Role of High Vancomycin Minimum Inhibitory Concentration in the Outcome of Methicillin-Susceptible Staphylococcus aureus Bacteremia

To the Editor—We read with great interest the article by Holmes et al [1] and the editorial commentary published in the same issue [2] regarding the novel topic of the potential role of high minimum inhibitory concentration (MIC) levels of vancomycin in the prognosis of patients with bacteremia by methicillin-susceptible Staphylococcus aureus (MSSA), as has been previously observed in patients with methicillin-resistant S. aureus (MRSA) bacteremia. The population included in the present study comes from a large multicenter prospective cohort of patients with S. aureus bacteremia and focused on those patients with MSSA bacteremia treated with vancomycin who were matched with those treated with flucloxacillin according to date order and participating site. Even taking into account some limitations of the study (mostly the clear preponderance of endocarditis in the group of patients with MSSA bacteremia), the main results of the study showed that S. aureus vancomycin MIC $\geq 1.5$ μg/mL (ie, high vancomycin MIC [HVM]) was associated with a significantly higher mortality in patients with MSSA bacteremia irrespective of the type of antimicrobial that was used. Although the empirical treatment used in the first days of the bacteremia was not preliminarily considered in the study, the authors performed a subanalysis in 72 patients who received exclusive $\beta$-lactam treatment and confirmed the same results in these cases.

We were pleased to find that the main message of this article reinforces the conclusions of our own research that were previously communicated 1 year ago at an international congress [3] and recently published elsewhere [4]. In contrast to the design of the study of Holmes et al, we performed a retrospective analysis of a cohort of patients with MSSA bacteremia, selecting a more homogeneous population (exclusively patients with catheter-related bacteremia) and, therefore, excluding patients in whom biases regarding outcome were more difficult to minimize even with multivariate analysis (ie, those with endocarditis). Apart from observing a higher attributable mortality in patients with HVM strains (within the limits of statistical significance), we demonstrated that vancomycin MIC $\geq 1.5$ μg/mL was the only variable independently related to the risk of development of complicated bacteremia (odds ratio, 22.9 [95% confidence interval, 6.7–78.1]). Although the number of patients treated from the start with antistaphylococcal $\beta$-lactams was limited in our study, we also observed a higher incidence of complicated bacteremia due to HVM strains in patients in this subgroup. Therefore, we postulated that certain structural modifications might occur in the cell wall of strains with HVM, including a thicker cell wall, as has been described in MRSA [5]. Thickness of the cell wall should not only hinder the action of vancomycin but also the arrival to the target (penicillin-binding proteins) of $\beta$-lactams. If this hypothesis is correct, a MIC of 1.5–2 μg/mL to vancomycin in MSSA could be not only a marker of poor response to vancomycin but also a surrogate marker of suboptimal response to $\beta$-lactams and even pathogenicity, as has been recently suggested in MRSA isolates [6].

In summary, we would like to clarify that the first report regarding the influence of HVM in the outcome of MSSA bacteremia was previously communicated by our study group, although the robustness of the study of Holmes et al [1] clearly reinforces our preliminary conclusions. In any case, we agree that a prospective approach is required to investigate specifically the relationship between vancomycin MIC and outcome in S. aureus bacteremia. Our group is currently performing such a prospective study that we hope will shed light on this topic.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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