

Chapter 11. Ventilator-Associated Pneumonia: Brief Update Review

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Introduction

Ventilator associated pneumonia (VAP) is defined as a hospital-acquired pneumonia that develops within 48 to 72 hours after endotracheal intubation; the diagnosis hinges on a lack of evidence suggesting that the infection developed prior to intubation. VAP is the most common intensive care unit (ICU)-acquired infection, accounting for 25 percent of all ICU infections and 50 percent of ICU antibiotic use. At least 250,000 VAPs occur in the United States (U.S.) each year. This condition causes complications in 8 to 28 percent of mechanically ventilated patients and carries a mortality risk of approximately 10 percent (range 6% to 27%), resulting in a possible 25,000 VAP-attributable deaths every year. Patients who develop VAP stay, on average, 4 days longer in the ICU. The per-case cost of VAP is estimated to be \$23,000, and the total incremental costs to the U.S. health care system are high: \$2.19 to 3.17 billion USD per year¹⁻³ The wide range of these estimates results from the lack of universally accepted, reliable diagnostic criteria for VAP is present. The diagnosis of VAP may be based on any of a variety of definitions, including a surveillance definition, a clinical definition, a microbiologically confirmed definition, or a combination of the three methods. Microbiologically confirmed definitions also may be differentially based on blind tracheal aspirates, directed bronco-alveolar lavage, or even protected brush specimens.²

The original “Making Health Care Safer” report examined four interventions related to VAP: variation of position (semi-recumbent positioning and continuous oscillation), continuous subglottic suctioning, selective decontamination of the gastro-intestinal tract and the use of sucralfate. While the data in favor of semi-recumbent positioning was limited (reduced VAP but did not change mortality), the practice was judged to be easy to implement and had essentially no cost or adverse effects. Oscillation was less clear in its benefit secondary to poor methodological quality of the studies. While no evidence for harm was found, there were increased costs, estimated to be about \$100/day at the time of that report. Subglottic suctioning was judged to be a promising strategy. At the time of the report, it was infrequently used and there were only a few studies. Harmful effects were felt to be negligible but there were incremental costs for the specialized endotracheal tubes required for this strategy. Selective gastro-intestinal decontamination was found to have strong benefit for reducing VAP, though cost-effectiveness was unclear. Of the trials examined, none reported adverse events from this practice; however, there is continued concern that this practice may have a deleterious effect on antibiotic sensitivity in general, leading to more resistant organisms over time in individuals as well as on a population basis. Sucralfate as a VAP prevention strategy was judged to be inconclusive. Additionally, sucralfate is inferior compared with H-2 blockers for preventing gastro-intestinal bleeding. Given the increased risk of mortality with gastrointestinal bleeding and the increased costs should this complication occur, sucralfate can no longer be recommended for VAP prevention and H-2 blockers are the preferred agent for preventing gastro-intestinal bleeding in critically ill patients.

This updated review focuses on four strategies as well; elevation of the head of the bed, sedation vacations, oral care with chlorhexidine and subglottic suctioning.

What Are the Patient Safety Practices for Preventing Ventilator-Acquired Pneumonia?

We conducted a systematic review of the literature to update a 2001 review conducted for the original report. A recent study estimates that 14,000 to 20,000 lives could be saved each year in the U.S. if best practices to prevent VAP were universally applied to all patients on mechanical ventilation.³ The four primary recommended practices include: elevating the head of the bed to 30 degrees, sedation vacations, oral care with chlorhexidine (CHG), and subglottic suctioning endotracheal tubes. Ventilator “bundles” usually include other elements such as deep venous thrombosis (DVT)/pulmonary embolism (PE) prophylaxis and Peptic Ulcer Disease prophylaxis, but these procedures are designed to prevent other ventilator-associated conditions and do not address VAP prevention specifically. In fact, Peptic Ulcer Disease prophylaxis may increase the risk of VAP. Other VAP-specific preventive interventions may include use of closed suctioning circuits, scheduled circuit changes and a preference for orotracheal over nasotracheal intubation. The remainder of this section describes the evidence in support of the four primary VAP specific practices.

