Increased resistance to first-line agents among bacterial pathogens isolated from urinary tract infections in Latin America: time for local guidelines?

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Emerging resistance phenotypes and antimicrobial resistance rates among pathogens recovered from community-acquired urinary tract infections (CA-UTI) is an increasing problem in specific regions, limiting therapeutic options.

As part of the SENTRY Antimicrobial Surveillance Program, a total of 611 isolates were collected in 2003 from patients with CA-UTI presenting at Latin American medical centers. Each strain was tested in a central laboratory using Clinical Laboratory Standard Institute (CLSI) broth microdilution methods with appropriate controls.

Escherichia coli *was the leading pathogen (66%), followed by* Klebsiella *spp. (7%),* Proteus mirabilis *(6.4%),* Enterococcus *spp. (5.6%), and* Pseudomonas aeruginosa *(4.6%). Surprisingly high resistance rates were recorded for* E. coli *against first-line orally administered agents for CA-UTI, such as ampicillin (53.6%), TMP/SMX (40.4%), ciprofloxacin (21.6%), and gatifloxacin (17.1%). Decreased susceptibility rates to TMP/SMX and ciprofloxacin were also documented for* Klebsiella *spp. (79.1 and 81.4%, respectively), and* P. mirabilis *(71.8 and 84.6%, respectively). For* Enterococcus *spp., susceptibility rates to ampicillin, chloramphenicol, ciprofloxacin, and vancomycin were 88.2, 85.3, 55.9, and 97.1%, respectively. High-level resistance to gentamicin was detected in 24% of* Enterococcus *spp. Bacteria isolated from patients with CA-UTI in Latin America showed limited susceptibility to orally administered antimicrobials, especially for TMP/SMX and fluoroquinolones. Our results highlight the need for developing specific CA-UTI guidelines in geographic regions where elevated resistance to new and old compounds may influence prescribing decisions.*

Key words: urinary tract infection - SENTRY - Latin America

Community-acquired urinary tract infections (CA-UTI) are a frequent problem worldwide. In the United States, surveys have estimated an incidence of eight million UTI episodes per year (Foxman 2002). These infections are usually caused by *Escherichia coli*, but other uropatho-gens, such as *Klebsiella* spp. and *Staphylococcus saprophyticus*, have also been frequently isolated (Ronald 2002, Lau et al. 2004).

Effective management of UTIs in the outpatient setting has been hampered by the fact that many strains have developed resistance to several oral antimicrobial agents. The increasing frequency of thrimetoprim/sulfamethoxazole (TMP-SMX) resistance is worrisome, since this agent is frequently prescribed for uncomplicated UTIs in many developed and developing countries (Talan et al. 2000, Hay et al. 2005, Sader et al. 2005). Reports from North America indicate an elevated prevalence of TMP-SMX-resistant isolates in this region associated with increased clinical failure rates (Manges et al. 2004). Although the Infectious Diseases Society of America (IDSA) guidelines and some studies have suggested that fluoroquinolones may be used as first-line therapy for treatment of uncomplicated bacterial cystitis in woman (Warren et al. 1999,Talan et al. 2004) reports of uropathogens resistant to these agents have increasingly been reported (Alos et al. 2005).

The continuous trend of empirically treating CA-UTI episodes poses a great challenge for researchers, since data on uropathogens prevalence and antimicrobial susceptibility have been increasingly more difficult to obtain. Moreover, regional variations in resistance patterns do occur, and must be as well documented (Gupta 2003). In Latin America, few data are available on the frequency and resistance rates of CA-UTI. In this study, we have evaluated the pathogen frequency and susceptibility patterns of CA-UTI in Latin American medical centers as part of the SENTRY Antimicrobial Surveillance Program.

MATERIALS AND METHODS

Bacterial strains - Each medical center was responsible to collect consecutive isolates from CA-UTI, including urinary pathogens from patients presenting to outpatient clinics or emergency department. Urinary specimens were collected in the course of routine clinical management, and infections were considered to be clinically significant and of community origin by local criteria. A number of demographic information, such as antibiotic use, and presence of complicated UTI, were not collected or might have not been available. A total of 611 non-dupli-

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cate bacterial isolates were collected from patients with CA-UTI presenting at Latin America medical centers participating in the SENTRY Program between January and December 2003 (Argentina, Chile, Brazil, Mexico, and Venezuela). All isolates were identified at the participating institution by the routine methodology in use at each laboratory. Upon receipt at the monitoring laboratory (JMI Laboratories, North Liberty, IA, US), isolates were subcultured onto blood agar to ensure viability and purity. Confirmation of species identification was performed with Vitek (bioMérieux Vitek, St Louis, MO) or conventional methods as required.

