper.[74] In essence, this is a modification of a Hi-Lo Evac ETT. The suction lumen is extended to the very tip and connects to a hollow, concentric, vinyl suction ring mounted at its tip. Mucus aspiration is performed through eight small holes situated on the suction ring. An external controller synchronizes activation of suction through a pressure switch activated when expiratory airway pressure is decreased 3–5 cm H_2O below the inspiratory plateau pressure. Li Bassi *et al.* evaluated the efficacy of Mucus Slurper in a prospective randomized animal study concerning 12 healthy sheep mechanically ventilated for 72 h.[75] They found that Mucus Slurper combined with orientation of trachea below horizontal level prevented accumulation of secretions within the lumen of ETT and trachea without need for conventional tracheal suctioning. Clinical studies are required to confirm these findings in mechanically ventilated patients.

Elimination of ETT Biofilm

The removal of mucus secretions accumulated in the internal surface of ETT in mechanically ventilated patients is performed by using small, flexible, plastic suction catheters. Nevertheless, residual secretions are always retained on ETT surface, promoting biofilm formation. A new device designed for complete mechanical cleansing of the interior surface of ETT has been recently introduced. The so-called mucus shaver (MS) is a tube equipped with an inflatable balloon with two rings on the end.[76] The MS is introduced through the connector piece of the ETT until its tip reaches just beyond the end of the ETT. The balloon is then inflated so that the shaving rings are firmly forced against the

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lumen of the ETT. Subsequently, the MS is then gently pulled out of the ETT during a period of 3 to 5s, removing the remaining accumulated mucus from the lumen of the ETT. MS was tested for its efficacy in six mechanically ventilated sheep.[76] No technical problems or ventilatory side effects were reported, and an average of 0.35 ± 0.29 g of mucus was removed with each use. After using this device, the ETT was free of visible secretions. In the study group, scanning electron microscopy of the internal lumen of the ETT showed no biofilm or proteinaceous material; in the control group, there was extensive biofilm formation.

The same group of investigators conducted an experimental control study in 12 intubated sheep to assess whether or not keeping the internal surface of a silver-sulfadiazine coated ETT clean by regular use of the MS may retain the tube's full bactericidal effects.[77] They found that silver-based coating of ETT significantly reduces accumulation of mucus/secretion and bacterial growth within the ETT after 72 h of mechanical ventilation.

There are various new approaches for dealing with ETT biofilm formation. Most of them have been tested separately or in combination, mainly in short-term experimental animal studies. Further clinical studies are needed to straighten out their efficacy as preventive strategies against VAP.

Overcoming the Disadvantages Of Endotracheal Tube

Early Tracheostomy

Tracheostomy has several advantages in patients who will require long orotracheal intubation and mechanical ventilation. It improves patients comfort, allows better oral hygiene, greatly facilitates secretion management, minimizes airway resistance and anatomic dead space, and reduces the risk of laryngeal injury.

The role of early tracheostomy (usually fewer than 7 days after translaryngeal intubation) in VAP prevention remains controversial. Some studies have found that early tracheostomy is more greatly associated with a lower incidence of VAP than late tracheostomy.[78,79] However other studies have found no such association.[80–86]

In a recent meta-analysis by Griffiths *et al.*[87] that enrolled 406 patients from five studies,[78–82] early tracheostomy did not significantly decrease the risk of pneumonia (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 days; 95% CI, −15.3 to −1.7 days), and length of stay in intensive care (mean difference, −15.3 days; 95% CI, −24.6 to −6.1 days). One obvious limitation of this meta-analysis is the small number of available randomized studies. Another limitation is the heterogeneity among the studies that arises because the exclusion and inclusion criteria differed across the trials and because each trial used a different definition of what constituted an early or late tracheostomy. Further studies are needed to clarify the timing of early tracheostomy and its efficacy in the incidence of VAP. At present, no recommendations can be addressed on this topic because of insufficient evidence.

Noninvasive Ventilation

Theoretically, the avoidance of intubation and mechanical ventilation would be the first defense against VAP. Noninvasive ventilation, the provision of ventilatory support with no use of an ETT, has revolutionized the management of acute respiratory failure, and it can decrease the tracheal intubation rates and even mortality.[88] Moreover, in patients who are appropriate candidates for noninvasive ventilation, the available evidence suggests a clear benefit in terms of a lower risk of pneumonia.[89,90] This is obviously related to the avoidance of intubation rather than the use of ventilator. Perhaps "endotracheal tube–associated pneumonia" is a better term than "ventilator-associate pneumonia."

Although noninvasive ventilation is still used in only a select minority of patients with acute respiratory failure, it has assumed an important role in the therapeutic armamentarium. With technical advances and new evidence on its proper application, this role is likely to expand in the near future. When feasible and not medically contraindicated the use of noninvasive ventilation instead of tracheal intubation may result in lower risk for development of VAP.

Conclusions

During the past few decades, numerous studies have been focused on the role of ETT in the pathogenesis of VAP. The presence of a foreign body (such as the ETT) in the airway, although critical for the management of the mechanically ventilated patient, also contributes substantially to the development of VAP; it precludes cough, impairs mucocilliary clearance, permit microaspiration of contaminated subglottic secretions around the cuff, and allows the intraluminal formation of biofilm. Despite this demonstrated risk and ongoing concern, the perfect design of an ETT for achieving a complete seal without compromising mucosal perfusion remains a matter of ongoing debate. However, ETT cuff pressure is recommended to be managed persistently within 20–30 cm H_2O to avoid aspiration.

The use of an endotracheal or tracheostomy tube with aspiration of subglottic secretions seems to decrease the incidence of VAP and should be recommended in patients expected to require more than 72 h of mechanical ventilation. The decontamination of subglottic space remains an attractive idea that needs further confirmation.

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The use of antiseptic-coated ETT is a promising method, but the evidence does not yetl permit its recommendation. The role of specifically designed devices aimed to prevent or eliminate ETT biofilm formation remains uncertified in clinical practice. Finally, the benefits from the early tracheostomy remain uncertain.

In conclusion, VAP is a nosocomial lung infection more related with the presence of an endotracheal tube in the patient's airway than with the ventilator *per se*. The term "*endotracheal tube–associated pneumonia"* could be recommended as describing better the pathogenesis than the term *"ventilator–associated pneumonia."*

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