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Trends in Antimicrobial Susceptibility to Ceftolozane/Tazobactam and Comparators of *Pseudomonas aeruginosa* from Patients with Respiratory Tract Infections in Five Latin American Countries – SMART 2017-2020

S. Lob[1], M. Hackel[1], F. Siddiqui[2], J. Pavia[3], A. DeRyke[2], K. Young[2], M. Motyl[2], D. Sahm[1]

[1]IHMA, Schaumburg, IL, USA
[2]Merck & Co., Inc., Rahway, NJ, USA
[3]MSD, Bogota, Colombia

IHMA
2122 Palmer Drive
Schaumburg, IL 60173 USA
www.ihma.com

Introduction

Ceftolozane is a cephalosporin specifically developed to have enhanced antibacterial activity against *P. aeruginosa*. Combined with tazobactam, it was approved by the US Food and Drug Administration and the European Medicines Agency for hospital-acquired/ventilator-associated bacterial pneumonia. We evaluated trends in the activity of ceftolozane/tazobactam (C/T) against *P. aeruginosa* isolates collected as part of the Study for Monitoring Antimicrobial Resistance Trends (SMART) global surveillance program from patients with lower respiratory tract infections in Argentina, Brazil, Chile, Colombia, and Mexico.

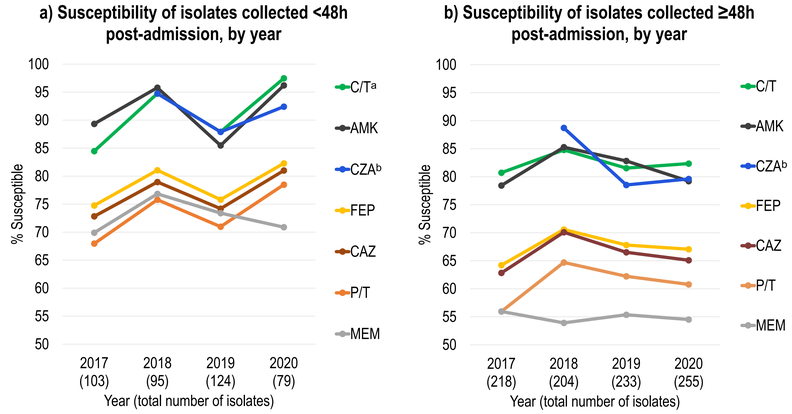
Methods

In 2017-2020, 29 clinical labs each collected up to 100 consecutive gram-negative pathogens per year from patients with lower respiratory tract infections. A total of 6,036 isolates were collected <48 or ≥48 hours post-admission, of which 1,679 (27.8%) were *P. aeruginosa*. MICs were determined using CLSI broth microdilution and interpreted with 2022 CLSI breakpoints [1, 2]. Ceftazidime/avibactam was only tested in 2018-2020. Isolates that were ceftolozane/tazobactam-, imipenem-, or imipenem/relebactam-nonsusceptible were screened for β-lactamase genes by short read whole-genome sequencing (ResFinder database; only isolates collected in 2020) or PCR and Sanger sequencing [3-5]. Some isolates that met the testing criteria were not molecularly characterized and were taken into account when calculating carbapenemase rates.

For the trend analyses, only isolates from the 21 sites that participated in all 4 study years were included. The Cochran-Armitage test for trend was used to test for significant linear trends for all agents that were tested in all 4 years. A p value <0.05 was considered statistically significant.

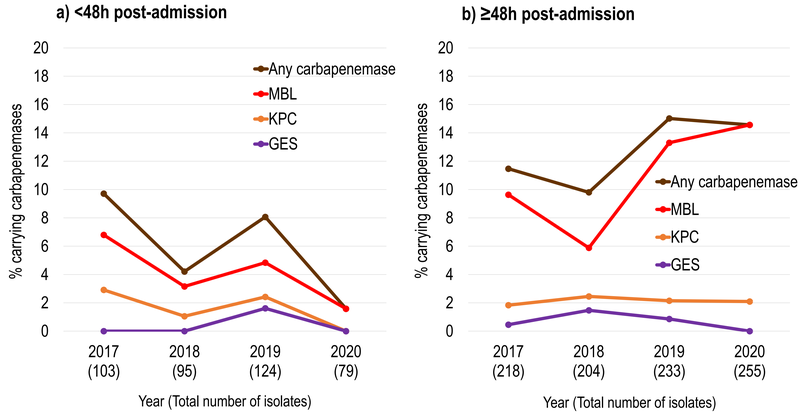
Results

Figure 1 a and b. Trends in susceptibility of *P. aeruginosa* isolates collected a) <48 hours post-admission and b) ≥48 hours post-admission by clinical labs that participated each study year 2017-2020



[a] Statistically significant increasing trend in susceptibility (p<0.05).
[b] CZA was tested only in 2018-2020; no trend analysis performed.
C/T, ceftolozane/tazobactam; AMK, amikacin; CZA, ceftazidime/avibactam; FEP, cefepime; CAZ, ceftazidime; P/T, piperacillin/tazobactam; MEM, meropenem.

