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Changing Susceptibility Patterns Among *Escherichia coli* in Latin America: 6-Year Report of the SENTRY Antimicrobial Surveillance Program

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AMENDED ABSTRACT

Background: Increasing resistance to antimicrobial agents among *E. coli* have been documented worldwide. We evaluated temporal changes in susceptibility (S) patterns of *E. coli* to nalidixic acid (NA), ß-lactams, aminoglycosides (AM) and fluoroquinolones (FQ) in Latin American (LA) hospitals.
Methods: A total of 3,748 *E. coli* isolates were collected as part of the SENTRY Program (1997-2002) in LA hospitals and tested at a central laboratory using NCCLS methods. Yearly S rates were calculated for amikacin (AK), cefepime (CPM), ceftazidime (CAZ), ceftriaxone (CT), ciprofloxacin (CIP), gatifloxacin (GAT), gentamicin (GT), levofloxacin (LEV), NA and piperacillin/tazobactam (P/T). Trend of S rates was ascertained between the years 1997 and 2002 for each antimicrobial agent by the chi-square test.
Results: The overall 6 years S rates to the tested agents were: AK 96.9%; CPM 96.1%; CAZ 95%; CT 93.8%; CIP 81.6%; GAT 81.9%; GT 87.8%; LEV 81.6%; NA 76.6%; P/T 91.4%. In comparison to 1997, S rates experienced a marked decrease to some tested antimicrobials in 2002.
Conclusions: The results of our study indicated the occurrence of a continuous and significant loss of the activities of antimicrobial agents against *E. coli* isolated from Latin American hospitals participating in the SENTRY Program.

INTRODUCTION

Escherichia coli is the most common cause of infection among gram-negative organisms and a major pathogen isolated from urinary tract infections and bacteremia worldwide. Isolates of *E. coli* have a relatively large potential for developing resistance. Indeed, resistance to ß-lactams and other antimicrobial agents has been reported from many regions, including Latin American (LA).

Fluoroquinolone resistance remained relatively low among *E. coli* until recently, when the widespread use of these compounds became associated with the emergence of resistant strains. Moreover, these resistant mutants usually exhibit cross-resistance to other quinolones.

Although reports on the antimicrobial susceptibility of *E. coli* have been frequently published, the overall progression of resistance of these organisms along the years in Latin America is still unclear. In this study we describe the evolution of the antimicrobial resistance of *E. coli* isolates collected from Latin American medical centers participating in the SENTRY Antimicrobial Surveillance Program (1997-2002).

MATERIALS & METHODS

Study Design. The SENTRY Surveillance Program monitors pathogen frequency and antimicrobial resistance patterns of nosocomial and community-acquired infections through sentinel hospitals worldwide. In Latin America, participant laboratories were distributed throughout seven countries: Argentina, Brazil, Chile, Colombia, Mexico, Uruguay and Venezuela. The monitored events included mainly bloodstream infections, pneumonia, skin/soft tissue infections and urinary tract infections.

Bacterial Isolates. A total of 3,748 *E. coli* isolates were analyzed in this study. Only one isolate per patient was included. The isolates were identified at the participating institutions by the routine methodology in use at each laboratory. Upon receipt at the coordinating center (The JONES Group/JMI Laboratories, North Liberty, Iowa), isolates were subcultured onto blood agar to ensure viability and purity. Confirmation of species identification was performed with Vitek (bioMerieux Vitek, Saint Louis, MO) or conventional methods as required.

Antimicrobial Susceptibility. Antimicrobial susceptibility testing was performed using the reference broth microdilution method as described by the National Committee for Clinical Laboratory Standards. Antimicrobial agents were obtained from the respective manufacturers. Quality control was performed by testing *E. coli* ATCC 25922, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, *E. faecalis* ATCC 29212, *H. influenzae* ATCC 49247, and *S. pneumoniae* ATCC 49619.

