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1241. In Vivo Efficacy of Meropenem Against Metallo-B-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. Herein, 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 vivo (neutropenic murine thigh infection model) and in vitro (broth microdilution). The 24h 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 0 h 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 -2.59 CFU reduction to +4.81 CFU growth against VIM isolates. All MEM 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- (6-fold) compared with NDM-harboring PSA (4-fold) in CAMHB-EDTA 300 mg/L relative to CAMHB. Average 0 h bacterial densities were >64 µg/mL for NDM and ranged from 8 to >64 µg/mL for VIM isolates in conventional CAMHB. MEM MICs were >64 µg/mL for NDM and ranged from 8 to >64 µg/mL for VIM isolates in conventional CAMHB.

Conclusion. Results indicate that MIC values generated in conventional CAMHB do not appropriately characterize the in vivo efficacy of meropenem against MBL-harboring PSA, and addition of EDTA (30 mg/L) to CAMHB appears to be a viable option for in vitro testing of these organisms.

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1242. Efficacy and Safety of Intravenous Fosfomycin for the Treatment of Multi-resistant Gram Negative Infections

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Session: P-72. Resistance Mechanisms

Background. Efficacy, efficiency and safety of intravenous (IV) fosfomycin in the treatment of infections caused by Gram-negative bacteria (GNB).

Methods. Hospitalized patients who received ≥24 hours of IV fosfomycin therapy between September 27, 2017 thru January 31, 2020 were included. The primary outcome was the proportion of subjects with clinical improvement at the end of IV fosfomycin therapy; defined as resolution of baseline signs and symptoms of infection.

Results. Thirty patients were included, of which 19 (63.3%) were males, and the median age was 63.5 years (interquartile range 46–73). Frequent risk factors for GNB infection included hospitalization (23, 76%), receipt of broad-spectrum antibiotics (15, 50%), and surgery (10, 33%), all within the preceding 90 days. Urinary tract infection (17, 56.7%) was the most common indication for use of IV fosfomycin, followed by bacteremia (4, 13.3), and skin and soft tissue infections (4, 13.3%). Klebsiella pneumoniae (17, 56.7%), Escherichia coli (7, 23.3%) and Pseudomonas species (4, 13.3%) were the most common target pathogens. Almost all target pathogens (28, 96.7%) were resistant in vitro to ≥1 agent from ≥3 different antimicrobial classes. The primary outcome was achieved in 22 (73.3%) patients. The most frequently observed adverse events were hypokalemia (13, 43.3%) and hypernatremia (7, 23.3%). However, the majority of adverse events were classified as Grade 1 or Grade 2 severity.

Microbiological characteristics

| Organism                  | E. Coli | Klebsiella pneumonia | Pseudomonas aeruginosa | Other | MDRO |
|---------------------------|---------|----------------------|------------------------|-------|------|
|                           | 7       | 17                   | 1                      | 2     | 8    |
|                           | 23.3%   | 56.7%                | 10.0%                  | 8.7%  | 96.7%|

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

Management outcomes and safety profile

The table describes percentage of primary outcome (clinical success) along with safety profile and mortality rate.

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

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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). Patient 2 treated for MSSA bacteremia with cefazolin and subsequent VRE faecium on day 9, regimen modified to ERV on day 12. Repeat BC on day 15 finalized to no growth with no recurrence of bacteremia until discharged (day 78). Patient 2 treated for MSSA bacteremia with cefazolin and subsequent K. pneumoniae VAP treated with ceftiraxone (CRO) (day 18-26). On day 27, meropenem (MEM) was initiated for gram-negative bacteremia and started on IV trimethoprim/