Reducing antibiotics use for ventilator-associated pneumonia in brain-injured patients

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A new score may help optimise the empiric antibiotic treatment of ventilator-associated pneumonia after brain injury http://ow.ly/XlR77

Ventilator-associated pneumonia (VAP) is a major contributor of morbidity and mortality in critically ill patients under mechanical ventilation [1, 2]. While inappropriate initial antibiotic therapy is a major determinant of mortality in patients with intensive care unit (ICU)-acquired pneumonia [3], emphasising the importance of a timely and accurate therapy for this infection [4], the unnecessary use of broad-spectrum antibiotic therapy may result in widespread bacterial resistance [5]. For this reason, the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) proposed some criteria to restrict the use of broad-spectrum antibiotics to patients at an increased high risk of drug-resistant pathogens [1].

The accuracy of these guidelines to predict potentially drug-resistant microorganisms has been questioned by several studies [6, 7]. Adaptation of these guidelines to specific populations such as surgical trauma patients significantly improved the outcomes and cost of care [8]. Among trauma patients ventilated in ICUs, the increased severity of head and neck injury is a major determinant in the risk of developing pneumonia [9].

In this issue of the *European Respiratory Journal*, Roquilly *et al.* [10] have developed and validated a score to guide empiric antimicrobial therapy in brain-injured patients. They studied a prospective cohort of 379 patients, predominantly with traumatic brain injury and subarachnoid haemorrhage, who developed an episode of VAP in five French ICUs. Preceding antimicrobial therapy for ⩾48 h and VAP onset ⩾10 days after hospital admission were independent predictors for antibiotic resistance of aetiological pathogens in this study. The authors developed a predictive score consisting of both variables that was externally validated in an independent cohort of 252 brain-injured patients, with very similar results and accuracy.

The predictive accuracy of this score for antibiotic resistance of aetiological pathogens had better performance than the 2005 ATS/IDSA guidelines [1] in this population. Applying the proposed score to both cohorts of patients would have resulted in less use of broad-spectrum antibiotics, compared with application of the 2005 ATS/IDSA guidelines criteria. In particular, among patients free of resistant bacteria, 140 (29%) would have been unnecessarily treated with broad-spectrum antibiotics using the proposed score, compared with 423 (81%) if the 2005 ATS/IDSA guidelines [1] had been applied. Conversely, among patients with bacteria resistant to limited-spectrum antibiotics, 17 (16%) would not

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have received appropriate empiric treatment using the proposed score, compared with none when using the 2005 ATS/IDSA guidelines. Overall, 466 (75%) patients were correctly classified with the proposed score, compared with 200 (32%) using the 2005 ATS/IDSA guidelines.

Several characteristics of this population may explain these results. First, the most frequent aetiological pathogen in these patients was methicillin-sensitive *Staphylococcus aureus*, followed by *Haemophilus influenzae*, *Escherichia coli* and *Pseudomonas aeruginosa*. In addition, this is a relatively young population, with a mean age of ∼50 years. This is substantially different from large multinational series, where *P. aeruginosa* or other hospital-acquired Gram-negative bacilli are the predominant pathogens, and the mean age of patients is substantially higher [11, 12]. Previous series in a similar population of patients with structural coma, mainly due to head trauma or stroke [13], as well as trauma patients with a high proportion of head trauma [9], showed similar aetiology of VAP and mean age to the present study.

Secondly, the frequency of patients with bacteria resistant to limited-spectrum antibiotic therapy, predominantly Gram-negative bacilli, was relatively low (16–17%) compared with the multinational series [11]. It is unlikely that the proposed score can be extrapolated to other critically ill populations or settings with higher rates of antimicrobial resistance, as the authors have demonstrated in burn patients.

This study found a poor ability of the proposed score to predict methicillin-resistant *S. aureus* (MRSA) when compared with the prediction of resistant Gram-negative bacteria. Treatment of VAP caused by MRSA remains a challenge for ICU clinicians, since this pathogen is not often adequately covered by the empiric antibiotic therapy proposed by guidelines [1]. Hence, MRSA as aetiology of pneumonia was a predictive factor for hospital mortality in patients with ICU-acquired pneumonia [14]. However, MRSA is an infrequent cause of VAP in patients with brain injury, as shown in this study as well as in previous series [13].

The association between previous prolonged antimicrobial therapy and bacteria resistant to limited-spectrum antibiotic therapy strongly advocates limiting antibiotic prophylaxis to <48 h in order to reduce the emergence of resistant pathogens. Indeed, a 24-h course of intravenous cefuroxime was an effective prophylactic strategy to decrease the incidence of VAP in patients with structural coma [13].

In summary, assessment of two easy-to-detect variables, such as previous prolonged antimicrobial therapy and late onset of pneumonia, may help to optimise the empiric antibiotic treatment of patients with brain injury who develop VAP in the ICU. The substantial reduction of unnecessary broad-spectrum antibiotics, with the potential decrease in developing antimicrobial resistance, should be balanced with the cost of a small proportion of patients with bacteria resistant to limited-spectrum antibiotics who would not have received appropriate empiric treatment. In addition, these variables, especially prior antimicrobial therapy, can help select patients for randomised clinical trials that recruit patients with VAP caused by multidrug-resistant pathogens.

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