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Increasing Prevalence of Antimicrobial Resistant *P. aeruginosa* isolates in Latin American Medical Centers: 5-Year Report of the SENTRY Antimicrobial Surveillance Program

Soraya Andrade-Baiocchi, Ronald N. Jones, Rodrigo E. Mendes, Helio S. Sader, The SENTRY Participants Group-Latin America
Universidade Federal de São Paulo, Brazil; The Jones Group / JMI Laboratories, North Liberty, IA, USA [www.jmilabs.com].

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ABSTRACT

Background: *Pseudomonas aeruginosa* (PSA) is a leading pathogen of hospital-acquired infections. Resistance to antimicrobial agents has become increasingly more prevalent among clinical isolates.

Methods: As part of the SENTRY Program, 1,894 PSA isolates were collected from Latin America (LA) centers between January 1997 and December 2001. Susceptibility (S) testing by broth microdilution was undertaken according to NCCLS protocols. S rates were calculated for imipenem (IMP), meropenem (MER), ceftazidime (CAZ), cefepime (CPM), piperacillin/tazobactam (P/T), amikacin (AK) and ciprofloxacin (CIP) according to the year of isolation. Trend of S rates was ascertained for each compound by chi-square for trend test.

Results: Overall S rates were as follows: MER 74.8%; P/T 72.2%; IMP 71.9%; AK 69.9%; CPM 62.7%; CAZ 62.5% and CIP 56.6%. Susceptibility rates significantly decreased to all mentioned antimicrobial agents when comparing the years of 1997 and 2001, as follows (S1997/S2001): MER 83.0/64.4%; P/T 73.4/64.9%; IMP 77.1/62.2%; AK 77.7/65.4%; CPM 66.2/54.8%; CAZ 66.6/56.3% and CIP 67.2/49.9%. An increasing annual trend towards resistance was detected for all mentioned antimicrobials through the 1997-2001 period (p < 0.001), as estimated by chi-square for trend.

Conclusion: A rapid increase of antimicrobial resistance among PSA strains was documented in LA hospitals. This continuous increase in resistance jeopardizes adequate antimicrobial treatment of PSA infections in the region. Longitudinal surveillance programs such as SENTRY provide valuable insights on monitoring antimicrobial resistance patterns.

INTRODUCTION

Pseudomonas aeruginosa is an opportunistic human pathogen, inherently resistant to many antimicrobial agents owing to multiple mechanisms, including impermeability and multi-drug efflux. This organism also has the ability to develop acquired multidrug resistance during chemotherapy. These characteristics contribute to its role as a leading source of often fatal nosocomial and, to a less extent, community-related infections.

Recent studies have focused on the decreased susceptibility of *P. aeruginosa* to currently used antipseudomonal agents, including ß-lactams, aminoglycosides and fluoroquinolones. Although carbapenems are usually considered an effective alternative for infections caused by *P. aeruginosa*, resistance to compounds of this class (imipenem, meropenem) has also been reported as a growing problem, worldwide. The recently released new carbapenem, ertapenem, has no activity against *P. aeruginosa*.

The SENTRY Antimicrobial Surveillance Program is an international surveillance program designed to monitor antimicrobial resistance trends worldwide. The present study was conducted to determine the prevalence of *P. aeruginosa* as a reported pathogen in Latin American (LA) participant centers and the variation in susceptibility rates to selected antimicrobial agents over a consecutive 5-year period (1997-2001).

MATERIALS AND METHODS

Study Design. The SENTRY Antimicrobial Surveillance Program monitors pathogen occurrences and antimicrobial resistance patterns of nosocomial and community-acquired infections through sentinel hospitals worldwide. In Latin America, participant laboratories were initially distributed throughout six countries: Brazil, Argentina, Chile, Colombia, Mexico and Uruguay. In 1998, the center located in Montevideo was replaced by a center in Venezuela, and in 2001 the Medellin (Colombia) center was replaced by a fourth center in Brazil. The monitored infectious events included bloodstream infection, pneumonia, skin/soft tissue infection and urinary tract infections. *P. aeruginosa* isolates were collected from clinically significant infections; duplicate isolates from the same patient were excluded from the study.

