

COMMENTARY

# A week seems to be weak: tailoring duration of antibiotic treatment in Gram-negative ventilator-associated pneumonia

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See related research by Kollef *et al.*, <http://ccforum.com/content/16/6/R218>

## Abstract

The optimal length of antimicrobial therapy has not been extensively studied for a great majority of infections and, in critically ill patients affected by ventilator-associated pneumonia, is a persisting and unsolved issue confronting clinicians. The integration of biomarkers, clinical judgment, and microbiologic eradication might help to define a shorter duration for some ventilator-associated pneumonia episodes due to non-fermenting Gram-negative bacilli, but until these strategies are implemented in clinical practice for individualizing antibiotic treatment, a short-course duration does not seem to tailor a long benefit.

## Introduction

In the previous issue of *Critical Care*, Kollef and colleagues [1] compared 7 days of doripenem with 10 days of imipenem in patients with ventilator-associated pneumonia (VAP) caused by Gram-negative bacilli (GNB). The 7-day course arm was found to have non-significant higher rates of clinical failure and mortality compared with the 10-day course arm. On the basis of the reported data, an independent data monitoring committee, which was blinded to treatment arm assignment, wisely decided to stop the present trial.

The impact of potential resistant microorganisms (PRMs), including non-fermenting GNB (NF-GNB), that cause nosocomial infection is a major health problem [2] and contributes to unfavorable clinical outcome and

increased resource utilization [3]. The greater hospital mortality associated has been attributed to the increased occurrence of inadequate initial antibiotic treatment and virulence factors [4]. Although several guidelines recommend treating patients according to defined patient risk factors, the consideration of intensive care unit (ICU) ecology must provide a more rational basis for selecting initial therapy for VAP patients before culture results are available [5,6].

The optimal length of antimicrobial therapy has not been extensively studied for a great majority of infections and, in critically ill patients affected by VAP, is a persisting and unsolved issue confronting clinicians. Does a shorter duration achieve a longer benefit? The answer is not easy. In clinical practice, several strategies have been used for shorter antibiotic therapy in VAP. Micek and colleagues [7] performed a randomized prospective study in patients with VAP and found that reevaluation strategies decreased antibiotic duration ( $6.0 \pm 4.9$  days versus  $8.0 \pm 5.6$  days). Chastre and colleagues [8] performed a randomized study that found that an 8-day duration of treatment was associated with an outcome similar to that of a 15-day treatment in terms of mortality, ventilator-free days, and stay in the ICU; interestingly, there were no differences in super-infection and relapse of pneumonia, but for primary infections caused by NF-GNB, a higher percentage of patients developed documented pulmonary infection recurrence in the 8-day than the 15-day group (41% versus 26%). Nevertheless, a retrospective study could not find a higher recurrence rate in patients with NF-GNB-caused VAP who received not more than 8 days of antibiotic therapy compared with at least 9 days. Also, in the study by Kollef and colleagues [1], the clinical pulmonary infection score (CPIS) was similar for the first 8 days of treatment and remained stable in the 1-week course but in the 10-day arm continued to decrease. In a study by Singh and colleagues [9] more than a decade ago, antibiotics were maintained for 10 to 21 days for patients with a high CPIS, but for

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those with a low CPIS (<6), the antibiotic either was free choice or was based on a reevaluation strategy after 72 hours: the antibiotic was stopped if the score decreased or remained constant and was continued if the CPIS increased. No differences in mortality and ICU stay were found; however, less time on antibiotic therapy and lower cost were achieved in the reevaluation group.

Current guidelines for VAP recommend a fixed duration of antibiotic therapy (7 to 8 days) for patients with uncomplicated VAP with good clinical response but not for patients with VAP episodes caused by NF-GNB [10]. One of the several unique characteristics and pathogenic properties of NF-GNB is the structure of the outer membrane. In recent years, there have been some notable studies that might help clinicians to better customize treatment duration and that include the use of a single biomarker or a combination of them. Although biomarkers have been extensively investigated for the management of infections from different sources in critically ill patients, the number of patients with VAP included is low for solid recommendations [11]. On the other hand, microbiologic eradication might be a useful end-point [12]. Montravers and colleagues [13], in a study of quantitative cultures of bronchoscopic protected specimen brush (PSB) obtained after the administration of effective antibiotic therapy, showed complete eradication of the causative organisms after only 3 days of treatment in two thirds of patients. More recently, Mueller and colleagues [14] found that the use of repeat bronchoalveolar lavage decreased the duration of antibiotic therapy for NF-GNB VAP from 14 to 10 days, but this approach requires an invasive technique.

## Conclusions

In summary, it is clear that a period of 7 days of antibiotic treatment in NF-GNB is not enough, and more exploratory trials for VAP due to NF-GNB are clearly not recommended. Until a strategy based on the integration of clinical judgment, dynamic changes in biomarkers, and microbiologic eradication can be implemented for tailoring antibiotic treatment in daily clinical practice, a week of antibiotic treatment seems to be weak.

## Abbreviations

CPIS, Clinical Pulmonary Infection Score; ICU, intensive care unit; NF-GNB, non-fermenting Gram-negative bacilli; PRM, potentially resistant microorganism; PSB, protected specimen brush; VAP, ventilator-associated pneumonia.

## Competing interests

The authors declare that they have no competing interests.

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Published: 21 January 2013

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doi:10.1186/cc11899

**Cite this article as:** Martin-Loeches I, Torres A: **A week seems to be weak: tailoring duration of antibiotic treatment in Gram-negative ventilator-associated pneumonia.** *Critical Care* 2013, **17**:106.