VENTILATOR-ASSOCIATED PNEUMONIA: THE POTENTIAL CRITICAL ROLE OF EMERGENCY MEDICINE IN PREVENTION

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Abstract—Background: Delivery of critical care within a certain window of opportunity is paramount in many disease states, and providing the right care to these patients at the right time in the Emergency Department (ED) can significantly reduce mortality. However, aggressive treatment of these patients often requires endotracheal intubation and mechanical ventilation either in the pre-hospital or ED phase of care. Care of mechanically ventilated patients in the ED is not trivial or without potential complications, including ventilator-associated pneumonia (VAP). Objective/Discussion: This article summarizes the epidemiology, pathophysiology, and specific risk factors associated with VAP and provides evidence-based recommendations for its prevention. We emphasize practices that are particularly important in the early stages of care of intubated, mechanically ventilated patients; thus, they should be instituted in the ED. Conclusion: Specifically, we recommend continuous backrest elevation of 30—45°, chlorhexidine application to the oral cavity after intubation and every 12 h thereafter, orotracheal intubation with a tube that enables continuous subglottic suctioning, and cuff pressure assessments after intubation and every 4 h thereafter to maintain pressure between 20 and 30 cm H2O. © 2010 Elsevier Inc.

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INTRODUCTION

Delivery of critical care within a certain window of opportunity is paramount in many disease states (e.g., myocardial infarction, trauma, stroke, respiratory failure, and sepsis). Providing the right care to these patients at the right time in the Emergency Department (ED) can significantly reduce mortality (1). However, aggressive treatment of these patients, as well as many patients with other disorders, often requires endotracheal intubation and mechanical ventilation either in the prehospital or ED phase of care. Care of mechanically ventilated patients in the ED is not trivial or without potential complications, including ventilator-associated pneumonia (VAP). VAP is defined as pneumonia occurring in a mechanically ventilated patient that is neither present nor developing at the time of intubation. Unfortunately, clinical evidence of VAP occurs only 48 h or more after intubation and thus, it may become manifest only days after the disease process has begun in the ED (2,3). In addition, because ED length of stay is increasing significantly, implementation of interventions to reduce VAP risk should optimally occur in the ED setting (4).

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and provides evidence-based recommendations for its prevention. We emphasize practices that are particularly important in the early stages of care of intubated, mechanically ventilated patients, and that should be instituted in the ED.

**DISCUSSION**

**Ventilator-associated Pneumonia: Epidemiology**

VAP is estimated to be responsible for 27–47% of intensive care unit (ICU)-acquired infections, and it is the second most common nosocomial infection in the United States (5,6). A recent systematic review concluded that VAP occurs in 10–20% of patients receiving mechanical ventilation for more than 48 h, and it is associated with increased ICU length of stay (mean = 6.10 days; 95% confidence interval [CI] 5.32–6.87 days) and mortality (pooled odds ratio, 2.03; 95% CI 1.16–3.56) (7). It is estimated that VAP leads to an average additional $40,000 cost of hospital services (8).

Traditionally, early-onset VAP is diagnosed 48–72 h after intubation, whereas late-onset VAP occurs after 72 h of intubation (2). The average time between intubation and diagnosis is 3.3 days (8). However, there is also recognition that pulmonary infection associated with mechanical ventilation occurs on a continuum that begins with colonization of the respiratory tract and can proceed to VAP, and may not be easily categorized as early vs. late. Recently, an intermediate on this continuum, ventilator-associated tracheobronchitis (VAT) has been identified. In VAT, clinical signs indicate pulmonary infection, but there are no accompanying changes on chest radiograph indicative of pneumonia (9). The overall mortality rate for VAP ranges from 24% to as high as 76% (10,11). Organisms responsible for VAP in the prehospital intubations differ significantly from those responsible for ED and inpatient trauma intubations (12). Community-acquired organisms such as *Haemophilus influenzae* and *Streptococcus spp.* are responsible for 74% of VAP related to field intubations and only 30–36% of VAP cases after ED and inpatient trauma intubations. Enteric Gram-negative rods and methicillin-sensitive *Staphylococcus aureus* are responsible for 26–35% of VAP in ED and inpatient intubated trauma patients, but account for only 0–13% of VAP in trauma patients intubated in the field (12).

Data reported by the Centers for Disease Control and Prevention (CDC) through the National Nosocomial Infections Surveillance reporting system indicate that the VAP rate is higher in trauma patients than in other patient groups (13,14). Trauma patients with severe head or neck injury seem to be at particularly high risk for VAP and they experience an increased ICU length of stay and increased mortality (15,16). Although the incidence of VAP in critically ill and injured patients coming from the ED is not known, there is compelling evidence in the trauma literature that it is substantial and that prehospital and ED intubation, as well as ED length of stay, are independent risk factors for the development of VAP (12,17,18). Research on VAP development in patients intubated in the ED is sparse and has focused mainly on trauma patients.