Head-of-Bed Elevation

The practice of head-of-bed elevation to prevent VAP has been recommended by several medical groups including the Canadian Critical Care Trials Group, the American Thoracic Society and Infectious Diseases Society of America, and the Centers for Disease Control and Prevention. This recommendation is based on early data showing that being supine was an independent risk factor for VAP.⁴ Importantly, a study in 1999 by Drakulovic and colleagues⁵ demonstrated a reduction in VAP with patients in the semi-upright position.⁵

A recent systematic review by Niel-Weisse and colleagues that applied strict inclusion criteria (randomized or quasi-randomized trial, published as a full paper and not an abstract, state the outcome measures used and present data sufficient to calculate the risks in both groups) and included only three of 208 potential studies, representing a total of 337 patients questioned whether patients’ head elevation can be maintained continuously above 30 degrees in ICUs, and point prevalence assessments used in many studies may overstate how often the goal is met.⁴ The effect of head-of-bed elevation on the incidence of both clinically diagnosed and microbiologically confirmed VAP was found to be non-significant (RR = 0.47, 95% CI = 0.19 to 1.17 and RR = 0.67, 95% CI = 0.23 to 2.01, respectively). A second study used broncho-alveolar lavage, and the other two used tracheal aspirates for the microbiological assessment. The third study found no significant increase in harm (decubitus ulcers); other potential harms (such as DVT) were not assessed. These same three trials also found no significant impact on mortality (pooled RR = 0.90, 95% CI = 0.64 to 1.27). The data were also judged to be of low quality for methodological reasons. Despite these findings, an evaluation of the results using an online Delphi process recommended the practice of keeping the head of the bed elevated by greater than 30 degrees to prevent VAP (most studies had actually used 45 degrees as their target).⁴ The favorable point estimates (all favored the intervention despite lack of statistical significance) and the lack of measurable harm may have influenced this recommendation.

Sedation Vacations

The use of sedation vacations, or sedation holds, has been shown to help patients wean from mechanical ventilation more quickly than when these techniques are not employed.^{6,7} Further, sedation vacations reduce patients’ exposure and subsequent risk of VAP as well as several other

mechanical ventilation-associated complications,^{6,7} and are, themselves, considered to be safe⁷. One pre-post study that examined a sedation protocol that specified daily interruption of sedatives in combination with spontaneous breathing trials demonstrated reduced ventilator days and reduced length of hospital stay. Although the sedation interruption group had a higher rate of self-extubation, the proportion of patients that required re-intubation was similar pre- and post intervention.⁷ These findings suggest that sedation vacations should be part of all ventilator and VAP prevention bundles.

Oral Care Using Chlorhexidine

Oral care using chlorhexidine (CHG) to reduce VAP is based on evidence that in intubated patients, gingival and dental plaque become rapidly colonized with bacterial overgrowth due to loss of natural mechanical elimination and poor hygiene. This microbiological burden becomes a source for aspiration of bacteria around the endotracheal tube cuff, resulting in pulmonary infection. Instituting meticulous oral care can reduce this microbiological burden and the potential for VAP. A systematic review in 2007⁸ that included seven randomized controlled trials (RCTs; 1,650 patients) evaluating CHG found a statistically significant reduction in the risk for VAP using a fixed effects model (RR=0.74 95% CI=0.56-0.96). Although the effect was found to be non-significant when a random effects model was applied, the absolute risk reduction was slightly better (RR=0.70, 95% CI= 0.47-1.04).⁸ A sub-group analysis of oral care using CHG in cardiac surgery patients did support the finding of a statistically significant reduction in the risk for VAP (RR=0.41, 95% CI=0.17-0.98)⁸

In 2008, the Canadian VAP Prevention Guidelines⁹ advised that oral care with CHG should be considered for VAP prevention, and the SHEA guidelines¹⁰ recommended regular oral care with an antiseptic solution. Although the SHEA guidelines did not specifically recommend CHG, all three of the studies that were cited as a basis for the recommendation used CHG.¹⁰

A 2011 systematic review of the effects of CHG¹¹ that included 12 RCTs (2,341 patients) further supported the previous findings. The relative risk of VAP after oral care with CHG was reduced 28 percent for all patients (RR, 0.72; 95% CI, 0.55 to 0.94); 59 percent for cardiac surgery ICU patients (RR, 0.41; 95% CI, 0.17 to 0.98); 33 percent for trauma/surgical ICU patients (RR, 0.67; 95% CI, 0.50-0.88); and 28 percent for mixed ICU patients (RR, 0.77; 95% CI, 0.58-1.02 for mixed ICUs). Evidence has also shown that using a 2% solution of CHG is superior to a 0.2% solution, which is superior to 0.12%.¹¹

