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Antimicrobial Susceptibility of *P. aeruginosa* and *Acinetobacter* spp. from Bloodstream Infections (BSI): Comparison of SENTRY Program Results from North America, Latin America and Europe

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AMENDED ABSTRACT

Background: *P. aeruginosa* (PSA) and *Acinetobacter* spp. (ACB) are frequent causes of nosocomial infections and usually present with high rates of resistance (R). Susceptibility (S) patterns of isolates collected from BSI through the SENTRY Antimicrobial Surveillance Program (2003) were analyzed.

Methods: Participants from North America (NA; 23), Europe (EU; 29) and Latin America (LA; 10 from 5 countries) were instructed by common protocol to send the first 20 unique strains from each month. The (PSA, 992; ACB, 414) isolates were tested by reference broth microdilution methods in the coordinating laboratory (JMI Laboratories, USA).

Results: Results for the most active compounds are listed below:

	% Susceptible (n)		
Organism/antimicrobial	North America	Europe	Latin America
P. aeruginosa	(289)	(445)	(188)
Amikacin (AMK)	97	89	71
Cefepime (CPM)	88	72	63
Piperacillin/Tazobactam (P/T)	91	77	71
Ciprofloxacin (CIP)	80	71	62
Imipenem (IMP)	90	80	68
Polymyxin B (PB)	100	100	100
Acinetobacter spp.	(124)	(177)	(113)
Ampicillin/Sulbactam (A/S)	75	51	48
AMK	82	62	53
CPM	59	48	48
P/T	57	44	44
CIP	51	42	49
IMP	88	79	91
PB	98	99	98

The most active compounds against PSA were PB (100% S), AMK (71 - 97%) and IMP (68 - 90%), with great regional variation. Significantly ($p < 0.05$) higher S rates were observed in NA while the lowest were observed in LA. Against ACB, the most active compound was also PB (98 - 99% S), followed by IMP (79 -91%) and AMK (53 - 82%). ACB S rates were markedly lower in EU and LA when compared to NA. CIP activity was compromised (% S, 42 - 80) overall.

Conclusions: PSA and ACB from BSI showed high R rates to antimicrobials evaluated, but with great regional variation. Only PB consistently demonstrated a wide-spectrum against both non-fermentors.

INTRODUCTION

Pseudomonas aeruginosa and *Acinetobacter* spp. are ubiquitous organisms widely distributed in nature. These gram-negative bacilli are usually commensal, but in the past few decades they have emerged as important opportunistic pathogens, especially in the nosocomial setting. They are capable of causing a range of infections, including pneumonia, bacteremia, secondary meningitis, urinary tract infections, and surgical wound infections, among others.

Resistance to antimicrobials contributes to their role as important opportunistic pathogens. ß-lactam resistance is due to a variety of mechanisms including AmpC ß-lactamase production, extended-spectrum ß-lactamases, a barrier to diffusion at the outer membrane, and efflux mechanisms being described. Loss of permeability and active antimicrobial efflux may affect other types of drugs such as aminoglycosides or quinolones. This may be complemented with alterations in DNA gyrase and the presence of aminoglycoside-modifying enzymes, leading to the emergence of multidrug-resistant strains, against which there are very few therapeutic options, such as polymyxins.

The frequency and antimicrobial susceptibility pattern of these pathogens varies widely according to geographic region. The objective of the present study was the analyze and compare the antimicrobial susceptibility of *P. aeruginosa* and *Acinetobacter* spp. collected from patients with bloodstream infections in North America, Latin America, and Europe in 2003.

MATERIALS AND METHODS

Participant Institutions and Bacterial Isolates: The SENTRY Antimicrobial Surveillance Program has monitored pathogen frequency and antimicrobial resistance patterns of nosocomial and community-acquired infections since 1997 through sentinel medical centers distributed worldwide. Participating medical centers from North America (23), Latin America (10) and Europe (29) were instructed to send the first 20 unique strains from blood stream infections (BSI) each month. A total of 992 *P. aeruginosa* and 414 *Acinetobacter* spp. strains were collected from BSI in 2003 and included in the present study.

Susceptibility testing. All isolates were susceptibility tested by the reference broth microdilution method as described by the NCCLS. Antimicrobial agents were obtained from the respective manufacturers and quality control was performed by concurrent testing of *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *S. aureus* ATCC 29213, and *E. faecalis* ATCC 29212.

