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1241. In Vivo Efficacy of Meropenem Against Metallo-β-Lactamase (MBL)-Harboring Pseudomonas aeruginosa and Correlation to In Vitro Susceptibility: Upon Addition of EDTA

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Session: P-72. Resistance Mechanisms

Background. Prior investigations evaluating the predictive value of zinc-depleted media for MBL susceptibility testing have focused on Enterobacteriaceae. Therein, bacterial killing observed with meropenem (MEM) in vitro was concordant with its pharmacodynamic profile using MIC values determined in zinc-depleted media compared with conventional cation-adjusted Mueller-Hinton broth (CAMHB). This study aims to evaluate the exposure-response relationship of MEM against VIM- and NDM-harboring P. aeruginosa (PSA) using the murine thigh infection model and zinc-depleted MICs.

Methods. MBL-harboring PSA isolates (VIM n=11; NDM n=10) were tested both in vitro (neutropenic murine thigh infection model) and in vitro (broth microdilution). The 24 h murine thigh study was conducted with treatment groups receiving a humanized MEM 2g q8h (3h infusion) dose. Six different zinc-limited media were prepared by the addition of EDTA at concentrations ranging from 3 to 300 mg/L to CAMHB. MEM MICs were determined in triplicate in conventional CAMHB and zinc-limited media. Time > MIC values (generated in each zinc-depleted media) were then plotted against the change in 24h bacterial density count in an Emax model.

Results. Average 0h bacterial densities were 5.21 ± 0.40 and 5.13 ± 0.81 log CFU/ml for NDM and VIM isolates, respectively. MEM resulted in -0.89 CFU reduction to +3.69 CFU growth against NDM isolates. MEM resulted in -25.9 CFU reduction to +4.81 CFU growth against VIM isolates. For both NDM- and VIM-harboring PSA, an Emax model with MICs generated in zinc-depleted media provided the highest correlation with MEM activity compared with CAMHB (r² = 0.88). Increasing EDTA concentrations resulted in several-fold MIC reductions and on average, a larger magnitude of reduction was observed among VIM (6-fold) compared to NDM isolates.

Average 0h bacterial densities were >64 µg/mL for NDM and ranged from 8 to >64 µg/mL for VIM isolates. MEM resulted in -2.59 CFU reduction to +3.69 CFU growth against NDM isolates. MEM resulted in -0.79 CFU reduction to +4.91 CFU growth against VIM isolates. MEM and VIM MICs in conventional CAMHB were >64 µg/mL for NDM and ranged from 8 to >64 µg/mL for VIM isolates. Increasing EDTA concentrations resulted in several-fold MIC reductions and on average, a larger magnitude of reduction was observed among VIM- compared to NDM-harboring PSA (4-fold) in CAMHB-EDTA 300 mg/L relative to CAMHB.

Conclusion. Correlation to in vivo activity compared with CAMHB (r² = 0.55).

The table describes microbiological characteristics of the isolated organism species, resistance pattern, development of fosfomycin resistance.

Management outcomes and safety profile

1243. Eravacycline in Bacteremia: A Case Series

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Session: P-72. Resistance Mechanisms

Background. Eravacycline (ERV) is FDA-approved for the treatment of complicated intra-abdominal infections, but there is limited experience for non-FDA approved indications.

Methods. We present five cases that utilized ERV for treatment of bacteremia.

Results. Patient 1 in septic shock (SS) started on vancomycin (VAN) and ceftazidime-avibactam (CZA). Blood culture (BC) finalized to E. coli and regimen narrowed to CZA. On day 9, gram-positive cocci in chains in BC grew and VAN was added. BC finalized to VRE faecium and regimen was modified to ERV on day 12. Repeat BC on day 15 finalized to no growth with no recurrence of bacteremia until discharged (day 78).

Conclusion. IV fosfomycin is a potentially effective and safe option for the treatment of patient with GNB infections.

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