

Prevention of ventilator-associated pneumonia in adults

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Abstract

Ventilator-associated pneumonia, broadly defined as pneumonia that develops after 48 hours of intubation, is a common mechanical ventilation complication that causes significant morbidity and mortality in critically ill patients. Prevention strategies are continually evolving to decrease the impact of this serious and costly disease.

Introduction and context

Ventilator-associated pneumonia (VAP) is thought to develop from microorganisms entering the sterile lower respiratory tract by aspiration of oropharyngeal secretions containing bacteria endemic to the digestive tract or exogenous pathogens acquired from contaminated equipment or health care workers [1,2]. Less commonly, the lower respiratory tract may be inoculated by direct inhalation of pathogens, hematogenous spread from a remote infection, or direct extension of a contiguous infection [1,2]. The most common etiologic agents are *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter*, and *Staphylococcus aureus* [1]. In healthy hosts, mucociliary clearance and innate immunity protect against pneumonia [2]. However, placement of an endotracheal tube impairs mucociliary clearance and provides a direct pathway for inoculation of the lower respiratory tract while critical illness weakens the immune system, putting critically ill, ventilated patients at high risk for developing pneumonia [2].

Prevention strategies focus on decreasing bacterial colonization of the oropharynx, reducing the frequency of aspiration, maintaining the immune system, and liberating patients from the ventilator as early as possible. These strategies have improved over the past decade and decreased the burden of disease. VAP previously occurred in 9-18% of mechanically ventilated patients [3] and was associated with a 20-50% mortality rate and a 7- to 9-day increase in hospitalization [4].

Newer data suggest that VAP incidence is 2-10 per 1000 ventilator days [5]. The cost of diagnosing and treating VAP is US \$5,000 to \$40,000 per incident [6,7]. Routine prevention strategies are summarized in Table 1. Emerging prevention strategies to consider in selected patient populations are summarized in Table 2.

Recent advances

Decreasing bacterial colonization of the oropharynx

In 2005, the Infectious Diseases Society of America and the American Thoracic Society published a comprehensive guideline for VAP prevention focusing on modifiable risk factors [1]. In 2008, the Canadian Critical Care Trials group published a similar guideline [8]. To decrease bacterial colonization of the oropharynx and endotracheal tube, these guidelines advocate using orotracheal rather than nasotracheal intubation, continuous subglottic secretion drainage, and standard infection control measures, including frequent hand washing, sterile central venous catheter placement, and isolation of resistant organisms. While continuous subglottic secretion drainage requires a special endotracheal tube that costs about US \$12 more than a standard tube, several studies have shown a significant reduction of VAP incidence with this intervention, as summarized in a recent review [9].

Decontamination of the oropharynx and digestive tract with systemic antibiotics, selective digestive decontamination, and selective oropharyngeal decontamination have all been shown to decrease bacterial colonization and VAP

Table 1. Recommended prevention strategies for ventilator-associated pneumonia in adult intensive care units

Avoidance of intubation and reintubation if possible
Orotracheal intubation over nasotracheal intubation
Continuous aspiration of subglottic secretions
Semi-recumbent positioning (head of bed elevated 30-45 degrees when possible)
Enteral feeding with post-pyloric feeding tube
Standard infection control measures
Daily sedation interruption paired with ventilator weaning protocol
Conservative transfusion policy
Sucralfate or H2 blockers over proton pump inhibitors for stress ulcer prophylaxis

Table 2. Ventilator-associated pneumonia prevention strategies to consider in selected patients

Early tracheostomy
Chlorhexidine mouthwash
Coated endotracheal tubes

incidence [10], but the practice remains controversial. While many studies have demonstrated decreased VAP incidence in patients treated with prophylactic antibiotics [10], the guidelines recommend against their use until more data on the effect on mortality and the risk of developing resistant organisms emerge [1,8]. In 2009, De Smet *et al.* [11] published the largest randomized trial to date on selective gut decontamination. After baseline differences between the treatment arms were adjusted for, there was a significant decrease in mortality for those treated with selective gut decontamination [11]. However, concerns about the external validity of the study remain because of the low incidence of resistant organisms encountered in the study population [12].

Oral cleansing with topical antiseptics such as chlorhexidine also reduces bacterial colonization with less potential for selecting resistant organisms but is similarly controversial. The 2005 guidelines recommend against using antiseptics because of the paucity of data [1]. Many subsequent trials on chlorhexidine have been published, but the results are conflicting so the controversy persists. Several meta-analyses [1,13] and clinical trials [14,15] suggest a benefit of chlorhexidine in decreasing VAP, whereas others have yielded negative results [16-18]. The 2008 guidelines recommend that oral chlorhexidine be considered [8].