Bacterial Isolates. During the study period, a total of 1,894 *P. aeruginosa* clinical isolates were processed. They were consecutively recovered from multiple infectious sites during the period of January 1997 through December 2001. The isolates were identified at the participating institution by the routine methodology in use at each laboratory. Upon receipt at the coordinator center (Iowa, USA), isolates were subcultured onto blood agar to ensure viability and purity. Species identification was confirmed with the Vitek system (bioMerieux Vitek) or by conventional methods, as required.

Susceptibility Testing. Antimicrobial susceptibility testing was performed according to the reference broth microdilution method recommended by the National Committee for Clinical Laboratory Standards (NCCLS). Antimicrobial agents were obtained from the respective manufacturers. Polymyxin B was included in the study in 2001 and only 407 isolates were tested against this compound. The MICs were defined as the lowest antibiotic concentration that inhibited bacterial growth. Quality control was performed by testing *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853. Evaluation of antimicrobial resistance rates were calculated by chi-square test for trend and *p* values of <0.05 were considered to be statistically significant.

RESULTS

- The majority of *P. aeruginosa* clinical isolates were collected from medical centers located in Brazil (48.3%) and Argentina (24.8%) (Table 1).
- The most common source of *P. aeruginosa* isolation was from respiratory tract infections (43.3%), followed by bloodstream infections (31.7%), skin/soft tissue infections (11.7%), and urinary tract infections, which accounted for only 8.6% of total isolates (Figure 1).
- Polymyxin B (MIC_{50}, 2 µg/mL; 96.3% susceptibility) was the only compound highly active against this pathogen in Latin America. The most active compounds overall were meropenem (MIC_{50}, 1 µg/mL; 74.8% susceptibility), piperacillin/tazobactam (MIC_{50}, 16 µg/mL; 72.2% susceptibility), and imipenem (MIC_{50}, 2 µg/mL; 71.9% susceptibility). However, the lowest resistance rate was achieved for cefepime (18.1%; see Table 2).

Table 1. Distribution of *Pseudomonas aeruginosa* strains, according to the country and year of isolation.

Country of isolation	No. of isolates by year of isolation					
	1997	1998	1999	2000	2001	Total (%)
Argentina	103	98	95	93	81	470 (24.8)
Brazil	138	189	169	170	247	913 (48.3)
Chile	23	60	52	38	66	239 (12.6)
Colombia	13	20	34	21	-	88 (4.6)
Mexico	41	40	-	7	-	88 (4.6)
Uruguay	17	-	-	-	-	17 (0.9)
Venezuela	-	17	21	28	13	79 (4.2)
Total (% of total)	335 (17.7)	424 (22.4)	371 (19.6)	357 (18.8)	407 (21.4)	1,894 (100.0)

Table 2. Antimicrobial activity and spectrum of drugs tested against 1,894 clinical isolates of *Pseudomonas aeruginosa* in Latin America (SENTRY Antimicrobial Surveillance Program 1997- 2001).

Antimicrobial class/agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	% Susceptible	% Resistant
Cephalosporins				
Ceftazidime	4	>16	62.5	31.2
Cefepime	8	>16	62.7	18.1
Other ß-lactams				
Aztreonam	16	>16	44.5	38.3
Piperacillin	16	>128	65.5	34.5
Piperacillin/Tazobactam	16	>64	72.2	27.9
Imipenem	2	>8	71.9	21.1
Meropenem	1	>8	74.8	19.5
Aminoglycosides				
Amikacin	4	>32	69.9	27.6
Gentamicin	4	>16	58.2	38.4
Fluoroquinolones				
Gatifloxacin	2	>4	54.4	39.2
Levofloxacin	1	>4	56.8	38.5
Ciprofloxacin	0.5	>2	56.6	38.2
Polymyxin B[a]	2	2	96.3	3.6

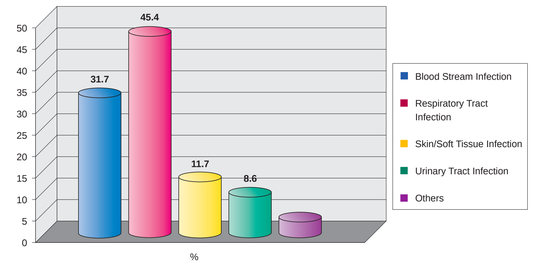
a. Polymyxin B was tested only in 2001 (407 isolates).

