Increasing Resistance of *Pseudomonas aeruginosa, Staphylococcus aureus, Klebsiella* spp., and *Acinetobacter* spp. in Patients with Pneumonia in Latin America: Report from the SENTRY Antimicrobial Surveillance Program, 2002

ICID 2004
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SENTRY ANTIMICROBIAL SURVEILLANCE

ABSTRACT

Background: Non-fermentative bacilli (NFB) comprise almost 40% of pneumonia cases in Latin America (LA) compared to 23% in the USA and Canada. Resistance (R) in NFB to carbapenems (CARBs), primarily due to the presence of metallo-ß-lactamases, has become widespread in LA and joins other emerging R problems including extended-spectrum ß-lactamases (ESBL) in Enterobacteriaceae and oxacillin (OXA) R in *S. aureus* (SA). In this study, contemporary susceptibility (S) profiles for the most commonly occurring pneumonia agents in LA were compared with LA SENTRY Program results for 1998 (712 strains; Lewis et al., Diagn Microbiol Infect Dis, 37; 63, 2000).

Methods: 823 strains from patients hospitalized with pneumonia were submitted in 2002 from 10 medical centers in LA, and were analyzed using NCCLS broth microdilution methods and interpretive criteria.

Results: Rank order of principal pathogens and changes in selected S are in the Table:

		$MIC_{50/90}$ in µg/ml (% S)	
Species* & frequency of occurrence (1998/2002)	Antimicrobial	1998	2002
P. aeruginosa (26.8/32.9)	Imipenem	2/>8 (71.7)	1/>8 (60.1)
	Meropenem	1/>8 (72.8)	2/>8 (60.5)
S. aureus (24.0/17.9)	Oxacillin	>8/>8 (47.7)	>8/>8 (43.5)
	Gatifloxacin	1/4 (87.7)	2/4 (84.4)
Klebsiella spp. (KSP; 12.1/9.8)	Aztreonam	≤0.12/>16 (75.6)	≤0.12/>16 (66.7)
	Ceftazidime	0.25/>16 (77.9)	≤1/>16 (75.3)
	Ceftriaxone	≤0.25/>32 (72.1)	≤0.25/>32 (70.4)
	Cefoxitin	4/16 (89.5)	4/16 (82.7)
Acinetobacter spp. (ASP; 10.5/7.3)	Imipenem	1/>8 (81.3)	1/>8 (63.3)
	Meropenem	2/>8 (78.3)	2/>8 (63.3)

*One or more clonal outbreaks were detected for each species.

Conclusions: NFB, SA and KSP comprise 68% of bacterial pneumonia in LA. NFBs are increasingly resistant to CARBs, and parallel the recovery of resistant NFB in bloodstream infections. Likewise, the recovery of KSP displaying a ESBL phenotype (aztreonam or ceftazidime or ceftriaxone MIC ≤2 µg/ml) has increased from approximately 22 to 35%; R to CARB has not been detected. SA remains uniformly S to vancomycin, linezolid and quinupristin/dalfopristin. However, the frequency of R to OXA, fluoroquinolones and other antimicrobial classes continues to escalate.

MATERIALS AND METHODS

Specimen Collection. A total of 823 non-duplicate bacterial strains from patients hospitalized with pneumonia were submitted from 10 medical centers in Latin America (Argentina, Brazil, Chile, Columbia, Mexico, Venezuela) during 2002. Isolates were initially identified by the submitting laboratory and subsequently shipped to the monitoring laboratory (The JONES Group/JMI Laboratories, Iowa, USA) where identifications were confirmed and antimicrobial susceptibility testing was performed. Genotyping using ribotyping (Riboprinter, Qualicon, Inc., DE, USA) and pulsed-field gel electrophoresis (PFGE) was performed on temporally-related multiresistant strains with identical antimicrobial susceptibility profiles isolated in the same medical center.

Susceptibility Testing. All strains were tested by the reference broth microdilution method in Mueller-Hinton broth (with 5% lysed horse blood added for testing of streptococci) against a variety of antimicrobial agents representing the most common classes and examples of drugs used in the empiric or directed treatment of serious respiratory tract disease. Dry-form microdilution panels and broth reagents were purchased from TREK Diagnostics (Ohio, USA). Interpretation of quantitative MIC results was in accordance with NCCLS methods and criteria. Enterobacteriaceae with elevated MICs (≤2 µg/ml) for ceftazidime and/or ceftriaxone and/or aztreonam were considered as extended-spectrum ß-lactamase-producing phenotypes according to NCCLS criteria. Quality control strains utilized included *Escherichia coli* ATCC 25922 and 35218, *Pseudomonas aeruginosa* ATCC 27853, *Haemophilus influenzae* ATCC 49247, *S. aureus* ATCC 29213, *Streptococcus pneumoniae* ATCC 49619 and *Enterococcus faecalis* ATCC 29212.