Subglottic Suctioning Endotracheal Tubes

Subglottic suctioning tubes address the tendency for nasal-oral secretions and debris to pool above the endotracheal tube cuff and below the vocal cords. This pooling creates a rich culture medium for micro-organisms found in the nasal-opharynx, which leads to overgrowth and is thought to be a major cause of VAP. Subglottic suctioning endotracheal tubes use a port or ports just above the cuff to allow removal of this pooled material so it cannot act as a culture medium or be aspirated. Some of the systems use a simple single suctioning port, whereas others use an active lavage system with an inflow and outflow port to “wash “out the material. Our review identified no studies that directly compared these types of subglottic suctioning tube design (or continuous vs. intermittent suction); nevertheless, the evidence is strongly in favor of these devices for the reduction of VAP. Among 13 RCTs (2,442 patients) identified for a recent systematic review,¹² 12 of the RCTs found that subglottic suctioning reduced VAP; the pooled risk-reduction was 0.55 (95% CI=0.46 to 0.66, $p<0.00001$) with no heterogeneity in the studies.

This practice also significantly reduced the duration of mechanical ventilation and length of stay in the ICU, although it had no impact on ICU- or hospital mortality.

How Have Practices To Prevent Ventilator-Acquired Pneumonia Been Implemented and What Has Been Learned?

Practices to prevent VAP are usually “bundled” into a care package of several elements as described above. The package may also incorporate elements beyond the four discussed above, including closed in-line endotracheal suctioning systems, humidification systems, and non-VAP specific interventions such as DVT/PE prophylaxis, for which ventilated patients are at increased risk. In a 2005 pre-post study, Resar and colleagues reported a 45 percent reduction in VAP across 35 ICUs that used such a bundled approach in a collaborative. This particular bundle used only sedation vacations and head-of-bed elevation as VAP-specific elements.¹³ Subsequent pre-post studies have also found that bundled elements synergistically reduced the rate of VAP by as much as 40 percent in both adult and pediatric patient populations.^{14,15}

One factor that has been noted in most of these publications is the difficulty of ensuring that all patients who qualify for the bundle and the individual elements within the bundle (e.g., for some patients—such as spine surgery patients with a dural tear—head-of-bed elevation may be contraindicated,) actually receive the bundle’s elements consistently. The Michigan Keystone Project addressed this quality gap through a process of developing and applying technical tools such as checklists and ensuring their use through improvements in teamwork and the safety climate within 112 ICUs. This pre-post study found a 71 percent risk reduction in VAP, while at the same time demonstrating an increase in the adherence to evidence-based practices from 32 percent at baseline to 84 percent after 30 months.¹⁶ This finding suggests that a combination of effective evidence-based bundle elements reinforced with strategies to improve teamwork and safety can ensure that patients receive appropriate care and that outcomes improve substantially.

Others have also noted this positive effect of collaboratives on closing the quality gap. In their evaluation of the routine use of VAP prevention practices, Krein and colleagues (2008)¹⁷ found that use of semi-recumbent positioning was much more prevalent than the use of subglottic drainage (73% vs. 21% of hospitals that reported use of VAP practices). They also found that use of semi-recumbent positioning was strongly influenced by participation in collaboratives (such as the Keystone Project) and is considered primarily a responsibility of nursing staff. In contrast, use of subglottic suctioning endotracheal tubes is not influenced very much by collaboratives and is primarily a physician decision. It is unclear whether these differences are secondary to the participation in collaboratives, depend on who has the primary responsibility for decisionmaking, or both. Interestingly, the authors also noted that whereas the prevalence of semi-recumbent positioning was dramatically higher than that of subglottic drainage, when the effectiveness of the techniques was compared, the supportive evidence for subglottic drainage was found to be much stronger than for semi-recumbent positioning (five randomized studies vs. two). More recently, Krein (2011)¹⁸ reported that the prevalence of use of VAP prevention measures was also strongly influenced by the threat of non-payment for this hospital-acquired infection, although the use of any one bundle component for preventing VAP varied across respondents to their survey. This finding would suggest that efforts to close the quality gap and improve the prevalence of use of prevention practices will need to be multi-factorial.

