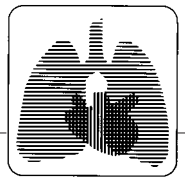

Early Antibiotic Treatment for BAL-Confirmed Ventilator-Associated Pneumonia*

A Role for Routine Endotracheal Aspirate Cultures

Fabrice Michel, MD; Bruno Franceschini, MD; Pierre Berger, MD; Jean-Michel Arnal, MD; Marc Gainnier, MD; Jean-Marie Sainty, MD; and Laurent Papazian, MD

Study objectives: **To test whether routine quantitative cultures of endotracheal aspirates obtained before the onset of ventilator-associated pneumonia (VAP) could help to predict the causative microorganisms and to select early appropriate antimicrobial therapy before obtaining BAL culture results.**
Design: **Prospective observational study.**
Setting: **French medical ICU.**
Patients: **A total of 299 patients received mechanical ventilation for at least 48 h.**
Interventions: **Endotracheal aspiration (EA) was performed twice weekly in all mechanically ventilated patients. A diagnosis of VAP was made by BAL culture. Only the EA performed just before the suspicion of VAP (EA-pre) were evaluated. This strategy (*ie*, the EA-pre-based strategy) was compared with an antibiotic therapy that would have been prescribed if the recommendations of both the American Thoracic Society (ATS) and Trouillet et al (Am J Respir Crit Care Med 1998; 157:531–539) had been applied.**
Measurements and results: **VAP was diagnosed (by BAL culture) in 41 of the 75 patients in whom BAL was performed. Among the 41 BAL specimens that were positive for VAP, EA-pre had identified the same microorganisms (with the same antibiotic resistance patterns) in 34 cases (83%). In one case, EA-pre was not available at the time BAL was performed (a case of early-onset VAP), but the empiric antibiotic therapy was adequate. While EA-pre did not give the same results as the BAL culture, the antibiotic therapy based on the results of the EA-pre was adequate in four other cases. Finally, antibiotic therapy was delayed in only two cases. Antibiotic treatment was therefore adequate in 38 of the 40 assessable cases (95%). If the Trouillet-based strategy had been used, the antibiotic treatment would have been adequate in 34 of the 41 cases (83%; p = 0.15 [vs EA-pre strategy]). Based on the ATS classification, the antibiotic treatment would have been adequately prescribed in only 28 of the 41 cases (68%; p = 0.005 [vs EA-pre strategy]).**
Conclusions: **Routine EA performed twice a week makes it possible to prescribe adequate antibiotic therapy (while waiting for BAL culture results) in 95% of the patients in whom a VAP is ultimately diagnosed by BAL culture.** ***(CHEST 2005; 127:589–597)***

Key words: ARDS; BAL; empiric antibiotic therapy; endotracheal aspirate; mechanical ventilation; pneumonia

Abbreviations: ATS = American Thoracic Society; CI = confidence interval; CPIS = clinical pulmonary infection score; EA = endotracheal aspiration; EA-pre = endotracheal aspiration performed just prior to the suspicion of ventilator-associated pneumonia; F_{IO_2} = fraction of inspired oxygen; IQR = interquartile range; OR = odds ratio; SAPS = simplified acute physiology score; SOFA = sequential organ failure assessment score; VAP = ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is the most frequent ICU-acquired infection among patients receiving mechanical ventilation. The incidence varies from 9 to 20%.[1,2] Although the attributable mortality rate for VAP is still debated,[3,4] it has been shown that these infections prolong both the