RESULTS

- The seven most common pathogens producing 82.4% of pneumonia cases seen in this patient population are: *P. aeruginosa, S. aureus, Klebsiella* spp. (91% *K. pneumoniae*), *Acinetobacter* spp. (77% *A. baumannii*), *E. coli, Enterobacter* spp. (69% *E. cloacae*), and *S. pneumoniae* (Table 1).
- Prevalence of *P. aeruginosa* as an agent of hospital-acquired pneumonia has eclipsed all other bacterial agents, increasing from 26.8% in 1998 to 32.9% in 2002. Changing patient demographics (serious predisposing disease, prolonged hospital stay, prior antimicrobial therapy, chemotherapy, structural lung disease) are likely to be responsible. Corresponding decreases were noted in prevalence of *S. aureus, Klebsiella* spp. and *Acinetobacter* spp. pneumonia.
- Among 2002 *P. aeruginosa* isolates, decreased susceptibility to extended-spectrum cephalosporins, carbapenems, aminoglycosides and fluoroquinolones was apparent compared with 1998 (Table 2). Decreasing effectiveness of carbapenems against *Acinetobacter* spp. was also seen during this interval.
- Decreased susceptibility of *S. aureus* to oxacillin and other agents was also noted during this period although susceptibility to vancomycin, linezolid and quinupristin/dalfopristin remained at 100%.
- Changes in susceptibility profiles of Enterobacteriaceae (*Klebsiella* spp., *E. coli* and *Enterobacter* spp.) were more variable, with modest declines in susceptibilities to extended-spectrum cephalosporins, aztreonam, aminoglycosides and ciprofloxacin, but with no decline in activity of piperacillin/tazobactam or carbapenems.
- Approximately 35% of *Klebsiella* spp. and 27% of *E. coli* displayed ESBL phenotypes, based upon NCCLS screening criteria, a marked increase from phenotype rates of 22 and 12.5%, respectively, in 1998.
- One or more epidemic clusters (clones) of resistant *P. aeruginosa, S. aureus, K. pneumoniae, E. cloacae* and *Acinetobacter baumannii* were detected in 5 participating medical centers using molecular typing methodologies (riboprints and PFGE).

CONCLUSIONS

- Non-fermentative bacilli (primarily *P. aeruginosa* and *Acinetobacter* spp.), *S. aureus, Klebsiella* spp., *E. coli, Enterobacter* spp. and *S. pneumoniae* comprised 82.4% of the etiologic agents producing bacterial pneumonia in hospitalized patients in Latin America (2002).
- Non-fermentative bacilli are increasingly resistant to carbapenems and other classes of antimicrobials, and parallel the recovery of resistant non-fermentative bacilli in bloodstream infections.
- ESBL phenotypes are increasingly being recognized, especially in *K. pneumoniae*, and have increased from approximately 22% to 35% between 1998 and 2002.
- Resistance among Enterobacteriaceae to carbapenems was not detected.
- Oxacillin and fluoroquinolone resistances among *S. aureus* isolates continues to escalate; however, all strains remain uniformly susceptible to vancomycin, linezolid and quinupristin/dalfopristin.
- Use of routine surveillance for detection of antimicrobial resistance coupled with methodologies for molecular typing proved useful in detecting clonal outbreaks of nosocomial pathogens.

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INTRODUCTION

Pneumonia is a leading cause of morbidity and mortality world-wide, and in many areas is the most frequent nosocomial infection occurring in intensive care units. Evolution of antimicrobial resistance in respiratory pathogens producing pneumonia has been rapid and is occurring simultaneously with rising resistance rates in a variety of other bacterial infections. The selection of empiric therapies is a critical factor, and is usually based upon knowledge of local and national resistance rates for the most likely pathogens. The SENTRY Antimicrobial Surveillance Program was initiated in 1997 as a longitudinal study to monitor the appearance of antimicrobial resistance among bacterial pathogens producing bloodstream infections, pneumonia, skin and soft tissue infections, and urinary tract infections, among others. In this study we report on the frequency of occurrence and antimicrobial susceptibility of pathogens isolated from patients hospitalized with pneumonia in medical centers located in Mexico and South America, and compare results with those of a previous study conducted in 1998.

Table 1. Distribution of pathogens identified from lower respiratory tract cultures of patients hospitalized with pneumonia in SENTRY Antimicrobial Surveillance Program hospitals in Latin America (South America and Mexico).

	1998* (n=712)	2002 (n=823)
Organism	Rank (%)	Rank (%)
Pseudomonas aeruginosa	1(26.8)	1(32.9)
Staphylococcus aureus	2(24.0)	2(17.9)
Klebsiella spp.	3(12.1)	3(9.8)
Acinetobacter spp.	4(10.5)	4(7.3)
Enterobacter spp.	5(4.8)	6(4.3)
Escherichia coli	6(3.4)	5(6.1)
Serratia marcescens	7(2.8)	9(2.6)
Streptococcus pneumoniae	8(2.0)	7(4.1)
Stenotrophomonas maltophilia	9(2.0)	10(1.9)
Enterococcus spp.	10(1.8)	11(1.7)
Haemophilus influenzae	16(0.8)	8(2.9)
Others	-(9.0)	-(8.5)

*From Lewis et al., 2000. Diagn. Microbiol. Infect. Dis. 37:63-74.

