EV0402
ePoster Viewing
Susceptibility testing methods

Colistin-based and colistin-sparing antimicrobial combinations against carbapenem-resistant Klebsiella pneumoniae

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Background: The aim of the study was to evaluate the *in-vitro* activity of different antimicrobial combinations (with and without colistin) against carbapenem-resistant *Klebsiella pneumoniae*. Furthermore, different methods used for MICs determination of colistin and tygecicline [macro broth dilution (MBD), automated system (VITEK-2) and gradient strip diffusion (E-test)] were compared.

Material/methods: A series of carbapenem-resistant *Klebsiella pneumoniae* (CR-Kp) collected from hospitalized patients with CR-Kp colonization or infection at the Department of Public Health and Infectious Diseases (Sapienza University of Rome) was included in the study. MICs50/90 of ertapenem (ERT), doripenem (DOR), meropenem (MEM), colistin (COL), rifampin (RIF) and tigecycline (TIG) were determined by BMD. Checkerboard method was used to evaluate the synergistic activity of COL-based (COL+MEM, COL+DOR, COL+RIF, COL+TIG) and COL-sparing combinations (MEM+ERT). Synergism was defined as FIC index ≤0.5. Additionally, killing curves were performed for MEM+ERT.

Results: Overall, 39 strains from 39 subjects (mean age 57.2±15 years; 11 F, 28 M) with CR-Kp infection (n=33) or colonization (n=6) were collected. Fluoroquinolones, gentamicin, amikacin and trimethoprim-sulfamethoxazole resistance was observed in 39/39 (100%), 30/39 (76.9%), 33/39 (84.6%) and 37/39 (94.8%) of the strains, respectively. COL and TIG resistance was present in 15/39 (38.4%) and 22/39 (56.4%), in 10/39 (25.6%) and 21/39 (53.8%), in 15/39 (38.4%) and 3/39 (7.6%) throughout VITEK-2, E-test and MBD, respectively. Compared to MBD, concordance of VITEK-2 and E-test was 0.462 and 0.538 for TIG and 0.846 and 0.769 for COL, respectively. By MBD, MICs50/90 were 128/512 mcg/ml for both ERT and MEM, 64/128 mcg/ml for DOR and 2/128, 32/512 mcg/mL for COL and RIF, respectively. Synergy was observed in 17/39 (43.5%), 26/39 (66.6%), 39/39 (100%), 31/39 (79.4%) and 26/39 (66.6%) for MEM+ERT, COL+MEM, COL+RIF, COL+TIG and COL+DOR, respectively. Among the 15/39 (38.4%) COL resistant strains throughout MBD, synergism was detected in 12/15 (80%), 15/15 (100%), 12/15 (80%) and 15/15 (100%) of COL+MEM, COL+RIF,

COL+DOR and COL+TIG combinations, respectively. In the killing curves (performed on 33 CR-Kp strains), synergy was observed in 5/33 (15.1%), 20/33 (60.6%), 30/33 (90.9%) and 33/33 (100%) for 0.5xMIC MEM+0.5xMIC ERT, 0.5xMIC MEM+1xMIC ERT, 1xMIC MEM+1xMIC ERT and 2xMIC MEM+1xMIC ERT, respectively.

Conclusions: Colistin-based regimens showed high levels of synergistic *in-vitro* activity, even in the presence of COL-resistant strains. In case of TIG susceptibility, MBD should be preferred to both VITEK-2 and E-test methods. Synergy testing should be performed whenever a CR-Kp is detected, especially when unconventional therapeutic approaches are considered.