Participant medical centers - The medical centers were located in San Isidro and Buenos Aires (Argentina); Brasília, Florianópolis, Porto Alegre, São Paulo (Brazil); Santiago (two medical centers, Chile); Ciudade del Mexico, (Mexico); and Caracas (Venezuela).

Susceptibility testing - Antimicrobial susceptibility testing was performed and interpreted following the guidelines for reference broth microdilution method described by the Clinical and Laboratory Standards Institute (CLSI, formerly National Committee for Clinical and Laboratory Standards) (NCCLS 2003). The minimal inhibitory concentrations (MICs) were defined as the lowest antimicrobial concentration able to totally inhibit bacterial growth. The diverse antimicrobial agent powders were obtained from the respective manufacturers or purchased from Sigma (St Louis, MO, US). Dry-form microdilution panels and broth for inoculation were purchased from Trek Diagnostic Systems (Westlake, OH, US). Testing of quality control strains *E. coli* ATCC 25922 and 35218, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, and *Enterococcus faecalis* ATCC 29212 was performed for quality assurance purposes. Isolates of *E. coli* and *K. pneumoniae* with increased MIC values (≥ 2 μg/ml) for ceftazidime and/or ceftriaxone and/or aztreonam were considered as possible extended-spectrum β-lactamase (ESBL)-producing phenotypes according to CLSI criteria (2005). Production of ESBL was confirmed by disk-approximation test (Thomson & Sanders 1992).

RESULTS AND DISCUSSION

E. coli (66%) was the most common pathogen isolated from CA-UTI in Latin American countries, followed by *P. mirabilis* (6.4%) and *K. pneumoniae* (5.9%) (Table I). *Enterococcus* spp. was the most common gram-positive uropathogen, responsible for 5.6% of all CA-UTI. These data are similar to those presented by other surveillance studies, in which gram-negative agents were the most common pathogens associated with CA-UTI (Zhanel et al. 2000, Kahlmeter 2003).

Overall, the majority of isolates (75.6%) were collected from female patients with *E. coli* being also the most common uropathogen (Table II). The median age of patients with CA-UTI was similar in both groups: 41.4 years (female sex) and 43.7 years (male sex) (data not shown). The predominance of *E. coli* as the leading agent of CA-UTI in women had been also verified by other surveillance reports from distinct geographic regions, such as the ECO SENS report from Europe and Canada, and the TSN study from the United States (Kahlmeter 2000, Gupta et al. 2001).

TABLE I

Occurrence of the top ten pathogens isolated from community-acquired urinary tract infections in Latin American medical centers (SENTRY Antimicrobial Surveillance Program 2003)

Organism or group	No. of isolates (%)
Escherichia coli	403 (66)
Klebsiella spp.	43 (7)
Proteus mirabilis	39 (6.4)
Enterococcus spp.	34 (5.6)
Pseudomonas aeruginosa	28 (4.6)
Group B streptococci	14 (2.3)
Staphylococcus saprophyticus	8 (1.3)
Klebsiella oxytoca	7 (1.1)
Enterobacter cloacae	6 (1)
Serratia marcescens	5 (0.8)

Among gram-positive uropathogens, *Enterococcus* spp. and group B streptococci were the most common agents isolated from women, responsible for 5.2 and 2.8%, respectively, of all CA-UTI (Table II). In this study, however, only 8 isolates of *S. saprophyticus* were recovered. These results contrast with other reports, where *S. saprophyticus* remains a significant pathogen causing CA-UTI in women (Kahlmeter 2003, Muratani & Matsumoto 2004). This finding may indicate a distinct pattern of Gram-positive uropathogen distribution in the Latin American region.

