What's New about Ventilator-associated Pneumonia

IN this issue of Anesthesiology, Bregeon et al.\textsuperscript{1} report their clinical investigation to determine whether ventilator-associated pneumonia (VAP) is an independent risk factor for death. They matched 108 nonsurvivors of mechanical ventilation with 108 survivors for their underlying diagnoses, age, gender, admission date, severity of illness, and duration of mechanical ventilation. VAP developed in the same number of patients in both groups (39 patients in each group). The authors concluded that VAP is not an important risk factor for hospital mortality. This finding is in contrast to other investigations, which have identified the occurrence of VAP as an independent determinant of hospital mortality.\textsuperscript{2,3}

This discrepancy may be caused by the relatively small number of patients examined in the study by Bregeon et al.\textsuperscript{1} Additionally, other factors beyond the simple development of VAP may be more important determinants of outcome for patients in whom VAP as well as other nosocomial infections develop.

Ventilator-associated pneumonia is the most common hospital-acquired infection among patients with acute respiratory failure.\textsuperscript{4} In general, VAP can be categorized according to its onset in relation to the start of mechanical ventilation. Early onset VAP (i.e., occurring within 96 h of the onset of ventilatory support) usually is attributed to antibiotic-sensitive bacteria, including oxacillin-sensitive Staphylococcus aureus, Haemophilus influenzae, and Streptococcus pneumoniae.\textsuperscript{5} Late-onset VAP refers to infection occurring more than 96 h after the start of mechanical ventilation and usually is caused by antibiotic-resistant bacteria, including oxacillin-resistant S. aureus, Pseudomonas aeruginosa, and Acinetobacter species. Prolonged hospital stay and exposure to antibiotics before the onset of infection seem to be important risk factors for VAP attributed to antibiotic-resistant bacteria.\textsuperscript{6,7}

In a larger case–control study that compared patients who had VAP with those who did not have VAP, the occurrence of VAP was found to be an independent risk factor for hospital mortality.\textsuperscript{8} More importantly, it seemed that VAP caused by antibiotic-resistant bacteria was associated more closely with excess hospital mortality. Our own group has demonstrated that VAP is an independent risk factor for hospital mortality and multi-organ dysfunction.\textsuperscript{7,9} Again, it seemed that most of the pathogens associated with VAP in these studies were high-risk antibiotic-resistant bacteria. This may explain the increased mortality observed in these studies. Inadequate initial antibiotic therapy is more likely to occur in patients infected with antibiotic-resistant bacteria. Several studies have shown that patients with VAP, as well as other nosocomial infections, who receive inadequate initial antibiotic therapy are more likely to die compared with patients treated with initial adequate antibiotic treatment.\textsuperscript{10–13} Inadequate antibiotic treatment of infection is usually defined as (1) the microbiological documentation of an infection (i.e., a positive culture result) that was not being effectively treated at the time of its identification, (2) the absence of antimicrobial agents directed against a specific class of microorganisms (e.g., absence of therapy for fungemia due to Candida albicans), or (3) the administration of an antimicrobial agent to which the microorganism responsible for the infection was resistant (e.g., empiric treatment with oxacillin for VAP subsequently attributed to methicillin-resistant S. aureus based on appropriate culture results).

Even if VAP always was treated effectively and did not contribute to excess mortality, the prevention of this hospital-acquired infection would presumably result in shorter intensive care unit stays and less medical care costs.\textsuperscript{14} Therefore, systematically applied interventions have been developed for VAP prevention and have been shown to be successful at the local hospital level.\textsuperscript{15,16} Drakulovic et al.\textsuperscript{17} demonstrated that semi-recumbent positioning decreased the occurrence of VAP and decreased hospital mortality. Similarly, oral intubation has been shown to decrease the incidence of VAP and hospital mortality compared with nasal intubation.\textsuperscript{18,19} Reducing the duration of tracheal intubation also has been associated with lower rates of VAP.\textsuperscript{20–22} Finally, new techniques are undergoing development to prevent biofilm formation on endotracheal tubes, which have been implicated in the pathogenesis of VAP.\textsuperscript{23}

Establishing an accurate diagnosis of VAP is controversial because of the nonspecific clinical and microbiologic markers associated with this infection (e.g., fever, leukocytosis, radiographic infiltrates, tracheal secretions, and tracheal cultures). Nevertheless, several clinical definitions have been proposed for VAP.\textsuperscript{24,25} Other diagnostic markers, including quantitative lower airway cultures and endotoxin measurements from bronchoalveolar lavage fluid, also have been used to diagnose VAP.\textsuperscript{20–28} Three studies have found no improvement in survival for

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\caption{This Editorial View accompanies the following article: Bregeon F, Ciais V, Carret V, Gregoire R, Saux P, Gannier M, Thirion X, Drancourt M, Auffray J-P, Papazian L: Is ventilator-associated pneumonia an independent risk factor for death? Anesthesiology 2001; 94:554–60.}
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patients with VAP diagnoses clinically compared with the use of bronchoscopically obtained lower airway cultures using bronchoalveolar lavage or protected specimen brush samples. These results differ from a recent multicenter study that showed statistically lower hospital mortality and less antibiotic use with the application of bronchoscopy methods to diagnose VAP. However, more patients in the clinical diagnosis part of this study (11.5%) compared with the bronchoscopic diagnosis part (0.5%) were treated initially with inadequate antimicrobial therapy, confounding the mortality analysis.

The optimal antibiotic treatment for VAP is unknown. In general, when a decision is made to treat VAP, antibiotics with demonstrable in vitro activity against the causative bacteria should be used. Additionally, unnecessary antibiotic treatment should be avoided to limit the emergence of resistance. Singh et al. used a simple clinical scoring system to identify patients at lower risk of having VAP. They found that 3 days of antibiotic treatment in these patients was as effective as 10–21 days of treatment and was associated with less emergence of subsequent bacterial resistance. Similarly, in a before-after trial, we have demonstrated that 7 days of antibiotic treatment is as effective as 14 days of treatment in patients with VAP. Additionally, several clinical studies have found that anaerobic bacteria are uncommon in the lower airways of patients with VAP or aspiration pneumonia occurring in the hospital setting. This may explain the lack of greater efficacy among antibiotic regimens with intrinsic anaerobic activity for patients with VAP.

In summary, VAP is an important nosocomial infection because of increased patient morbidity, greater hospital costs, and longer lengths of hospital stay. Clinicians practicing in the intensive care unit should support the development and routine implementation of interventions aimed at preventing VAP and encouraging rational use of antibiotic therapy.

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