The cost-effectiveness of several VAP prevention practices—both subglottic suctioning endotracheal tubes and VAP bundles—has been assessed. For subglottic suctioning tubes, it is

estimated that 11 people need to be treated (number needed to treat) in order to prevent one VAP. Although the cost of these endotracheal tubes is approximately \$18 USD, one model of continuous washing tubes (inflow/outflow ports with pumping system) costs about \$200 USD. In comparison, the cost of a standard endotracheal tube is approximately \$1 USD. If the number needed to treat is accurate, these special endotracheal tubes (even the most expensive versions) are cost-effective, especially if reserved for patients likely to remain intubated for more than 48 to 72 hours (the risk for VAP in those requiring intubation less than 48- to 72 hours is considered low). This conclusion is further supported by Hallais and colleagues,¹⁹ who compared the cost of these tubes to the cost of VAP, using very conservative values. The authors found that averting only three VAPs would offset the cost of the special tubes. Based on this cost analysis, any ICU with at least 3 VAPs per year would find that switching to these tubes reduces harm as well as costs.

Ventilator bundles have also recently been evaluated for their cost-effectiveness. A Danish study²⁰ retrospectively examining ventilated patients in a single ICU found that the cost of preventing one VAP was 4451 €(approximately \$6,000 USD), and the cost of preventing one death was 31792 €(approximately \$42,000 USD). While the cost and incidence of each VAP varies across patient populations, the study concluded that the ventilator bundle would likely be cost-effective in most environments.

Conclusions and Comment

In conclusion, of the four key practices for preventing VAP, subglottic suctioning endotracheal tubes have strong evidence to support their ability to reduce VAP and to do it cost-effectively, based on a systematic review of multiple RCTs. Strong evidence from a recent systematic review of multiple RCTs also supports oral care using CHG. Evidence from a few non-randomized studies supports sedation vacations directly. This evidence is of moderate strength. The maintenance of a head-of-bed elevation of at least 30 degrees (a ubiquitous element of VAP prevention bundles) is supported by very little evidence, yet remains part of virtually all recommendations by U.S. quality and safety organizations. This tacit support is likely a result of its ease and lack of evidence of harm, although the ability to effectively implement this element consistently has been questioned. Other elements often advocated for VAP prevention but not specifically addressed in this chapter include using antimicrobial-coated endotracheal tubes (evidence supports effectiveness),²¹ closed circuit in-line suctioning systems (evidence does not support their effectiveness)²² and humidification circuits on ventilators (evidence does not support their benefit).²³

Evidence from multiple large pre-post studies also supports the effectiveness of VAP bundles. While the evidence for each specific VAP prevention bundle element may vary, two principles are clear. First, VAP is most effectively reduced by the bundling of several elements together for a potentially synergistic effect, and bundles should be developed locally based on both institutional expertise and evidence, with ongoing evaluation of the success of the interventions. Second, the consistent application of each of the bundle elements to all patients who qualify for them is essential to success. The use of teamwork tools and strategies to ensure this consistency can have a tremendous impact on closing this quality gap and improving patient outcomes. Technical work (the bundle) needs to be supported by adaptive work (the processes needed to apply the bundle consistently) for the best success.¹⁸ A summary table is located below (Table 1).

Table 1, Chapter 11. Summary table

| Scope of the Problem targeted by the PSP (Frequency/Severity) | Strength of Evidence for Effectiveness of the PSPs | Evidence or Potential for Harmful Unintended Consequences | Estimate of Cost | Implementation Issues: How Much do We Know?/How Hard Is it? |
|---|--|---|------------------|---|
| Common/High | Moderate-to-high | Low | Low-to-moderate | Moderate/Moderate |