The antimicrobial susceptibility results of the most frequent pathogens associated with CA-UTI in Latin America is shown in Table III. The β-lactam agents ceftriaxone (MIC_{50}, ≤ 0.25 μg/ml), ceftazidime (MIC_{50}, ≤ 1 μg/ml), and cefepime (MIC_{50}, ≤ 0.12 μg/ml), displayed excellent activity against *E. coli* (98.3-98.5% susceptible). All of the 403 clinical isolates of *E. coli* were susceptible to imipenem and meropenem, indicating that carbapenem resistance is still an unusual phenotype among Enterobacteriaceae isolated from CA-UTI in the region. On the other hand, decreased susceptibility rates were detected among *E. coli* for common orally administered agents, such as ampicillin (46.2% susceptible), ciprofloxacin (77.4% susceptible), and TMP-SMX (59.6% susceptible). In fact, among the orally prescribed agents, cefuroxime (2.2% resistant), amoxicillin/clavulanate (1.2% resistant), and nitrofurantoin (6.9% resistant) achieved the lowest resistance rates for *E. coli*.

Our study have detected much higher resistance rates when compared to the ECO SENS and TSN Programs for some oral prescribed agents (Gupta et al. 2001, Kahlmeter 2003). Most surprisingly, the *E. coli* resistance rates found in the current study are even higher than those described by some surveillance programs evaluating hospitalized patients. The EARSS study in Spain reported lower resistance rates to ciprofloxacin (19.3%), and TMP/SMX (32.6%), among *E. coli* strains from Spanish hospitals (Oteo et al. 2005). The current study showed similar susceptibility rates for some orally prescribed agents among

TABLE II

Occurrence of the top five pathogens isolated from community-acquired urinary tract infections in Latin American medical centers according to gender distribution (SENTRY Antimicrobial Surveillance Program 2003)

Organism or group (%)	
Gender	
Female (n = 462)	Male (n = 148)
1 *Escherichia coli* (71.6)	*Escherichia coli* (48.0)
2 *Proteus mirabilis* (5.4)	*Pseudomonas aeruginosa* (11.5)
3 *Klebsiella pneumoniae* (5.2)	*Proteus mirabilis* (9.5)
Enterococcus spp. (5.2)	
4 Group B streptococcus (2.8)	*Klebsiella pneumoniae* (8.1)
5 *Pseudomonas aeruginosa* (2.4)	*Enterococcus faecalis* (6.8)

Gender information was not available for one patient.

CA-UTI isolates similar to those showed by *E. coli* strains from other infection sites previously evaluated by the SENTRY Program in Latin America, such as bloodstream infections (Sader et al. 2002), and hospital-acquired UTI (Gales et al. 2002).

The increased resistance rates detected for TMP/SMX in Latin America is of great concern. These rates may reflect a possible widespread use of this low cost antimicrobial agent for treatment of CA-UTI in the region, or as a prophylactic agent against *Pneumocystis jiroveci* infections in the HIV-infected population.

Increased resistance rates of *E. coli* against the studied quinolones were also verified in contrast to other surveillance studies evaluating CA-UTI in United States and Europe, which have documented resistance rates of approximately 2% (Gupta et al. 2001, Kahlmeter 2003) for some fluoroquinolones (Table III). In fact, the susceptibility rates to the fluoroquinolones were lower than those observed for hospital-acquired *E. coli* isolates previously collected by the SENTRY in Latin America (Gales et al. 2002). These increased resistance rates among community-acquired *E. coli* was addressed by the EARSS study in Spain, where 19.3% of all invasive clinical isolates evaluated in 2003 were resistant to ciprofloxacin (Oteo et al. 2005). These high resistance rates were attributed to an increase in fluoroquinolone consumption over the years in Spain. Prior exposure to fluoroquinolones has been recently acknowledged to be an independent risk factor for ciprofloxacin-resistant *E. coli* from CA-UTI (Killgore et al. 2004).

Among the participating countries, Brazil and Chile displayed the highest susceptibility rates to the evaluated fluoroquinolones against *E. coli* (Table IV). Although Mexico contributed with only 36 *E. coli* isolates, very low susceptility rates were detected among all tested oral agents. Overall, rates of TMP/SMX resistance were significantly decreased for all Latin American countries. The current data may reflect the increased use of orally prescribed agents in some Latin American countries, to treat hospital or community-acquired infections, such as UTI or respiratory tract infections. This overuse may select for multidrug-resistant *E. coli* phenotypes, harboring the potential to disseminate within a specific region. Further antimicrobial consumption studies at community level are needed in the Latin American region to verify this assumption.