- The most active compounds in the last year of this study period (2001) were polymyxin B (96.3% susceptibility) > amikacin (65.4% susceptibility) = piperacillin/tazobactam (64.9% susceptibility) = meropenem (64.4% susceptibility; see Table 3).
- The fluoroquinolones evaluated (ciprofloxacin, levofloxacin, and gatifloxacin) demonstrated similar in vitro activity against *P. aeruginosa* isolates (54.4% to 56.8% susceptibility; p > 0.05).
- Susceptibility rates decreased significantly for all anti-pseudomonal drugs evaluated (Table 3).

Table 3. Susceptibility rates according to the year of isolation in Latin America (SENTRY Antimicrobial Surveillance Program, 1997- 2001).

Antimicrobial class/agent	% susceptible by year (no. tested)					
	1997 (335)	1998 (424)	1999 (371)	2000 (357)	2001 (407)	*p* value
Cephalosporins						
Ceftazidime	66.6	64.4	65.8	59.7	56.3	< 0.001
Cefepime	66.2	67.9	65.2	59.4	54.8	< 0.001
Other ß-lactams						
Aztreonam	55.5	45.0	46.6	34.7	41.3	< 0.001
Piperacillin	71.9	66.7	66.6	61.9	60.9	< 0.001
Piperacillin/Tazobactam	79.4	77.1	73.3	66.4	64.9	< 0.001
Imipenem	77.1	76.7	73.6	70.6	62.2	< 0.001
Meropenem	83.0	79.7	76.0	71.7	64.4	< 0.001
Aminoglycosides						
Amikacin	77.7	73.3	69.0	65.0	65.4	< 0.001
Gentamicin	63.6	61.8	60.1	56.9	49.6	< 0.001
Fluoroquinolones						
Gatifloxacin	60.9	57.1	56.3	52.1	46.4	< 0.001
Levofloxacin	63.6	59.0	59.3	53.5	49.6	< 0.001
Ciprofloxacin	67.2	60.8	60.6	53.2	49.9	< 0.001

Figure 1. Distribution of 1,894 *Pseudomonas aeruginosa* isolates according to the site of infection.



CONCLUSIONS

- A rapid and continuous decrease in the susceptibility to antimicrobial agents among *P. aeruginosa* strains was documented in participating Latin American hospitals. This continuous rise in resistance jeopardizes adequate antimicrobial treatment of *P. aeruginosa* infections in the region.
- Comprehensive longitudinal surveillance programs such as the SENTRY Antimicrobial Surveillance Program provide valuable insights on monitoring antimicrobial resistance patterns and can guide empiric treatments.

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SENTRY Program Participant Group (Latin America)

• Argentina
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Jorgelina Smayevsky (1997-2001) - Microbiology Laboratory C.E.M.I.C., Buenos Aires

• Brazil
Helio S. Sader (Latin America Coordinator; 1997-2001) – Universidade Federal de São Paulo
Cassia Zoccoli (1997-2001) - Laboratório Médico Santa Luzia , Florianopolis
Jorge Sampaio (1997 – 1998) – Laboratório Lâmina , Rio de Janeiro
Afonso Barth (1999 – 2001) – Hospital de Clínicas, Porto Alegre
Julival Ribeiro (2001) – Hospital de Base, Brasilia

• Chile
Valeria Prado (1997-2001) - Faculdad de Medicina de Chile, Santiago
Elizabeth Palavecino e Patricia Garcia (1997-2001) - Universidad Catolica del Chile, Santiago

• Colombia
Jaime A. Robledo (1997-2000) - Corporation para Investigaciones Biológicas, Medellin

• Mexico
Jose Sifuentes-Osornio (1997-2001) - Instituto Nacional de la Nutricion, Ciudad del Mexico

• Uruguay
Homero Bagnulo (1997) - Hospital Maciel, Montevideo.

• Venezuela
Manuel Gúzman Blanco (1998-2001) – Centro Medico de Caracas