Other mechanically ventilated patient groups cared for in the ED are also likely to be at greater risk than their counterparts intubated in other hospital areas. Reasons for the increased incidence of VAP in ED patients are unclear, but may be related to the less-than-ideal environment in which intubation takes place (prehospital setting) and the fact that fewer VAP-related precautions are taken in the ED than in the ICU setting.

**Ventilator-associated Pneumonia: Pathogenesis**

The pathogenesis of VAP is thought to result primarily from the leakage of contaminated oropharyngeal secretions around the endotracheal tube cuff and into the lung. Thus, the major efforts to prevent VAP focus on aspects of care that affect this process.

**Role of oral health.** Oral flora change within the first 48 h of critical illness from the usual predominance of streptococci to more potentially pathogenic microbes, and these microorganisms have been hypothesized to contribute to VAP (19–22). Dental plaque, which may serve as a reservoir for potential VAP pathogens, also has been associated with nosocomial pneumonia (23–27).

**Role of the endotracheal tube (ETT).** Although the use of a cuffed ETT is considered the gold standard of airway management and airway protection against large volume aspiration, this does not guarantee prevention of VAP, which is most often caused by aspiration of small volumes around the cuff (microaspiration). An ETT also increases mucosal injury, reduces mucociliary function, and impairs upper airway defenses as a result of ineffective coughing and bypass of other upper airway defense mechanisms (28). The ETT can create binding sites for bacteria in the bronchial tree and it increases mucus secretion and the stagnation of secretions, promoting bacterial adherence. In addition, the ETT enhances bacterial entry into the lung by serving as a reservoir where bacteria remain inaccessible to host defenses (29). Also, ETT biofilm is a reservoir of potential VAP pathogens, because once the polyvinyl-chloride ETT is placed, the inside surface is rapidly colonized (30–32).

**Role of subglottic secretion accumulation.** Although an inflated ETT cuff provides protection against rapid
aspiration of large amounts of secretions, it is not totally preventative. When the cuff is inflated, creation of microchannels between the cuff and the tracheal mucosa is possible, and these are thought to contribute to the development of VAP. The anatomy of the airway and the presence of the ETT, coupled with inability of the patient to swallow and cough, allows accumulation of bacteria-laden secretions in the subglottic space, which can hold as much as 10.5 ± 5 mL of secretions (33,34). This accumulation has been shown to occur frequently (33,35). Movement of the patient or ETT is thought to increase the opportunities for microaspiration through a combination of microchannels and subglottic secretion accumulation.

**Role of backrest elevation.** The CDC recommendations for the prevention of nosocomial bacterial pneumonia in patients receiving mechanical ventilation include elevation of the head of the bed at an angle of 30°–45° if there are no contraindications, with more recent recommendations of even higher elevations (45° or greater) (36–38). The supine position has been shown to be an independent risk factor for mortality in mechanically ventilated patients (39,40). In those patients receiving enteral feeding, low backrest position (angle < 30°) is a risk factor for aspiration and pneumonia, whereas Fowler’s position (head of bed 45° or higher) has been associated with lower incidence of gastric aspiration and pneumonia (41–44).

**Role of gastric alkalinization.** Gastric alkalinization, using H2-antagonists and antacids, is beneficial in reducing stress ulcers in the critically ill. However, increasing gastric pH may increase gastric colonization with pathogenic organisms that can then be aspirated and increase VAP risk (45–47). Meta-analyses of stress ulcer prophylaxis studies have shown that prophylaxis with sucralfate or histamine-2 receptor antagonists is associated with minimal risk of VAP, although there is still controversy about which is optimal (48–50). Two groups that examined the effect of proton pump inhibitors on nosocomial pneumonia found no significant differences in pneumonia rates compared to histamine-2 receptor antagonists or sucralfate (51,52). However, in a very recent, large, prospective pharmacoepidemiologic cohort study in hospitalized (but not ICU patients), Herzig et al. found that the incidence of hospital-acquired pneumonia was higher in patients exposed to acid-suppressive medication than in the unexposed group (4.9% vs. 2.0%, respectively; odds ratio [OR], 2.6; 95% confidence interval [CI], 2.3–2.8) (53). The association was significant for proton-pump inhibitors (OR, 1.3; 95% CI, 1.1–1.4) but not for histamine-2 receptor antagonists (OR, 1.2; 95% CI, 0.98–1.4).