High resistance rates were also documented for TMP/SMX among the other Enterobacteriaceae causing CA-UTI, ranging from 19.4% for *K. pneumoniae*, to 28.2% for *P. mirabilis* (Table III). Resistance rates for the tested fluoroquinolones were lower than those described for *E. coli*, but also significantly elevated. Overall, more than 85% of clinical isolates of *K. pneumoniae* and *P. mirabilis* were susceptible to third- and fourth-generation cephalosporins. No isolate was found to be resistant to imipenem or meropenem. These two Enterobacteriaceae pathogens have been described as frequent uropathogens associated with CA-UTI among non-*E. coli* isolates, especially among adult and elderly patients (Gupta et al. 2001). Other surveillance studies, however, have found distinct and much lower resistance rates for orally administered antimicrobial agents for these pathogens (Gupta et al. 2001, Kahlmeter 2003).

A total of 88.2% of *Enterococcus* spp. isolates were susceptible to ampicillin (Table III). Among other orally administered agents, nitrofurantoin (94.1%) and chloramphenicol (85.3%) demonstrated the higher susceptibility rates. Linezolid was the only agent able to inhibit the growth of 100% of all *Enterococcus* spp. isolates, and 2.9% of isolates were resistant to both, teicoplanin and vancomycin (vanA phenotype). The majority of group B streptococci collected from CA-UTI were susceptible to the tested antimicrobial agents, including the tested fluoroquinolones.

Surprisingly, a total of 28 isolates of *P. aeruginosa* were reported (Table III). Previous surveillance studies have also documented *P. aeruginosa* among patients with CA-UTI (Barrett et al. 1999, Lau et al. 2004). These data may correspond, in the current study, to infections developed in the community setting from patients with recent hospitalization and/or antimicrobial treatment.

Rates of ESBL-producing isolates were 1.7, 16.3, and 5.1%, respectively, for *E. coli*, *Klebisella* spp., and *P. mirabillis* (data not shown). The increasing frequency of

TABLE III

Antimicrobial susceptibility of community-acquired urinary tract infection isolates collected from Latin American medical centers (SENTRY Antimicrobial Surveillance Program 2003)

	MIC_{50}	MIC_{90}	% susceptible	% resistant
Escherichia coli (n = 403)				
Ampicillin[a]	> 16	> 16	46.2	53.6
Ampicillin/sulbactam	8	32	56.6	23.3
Amoxicillin/clavulanate[a]	8	16	83.6	1.2
Piperacillin/tazobactam	2	4	97.3	0.2
Cefoxitin	4	8	93.1	1.7
Cefuroxime[a]	4	8	76.4	2.2
Ceftriaxone	≤ 0.25	≤ 0.25	98.5	1.2
Ceftazidime	≤ 1	≤ 1	98.3	1.5
Cefepime	≤ 0.12	≤ 0.12	98.8	1.0
Aztreonam	≤ 0.12	≤ 0.12	98.3	1.7
Imipenem	≤ 0.5	≤ 0.5	100.0	0.0
Amikacin	2	4	100.0	0.0
Gentamicin	≤ 2	4	90.1	8.4
Nalidixic acid[a]	4	> 32	72.7	29.3
Ciprofloxacin[a]	≤ 0.03	> 4	77.4	21.6
Gatifloxacin[a]	≤ 0.03	> 4	79.2	17.1
Levofloxacin[a]	≤ 0.03	> 4	78.7	18.6
Nitrofurantoin[a]	≤ 16	32	93.1	6.9[b]
Trimethoprim/sulfamethoxazole[a]	≤ 0.5	> 2	59.6	40.4
Klebsiella spp. (n = 43)				
Ampicillin[a]	> 16	> 16	9.3	74.4
Ampicilllin/sulbactam	8	> 32	67.4	25.6
Amoxicillin/clavulanate[a]	2	16	76.7	7.0
Piperacillin/tazobactam	2	32	88.4	9.3
Cefuroxime[a]	2	> 16	74.4	16.3
Ceftriaxone	≤ 0.25	32	86.0	9.3
Ceftazidime	≤ 1	16	88.4	4.7
Cefepime	≤ 0.12	2	90.7	7.0
Aztreonam	≤ 0.12	> 16	83.7	11.6
Imipenem	≤ 0.5	≤ 0.5	100.0	0.0
Amikacin	2	16	95.3	4.7
Gentamicin	≤ 2	> 8	86.0	14.0
Nalidixic acid[a]	4	> 32	74.4	25.6
Ciprofloxacin[a]	0.12	> 4	81.4	18.6
Gatifloxacin[a]	0.06	> 4	83.7	16.3
Levofloxacin[a]	0.06	> 4	81.4	16.3
Nitrofurantoin[a]	32	> 32	51.2	48.8[b]
Trimethoprim/sulfamethoxazole[a]	≤ 0.5	> 2	79.1	20.9
Proteus mirabilis (n = 39)				
Ampicillin[a]	≤ 1	> 16	59.0	41.0
Ampicillin/sulbactam[a]	1	32	76.9	10.3
Amoxicillin/clavulanate[a]	≤ 1	8	94.9	0.0
Piperacillin/tazobactam	≤ 0.5	1	100.0	0.0
Cefuroxime[a]	2	8	89.7	7.7
Ceftriaxone	≤ 0.25	≤ 0.25	94.9	5.1
Ceftazidime	≤ 1	≤ 1	100.0	0.0
Cefepime	≤ 0.12	0.5	94.9	5.1
Aztreonam	≤ 0.12	≤ 0.12	100.0	0.0
Imipenem	1	2	100.0	0.0
Meropenem	≤ 0.06	≤ 0.06	100.0	0.0
Amikacin	4	8	97.4	2.6
Gentamicin	≤ 2	> 8	79.5	20.5
Nalidixic acid[a]	4	> 32	84.6	15.4
Ciprofloxacin[a]	≤ 0.03	4	84.6	10.3
Gatifloxacin[a]	0.12	4	87.2	7.7
Levofloxacin[a]	0.06	2	92.3	5.1
Nitrofurantoin[a]	> 32	> 32	2.6	97.4[b]
Trimethoprim/sulfamethoxazole[a]	≤ 0.5	> 2	71.8	28.2

