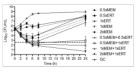

Clinical Microbiology and Infection

Volume 22, Issue 2, February 2016, Pages 147–153

Original article

Bactericidal and synergistic activity of double-carbapenem regimen for infections caused by carbapenemase-producing *Klebsiella pneumoniae*

A. Oliva , F. Gizzi, M.T. Mascellino, A. Cipolla, A. D'Abramo, C. D'Agostino, V. Trinchieri, G. Russo, F. Tierno, M. Iannetta, C.M. Mastroianni, V. Vullo

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doi:10.1016/j.cmi.2015.09.014

Abstract

Available therapeutic options against carbapenem-resistant *Klebsiella pneumoniae* (CR-Kp) are limited because of the high level of resistance to other antimicrobial classes including polymyxins. The double-carbapenem regimen has been recently considered a possible therapeutic strategy. In the present study, we evaluated the *in vitro* bactericidal and synergistic activity of a double-carbapenem regimen consisting of ertapenem plus high-dose meropenem in a series of patients with healthcare-associated CR-Kp infections in whom the use of colistin was not indicated because of potential nephrotoxicity and/or resistance. *In vitro* synergy was evaluated using checkerboard and killing studies. A total of 15 patients were included in the study, with sepsis, severe sepsis and septic shock found in two (13.3%), five (33.3%) and one (6.7%) patients, respectively. Overall, the clinical/microbiological response was 12/15 (80%). Synergy was observed in 11/14 (78.6%) isolates using the checkerboard method whereas in killing studies 12/14 (85.7%) and 14/14 (100%) strains were synergistic and bactericidal at 24 h at concentrations of 1 × MIC MEM + 1 × MIC ERT and 2 × MEM + 1 × MIC ERT, respectively, with a significant decrease of log CFU/mL compared with other combinations ($p < 0.0001$). The double-carbapenem regimen showed clinical and *in vitro* effectiveness in patients with CR-Kp infections.

Keywords

Bactericidal activity; carbapenem-resistant *Klebsiella pneumoniae*; double-carbapenem regimen; sepsis; synergy; time-kill studies

Corresponding author: A. Oliva, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

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