**VAP Prevention Strategies**

**Oral care.** Several studies have examined the effectiveness of oral care interventions, both mechanical (tooth brushing) and pharmacologic (chlorhexidine, povidone-iodine), in reducing VAP. Chlorhexidine (CHX), an antiseptic agent, is extensively used in healthy populations as an oral rinse or gel to control dental plaque and prevent or treat gingivitis. Several randomized controlled trials have examined the effect of topical oral CHX on the incidence of nosocomial pneumonia (26,54–57). Some studies suggest that oral application of CHX can prevent infectious complications (including both surgical wound infections and respiratory infections) in patients undergoing elective cardiovascular surgery (54,55,58).

Two recent meta-analyses have evaluated the effect of oral decontamination on the incidence of VAP. Chan et al. reviewed 11 trials with a total of 3242 patients (59). Seven trials demonstrated significantly reduced VAP with oral application of antiseptics (CHX or povidone iodine), and 4 did not. When the results of the 11 trials were pooled, VAP rates were lower in those receiving either method of oral decontamination, although duration of mechanical ventilation, ICU length of stay, and mortality were not reduced by either method (59). A meta-analysis by Chlebicki and Safdar to evaluate the efficacy of CHX in VAP prevention found that in seven randomized, controlled trials, CHX significantly reduced VAP (p = 0.02); the greatest benefit was found in cardiac surgery patients (60).

Although tooth brushing is effective for mechanical removal of dental plaque, there is no convincing evidence that tooth brushing reduces VAP risk (61). Most studies of the effectiveness of mechanical oral care have been anecdotal or used a non-experimental design, and many studies included oral care along with other interventions with proven efficacy (e.g., head of bed elevation), and tested all the interventions together as a bundle. More studies using randomized controlled designs are needed to clarify the effect of tooth brushing on VAP.

In the only randomized, controlled trial to date that evaluated both mechanical (tooth brushing) and pharmacologic (CHX) oral interventions implemented up to 7 days after intubation, Munro et al. found that in 249 subjects, CHX alone reduced VAP among subjects who were without pneumonia at baseline (p = 0.0065), whereas tooth brushing had no effect on VAP (62). When subjects with and without pneumonia at baseline were analyzed together, no effect of either CHX (p = 0.6903) or tooth brushing (p = 0.95) was found. In addition, in a recent randomized trial of an early (within 12 h), single application of CHX in trauma victims (n = 145), Grap et al. found a significant reduction (p = 0.023) in VAP in the treatment group at both 48 and 72 h after the CHX intervention.
Cubation, cultures of antiseptic ETTs revealed pathogen ETT contamination with VAP pathogens and 5 days of incubation with VAP. Several approaches have been suggested to overcome this problem. Recently, ETTs coated with antiseptics have been developed. In a laboratory model to evaluate the effect of ETTs impregnated with CHX and silver carbonate, Pacheco-Fowler et al. found that after ETT contamination with VAP pathogens and 5 days of incubation, cultures of antiseptic ETTs revealed pathogen colonization ranging from 1–106 cfu/tube, compared with approximately 106 cfu/tube for the control ETTs (p < 0.001) (64). Subcultures from proximal and distal ends showed minimal or no growth in the antiseptic ETTs compared with the control ETTs (p < 0.001). The authors concluded that the antiseptic ETTs prevented bacterial colonization in the airway and also retained significant amounts of the antiseptic, but reduction in ETT VAP pathogens could vary with different organisms. In an animal model, Olson et al. also showed that an ETT coated with antimicrobial silver hydrogel delayed bacterial appearance on the inner surface of the ETT by 3.2 ± 0.8 days (65). The bacterial load in the lung parenchyma was also significantly lower among dogs receiving the silver-coated ETTs than in those receiving standard ETTs (P = 0.010). Recently, silver-coated endotracheal tubes have been developed in an effort to reduce bacteria in the airways. In a prospective, randomized, single-blind, multi-center trial, Rello et al. found slower colonization from the oral cavity into the subglottic space and eventually into the lung increases the risk of VAP, and an effective ETT cuff seal may reduce secretion movement. The recommended range for ETT cuff pressure is 20–30 cm H2O (14,70). However, Sole et al. found that cuff pressures decreased within 4 h of inflation (average decrease of 2.8–3.8 cm H2O) and dropped to as low as 9 cm H2O (72). Greater pneumonia risk has been associated with cuff pressures below 20 cm H2O (72,84). At the same time, high ETT cuff pressure has been associated with tracheal mucosal damage, and Galinski et al. found that in patients intubated outside of the hospital setting, the first recorded mean cuff pressure was higher than that considered safe (85,86). Therefore, ETT cuff pressure monitoring should be performed as soon as possible after intubation, and pressures maintained between 20 and 30 cm H2O, including in the ED and continued at regular intervals, for instance, every 4 h.