↳

Pseudomonas aeruginosa (n = 28)				
Ceftazidime	4	> 16	67.9	32.1
Cefepime	4	> 16	64.3	14.3
Aztreonam	8	> 16	57.1	39.3
Imipenem	1	> 8	71.4	25.0
Meropenem	0.5	> 8	71.4	14.3
Piperacillin/tazobactam	8	> 64	67.9	32.1
Amikacin	4	> 32	71.4	21.4
Gentamicin	4	> 8	60.7	35.7
Nalidixic acid[a,c]	> 32	> 32	3.6	96.4
Ciprofloxacin[a]	0.25	> 4	67.9	32.2
Gatifloxacin[a]	2	> 4	60.7	32.1
Levofloxacin[a]	1	> 4	60.7	32.1
Nitrofurantoin[a,c]	> 32	> 32	0.0	100.0[b]
Polymyxin B	≤ 1	≤ 1	96.4	3.6
Enterococcus spp. (n = 34)				
Ampicillin[a]	≤ 1	> 16	88.2	11.8
Chloramphenicol[a]	8	> 16	85.3	11.8
Ciprofloxacin[a]	1	> 4	55.9	35.3
Gatifloxacin[a]	0.5	> 4	64.7	35.3
Levofloxacin[a]	1	> 4	64.7	35.3
Linezolid[a]	≤ 2	≤ 2	100.0	0.0
Nitrofurantoin[a]	≤ 16	≤ 16	94.1	5.9[b]
Quinupristin/Dalfopristin	≥ 2	> 2	11.8	76.5
Gentamicin HL	≤ 500	> 1000	76.5	23.5
Streptomycin HL	≤ 1000	> 2000	70.6	29.4
Teicoplanin	≥ 2	≥ 2	97.1	2.9
Vancomycin	2	2	97.1	2.9
Group B streptococci (n = 14)				
Ampicillin[a]	≤ 1	≤ 1	100	0.1
Penicillin[a]	0.06	0.06	100	0.0
Chloramphenicol[a]	≤ 2	≤ 2	100	0.0
Clindamycin[a]	≤ 0.06	≤ 0.06	100	0.0
Erythromycin[a]	≤ 0.06	≤ 0.06	92.9	7.1
Gatifloxacin[a]	0.25	0.25	100	0.0
Levofloxacin[a]	0.25	1	100	0.0
Linezolid[a]	1	1	100	0.0
Quinupristin/Dalfopristin	≤ 0.25	≤ 0.25	100	0.0
Vancomycin	0.5	0.5	100	0.0

a: orally administered antimicrobial agents; *b*: includes intermediate and resistant strains; *c*: susceptibility breakpoints for Enterobacteriaceae were used (CLSI 2005).