E. coli isolates with elevated MIC values (≥ 2 µg/ml) for ceftazidime and/or ceftriaxone and/or aztreonam were considered as extended-spectrum ß-lactamase (ESBL)-producing phenotypes according to NCCLS criteria. The ESBL phenotype was confirmed by using the ESBL Etest strips™ (AB BIODISK, Solna, Sweden), and/or disk approximation test. Comparisons of antimicrobial resistance rates along the years were evaluated by chi-square and/or chi-square for trend test.

COMMENTS

- Chile (29.5%) and Brazil (26.9%) contributed the largest number of isolates (Table 1).
- The most common source of *E. coli* was bloodstream infections (55.4%), followed by urinary tract infections (29.9%) and skin/soft tissue infections (8.3%).
- Among the ß-lactams evaluated, cefepime showed the lowest resistance rate overall (3.8%) and piperacillin/tazobactam the highest (8.6%; Table 2).
- All fluoroquinolones evaluated (ciprofloxacin, gatifloxacin, levofloxacin) demonstrated similar resistance rates (17.9 - 18.5%; Table 2). A dramatic decrease in the susceptibility rates to all quinolones was noticed between 2001 and 2002 (Table 3 and Figure 1).
- Comparison between 1997 and 2002 data revealed a significant decrease in susceptibility rates to the following antimicrobial agents, as statistically confirmed by chi-square test (1997/2002): ceftazidime (95.0/90.7%), cefepime (96.1/91.9), ceftriaxone (94.0/90.0), gentamicin (87.4/82.2%), nalidixic acid (77.7/68.0%), ciprofloxacin (83.0/73.7%), gatifloxacin (83.7/74.2%), and levofloxacin (82.6/73.8%). However, the main drop in susceptibility rates occurred between 2001 and 2002 for most antimicrobial agents (Table 3 and Figure 1).
- The prevalence of ESBL-producing *E. coli* increased from 8.0% in 1998 to 13.3% in 2002 (p=0.001, chi-square for trend test). Among isolates from bloodstream infections, the main increase occurred in the 2000-2002 period (from 6.1 to 10.5%, p=0.02) (Table 4). The increasing prevalence of ESBL-producing *E. coli* in Latin America contrasts to results in other regions evaluated by the SENTRY Program, such as North America and Europe, where the frequency of this phenotype has been considerably lower.

Table 1. Distribution of 3,748 *E. coli* isolates according to the respective country of isolation. SENTRY Antimicrobial Surveillance Program (Latin America, 1997-2002).

	Number of organisms (%)							
Year	Argentina	Brazil	Chile	Colombia	Mexico	Uruguay	Venezuela	Total
1997	99	151	148	54	109	67	---	619
1998	110	171	173	94	163	---	24	735
1999	142	194	181	106	---	---	47	679
2000	129	162	205	60	44	---	74	674
2001	60	158	214	---	3	---	22	457
2002	64	173	185	---	126	---	36	584
Total	604(16.1)	1009(26.9)	1,106(29.5)	314(8.3)	445(11.9)	67(1.8)	203(5.4)	3748

Table 2. MIC distribution for 10 antimicrobial agents against 3,748 *E. coli* isolates from the SENTRY Antimicrobial Surveillance Program (Latin America, 1997-2002).

	Cumulative % of isolates at MIC (µg/ml)						MIC (µg/ml)		% by category	
Antimicrobial class/agent	1	2	4	8	16	32	50%	90%	Susceptible	Resistant
ß-lactams										
Ceftriaxone	92.5	93.0	93.3	93.9	94.6	95.1	≤0.25	0.25	93.9	6.1
Ceftazidime	81.6	92.7	93.8	95.0	96.4	---	0.25	2	95.0	5.0
Cefepime	93.6	94.8	95.5	96.2	96.8	---	≤0.12	0.5	96.2	3.8
Piperacillin/Tazobactam	39.2	74.0	84.1	88.3	91.4	93.8	2	16	91.4	8.6
Aminoglycosides										
Amikacin	16.4	61.8	86.6	94.5	97.0	98.5	2	8	97.0	3.0
Gentamicin	58.9	85.2	87.9	89.5	96.6	---	1	16	87.9	12.1
Quinolones										
Nalidixic acid	1.5	21.9	33.9	63.5	76.9	86.0	8	>32	76.9	23.1
Ciprofloxacin	81.5	81.7	---	---	---	---	0.25	>2	81.5	18.5
Gatifloxacin	81.4	82.1	85.4	---	---	---	0.03	>4	82.1	17.9
Levofloxacin	81.4	81.7	84.5	---	---	---	0.25	>4	81.7	18.3

