Combination Regimens for Treatment of Carbapenem-Resistant Klebsiella pneumoniae Bloodstream Infections

A. Gomez-Simmonds, B. Nelson, D. P. Eiras, et al.

Antimicrob Agents Chemother 2016; 60 : 3601-3607. doi:10.1128/AAC.03007-15

ABSTRACT

Previous studies reported decreased mortality in patients with carbapenemase-producing Klebsiella pneumoniae bloodstream infections (BSIs) treated with combination therapy but included carbapenem-susceptible and -intermediate isolates, as per revised CLSI breakpoints. Here, we assessed outcomes in patients with BSIs caused by phenotypically carbapenem-resistant *K. pneumoniae* (CRKP) according to the number of *in vitro* active agents received and whether an extended-spectrum beta-lactam (BL) antibiotic, including meropenem, or an extended-spectrum cephalosporin was administered.

We retrospectively reviewed CRKP BSIs at two New York City hospitals from 2006 to 2013, where all isolates had meropenem or imipenem MICs of ≥4 μg/ml. Univariate and multivariable models were created to identify factors associated with mortality. Of 141 CRKP BSI episodes, 23% were treated with a single active agent (SAA), 26% were treated with an SAA plus BL, 28% were treated with multiple active agents (MAA), and 23% were treated with MAA plus BL. Ninety percent of isolates had meropenem MICs of ≥16 μg/ml. Thirty-day mortality was 33% overall and did not significantly differ across the four treatment groups in a multivariable model (P = 0.4); mortality was significantly associated with a Pitt bacteremia score of ≥4 (odds ratio [OR], 7.7; 95% confidence interval [CI], 3.2 to 18.1; P = 0.1), and immunosuppression was protective (OR, 0.4; 95% CI, 0.2 to 1.0; P = 0.04). Individual treatment characteristics were also not significantly associated with outcome, including use of SAAs versus MAA (26% versus 38%, P = 0.1) or BL versus no BL (26% versus 39%, P = 0.1).

In summary, in patients with CRKP BSIs caused by isolates with high carbapenem MICs, the role of combination therapy remains unclear, highlighting the need for prospective studies to identify optimal treatment regimens.