duration of ventilation[5–7] and the duration of ICU stay.[8,9] Approximately 50% of all antibiotics prescribed in an ICU are administered for respiratory tract infections.[10] The absence of adequate antimicrobial therapy in patients with pneumonia, peritonitis, bacteremia, or meningitis is associated with an increased mortality rate.[11–19] Bronchoscopically directed sampling of lower respiratory tract secretions provides accurate microbiological data. However, it may do so too late in the course of VAP to improve survival. Indeed, Luna et al[12] showed that adequate antibiotic therapy can improve survival in patients with VAP only if administered early in the course of the illness, at a time when the microbiological data obtained by BAL are not available. Moreover, they also demonstrated that in case of inadequate initial empiric antibiotic therapy, the subsequent change in the antibiotic administered when BAL culture results are known did not decrease the mortality rate.[12] It can be argued that the outcome in VAP patients can be improved only if the initial antibiotic therapy is accurate and timely. The major drawback of a strategy based on bronchoscopically directed sampling of lower respiratory tract secretions (*ie*, a BAL-based strategy) is the necessary time to identify the etiologic agent of VAP leading physicians to prescribe broad-spectrum antibiotics during the 24 to 48 h preceding the obtaining of the BAL culture results. The initial empiric antibiotic treatment often requires modification when quantitative culture results become available.[13,14,20–23] When using a BAL-based strategy, the choice of antibacterial agents must be broad enough to ensure that adequate coverage of all likely bacterial pathogens is provided during the 24 to 48 h period preceding the obtaining of BAL culture results. Initial treatment covering Gram-negative and Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus*, should then be provided unless infection due to these organisms is excluded.[11] The American Thoracic Society (ATS) guidelines for hospital-acquired pneumonia[24] and the classification of Trouillet et al[25] can help to select an adequate initial antibiotic therapy. However, the extensive use of antibiotics, especially broad-spectrum antibiotics, is associated with the emergence of resistant pathogens and exposes patients to adverse effects.

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Routine surveillance for bacterial colonization by endotracheal aspirate cultures is used in a number of ICUs. However, to our knowledge, its appropriateness for the choice of initial antimicrobial treatment of suspected VAP, subsequently confirmed (or not) by BAL culture, has not been established. In the present study, we tested the hypothesis that the results of routine (*ie*, twice-a-week) quantitative cultures of endotracheal aspirates obtained before the onset of VAP can predict the causative microorganisms and thus make it possible to select appropriate early antimicrobial therapy before obtaining BAL culture results. In order to do this, we prospectively studied a series of consecutive adult patients who were suspected of having VAP in whom the causative bacteria were determined by BAL culture.

Materials and Methods

This prospective study was performed in the medical ICU of Sainte-Marguerite University Hospital in Marseille, France, over a 21-month period (*ie*, May 1, 2000, to January 31, 2002). In accordance with French law, no informed consent was mandatory, given that this epidemiologic study did not modify current diagnostic or therapeutic strategies.

Patients

Patients ($\geq$ 18 years of age) who had received mechanical ventilation for $>$ 48 h were prospectively included if VAP was suspected. Severely neutropenic patients ($< 0.5 \times 10^9$ neutrophils per liter) and AIDS patients were excluded.

Endotracheal Aspirates

Routine surveillance included a microbiological analysis of endotracheal aspirates twice weekly in all patients until the tracheostomy cannula or endotracheal tube was removed. Endotracheal aspiration (EA) was performed using a sterile catheter with a specimen trap kit (model 534–16; Vygon; Ecouen, France), as previously described.[26,27] The suction tube was blindly introduced through the intubation or tracheostomy tube and was wedged into the tracheobronchial tree before suction. Bacterial identification and antibiotic susceptibility tests using standard methods were performed only for microorganisms that were present at a concentration $\geq 10^3$ cfu/mL. The results of EA were not taken into account in the suspicion or diagnosis of VAP. Only the EAs that were performed just before the suspicion of VAP (EA-pre) were taken into account (Fig 1) for the evaluation of the strategy in question.

Diagnosis of VAP

One of the investigators made daily rounds in the ICU to identify eligible patients, to determine the onset of VAP based on

*From the Service de Réanimation Médicale (Drs. Michel, Franceschini, Arnal, Gainnier, Sainty, and Papazian), Hôpital Sainte-Marguerite, Unité Propre de Recherche de L'Enseignment Superior Equire D'Accueil, 2201, and the Service de Microbiologie (Dr. Berger), Hôpital de La Timone, Université de la Méditerranée, Marseille, France.
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Correspondence to: Laurent Papazian, MD, Réanimation Médicale, Hôpital Sainte-Marguerite, 13274 Marseille Cedex 9, France; e-mail: laurent.papazian@ap-hm.fr