Cuff pressure management. The movement of secretions from the oral cavity into the subglottic space and eventually into the lung increases the risk of VAP, and an effective ETT cuff seal may reduce secretion movement. The recommended range for ETT cuff pressure is 20–30 cm H2O (14,70). However, Sole et al. found that cuff pressures decreased within 4 h of inflation (average decrease of 2.8–3.8 cm H2O) and dropped to as low as 9 cm H2O (72). Greater pneumonia risk has been associated with cuff pressures below 20 cm H2O (72,84). At the same time, high ETT cuff pressure has been associated with tracheal mucosal damage, and Galinski et al. found that in patients intubated outside of the hospital setting, the first recorded mean cuff pressure was higher than that considered safe (85,86). Therefore, ETT cuff pressure monitoring should be performed as soon as possible after intubation, and pressures maintained between 20 and 30 cm H2O, including in the ED and continued at regular intervals, for instance, every 4 h.

Subglottic secretion removal. Removal of subglottic secretions has been recommended to reduce VAP risk (37,70,71,87). As a result, a special ETT has been designed with an additional length spanning the lumen and a port to allow continuous microaspiration of subglottic secretions (CASS). In a randomized controlled trial, Kollef et al. found no significant differences in VAP rate with or without CASS in 343 cardiac surgery patients, but the patients receiving CASS developed VAP later than patients who did not receive CASS (88). However, there were no differences in hospital mortality, overall duration of mechanical ventilation, or length of hospital stay. Other randomized controlled trials that investigated the effects of intermittent or continuous subglottic secretion drainage on VAP rate found that subglottic drainage reduced VAP rates (89,90). Recently, Dezfulian et al.
performed a pooled analysis of 896 patients in five studies and found that subglottic secretion drainage reduced the risk of VAP by 49% (relative risk 0.51, 95% CI 0.31–0.71), although there was no difference in mortality (91). Therefore, performing orotracheal intubation using a tube that enables continuous subglottic suctioning should be considered, especially in patients who may require intubation for 48 h or longer.

**Backrest elevation.** Use of higher backrest positions (> 30°–45°) may be most important in the early hours and days of mechanical ventilation. In a study to identify risk factors for VAP, Kollef found that supine head positioning during the first 24 h was one of the four most important VAP risk factors (which also included organ system failure, age > 60 years, and prior antibiotic use), and ICU mortality was greater for supine patients (30.2%) than for semi-recumbent patients (8.9%) (39). Interestingly, 32% of patients in the supine position had no clear indication for that position. In a longitudinal study of the effect of backrest elevation on VAP, Grap et al. continuously measured elevation in 66 subjects for up to 7 days (92). Subjects were at backrest elevations lower than 30° 72% of the time and lower than 10° 39% of the time. The final model predicting VAP using the Clinical Pulmonary Infection Score at Day 4 included baseline Clinical Pulmonary Infection Score, percent of time spent under 30° on study Day 1 (first 24 h of intubation), and the Acute Physiology and Chronic Health Evaluation II score, and explained 81% of the variance (F = 7.31, p = 0.0033). These results indicate that the combination of early low backrest elevation and severity of illness leads to VAP. Many of the first 24 h of intubation are frequently spent in the ED, highlighting the importance of instituting use of higher backrest elevation in this setting.

However, adherence to backrest elevation recommendations (30° or greater) is not common practice (93,94). Van Nieuwenhoven et al. attempted to examine the effect of 45° backrest elevation on VAP rate, but comparisons could not be made because this level of elevation was not achieved (95). In fact, actual elevations did not achieve the minimum standard (28.1° at day 1; 22.6° at day 7). Cook et al. interviewed 93 ICU clinicians (bedside nurses, respiratory therapists, physiotherapists, nutritionists, residents, fellows, and intensivists) about their knowledge and use of backrest elevation of 45° or more and concluded that under-utilization results from lack of awareness of its benefit, poor understanding of implementation responsibility, and a lack of enabling and reinforcing strategies (96). Recently, the implementation of national recommendations has increased, and quality improvement projects have shown that implementation of higher backrest positions, often in combination with other VAP prevention strategies, reduces the incidence of VAP (70,97–100).

