**ABSTRACT (Modified)**

**Background:** Challenges due to multidrug resistant Gram-negative bacterial pathogens such as *P. aeruginosa* (PSA) are increasing globally. Suboptimal antimicrobial therapy of infections caused by PSA is associated with increased morbidity and mortality. As a result, antimicrobial susceptibility (NS) studies are pivotal to identifying trends in antimicrobial resistance that inform decisions regarding choice of antimicrobial therapy. This study assessed the in vitro potencies of 7 antimicrobial agents including ceftolozane/tazobactam against PSA collected from numerous sites across the US.

**Methods:** Multiple US hospitals provided non-duplicate respiratory and blood isolates of PSA for potency testing. MICs against PSA were determined using broth microdilution methods according to CLSI for 7 antimicrobials with antimicrobial activity: aztreonam, cefepime, ceftazidime, cefepime/tazobactam, imipenem, meropenem and piperacillin/tazobactam. NS was defined per CLSI or FDA breakpoint criteria.

**Results:** Thirty-five US hospitals geographically spread across the US provided total of 1214 PSA isolates. Of the antibiotics assessed, NS to C/T was the highest at 95% with an MIC\(_{90}\) of 0.5 mg/mL and MIC\(_{2}\) of 2 mg/mL. In comparison, other NS (MIC\(_{90} /\) MIC\(_{2}\)) were as follows: aztreonam 66% (8 / 32); cefepime 76% (4 / 32); ceftazidime 78% (4 / 64); imipenem 68% (2 / 16); meropenem 74% (0.5 / 16); and piperacillin/tazobactam 73% (8 / 128).

**Conclusions:** For this geographically diverse PSA population, ceftolozane/tazobactam demonstrated the highest overall susceptibility (95%). Other antimicrobial agents included carbapenem susceptible isolates over 66-78%. In the era of escalating PSA resistance to the β-lactams, the potency of ceftolozane/tazobactam may represent an important clinical option.

**INTRODUCTION**

Challenges due to multidrug resistant Gram-negative bacterial pathogens such as *P. aeruginosa* are increasing globally.1

Suboptimal antimicrobial therapy of infections caused by *P. aeruginosa* is associated with increased morbidity.2

Antimicrobial susceptibility (%) studies are fundamental to identifying trends in antimicrobial resistance that inform decisions regarding choice of antimicrobial therapy.2

**OBJECTIVES**

To assess the in vitro potency of 7 antimicrobial agents including ceftolozane/tazobactam against *P. aeruginosa* collected from numerous sites across the US.

**MATERIALS & METHODS**

- Thirty-five US hospitals collected non-duplicate respiratory or blood isolates of *P. aeruginosa* (n=1214) from adult inpatients over 2017-2018.
- Isolates were shipped on trypticase soy agar slants and once received at the central processing laboratory (Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, CT, USA) isolates were transferred onto trypticase soy agar plates containing 5% sheep blood and 0.5% minimum inhibitory concentration (MIC) determination.
- MIC trays were prepared using the Biomek 3000 (Beckman Instruments, Inc., Fullerton, CA). To verify correct inoculum, colony counts were performed on each isolate.
- MICs for aztreonam, ceftolozane/tazobactam, cefepime, ceftazidime, imipenem, meropenem and piperacillin/tazobactam were tested using Clinical Laboratory Standards Institute (CLSI) broth microdilution methods.3
- As recommended by CLSI, *K. pneumoniae* 700603 and *P. aeruginosa* 27853 were utilized as quality control strains.
- Isolates were characterized using CLSI susceptibility breakpoints presented in Table 1.
- *P. aeruginosa* were classified as multidrug resistant (MDR) if they were resistant to ≥3 classes of antimicrobials (CIP, MIC ≥ 4 mg/L; IMP, MIC ≥ 8 mg/L; CAZ, MIC ≥ 32 mg/L; TZP, MIC ≥ 128 mg/L; and TOB, MIC ≥ 16 mg/L).

**RESULTS**

- Eighteen percent of the *P. aeruginosa* (n=216) were identified as MDR by reference broth microdilution methods.
- The MIC for which 50% and 90% were inhibited (MIC\(_{50}\) and MIC\(_{90}\)) for all agents are noted in Table 1.
- In this study, C/T and CAZ displayed the highest susceptibility, followed by FEP.
- All other antimicrobial agents, consisting of representative examples across classes, demonstrated a range of 66-76% susceptibility.
- The MIC distribution for all agents is displayed in Figure 1, further highlighting the relative activity of C/T as compared with the other agents.

**CONCLUSIONS**

- In this geographically diverse *P. aeruginosa* population, ceftolozane/tazobactam demonstrated the highest overall susceptibility (95%).
- Other antimicrobial agents including carbapenems displayed susceptibilities of 66-78%.
- In the era of escalating *P. aeruginosa* resistance to the β-lactams, the potency of ceftolozane/tazobactam may represent an important clinical option.

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**Figure 1.** MIC distribution of aztreonam (ATM), ceftolozane/tazobactam (C/T), cefepime (FEP), ceftazidime (CAZ), imipenem (IMP), meropenem (MEM) and piperacillin/tazobactam (TZP).