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1241. In Vivo Efficacy of Meropenem Against Metallo-ß-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 *Enterobacterales*. Therein, bacterial killing observed with meropenem (MEM) *in vivo* 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 $\log_{10}$ CFU/thigh for NDM and VIM isolates, respectively. MEM resulted in -0.09 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. For both NDM- and VIM-harboring PSA, an Emax model with MICs generated in CAMHB+EDTA 30 mg/L (r^2 = 0.88) provided the highest correlation with MEM *in vivo* activity compared with CAMHB (r^2 = 0.55).

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. To describe the clinical use, efficacy and safety of intravenous (IV) fosfomycin in the treatment of infections caused by Gram-negative bacteria (GNB).

Methods. Hospitalized patients who received ≥48 hours of IV fosfomycin therapy during 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, 33.3%), 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%). *Kelbsiella 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 (29, 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	7	23.3%
Klebsiella pneumoniae	17	56.7%
Pseudomonas aeruginosa	4	13.3%
Other	2	6.7%
MDRO	29	96.7%
Antibiotic resistance		
MERO	22	73.3%
Colistin	6	20%
Cipro	27	90%
AG	7	23.3%
Bacteremia	8	26.7%
Documented clearance		
Yes	12	40%
No	6	20%
Not applicable	12	40%
Fosfomycin resistance within 90 days		
Yes	5	16.7%
No	14	46.6%
Not done	11	36.7%

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

Management outcomes and safety profile

Clinical outcome	22	73.3%
Microbiological outcome	20/22	91%
Treatment success	21	70%
Side effect		
Hypokalemia	13	43.3%
Grade 1	9/13	69.2%
Grade 2	4/13	30.8%
Hypernatremia	7	23.3%
Grade 2	2/7	28.5%
Grade 3	3/7	43%
Grade 4	2/7	28.5%
Neutropenia	2	6.7%
Grade 2	2	
Eosinophilia	2	6.7%
Grade 1	2	
Allergy	1	3.3%
Premature discontinuation	6	20%
30 days Mortality	7	23.3%
ICU admission	11	36.7%

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 *K. pneumoniae* VAP treated with ceftriaxone (CRO) (day 18-26). On day 27, meropenem (MEM) was initiated for gram-negative bacteremia and started on IV trimethoprim/