Use of backrest elevation may be one of the fastest and easiest ways for emergency physicians, nurses, and respiratory therapists to help prevent VAP. In trauma patients, this requires ruling out contraindications such as spinal cord or spinal column injury. However, with greater use of imaging at trauma centers, such injuries can be excluded much earlier. Head of bed elevation is already widely used for patients with traumatic brain injury to assist in managing either documented or presumed intracranial hypertension. For other critically ill intubated patients, such as those with sepsis, cardiogenic shock, post-cardiac arrest, or non-traumatic cerebral catastrophe, the only potential contraindication to head of bed elevation may be hypotension, with inability to maintain a mean arterial pressure sufficient to assure an adequate cerebral perfusion pressure, assuming that cerebral autoregulation is intact. Therefore, use of backrest elevation of 30°–45° is recommended for all intubated ED patients without contraindications, but as the data show, a collaborative effort among all disciplines is required to ensure compliance.

**Multi-factorial VAP Reduction Approach**

Effective risk reduction for VAP is likely to require multiple interventions or bundles (interventions that when implemented together may achieve significantly better outcomes than when implemented alone). The 100 K Lives campaign, an effort to reduce patient morbidity and mortality in the ICU, began with the development of the VAP bundle. This bundle includes head of bed elevation, daily sedation assessments and awakenings, and peptic ulcer and deep vein thrombosis prophylaxis. Use of the ventilator bundle has been shown to significantly reduce rates of VAP, ventilator days, and ICU length of stay (97,101,102). However, compliance with bundle interventions is essential to achieve success, and these strategies are not typically instituted in the ED. Cocanour et al. found that in the ICU, VAP did not initially decrease with institution of the VAP bundle, but when compliance with implementation of the VAP bundle was audited daily and feedback was provided to the care providers on a weekly basis, VAP was significantly decreased, resulting in fewer ventilator days and decreased costs (103).

In a collaborative improvement project in 61 health care organizations, Resar et al. reported an average 44.5% reduction of VAP in 35 units that consistently collected data on ventilator bundle element adherence and VAP rates (102). In addition, after instituting the VAP bundle, Crunden et al. found reductions in ventilator days and ICU length of stay (102).

Other studies have shown that in addition to use of the ventilator bundle, educational strategies may reduce VAP.
Joiner et al. developed an evidence-based protocol to reduce VAP in an acute care teaching medical center, and after a 4-month introductory and learning period, the protocol resulted in a significant reduction in VAP as well as cost savings (99). Similarly, Zack et al. found that an intensive education program directed toward respiratory care practitioners and ICU nurses decreased the VAP rate by 57.6%, and dramatically reduced costs (100).

Given the rising number of ED patients admitted to ICUs, it is reasonable to expect that the patient’s waiting time in the ED before reaching the ICU will also increase. Thus, multidisciplinary decision-making on the use of bundle implementation in the ED is worthy of consideration.

CONCLUSIONS

Although further study is required to address all aspects of VAP reduction, certain interventions based on empirical support should be instituted now for mechanically ventilated patients (Table 1). Several of these (highlighted) are appropriate for initiation in the ED before the patient’s admission to an ICU. The success of these strategies, however, is highly dependent on when (how soon after intubation) and where they are carried out. None of the strategies discussed in this article have been reported to be carried out in the ED. Yet, the final success of any strategy is dependent on its execution within an optimal window of opportunity. Thus, early goal-directed therapy carried out in the ED is at least as important as goal-directed therapy carried out in the ICU many hours after a patient becomes ill.

VAP is a common complication of mechanical ventilation with significant morbidity and mortality. This article summarizes the data on specific risk factors associated with VAP (patient position, oral health, airway management, and gastrointestinal factors) and provides recommendations for practice based on current evidence. Only consistent use of evidence-based care for mechanically ventilated patients will help to improve outcomes for this population. Most importantly, these strategies must be tried and tested in the ED environment.

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ARTICLE SUMMARY

1. Why is this topic important?

Ventilator-associated pneumonia (VAP) is a significant complication of mechanical ventilation that results in increased morbidity, mortality, and health care costs. Efforts to enhance prevention are therefore a high priority, and prevention should begin in the emergency department (ED).

2. What does this review attempt to show?

This review shows that there are important strategies that should be implemented in the ED to reduce the risk of VAP.

3. What are the key findings?

We recommend continuous backrest elevation of 30°–45°, chlorhexidine application to the oral cavity after intubation and every 12 h thereafter, orotracheal intubation with a tube that enables continuous subglottic suctioning, and cuff pressure assessments after intubation and every 4 h thereafter to maintain pressure between 20 and 30 cm H2O.

4. How is patient care impacted?

The impact on patient care is a reduction in VAP risk with resulting decreases in duration of mechanical ventilation, intensive care unit and hospital stay.