Combination Therapy for Enterococcal Endocarditis

TO THE EDITOR—The recent comparison of ampicillin plus ceftriaxone to ampicillin plus gentamicin for the treatment of infective endocarditis due to Enterococcus faecalis was much appreciated, and we congratulate Fernández-Hidalgo et al on their impressive effort [1]. The editorial accompanying this article discusses both strengths and weaknesses of the study as well as potential implications for current clinical practice [2].

Although the debate about the relative efficacy and toxicity of the respective regimens is interesting, we would like to point out that combination therapy using ampicillin plus ceftriaxone has not been compared with ampicillin monotherapy in the treatment of endocarditis due to E. faecalis. Supporters of combination therapy frequently invoke the paper by Geraci and Martin to bolster their view that β-lactam monotherapy is only modestly effective [3]; however, in this study, the patients were often treated with low doses and short courses of penicillin G, and valve replacement surgery was not yet available [3].

The lack of efficacy of monotherapy using large doses of ampicillin by either intermittent or continuous infusions in this disease has not been established. Beaty et al reported the successful treatment of a patient with enterococcal endocarditis with intermittent administration of intravenous ampicillin [4]. The continuous infusion of ampicillin has been shown to be effective in an animal model of enterococcal endocarditis [5] and has been reportedly used to successfully treat a number of cases of enterococcal endocarditis [6]. We are unaware of a large series of patients in the modern era treated with high-dose ampicillin monotherapy for enterococcal endocarditis.

The need for prolonged aminoglycoside synergistic therapy has been questioned, and successful experience with a 2-week course of gentamicin added to ampicillin has been published [7, 8]. Is it possible that even a shorter course of gentamicin (perhaps zero days) would be as effective when combined with ampicillin?

Many patients in the study by Fernández-Hidalgo et al did not complete gentamicin therapy, whereas others underwent surgical valve replacement [1]. These factors make it difficult to compare efficacy of their regimen with those from the pre–cardiovascular surgery era.

With both in vitro and clinical data supporting the use of ampicillin plus ceftriaxone, a combination with a relatively low risk of direct toxicity, the move to this regimen may be irresistible, as discussed in the editorial [2]. Given that we are in an era with increasingly frequent infections due to extended-spectrum β-lactamase–producing gram-negative bacilli and Clostridium difficile, prolonged exposure to broad-spectrum cephalosporins may not be desirable.

Additional comparisons of high-dose ampicillin monotherapy with combination regimens in the treatment of enterococcal endocarditis might be helpful. Currently, available evidence does not clearly support the inferiority of high-dose ampicillin monotherapy in enterococcal endocarditis, and such therapy may be appropriate in select patients.

Note

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

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Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Michael S. Gelfand and Kerry O. Cleveland
Division of Infectious Diseases, Department of Medicine, University of Tennessee Health Science Center, Memphis

References


Correspondence: Kerry O. Cleveland, MD, University of Tennessee Health Science Center, 1325 Eastmoreland Ave, Ste 460, Memphis, TN 38104 (kcleveland@uthsc.edu).

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