RESULTS

Table 3. Yearly susceptibility rates to 10 antimicrobial agents among 3,748 *E. coli* isolates from the SENTRY Antimicrobial Surveillance Program (Latin America 1997-2002).

	1997	1998	1999	2000	2001	2002	p[a]
Antimicrobial class/agent	(n=619)	(n=735)	(n=679)	(n=674)	(n= 457)	(n=584)	
ß-lactams							
Ceftriaxone	94.0	93.7	94.1	95.7	95.6	90.0	0.01
Ceftazidime	95.0	95.0	96.3	96.9	96.1	90.7	0.004
Cefepime	96.1	96.5	96.8	98.2	97.2	91.9	0.002
Piperacillin/tazobactam	85.3	89.1	92.6	95.5	95.0	91.4	<0.001
Aminoglycosides							
Amikacin	96.9	97.0	97.3	98.4	97.2	95.4	0.15
Gentamicin	87.4	86.9	90.7	89.3	87.5	82.2	0.01
Quinolones							
Nalidixic acid	77.7	74.3	80.0	80.7	81.4	68.0	< 0.001
Ciprofloxacin	83.0	78.5	84.1	84.6	85.8	73.7	< 0.001
Gatifloxacin	83.7	78.8	84.1	85.2	87.1	74.2	< 0.001
Levofloxacin	82.6	78.2	84.2	84.9	87.1	73.8	< 0.001

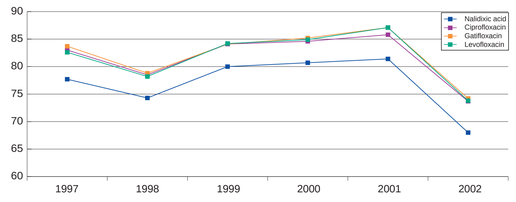
a. *p* value was calculated between the years 1997 and 2002.

Table 4. Occurrence and trends of ESBL-producing *E. coli* strains in the Latin American region (SENTRY Antimicrobial Surveillance Program, 1997-2002).

	Overall		Blood stream infection	
Year	No. of isolates tested	No. of isolates (%) with ESBL phenotype[a]	No. of isolates tested	No. of isolates (%) with ESBL phenotype[b]
1997	619	66 (10.7)	279	24 (8.6)
1998	735	59 (8.0)	344	31(9.0)
1999	679	48 (7.1)	337	24(7.1)
2000	674	43 (6.4)	279	17(6.1)
2001	457	36 (7.9)	381	28(7.3)
2002	584	78 (13.3)	455	48(10.5)

a. p = 0.001 by chi-square for trend test for the 1998-2002 period.
b. p = 0.02 by chi-square for trend test for the 2000-2002 period.

Figure 1: Yearly susceptibility rates to quinolones among 3,748 *E. coli* clinical isolates from the SENTRY Antimicrobial Surveillance Program (Latin America, 1997-2002).



CONCLUSIONS

- Our results indicate that antimicrobial susceptibility rates have been decreasing significantly among *E. coli* from Latin American medical centers participating in the SENTRY Program.
- The decrease in the antimicrobial susceptibility rates were mainly due to the increasing prevalence of ESBL-producing strains and fluoroquinolone resistance in the period evaluated.
- Major emphasis should be placed on local surveillance programs to determine changes in susceptibility rates and guide appropriate intervention measures.

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