Antimicrobial Susceptibility of *Burkholderia cepacia* in Latin America: Report from the SENTRY Antimicrobial Surveillance Program (1997-2002)

ICID 2004
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ABSTRACT

Background: *Burkholderia cepacia* (BC) has been recognized as a cause of opportunistic infection in hospitalized patients and susceptibility data to guide empiric therapy is scarce in Latin America (LA).

Methods: 80 BC were susceptibility tested by reference NCCLS broth microdilution as part of the SENTRY Program. The isolates were consecutively collected from January/1997 to December/2002 from hospitalized patients in LA medical centers.

Results: BC represented 0.3% of the isolates collected in LA and it was most frequently isolated from blood (65.0%) > respiratory tract (28.7%) > skin and soft tissue (2.5%) > urinary tract infection (3.8%). Susceptibility to the most active agents according to the year of isolation is summarized in the table:

	MIC_{50} in µg/ml / % susceptible (S) by year (no. tested)					
Antimicrobials	1997 (22)	1998 (19)	1999 (9)	2000 (10)	2001 (8)	2002 (12)
Ceftazidime (CAZ)	4 / 86.4	4 / 78.9	4 / 88.9	2 / 80.0	4 / 75.0	2 / 91.7
Levofloxacin (LEV)	1 / 72.7	2 / 78.9	1 / 66.7	0.5 / 100.0	0.5 / 100.0	1 / 83.3
Meropenem (MER)	4 / 54.5	2 / 89.5	2 / 88.9	2 / 70.0	1 / 100.0	2 / 91.7
Gatifloxacin (GAT)	1 / 54.5	1 / 73.7	2 / 66.7	0.5 / 100.0	0.5 / 100.0	1 / 83.3
Trim/Sulf* (T/S)	≤0.5 / 72.7	≤0.5 / 52.6	≤0.5 / 66.7	≤0.5 / 80.0	≤0.5 / 75.0	≤0.5 / 83.3

*Trimethoprim/Sulfamethoxazole

The most active compounds against the entire collection were CAZ (83.3% S), LEV (81.3%), MER (78.8%), GAT (78.8%) and T/S (70.0%). Some compounds in the same class had similar potency, but distinct S rates, such as cefepime (MIC_{50}, 8 µg/ml; 52.5% S) and CAZ, ciprofloxacin (MIC_{50}, 1 µg/ml; 60% S) and LEV; imipenem (MIC_{50}, 4 µg/ml; 58.8% S) and MER.

Conclusion: There was an important variation in the S rates of compounds from the same class. The comparison of 1997 and 2002 results showed that both the prevalence of BC and its resistance rates have decreased during the period of the study.

INTRODUCTION

Infections due to nonfermentative Gram-negative bacilli (NF-GNB) other than *P. aeruginosa* and *Acinetobacter* spp. are uncommon but their incidence is increasing in the last years. *Burkholderia cepacia* have been implicated as a cause of infections in immunocompromised hosts and patients with cystic fibrosis. This pathogen has also been linked to nosocomial outbreaks.

Decisions about performing susceptibility testing are complicated by the fact that automated systems may not perform appropriately and disk diffusion interpretative breakpoints have only been established very recently and for a limited number of compounds.

We report the antimicrobial susceptibility profile of *B. cepacia* isolated from the Latin American medical centers that participate in the SENTRY Antimicrobial Surveillance Program (1997-2002).

MATERIAL AND METHODS

Bacterial strains**.** A total of 80 clinical isolates were collected from the Latin America region through the SENTRY Program between January 1997 and December 2002. All strains were isolated from hospitalized patients. Only a single isolate per patient was evaluated. The isolates were identified to the species level by the participant medical center and sent to the coordinating laboratory for identification confirmation and reference susceptibility testing.

Medical centers**.** The participant medical centers were distributed throughout twelve cities in seven countries: Brasília (2001-2002), Florianópolis (1997-2002), Rio de Janeiro (1997-1998), São Paulo (1997-2002), and Porto Alegre (1999-2002) in Brazil; Buenos Aires (1997-2002) and San Isidro (1997-2002) in Argentina; Santiago in Chile (2 sites, 1997-2000); Medellin in Colombia (1997-2000); Mexico City in Mexico (1997-2002); Montevideo, Uruguay (1997); and Caracas in Venezuela (1998-2002).

Susceptibility testing**.** Antimicrobial susceptibility testing was performed using the reference broth microdilution method as described by the NCCLS. The susceptibility and resistance rates were calculated according to the NCCLS breakpoints established for testing non-Enterobacteriaceae isolates (M100-S14). Antimicrobial agents were obtained from the respective manufacturers. Quality control was performed by testing *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, and *Enterococcus faecalis* ATCC 29212.

Table 1. Frequency and distribution of 80 isolates of *B. cepacia* from multiple infectious sites from Latin American participant centers. SENTRY Antimicrobial Surveillance Program, 1997-2002.

