Commentary

Ventilator-associated tracheobronchitis (VAT): questions, answers, and a new paradigm?

Donald E Craven[1,2]

[1]Department of Infectious Diseases, Lahey Clinic Medical Center, 41 Mall Road, Burlington, MA 01805, USA
[2]Tufts University School of Medicine, Boston, MA, USA

Corresponding author: Donald E Craven, donald.e.craven@lahey.org

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Abstract

Nosocomial lower respiratory tract infections are a common cause of morbidity and mortality in intensive care unit (ICU) patients. Although many studies have investigated the management and prevention of ventilator-associated pneumonia (VAP), few have focused on ventilator-associated tracheobronchitis (VAT). In this issue of *Critical Care*, Nseir and coworkers present interesting data from a randomized controlled study of antimicrobial therapy for VAT. Patients randomly assigned to antibiotic therapy had more mechanical ventilation-free days ($P < 0.001$), fewer episodes of VAP (13% versus 47%; $P < 0.001$), and a lower ICU mortality rate (18% versus 47%; $P = 0.05$) than those without antibiotic therapy. Although this study has limitations, the data suggest that VAT may be an important risk factor for VAP or overlap with early VAP. More importantly, targeted antibiotic therapy for VAT may improve patient outcomes and become a new paradigm for prevention or early therapy for VAP.

In this issue of *Critical Care*, Nseir and coworkers [1] provide interesting data from a randomized trial of antibiotic therapy for ventilator-associated tracheobronchitis (VAT). Although ventilator-associated pneumonia (VAP) has been the major focus of critical care providers, perhaps our focus should also include VAT, which may be a precursor to VAP or overlap with early VAP [1-5]. Understanding VAT may have important implications for the early diagnosis, therapy, and prevention of VAP. In comparison with VAP, VAT is plagued by little clinical data and several questions: How do we define it? How much does it overlap with VAP? What level of bacteria in endotracheal aspirates is diagnostic? When is antibiotic therapy indicated and for how long [5]?

Most bacteria enter the lower respiratory tract by leakage of bacteria and oropharyngeal secretions around the endotracheal tube cuff, resulting in colonization, VAT, or VAP [2]. Furthermore, the primary exit route for bacteria out of the lower respiratory tract is impeded by the endotracheal tube, patient sedation, and a reliance on mechanical suctioning rather than spontaneous coughing. The lower respiratory tract in the ventilated patient is a continuous 'battleground' between the numbers, types, and virulence of the incoming bacteria versus the lung's incredible mechanical, cellular, and humoral defenses. The outcome for each patient is either lower airway colonization or shades of grey from VAT to VAP.

Diagnoses of both VAT and VAP rely on clinical and systemic signs of infection (fever, leukocytosis, reduced oxygenation) plus purulent sputum with high concentrations of bacteria ($\geq 10^{5\text{-}6}$ colony-forming units [cfu]/mL) in the endotracheal aspirate. Diagnoses of VAP rely on distal samples of bacteria obtained from bronchoscopic and non-bronchoalveolar lavage ($\geq 10^4$ cfu/mL) [2] or protected specimen brush (PSB) ($\geq 10^3$ cfu/mL). Definitions of VAT and VAP have been based on different sampling techniques and microbiologic thresholds, which may make discrimination between VAT and VAP difficult. Although VAP requires evidence of a new and persistent infiltrate on a chest x-ray, the sensitivity and specificity of x-rays are variable and, though improved with computerized tomographic scans, still have limitations, especially in patients with severe congestive heart failure or adult respiratory distress syndrome.

For VAP, and probably VAT, early appropriate antibiotic therapy improves patient outcomes [1,2]. Nseir and coworkers [4] reported an observational cohort of medical and surgical intensive care unit (ICU) patients who had a 10.6% incidence of VAT. VAT was associated with an increased length of stay (LOS) in the ICU and more mechanical ventilator days, but those receiving antimicrobial therapy had a trend toward decreased LOS, fewer mechanical ventilator

cfu = colony-forming units; ICU = intensive care unit; ITT = intention-to-treat; LOS = length of stay; PSB = protected specimen brush; VAP = ventilator-associated pneumonia; VAT = ventilator-associated tracheobronchitis.

days, and lower mortality. In a more recent case control study in ventilated patients with chronic respiratory failure, patients with VAT had a significantly longer duration of mechanical ventilation (17 versus 8 days; $P < 0.001$) and ICU stays (24 versus 12 days; $P < 0.001$) [6]. Nouria and coworkers [7] compared the impact of ofloxacin versus placebo in a randomized trial of mechanically ventilated patients with chronic lung disease and noted significantly better outcomes in the ofloxacin group.

A'Court and coworkers [8] studied the natural history of colonization in mechanically ventilated patients using serial non-bronchoscopic bronchial lavage with quantitative cultures collected every 48 hours. These investigators reported a significant increase in lower respiratory tract colony counts which started 2 days before the clinical onset of VAP, which may have represented either VAT or early VAP not detected by chest x-ray. In this issue, Nseir and coworkers [1] present interesting data from a small randomized, controlled, multicenter trial of patients with VAT who were randomly assigned to antibiotic therapy versus no therapy. VAT was defined as a first episode of fever of greater than 38°C, purulent sputum production, endotracheal aspirate having greater than or equal to 10^6 cfu/mL of a new pathogen, but no radiographic signs of VAP on a chest x-ray. *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and methicilllin-resistant *Staphylococcus aureus* (MRSA) were the most common pathogens isolated. Results were presented as intention-to-treat (ITT) and a modified ITT (MITT) analysis which excluded patients with potential confounders. In both analyses, the antibiotic-treated group had a significant decrease in VAP ($P < 0.01$), more mechanical ventilation-free days ($P < 0.001$), and a lower ICU mortality ($P < 0.05$). These data of Nseir and coworkers [1] are interesting and provocative and suggest that VAT caused by these pathogens may be a marker for patients at high risk for developing VAP and that early appropriate antibiotic therapy for VAT or preemptive therapy for early VAP may significantly improve patient outcomes. Study limitations of note include the following: lack of blinding; low numbers of patients; the study was stopped before randomization blocks were attained; an independent blinded committee did not evaluate the endpoints; and, finally, computer-assisted tomography was not performed systematically to exclude VAP.

The data of Nseir and coworkers [1] need confirmation but suggest a new paradigm to assess tracheal colonization, whether treating VAT or early VAP. Also, treatment of VAT may reduce lung inflammation, which may translate into earlier extubation and reduced risk for VAP. Finally, the presence of high concentrations of a bacterial pathogen in the endotracheal aspirate may be an important clinical clue that antibiotic therapy is needed to aid failing host defenses and reduce patient mortality, morbidity, and health care costs.

The limitations of the study by Nseir and coworkers [1] underscore the need for larger collaborative national and international networks to develop well-designed trials, with independent data analysis and data safety monitoring boards, that would greatly increase our understanding of disease pathogenesis, prevention, and treatment. Such a network could provide a foundation on which to build vitally needed 'gold standards' to improve patient care, outcomes, and prevention of VAP and other health care-associated infections. Progress usually is based on a series of small steps, but bigger and better steps are not only possible, but vitally needed.

Competing interests

The author declares that he has no competing interests.

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