Figure 2 a and b. Trends in estimated carbapenemase rates among *P. aeruginosa* isolates collected a) <48 hours post-admission and b) ≥48 hours post-admission, by year 2017-2020[a]



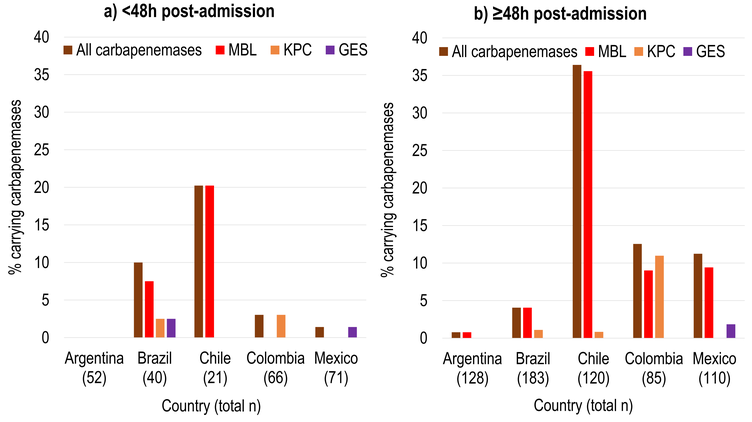
[a]Isolates that carried multiple carbapenemases were counted for each carbapenemase type

Table 1. Susceptibility of *P. aeruginosa* isolates collected at all participating sites in 2019 and 2020, by country[a]

	% Susceptible									
LOS at specimen collection/ Country (total n)	C/T	CZA	MEM	IMI	P/T	FEP	CAZ	ATM	LVX	AMK
<48 hours										
Argentina (52)	98.1	100	78.9	84.6	76.9	71.2	86.5	63.5	53.9	88.5
Brazil (40)	90.0	82.5	70.0	55.0	67.5	75.0	70.0	67.5	67.5	80.0
Chile (21)	81.0	71.4	61.9	57.1	71.4	66.7	61.9	66.7	47.6	81.0
Colombia (66)	95.5	95.5	72.7	57.6	69.7	83.3	72.7	74.2	71.2	95.5
Mexico (71)	91.6	90.1	70.4	52.1	74.7	81.7	78.9	76.1	67.6	91.6
≥48 hours										
Argentina (128)	96.1	93.0	77.3	70.3	65.6	73.4	71.1	60.9	65.6	85.9
Brazil (183)	92.4	88.5	65.0	39.9	67.2	72.1	71.6	57.4	61.8	86.9
Chile (120)	62.5	60.8	31.7	24.2	47.5	52.5	53.3	41.7	37.5	66.7
Colombia (85)	84.7	88.2	72.9	56.5	65.9	72.9	65.9	60.0	69.4	89.4
Mexico (110)	82.7	80.0	54.6	40.9	65.5	70.9	70.0	64.6	61.8	78.2

[a] Susceptibility values ≥90% are shaded green.
LOS, length of hospital stay; C/T, ceftolozane/tazobactam; CZA, ceftazidime/avibactam; MEM, meropenem; IMI, imipenem; P/T, piperacillin/tazobactam; FEP, cefepime; CAZ, ceftazidime; ATM, aztreonam; LVX, levofloxacin; AMK, amikacin.

Figure 3 a and b. Estimated carbapenemase rates among *P. aeruginosa* isolates collected a) <48 hours post-admission and b) >=48 hours post-admission, 2019-2020, by country[a]



[a]Isolates that carried multiple carbapenemases were counted for each carbapenemase type

Results Summary

- Variability in susceptibility was seen over the study period among isolates collected <48 hours post-admission, with a significant increasing trend in susceptibility only for C/T. For C/T and commonly used β-lactams, susceptibility was lower and more stable among isolates collected ≥48h, while a steeper decrease was seen for CZA from 2018 to 2019 (Figure 1 a and b).
- These patterns correlated with estimated carbapenemase rates, especially among isolates collected <48h post-admission. The majority of carbapenemase-positive isolates carried MBL (Figure 2 a and b).
- Using isolates from all sites from the two most recent years to assess country-level susceptibility, substantial variability was seen. For example, susceptibility to C/T of isolates collected after 48h ranged from 62.5% for Chile to ≥92% for Argentina and Brazil, 12-31 percentage points higher than meropenem and piperacillin/tazobactam and 2-4 percentage points higher than ceftazidime/avibactam (except in Colombia) (Table 1).
- This geographic pattern correlated with estimated carbapenemase rates (36% of isolates collected in Chile ≥48h post-admission [almost all MBLs] versus ≤4% for Argentina and Brazil) (Figure 3 a and b).

Conclusions

Variability in antimicrobial susceptibility of *P. aeruginosa* from lower respiratory tract infections was seen across Latin American countries, but the 4-year trend analyses showed no significant decreases in susceptibility. C/T remained the most active among the studied agents.

References:

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