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ePoster Viewing

Antimicrobials: antibiotic usage

Double-carbapenem therapy for systemic infections caused by carbapenemase-producing *Klebsiella pneumoniae*

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Objectives

Infections caused by carbapenemase-producing *Klebsiella pneumoniae* (CP-Kp) are associated with high mortality rate and limitations of therapeutic options. Aim of the study was to evaluate the *in-vivo* and *in-vitro* activity of double carbapenem regimen in patients with systemic infections due to CP-Kp.

Methods

Over a 2-years period, subjects who underwent therapy with double-carbapenem regimen (ertapenem+ high dosage of meropenem) because of systemic infections due to CP-Kp at Sapienza University of Rome were included in the study. For each subject, clinical and demographic characteristics were collected. Strain identification and antimicrobial susceptibility testing were performed throughout VITEK-2. Carbapenemase production was phenotypically confirmed by modified Hodge test and double disk synergy with oxacillin, dipicolinic and boronic acid was used to identify the type of carbapenemase. Broth macrodilution method (BMD) was used to perform the minimum inhibitory concentrations (MICs) of ertapenem (ERT) and meropenem (MEM). Synergy was *in-vitro* investigated throughout checkerboard method and killing tests.

Results

A total of 10 subjects (7M, 3F; mean age 61±12 years) was included in the study. Mean Apache III score and Charlson Index were 31 and 3.8, respectively. Bloodstream infections, urinary tract infections, pneumonia and cutaneous abscessus occurred in 4/10 (40%), 4/10 (40%) 1/10 (10%) and 1/10 (10%) of the subjects, respectively.

Six out of 10 (60%) had hospital-acquired infections whereas 4/10 (40%) had healthcare associated infections. As for infections risk factors, 8/10 (80%) had hospitalization in the previous 12 months and received beta-lactam therapy including carbapenems in the previous 3 months. No subject underwent endoscopy in the previous 72 hours. As clinical presentation of CR-Kp infection, six subjects (60%) had sepsis/severe sepsis/septic shock. The mean lenght of empiric therapy was 5 days whereas the mean duration of double-carbapenem therapy was 14 days, in the absence of adverse effects. We observed clinical success in 8/10 subjects (80%) whereas 2 patients died. The totality of CP-Kp was resistant to carbapenems (MICs>16 mg/mL throughout VITEK-2 system, MICs 128 mg/mL throughout MBD) and KPC-producers. *In-vitro* checkerboard analyses showed ERT+MEM synergy in 7/10 strains (70%). Killing tests showed a synergistic and bactericidal activity at both concentrations of ERT 1xMIC+MEM 1xMIC and ERT 1xMIC+MEM 2xMIC.

Conclusion

A previous hospitalization and therapy containing carbapenem-based regimen are risk factors for infections due to CP-Kp. Double-carbapenem regimen could be a promising option in selected patients in whom other antimicrobials cannot be administered because of resistance or toxicity. Despite a high level of carbapenem resistance, the high dosage of MEM together with the action of ERT as a carbapenemase suicide inhibitor might explain the efficacy of this combination both *in-vitro* and *in-vivo*.