		Source			
		% (N° of isolates)			
Country	Year (Total No. of isolates)	Blood	LRT[a]	SSTI[b]	Urine
Argentina	1997 (8)	62.5 (5)	37.5 (3)	-	-
	1998 (4)	75.0 (3)	-	-	25.0 (1)
	1999 (1)	100.0 (1)	-	-	-
	2000 (3)	66.7 (2)	-	33.3 (1)	-
	2001 (2)	50.0 (1)	50.0 (1)	-	-
Brazil	1997 (12)	66.6 (8)	16.6 (2)	-	16.6 (2)
	1998 (9)	77.7 (7)	22.3 (2)	-	-
	1999 (5)	60.0 (3)	40.0 (2)	-	-
	2000 (2)	50.0 (1)	50.0 (1)	-	-
	2001 (6)	33.3 (2)	66.7 (4)	-	-
	2002 (7)	85.7 (6)	14.3 (1)	-	-
Colombia	1997 (1)	100.0 (1)	-	-	-
	1998 (2)	100.0 (2)	-	-	-
	1999 (2)	50.0 (1)	33.3 (1)	-	
	2000 (5)	100.0 (5)	-	-	-
Mexico	1997 (1)	-	100.0 (1)	-	-
	1998 (1)	-	100.0 (1)	-	-
	2002 (1)	-	100.0 (1)	-	-
Venezuela	1998 (3)	25.0 (1)	75.0 (2)	-	-
	1999 (1)	100.0 (1)	-	-	-
	2002 (4)	50.0 (2)	25.0 (1)	25.0 (1)	-
Total n. of isolates (80)		65.0 (52)	28.7 (23)	2.5 (2)	3.8 (3)

[a] Lower respiratory tract,
[b] Skin and soft tissue infection

Table 2. Antimicrobial activity of five antimicrobial agents tested against *B. cepacia* according to the year of isolation in Latin America participant centers. SENTRY Antimicrobial Surveillance Program, 1997-2002.

	MIC_{50} (µg/ml) / % susceptible by year					
Antimicrobial	1997 (n=22)	1998 (n=19)	1999 (n=9)	2000 (n=10)	2001 (n=8)	2002 (n=12)
Ceftazidime	4 (86.4)	4 (78.9)	4 (88.9)	2 (80.0)	4 (75.0)	2 (91.7)
Levofloxacin	1 (72.7)	2 (78.9)	1 (66.7)	0.5 (100.0)	0.5 (100.0)	1 (83.3)
Meropenem	4 (54.5)	2 (89.5)	2 (88.9)	2 (70.0)	1 (100.0)	2 (91.7)
Gatifloxacin	1 (54.5)	1 (73.7)	2 (66.7)	0.5 (100.0)	0.5 (100.0)	1 (83.3)
Trim/Sulfa*	≤0.5 (72.7)	≤0.5 (52.6)	≤0.5(66.7)	≤0.5 (80.0)	≤0.5(75.0)	0.5 (83.3)

*Trimethoprim/Sulfamethoxazole

Table 3. Antimicrobial activity and spectrum of 10 antimicrobial agents tested against *B. cepacia* isolated patients hospitalized in Latin American medical centers participating in the SENTRY Program, 1997-2002.

	MIC (µg/ml)			
Burkholderia spp. (80)	MIC_{50}	MIC_{90}	% Susceptible	% Resistance
Piperacillin/Tazobactam	8	64	67.5	9.6
Ceftazidime	4	16	83.1	6.0
Cefepime	8	>16	51.8	30.1
Imipenem	4	>8	60.2	26.5
Meropenem	2	>8	79.5	12.0
Ciprofloxacin	1	>2	61.4	18.1
Gatifloxacin	1	>4	79.5	10.8
Levofloxacin	1	4	81.9	8.4
Trimethoprim/Sulfamethoxazole	≤0.5	>1	71.1	28.9

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COMMENTS

- The medical centers located in Brazil contributed with the largest number of isolates (41 isolates, 51.3%), followed by Argentina (18 isolates, 22.5%), Colombia (10 isolates, 12.5%), Venezuela (8 isolates, 10%) and Mexico (3 isolates, 3.8%; Table 1).
- The majority of isolates were from bloodstream infection (52 isolates, 65.0%), while 23 isolates (28.8%) were from lower respiratory tract infections, three isolates (3.8%) from urinary tract infections and two isolates (2.5%) from skin and soft tissue infection (Table 1).
- More than half of the isolates (51.3%) were collected in the first two years (1997 and 1998), and susceptibility rates to the fluoroquinolones and meropenem were lower in this period when compared to the last two years of the study (2001 and 2002; Table 2).
- An important variation in the susceptibility rates of compounds of the same class was noticed. Susceptibility rates varied from 79.5% for meropenem to 60.2% for imipenem; and from 83.1% for ceftazidime to 51.8% for cefepime.
- The most active compound was ceftazidime (83.1% susceptibility [S], MIC_{50}, 4 µg/ml), followed by levofloxacin (81.9% S; MIC_{50}, 1 µg/ml) > gatifloxacin (79.5% S, MIC_{50}, 1 µg/ml) = meropenem (79.5% S, MIC_{50}, 2 µg/ml) > trimethoprim/sulfamethoxazole (71.1% S, MIC_{50}, ≤ 0.5 µg/ml).

CONCLUSIONS

- The most active compounds (ceftazidime, levofloxacin, gatifloxacin and meropenem) showed susceptibility rates around 80%.
- There was an important variation in the in vitro activity of compounds from the same class.
- The comparison of 1997 and 2002 results indicated that both the prevalence of *Burkholderia cepacia* infections and its resistance rates have decreased during this period.