References

1. Calfee DP. Crisis in hospital-acquired, healthcare-associated infections. *Annu Rev Med* 2012; 63:359-71.
2. Vincent JL, de Souza Barros D, Cianferoni S. Diagnosis, management and prevention of ventilator-associated pneumonia: an update. *Drugs* 2010; 70(15):1927-44.
3. Umscheid CA, Mitchell MD, Doshi JA, et al. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. *Infect Control Hosp Epidemiol* 2011; 32(2):101-14.
4. Niel-Weise BS, Gastmeier P, Kola A, et al. An evidence-based recommendation on bed head elevation for mechanically ventilated patients. *Crit Care* 2011; 15(2):R111.
5. Drakulovic MB, Torres A, Bauer TT, et al. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet* 1999; 354(9193):1851-8.
6. Schweickert WD, Gehlbach BK, Pohlman AS, et al. Daily interruption of sedative infusions and complications of critical illness in mechanically ventilated patients. *Crit Care Med* 2004; 32(6):1272-6.
7. Dries DJ, McGonigal MD, Malian MS, et al. Protocol-driven ventilator weaning reduces use of mechanical ventilation, rate of early reintubation, and ventilator-associated pneumonia. *J Trauma* 2004; 56(5):943-51; discussion 951-2.
8. Chlebicki MP, Safdar N. Topical chlorhexidine for prevention of ventilator-associated pneumonia: a meta-analysis. *Crit Care Med* 2007; 35(2):595-602.
9. Muscedere J, Dodek P, Keenan S, et al. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: prevention. *J Crit Care* 2008; 23(1):126-37.
10. Coffin SE, Klompas M, Classen D, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals. *Infect Control Hosp Epidemiol* 2008; 29 Suppl 1:S31-40.
11. Labeau SO, Van de Vyver K, Brusselaers N, et al. Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. *Lancet Infect Dis* 2011; 11(11):845-54.
12. Muscedere J, Rewa O, McKechnie K, et al. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. *Crit Care Med* 2011;39(8):198591.
13. Resar R, Pronovost P, Haraden C, et al. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf* 2005; 31(5):243-8.
14. Bonello RS, Fletcher CE, Becker WK, et al. An intensive care unit quality improvement collaborative in nine Department of Veterans Affairs hospitals: reducing ventilator-associated pneumonia and catheter-related bloodstream infection rates. *Jt Comm J Qual Patient Saf* 2008; 34(11):639-45.
15. Rosenthal VD, Alvarez-Moreno C, Villamil-Gomez W, et al. Effectiveness of a multidimensional approach to reduce ventilator-associated pneumonia in pediatric intensive care units of 5 developing countries: International Nosocomial Infection Control Consortium findings. *Am J Infect Control* 2011.

16. Berenholtz SM, Pham JC, Thompson DA, et al. Collaborative cohort study of an intervention to reduce ventilator-associated pneumonia in the intensive care unit. *Infect Control Hosp Epidemiol* 2011;32(4):305-14.
17. Krein S, Kowalski CP, Damschroder L, et al. Preventing Ventilator-Associated Pneumonia in the United States: A Multicenter Mixed-Methods Study *Infect Cont and Hosp Epid* 2008; 29:933-940.
18. Krein S, Kowalski CP, Hofer TP, et al. Preventing Hospital-Acquired Infections: A National Survey of Practices Reported by U.S. Hospitals in 2005 and 2009. *J. Gen Int Med* 2011.
19. Hallais C, Merle V, Guitard PG, et al. Is continuous subglottic suctioning cost-effective for the prevention of ventilator-associated pneumonia? *Infect Control Hosp Epidemiol* 2011; 32(2):131-5.
20. Moller AH, Hansen L, Jensen MS, et al. A cost-effectiveness analysis of reducing ventilator-associated pneumonia at a Danish ICU with ventilator bundle. *J Med Econ* 2012; 15(2):285-92.
21. Kollef MH, Afessa B, Anzueto A, et al. Silver-Coated Endotracheal Tubes and Incidence of Ventilator-Associated Pneumonia The NASCENT Randomized Trial. *JAMA*. 2008;300:805-813.
22. Siempos II, Vardakas KZ, Falagas ME. Closed tracheal suction systems for prevention of ventilator-associated pneumonia. *Br J Anaesth*. 2008;100:299-306.
23. Siempos II, Vardakas KZ, Kopterides P, et al. Impact of passive humidification on clinical outcomes of mechanically ventilated patients: a meta-analysis of randomized controlled trials. *Crit Care Med*. 200;35:2843-51.