ESBL phenotypes in the community is an emerging problem (Pitout et al. 2005). Although we were not able to track demographic data on these patients, risk factors for the development of ESBL in the community have already been described, including recent hospitalization, previous antimicrobial treatment, and use of immunosuppressive therapy (Colodner et al. 2004). The current report further emphasizes the importance of routine screening, by clinical laboratories, of ESBL production among Enterobacteriaceae strains isolated from community-acquired infections.

In the Latin American region, international surveillance programs have already documented increased resistance rates for multiple pathogens among hospitalized patients (Andrade et al. 2003, Gordon & Jones 2003, Mendes et al. 2005), probably reflecting local antimicrobial usage patterns, leading to a high selective pressure, and/or dissemination of specific resistant clones. However, antimicrobial susceptibility among pathogens isolated from community-acquired infections is poorly investigated in this region.

Although this is the first surveillance study in the Latin American region to assess the frequency of pathogens from CA-UTI, a number of points should be raised. The classification of CA-UTI was based on local criteria, according to the study protocol, but some data, such as previous hospitalization, may not have been available for analysis. So, the presence of some pathogens, such as *P. aeruginosa* and *Enterococcus* spp., and the low prevalence of *S. saprophyticus*, might reflect infections acquired during hospitalization, followed by community-onset after hospital discharge. However, a larger surveillance study conducted in the US has also found even elevated frequencies of *Enterococcus* spp. (from 5 to 12%) and *P. aeruginosa* (from 1 to 4%) among CA-UTI in woman (Gupta et al. 2001). Since most cases of CA-UTI are treated empirically and cultures are not usually requested, we can predict that some urine cultures evaluated in the present

TABLE IV

Antimicrobial susceptibility of selected oral agents against 403 *Escherichia coli* isolates collected from community-acquired urinary tract infections at Latin American medical centers, according to country of isolation (SENTRY Antimicrobial Surveillance Program 2003)

Antimicrobial agent	Argentina[a] (n = 73)	Brazil[b] (n = 139)	Chile[c] (n = 74)	Mexico[d] (n = 36)	Venezuela[e] (n = 81)
Ampicillin	53.4	50.4	43.2	22.2	45.7
Amoxicillin/clavulanate	89.0	89.0	86.5	55.6	77.8
Cefuroxime	100	98.6	95.9	63.9	95.1
Nalidixic acid	67.1	84.9	82.4	25.0	69.1
Ciprofloxacin	75.3	89.9	86.5	27.8	71.6
Gatifloxacin	76.7	92.1	87.8	30.6	72.8
Levofloxacin	78.1	91.4	87.8	27.8	71.6
Nitrofurantoin	87.7	97.8	94.6	80.6	93.8
Trimethoprim/sulfamethoxazole	76.7	57.6	66.2	38.9	50.6

a: includes centers in San Isidro and Buenos Aires; *b*: includes centers in Brasília, Florianopolis, Porto Alegre, São Paulo; *c*: includes two medical centers in Santiago; *d*: includes a center in Ciudade del Mexico; *e*: includes a center in Caracas.

study were submitted to the laboratory because of treatment failure or complicated UTI, and probably represent a different patient population from those with first episode of UTI. Although these limitations are inherent to the retrospective nature of large surveillance studies, the inclusion of such specimens may have overestimated the resistance rates for some organisms.