Since the 2008 guidelines were published, a new silver-coated endotracheal tube designed to decrease bacterial colonization and biofilm formation was introduced. The NASCENT trial, a prospective, randomized, multi-center study comparing standard and coated endotracheal tubes, showed a significant reduction in VAP (4.8% versus 7.5%, $P = 0.03$) in patients treated with this coated tube. However, mechanical ventilation duration, hospital length of stay, and intensive care unit (ICU) length of

stay were unchanged between the control and intervention groups [4]. A numeric increase in mortality among patients assigned to the coated tubes (30.4% versus 26.6% for standard tubes, $P = 0.11$) needs to be evaluated further [4]. Furthermore, the cost of a coated tube is US \$90 compared with \$2 for a routine tube, but a recent cost-effectiveness analysis concluded that silver-coated tubes would likely save money because of their ability to prevent VAP [19].

Decreasing the frequency of aspiration

Enteral nutrition predisposes patients to aspiration of gastric contents and subsequent VAP [20] but is still considered preferable to parenteral nutrition because of the many complications associated with parenteral nutrition [20,21]. The 2005 guidelines recommend post-pyloric feeding tubes and semi-recumbent positioning with a head of bed angle of greater than 45 degrees to decrease the frequency of aspiration associated with enteral feeding [1]. Unfortunately, it is difficult to maintain patients at 45 degrees, and 30 degree elevation may not be as effective [22]. Some research suggests that postponing full-calorie nutrition may be another option [23]. A 2002 single-center study evaluating initial trophic feeding followed by delayed full-calorie nutrition found a significant reduction in VAP with no change in mortality compared with the control group [23]. A multicenter trial is now under way to confirm these results [24].

Maintaining natural immunity

Stress ulcer prophylaxis with acid suppression predisposes patients to developing VAP by raising the gastric pH levels and allowing bacterial overgrowth [25]. Sucralfate is an appealing option because it does not affect gastric pH, but it has been associated with increased bleeding and VAP incidence [26,27]. Citing conflicting evidence, the 2005 guidelines recommend using either sucralfate or H2 blockers for stress ulcer prophylaxis [1]. More recently, acid suppression therapy with more potent proton pump inhibitors has become widespread [25], but it was associated with a greater incidence of VAP than H2 blockers in a retrospective study [25]. To help maintain natural immunity, the guidelines also recommend a conservative transfusion policy and intensive insulin therapy since blood transfusion and hyperglycemia have been associated with increased infectious complications [1]. However, intensive insulin regimens have been increasingly scrutinized as new data suggesting their potential for harm emerge [28-30].

Liberating patients from the ventilator

The 2005 guidelines recommend avoiding intubation, and particularly reintubation whenever possible, as well

as installing protocols to reduce sedation and accelerate ventilator weaning [1]. In 2008, the Awakening and Breathing Controlled trial confirmed the importance of combining sedation and ventilator weaning protocols by showing a shorter duration of mechanical ventilation and significant mortality improvement in the intervention group [31].

For patients who are unlikely to be liberated from the ventilator quickly, early tracheostomy has been used to mitigate the risks associated with endotracheal intubation, but its role is controversial. A 2004 randomized clinical trial showed a significant reduction in VAP, duration of mechanical ventilation, and mortality in patients who received tracheostomy on ventilator day 2 rather than prolonged endotracheal intubation with tracheostomy on ventilator day 14 [32]. However, follow-up studies have not replicated these findings [33,34]. A 2006 meta-analysis showed decreased ventilation duration and ICU length of stay but no difference in mortality or VAP in those treated with early tracheostomy [34]. In 2008, a small randomized trial also showed no difference between tracheostomy within the first 4 days of intubation and prolonged intubation with tracheostomy allowed only after ventilator day 14, other than improved patient comfort, but the study was too underpowered to be conclusive [33].

Implications for clinical practice

VAP leads to excess morbidity, mortality, and costs in critically ill patients. While many prevention strategies have proven successful in decreasing the incidence of VAP by a small amount, significant reduction requires a multimodal approach encompassing positioning, equipment, nutritional support, infection control, sedation minimization, and ventilator weaning. Adjunctive therapies such as stress ulcer prophylaxis, glycemic control, and blood transfusion also play a role because of their impact on the immune system. Vigilant attention to all of these details by means of a ventilator bundle has been shown to significantly reduce the incidence of VAP [35,36]. Many other promising therapies, such as selective gut decontamination, early tracheostomy, and coated endotracheal tubes, remain controversial because of their mixed or limited data, so we await further trials to determine their role. VAP prevention remains an area of active research, with 28 clinical trials currently listed on www.clinicaltrials.gov.

Abbreviations

ICU, intensive care unit; VAP, ventilator-associated pneumonia.

Competing interests

The authors declare that they have no competing interests.

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