RESULTS

- The frequency of *P. aeruginosa* as a cause of BSI varied from 7.2% in Latin America to 6.6% in Europe and 4.2% in North America; while the frequency of *Acinetobacter* spp. varied from 4.4% in Latin America to 2.6% in Europe and 1.9% in North America (Table 1).
- Only polymyxin B was active against all *P. aeruginosa* isolates evaluated. The highest resistance rates to other compounds tested were observed in Latin America (20.0 to 40.4%), followed by Europe (8.1 to 26.3%) and North America (2.4 to 19.0%; Table 2).
- The second most active compound against *P. aeruginosa* was amikacin with susceptibility rates varying from 96.9% in North America to 89.4% in Europe and only 71.3% in Latin America.
- Meropenem was the third most active compound against *P. aeruginosa* in North America (91.9% susceptibility) and Europe (81.1% susceptibility), while in Latin America piperacillin/tazobactam susceptibility rate (70.7%) was slightly higher than that of meropenem (69.6%; Table 2).
- Polymyxin B was also the most active compound tested against *Acinetobacter* spp. with susceptibility rates varying from 97.6 to 98.9% (Table 2). Resistance rates to imipenem and meropenem were highest in Europe (17.5 and 12.9%, respectively), followed by North America (11.3 and 12.2%) and Latin America (7.1 and 7.4%). Conversely, resistance to amikacin was highest in Latin America (42.5%), followed by Europe (36.7%) and North America (12.9%).
- The activity of ampicillin/sulbactam against *Acinetobacter* spp. also varied considerably among regions. The highest susceptibility rate was observed in North America (75.0%), followed by Europe (51.4%) and Latin America (47.8%).

Table 1. Frequency of occurrence of bacterial pathogens as cause of bloodstream infections.

	Organism (% of total)		
Rank order	North America	Europe	Latin America
1	*S. aureus* (26.6)	*E. coli* (22.9%)	*S. aureus* (21.6%)
2	*E. coli* (16.7%)	*S. aureus* (20.0%)	*E. coli* (17.5%)
3	*Enterococcus* spp. (11.4%)	CoNS (11.9%)	CoNS (12.3%)
4	CoNS (8.7%)	*Enterococcus* spp. (7.9%)	*Klebsiella* spp. (8.8%)
5	*Klebsiella* spp. (8.5%)	*Klebsiella* spp. (7.0%)	*P. aeruginosa* (7.2%)
6	*Enterobacter* spp. (4.3%)	*P. aeruginosa* (6.6%)	*Enterobacter* spp. (5.4%)
7	*P. aeruginosa* (4.2%)	*Enterobacter* spp. (4.6%)	*Enterococcus* spp. (4.8%)
8	ß-haemolytic streptococci (4.2%)	*S. pneumoniae* (2.9%)	*Acinetobacter* spp. (4.4%)
9	*S. pneumoniae* (3.9%)	*Acinetobacter* spp. (2.6%)	*S. pneumoniae* (4.3%)
10	*Acinetobacter* spp. (1.9%)	ß-haemolytic streptococci (2.6%)	*S. maltophilia* (2.0%)
Total	(90.4%)	(89.0%)	(88.3%)

Table 2. Antimicrobial susceptibility of *P. aeruginosa* and *Acinetobacter* spp. strains from North America, Latin America and Europe.

		% susceptible/resistant (no. tested)		
Organism	Antimicrobial agent	North America (289)	Europe (445)	Latin America (188)
P. aeruginosa		(289)	(445)	(188)
	Cefepime	87.5/4.2	71.9/14.8	62.8/20.0
	Ceftazidime	84.8/9.3	72.8/22.7	57.4/34.6
	Piperacillin/Tazobactam	91.0/9.0	76.5/23.5	70.7/29.3
	Aztreonam	72.7/15.2	63.1/24.7	49.5/30.0
	Imipenem	89.6/6.6	79.8/15.5	67.6/22.9
	Meropenem	91.9/4.6	81.1/13.5	69.6/22.7
	Ciprofloxacin	79.6/15.9	71.2/26.7	62.2/37.3
	Gatifloxacin	74.0/19.0	68.8/26.3	59.0/36.7
	Levofloxacin	75.4/16.3	70.3/26.3	61.7/37.2
	Amikacin	96.9/2.4	89.4/8.1	71.3/22.3
	Gentamicin	89.6/8.3	72.1/25.8	58.0/40.4
	Polymyxin B	100.0/0.0	100.0/0.0	100.0/0.0
Acinetobacter spp.		(124)	(177)	(113)
	Cefepime	58.9/29.8	47.5/41.2	47.8/29.2
	Ceftazidime	51.6/37.9	39.5/53.1	46.0/50.4
	Ampicillin/Sulbactam	75.0/18.6	51.4/35.0	47.8/29.2
	Piperacillin/Tazobactam	57.3/26.6	43.5/46.9	44.2/45.1
	Imipenem	87.9/11.3	79.1/17.5	91.2/7.1
	Meropenem	82.9/12.2	74.3/12.9	91.7/7.4
	Ciprofloxacin	51.1/41.9	42.4/57.0	48.7/51.3
	Gatifloxacin	63.7/33.9	50.8/35.0	49.6/30.1
	Levofloxacin	62.9/35.5	49.7/40.7	49.6/40.7
	Amikacin	82.3/12.9	62.1/36.7	53.1/42.5
	Gentamicin	65.0/31.7	47.5/42.9	49.6/45.1
	Polymyxin B	97.6/2.4	98.9/1.1	98.2/1.8

CONCLUSIONS

- *P. aeruginosa* and *Acinetobacter* spp. represented important causes of bloodstream infections with the highest frequencies occurring in Latin America, followed by Europe and North America.
- The antimicrobial susceptibility patterns of these pathogens varied considerably among the geographic regions surveyed.
- Both pathogens showed very high rates of resistance in general, with only polymyxin B being active against >90% of isolates in all three regions evaluated.

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