Even tough, the decreased susceptibility rates found for some agents in the current study is worrisome, since some of them are currently prescribed as first-line agents for treatment of CA-UTI in the Latin American region. As most orally administered agents prescribed for CA-UTI usually achieve high urinary concentrations, it was originally thought that in vitro resistance could not result into therapeutic failure. However, recent studies have demonstrated therapeutic failure in more than 50% of patients infected with TMP/SMX-resistant uropathogens (Gupta & Stamm 2002). The Infectious Diseases Society of America (IDSA) guidelines consider TMP/SMX as the current standard therapy for uncomplicated CA-UTI in women (Warren et al. 1999). The IDSA guidelines recommend that local antimicrobial susceptibility patterns of community-acquired pathogens must be taken into account before prescribing such agents. As demonstrated by this study, TMP/SMX may no longer be considered a first-line orally administered agent for CA-UTI in the specific geographic regions covered by the SENTRY Program in Latin America. Based on the results reported here, it has become a difficult task to choose the most suitable oral agent for empiric treatment of CA-UTI. Fluoroquinolones, agents recommended for communities with elevated prevalence of TMP/SMX resistance, must be used with caution, since resistance rates may reach up to 21% among *E. coli*, as described in this study. Although cefuroxime and amoxicillin/clavulanate demonstrated lower resistance rates, β-lactam agents are less effective in bacteriuria erradication, leading to increased rates of recurrence (Daikos et al. 1987). Although nitrofurantoin had poor activity against *P. mirabilis* and only 51.2% of *Klebsiella* spp. were susceptible to this agent, it might constitute a good alternative agent for treatment of uncomplicated CA-UTI caused by *E.coli.*

The worldwide trend of empirically treating CA-UTI may not apply for specific geographical regions in which decreased susceptibility rates are documented for common uropathogens. In these communities with high rates of antimicrobial resistance, routine urine cultures may be necessary, since treatment failure is more likely to occur. International guidelines may no longer be suitable for some Latin American countries, where antimicrobial resistance rates for first-line agents were unexpectedly elevated in this study. The development of specific guidelines based on local susceptibility patterns may be necessary in these geographic regions. Continued surveillance programs, such as the SENTRY, are essential to provide local information for decision-makers and infectious diseases specialists developing CA-UTI guidelines.

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REFERENCES

Alos JI, Serrano MG, Gomez-Garces JL, Perianes J 2005. Antibiotic resistance of *Escherichia coli* from community-ac-

quired urinary tract infections in relation to demographic and clinical data. *Clin Microbiol Infect 11*: 199-203.

Andrade SS, Jones RN, Gales AC, Sader H S 2003. Increasing prevalence of antimicrobial resistance among *Pseudomonas aeruginosa* isolates in Latin American medical centres: 5 year report of the SENTRY Antimicrobial Surveillance Program (1997-2001). *J Antimicrob Chemother 52*: 140-141.

Barrett SP, Savage MA, Rebec MP, Guyot A, Andrews N, Shrimpton SB 1999. Antibiotic sensitivity of bacteria associated with community-acquired urinary tract infection in Britain. *J Antimicrob Chemother 44*: 359-365.

CLSI-Clinical and Laboratory Standards Institute 2005. Performance standards for antimicrobial susceptibility testing, 15th informational supplement M100-S15, NCCLS, Wayne, PA.

Colodner R, Rock W, Chazan B, Keller N, Guy N, Sakran W, Raz R 2004. Risk factors for the development of extended-spectrum beta-lactamase-producing bacteria in nonhospitalized patients. *Eur J Clin Microbio Infect Dis 23*: 163-167.

Daikos GL, Kathpalia SB, Sharifi R, Lolans VT, Jackson GG 1987. Comparison of ciprofloxacin and beta-lactam antibiotics in the treatment of urinary tract infections and alteration of fecal flora. *Am J Med 82*: 290-294.

Foxman B 2002. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med 113* (Suppl.): 5S-13S.

Gales AC, Sader HS, and Jones RN 2002. Urinary tract infection trends in Latin American hospitals: report from the SENTRY antimicrobial surveillance program (1997-2000). *Diag Microbiol Infect Dis 44*: 289-299.

Gordon KA and Jones RN 2003. Susceptibility patterns of orally administered antimicrobials among urinary tract infection pathogens from hospitalized patients in North America: comparison report to Europe and Latin America. Results from the SENTRY Antimicrobial Surveillance Program (2000). *Diag Microbiol Infect Dis 45*: 295-301.

Gupta K 2003. Emerging antibiotic resistance in urinary tract pathogens. *Infect Dis Clin North Am 17:* 243-259.

Gupta K, Stamm WE 2002. Outcomes associated with trimethoprim/sulphamethoxazole (TMP/SMX) therapy in TMP/SMX resistant community-acquired UTI. *Int J Antimicrob Agents 19*: 554-556.

Gupta K, Sahm DF, Mayfield D, Stamm WE 2001. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in women: a nationwide analysis. *Clin Infect Dis 33*: 89-94.

