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LETTER TO THE EDITOR OPEN ACCESS

Daptomycin or Vancomycin Plus Ceftaroline for Methicillin-Resistant Staphylococcus Aureus Bloodstream Infections

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To the Editor

Recently, one randomized clinical trial (RCT) by Tong et al showed that addition of an anti-staphylococcal β-lactam to daptomycin or vancomycin alone was not associated with improve outcome of patients with MRSA bacteremia (1). Moreover, more acute kidney injury occurred in combination group than monotherapy group in this RCT (1). However, another recent retrospective study by Jorgensen et al which investigated the effect of addition of a β-lactam to daptomycin in the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection and found that the combination of a β-lactam and daptomycin was associated with a better outcome than daptomycin monotherapy (2). In addition to different study design between these two studies (1, 2), the choice of β-lactam in each of them was significant different. In Jorgensen et al's study (2), 87.5% (63/72) of combination therapy used cephalosporin, but most of the patents treated with combining flucloxacillin or cloxacillin (1). Therefore, we wonder whether cephalosporin, especially the ceftaroline, which exhibits potent *in vitro* anti-MRSA activity can be the better choice of daptomycin-based combination therapy to improve the outcome of patients with MRSA bloodstream infections. To clarify this issue, we conducted this meta-analysis to compare the effect of adding ceftaroline to vancomycin or daptomycin and monotherapy in the treatment of MRSA bacteremia.

Four studies (3-6) which compared the effect of combining ceftaroline and vancomycin/daptomycin and standard therapy were identified from the literature search. Table 1 summarized the characteristics of these studies. One study

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Table 1. Characteristics of Included Studies

Author, year	Study Design	Study Site	Study Period	No of patients		Regimen	
				Combi-nation	Mono-therapy	Combination	Monotherapy
Cortes-Penfield et al, 2018[3]	Retrospective study	Single center, in US	2012-2015	4	5	Ceftaroline + Daptomycin	Daptomycin
Geriak et al, 2019[4]	Prospective randomized study	3 centers in US	2017-2015	17	23	Ceftaroline + Daptomycin	Vancomycin or Daptomycin
McCreary et al, 2019[5]	Retrospective, matched cohort study	4 centers in US	2013-2017	58	113	Ceftaroline + Daptomycin	Vancomycin or Daptomycin
Ahmad et al, 2019[6]	Retrospective study	Single center, in US	2015-2017	15	15	Ceftaroline + Daptomycin	Vancomycin or Daptomycin

was RCT (4) and other three were retrospective studies (3,5,6). Each two studies were single(3,6) and multicenter studies (4,5). Primary outcomes as 28-day mortality was recorded for analysis. Secondary outcome including 90-day mortality, microbiological relapse and the risk of acute kidney injury were extracted from the enrolled studies.

Overall, 94 and 156 patients received combination therapy with daptomycin plus ceftaroline and monotherapy - vancomycin or daptomycin, respectively. Although 28-day mortality rate of combination therapy group was numerically than monotherapy group (7.4% [7/94] vs 14.7% [23/156]), this difference did not reach statistical significance (risk difference, -0.07; 95% confidence interval [CI], -0.21 ~ 0.08). The similarity between combination therapy and monotherapy was also observed regarding the 90-day mortality (risk difference, 0.08; 95%CI, -0.77 ~ 0.94). In addition, combination therapy was similar to monotherapy (risk difference, -0.06; 95%CI, -0.22 ~ 0.1) in terms of micro biological relapse. Finally, the risk of acute kidney injury was similar between combination therapy and monotherapy (risk difference,-0.21; 95% CI,-0.62 ~ 0.2).

Based on the above findings, the clinical outcome of patients with MRSA bacteremia treated by the combination of ceftaroline and vancomycin or daptomycin was similar to those by monotherapy of vancomycin or daptomycin. However, the case and study number are limited in this analysis, further large-scale study is warrant to confirm these findings.

Conflicts of Interest

The author declared no conflict of interest.

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