Table 2. Antibiogram for selected antimicrobials tested against the six most frequently isolated (78% of all strains) pathogens causing patient pneumonias in SENTRY-participating Latin American medical centers; 1998 and 2002 comparison.

	$MIC_{50/90}$ in µg/ml (% susceptible)	
Pathogen/antimicrobial agent (no. tested 1998; 2002)	1998	2002[a]
P. aeruginosa (191; 271)		
Piperacillin/Tazobactam	16/>64(73.3)	16/>64(73.8)
Ceftazidime	8/>16(63.9)	8/>16(58.3)
Cefepime	8/>16(64.4)	8/>16(59.4)
Imipenem	2/>8(71.7)	1/>8(60.1)
Meropenem	1/>8(72.8)	2/>8(60.5)
Amikacin	4/>32(77.5)	8/>32(66.1)
Gentamicin	4/>16(62.3)	4/>8(55.8)
Ciprofloxacin	0.5/>2(63.9)	1/>4(52.4)
S. aureus (171; 147)		
Oxacillin	>8/>8(47.4)	>8/>8(43.5)
Gatifloxacin	1/4(87.7)	2/4(84.4)
Quinupristin/Dalfopristin	0.5/0.5(100.0)	0.5/0.5(100.0)
Rifampin	≤0.25/>2(74.3)	≤0.25/>2(58.5)
Tetracycline	≤4/>8(70.6)	≤4/>8(63.0)
Vancomycin	1/1(100.0)	1/1(100.0)
Trimethoprim/Sulfamethoxazole	≤0.5/>1(73.7)	1/>2(64.6)
Klebsiella spp. (86; 81)		
Piperacillin/Tazobactam	4/>64(74.4)	2/>64(79.0)
Cefoxitin	4/16(89.5)	4/16(82.7)
Ceftriaxone	≤0.25/>32(72.1)	≤0.25/>32(70.4)
Ceftazidime	0.25/>16(77.9)	≤1/>16(75.3)
Cefepime	≤0.12/16(84.9)	≤0.12/>16(80.2)
Aztreonam	≤0.12/>16(75.6)	≤0.12/>16(66.7)
Imipenem	0.25/0.5(100.0)	0.12/0.5(100.0)
Meropenem	≤0.06/≤0.06(100.0)	≤0.06/≤0.06(100.0)
Amikacin	2/32(86.0)	2/32(85.2)
Gentamicin	0.5/16(79.1)	≤2/>8(70.0)
Ciprofloxacin	0.03/2(89.5)	≤0.03/>4(76.5)
Trimethoprim/Sulfamethoxazole	≤0.5/>1(81.4)	≤0.5/>2(80.2)
Acinetobacter spp. (75; 60)		
Imipenem	1/>8(81.3)	1/>8(63.3)
Meropenem	2/>8(78.3)	2/>8(63.3)
E. coli (24; 50)		
Amoxicillin/Clavulanate	8/>16(58.3)	8/16(58.0)
Piperacillin/Tazobactam	2/>64(87.5)	2/16(94.0)
Cefoxitin	4/32(79.2)	4/32(64.0)
Ceftriaxone	≤0.25/32(87.5)	≤0.25/>32(77.6)
Ceftazidime	0.25/8(91.7)	≤1/>16(74.0)
Cefepime	≤0.12/8(91.7)	≤0.12/>16(80.0)
Aztreonam	≤0.12/8(91.7)	≤0.12/>16(75.5)
Imipenem	0.12/0.25(100.0)	0.12/0.12(100.0)
Meropenem	≤0.06/≤0.06(100.0)	≤0.06/≤0.06(100.0)
Amikacin	2/16(91.7)	2/32(88.0)
Gentamicin	1/>16(79.2)	≤2/>8(58.0)
Ciprofloxacin	≤0.015/>2(75.0)	≤0.03/>4(54.0)
Trimethoprim/Sulfamethoxazole	≤0.5/>1(58.3)	>2/>2(40.0)
Enterobacter spp. (34; 35)		
Piperacillin/Tazobactam	4/>64(67.6)	4/>64(68.6)
Ceftriaxone	≤0.25/>32(64.7)	≤0.25/>32(60.0)
Ceftazidime	1/>16(64.7)	≤1/>16(62.9)
Cefepime	≤0.12/>16(88.2)	≤0.12/>16(85.7)
Aztreonam	0.25/>16(70.6)	≤0.12/>16(62.9)
Imipenem	0.5/2(100.0)	0.5/1(100.0)
Meropenem	≤0.06/0.12(100.0)	≤0.06/0.25(100.0)
Amikacin	2/16(94.1)	2/>32(77.1)
Gentamicin	0.5/16(85.3)	≤2/>8(77.1)
Ciprofloxacin	≤0.015/2(85.3)	≤0.03/>4(85.7)
Trimethoprim/Sulfamethoxazole	≤0.5/>1(70.6)	≤0.5/>2(71.4)

a. Underlined results indicate ≥10% decrease in susceptibility for 2002 compared to 1998.