Hay AD, Thomas M, Montgomery A, Wetherell M, Lovering A, McNulty C, Lewis D, Carron B, Henderson E, MacGowan A 2005. The relationship between primary care antibiotic prescribing and bacterial resistance in adults in the community: a controlled observational study using individual patient data. *J Antimicrob Chemother 56*: 146-153.

Kahlmeter G 2000. The ECO.SENS Project: a prospective, multinational, multicentre epidemiological survey of the prevalence and antimicrobial susceptibility of urinary tract pathogens-interim report. *J Antimicrob Chemother 46* (Suppl.): 15-22.

Kahlmeter G 2003. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. *J Antimicrob Chemother 51:* 69-76.

Killgore KM, March KL, Guglielmo B J 2004. Risk factors for community-acquired ciprofloxacin-resistant *Escherichia coli* urinary tract infection. *Ann Pharmacother 38*: 1148-1152.

Lau SM, Peng MY, Chang FY 2004. Resistance rates to commonly used antimicrobials among pathogens of both bacteremic and non-bacteremic community-acquired urinary tract infection. *J Microbiol Immunol Infect 37*: 185-191.

Manges AR, Dietrich PS, Riley LW 2004. Multidrug-resistant *Escherichia coli* clonal groups causing community-acquired pyelonephritis. *Clin Infect Dis 38*: 329-334.

Mendes C, Oplustil C, Sakagami E, Turner P, Kiffer C 2005. Antimicrobial susceptibility in intensive care units: MYSTIC Program Brazil 2002. *Braz J Infect Dis 9:* 44-51.

Muratani T, Matsumoto T 2004. Bacterial resistance to antimicrobials in urinary isolates. *Int J Antimicrob Agents 24* (Suppl.): S28-S31.

NCCLS-National Committee for Clinical and Laboratory Standards 2003. Methods for dilution antimicrobial tests for bacteria that grow aerobically: Approved standard M7-A6. Wayne, PA.

Oteo J, Lazaro E, de Abajo F J, Baquero F, Campos J 2005. Antimicrobial-resistant invasive *Escherichia coli*, Spain. *Emerg Infect Dis 11*: 546-553.

Pitout JD, Nordmann P, Laupland KB, Poirel L 2005. Emergence of Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBLs) in the community. *J Antimicrob Chemother 56*: 52-59.

Ronald A 2002. The etiology of urinary tract infection: traditional and emerging pathogens. *Am J Med 113* (Suppl.): 14S-19S.

Sader HS, Biedenbach DJ, Streit JM, Jones RN 2005. Cefdinir activity against contemporary North American isolates from community-acquired urinary tract infections. *Int J Antimicrob Agents 25*: 89-92.

Sader HS, Jones RN, Andrade-Baiocchi S, Biedenbach D J 2002. Four-year evaluation of frequency of occurrence and antimicrobial susceptibility patterns of bacteria from bloodstream infections in Latin American medical centers. *Diagn Microbiol Infect Dis 44*: 273-280.

Talan DA, Klimberg IW, Nicolle LE, Song J, Kowalsky SF, Church DA 2004. Once daily, extended release ciprofloxacin for complicated urinary tract infections and acute uncomplicated pyelonephritis. *J Urol 171*: 734-739.

Talan DA, Stamm WE, Hooton TM, Moran GJ, Burke T, Iravani A, Reuning-Scherer J, Church DA 2000. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis pyelonephritis in women: a randomized trial. *JAMA 283*: 1583-1590.

Thomson KS, Sanders CC 1992. Detection of extended-spectrum beta-lactamases in members of the family *Enterobacteriaceae*: comparison of the double-disk and three-dimensional tests. *Antimicrob Agents Chemother 36*:1877-82.

Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE 1999. Guidelines for antimicrobial treatment of

uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). *Clin Infect Dis 29*: 745-758.

Zhanel GG, Karlowsky JA, Harding GK, Carrie A, Mazzulli T, Low DE, Hoban DJ 2000. A Canadian national surveillance study of urinary tract isolates from outpatients: comparison of the activities of trimethoprim-sulfamethoxazole, ampicillin, mecillinam, nitrofurantoin, and ciprofloxacin. The Canadian Urinary Isolate Study Group. *Antimicrob Agents Chemother 44*: 1089-1092.