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P2435 In vitro susceptibility testing of ceftolozane/tazobactam against carbapenem-resistant Pseudomonas aeruginosa and extended-spectrum betalactamase-producing Enterobacteriaceae

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Background: Against multidrug-resistant Gram-negative bacterial infections, our existing antibiotic armamentarium is limited. Ceftolozane/tazobactam (C/T) is a novel anti-pseudomonal cephalosporin/beta-lactamase inhibitor with potent activity against Enterobacteriaceae and *Pseudomonas aeruginosa*. Our study evaluated the *in vitro* efficacy of C/T against non-carbapenemase-producing carbapenem-resistant *P. aeruginosa* (CRPA) and ESBL-producing Enterobacteriaceae in our local setting.

Materials/methods: The MICs of 46 non-carbapenemase-producing clinical CRPA, 34 *Klebsiella* species (KS), 29 *Escherichia coli* (EC) and 22 *Enterobacter* species (ENT) from blood and respiratory sources against various antimicrobials were performed via broth microdilution methods, in accordance to CLSI guidelines. Categorical susceptibilities were evaluated according to to CLSI breakpoints.

Results: Against CRPA, meropenem $MIC_{50/90}$ were ≥64 / ≥64 mg/L; range: 4 - ≥64 mg/L. 28% (13/46) were susceptible to C/T, with $MIC_{50/90}$ at 32 / ≥512 mg/L; range: 0.5 - ≥256mg/L.
C/T displayed good antimicrobial activity against ESBL-producing Enterobacteriaceae, especially against KS and EC with 74% (25/34) susceptibility ($MIC_{50/90}$ at 0.5 / 64 mg/L; range: 0.25 - ≥256 mg/L) and 79% (23/29) susceptibility ($MIC_{50/90}$ at 0.5 / 8 mg/L; range: ≤0.125 - 64 mg/L), respectively. However, C/T exhibited decreased activity against ENT with only 41% (10/22) susceptibility ($MIC_{50/90}$ at 2 / 32 mg/L; range: 0.25 - ≥256 mg/L). The overall C/T susceptibility rates was 67% for all Enterobacteriaceae which were higher than that of other commonly used agents [aztreonam – 13%, cefepime (FEP) – 24%, piperacillin-tazobactam (TZP) – 28%, levofloxacin – 21%] (Figure 1).
High C/T susceptibility rates were observed against FEP-resistant/TZP-susceptible ESBL-producing Enterobacteriaceae [92%(22/24)] and FEP-susceptible/TZP-resistant ESBL-producing Enterobacteriaceae [85%(17/20)]. However, C/T achieved only 42% (16/38) susceptibility in the FEP-resistant/TZP-resistant phenotype. All 3 isolates with FEP-susceptible-dose-dependent/TZP-resistant phenotype were suseptible to C/T.

Conclusions: Susceptibility to C/T differs between Enterobacteriaceae species - C/T has better antimicrobial activity against ESBL-KS and ESBL-EC compared to ESBL-ENT. It appeared that C/T may not be an optimal agent of choice for carbapenemase non-producing CRPA in our local setting.

Figure 1: Antimicrobial activity of ceftolozane/tazobactam and various comparator agents against Enterobacteriaceae