Resistance Among the Most Frequent Pathogens Causing Urinary Tract Infections in Hospitalized Patients Compared to Resistance in the Same Species Isolated from Blood Stream Infections: Report from the SENTRY Antimicrobial Surveillance Program (Europe 2000)

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ABSTRACT

Background: Bacterial urinary tract infections (UTIs) are an important source of septicemia (BSI) resulting in higher mortality rates. 16 centers from 11 European countries participating in SENTRY Antimicrobial Surveillance Program assessed UTI and BSI in 2000.
Methods: 744 UTI and 3192 BSI isolates were forwarded to the coordinating center (Iowa). 44 antimicrobial agents were tested against UTI organisms and 45 against BSI isolates by NCCLS methods. Top five UTI isolates were: *E. coli* (45%), *Enterococcus spp* (13%), *P. aeruginosa* (9%), *Klebsiella spp*. (9%) and *P. mirabilis* (7%). The rank order and proportions of pathogens observed has remained stable in comparison to the previous three years of the SENTRY Program.
Results: Table below gives the percentage susceptible (3 top isolates) against selected antimicrobial agents:

	% susceptible (NCCLS breakpoints):					
	E. coli		Enterococci		*P. aeruginosa*	
Agent	UTI	BSI	UTI	BSI	UTI	BSI
Ampicillin	48	48	84	74	0	0
Amox/Clav	81	80	86	75	1	1
Cefepime	99	99	3	2	69	68
BMS284756	86	87	81	74	51	66
Ciprofloxacin	85	86	47	44	54	71
Gentamicin	90	94	(70)a	(68)a	54	69
Trim/Sulfa	66	68	68	70	1	2

a. % at ≤ 500 µg/ml (synergy screen).

Enterococci from UTI were generally more susceptible to ß-lactams and fluoroquinolones than BSI strains; *P. aeruginosa* from UTI were consistantly more resistant than BSI counterparts; and BMS284756, a new desfluoroquinolone, appears promising and clearly superior against enterococci isolated from urine compared to ciprofloxacin (≥ 30% wider spectrum).

INTRODUCTION

Urinary tract infections (UTIs) are the most common infections occurring in hospitals and extended-care settings. Many of these UTIs are recurrent, chronic or associated with the use of indwelling urethral catheters. Nosocomial UTIs have also become more prevalent as hospitalized patients have become more compromised and lengths of stay have increased due to the severity of disease. Antimicrobial resistance has increased not only among pathogens causing nosocomial infections, but also, among pathogens in patients admitted from the community setting. Because of the large number of catheterized hospitalized patients, bacteremias originating from urinary tract infections constituted nearly 15% of all nosocomial blood stream infections (BSI).

To address the problem of increasing antimicrobial resistance, surveillance programs are necessary both locally, nationally, and globally. Data on frequency of pathogen occurrence and resistance to commonly prescribed antimicrobials is a cornerstone for the empiric treatment of patients with antimicrobial agents.

In the present overview, we report the results of the European SENTRY Antimicrobial Surveillance Program for the year 2000 with regard to the rate of resistance against different antimicrobial agents in pathogens causing UTI and compare the rates of resistance with those species cultured from BSI to address the question whether there are significant differences in resistance pattern between these pathogen groups.

MATERIALS AND METHODS

The SENTRY Program is a global surveillance system which monitors the frequency of occurrence in antimicrobial susceptibility of both nosocomial- and community-acquired bacterial pathogens via an international network of sentinel hospitals that are distributed roughly equally by size and location. Sixteen centers from 11 European countries were asked to send 50 consecutive isolates from UTIs and additionally 20 isolates from BSI each month (240/year/center for 2000). No distinction was made between nosocomial and community-acquired infection for isolates from urinary tract although essentially all were from hospitalized patients. All isolates (only one isolate per patient) were deemed clinically significant by local relevance criteria. Each isolate was accompanied by demographical data, including the genus and species name and methods of identification. All isolates were forwarded to a central laboratory (Iowa, USA). Upon receipt, isolates were subcultured on blood agar to ensure purity. Isolate identify was confirmed, if necessary, using the Vitek or reference methods.

The distributions of processed isolates by nation was: Belgium (47), France (51), Germany (84), Israel (49), Italy (96), Poland (52), Spain (111), Sweden (59), Switzerland (49), Turkey (97), and UK (49).

All susceptibility testing used methods described by the NCCLS [2000] and were interpreted by the most recent publication, M100-S12 [2002]. Quality control (QC) of the trays prepared by TREK Diagnostics (Westlake, OH) was provided by routine testing of *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, *P. aeruginosa* ATCC 27853, *E. coli* ATCC 25922 and 35218, *H. influenzae* ATCC 49247 and *S. pneumoniae* ATCC 49619. All QC values were with NCCLS-specified ranges. ESBL enzyme phenotypes were detected by NCCLS MIC screening criteria (MIC, ≥ 2 µg/ml for aztreonam or ceftazidime or ceftriaxone) and confirmed by clavulanate inhibition (Etest, AB BIODISK, Solna, Sweden).

Definition of multi-resistance. Strains were considered to be multi-drug-resistant if they were refractory to four or more of the following agents was present: ampicillin, amoxicillin/clavulanate, cefotaxime or ceftriaxone, trimethoprim/sulfamethoxazole, ciprofloxacin, nitrofurantoin, gentamicin, cefepime or garenoxacin (formerly BMS284756, a novel desfluoro-quinolone).

Table 1. Variation in the occurrence of UTI pathogens for the year 2000 versus the rates identified in SENTRY Program hospitals in 1997-99 (Europe; 2,307 strains).

	Rank/% occurrence	
Organism	2000	1997-99
E. coli	1/45.6	1/48.6
Enterococci	2/13.4*	4/7.2
P. aeruginosa	3/9.4	3/7.5
Klebsiella spp.	4/8.7	2/9.6
P. mirabilis	5/7.1	5/5.4
Enterobacter spp.	6/4.2	6/4.2
Indole-positive Proteae	7/2.9	7/2.5
Citrobacter spp.	8/2.1	10/1.6
S. aureus	9/1.7	7/2.5
Acinetobacter spp.	10/1.6	11/1.3
No. of isolates	774	2,307

*Significant recent change in pattern of pathogen occurrence.

Table 2. Organisms causing UTI and BSI in European SENTRY Program medical centers during 2000.

	Rank/No. of isolates/% of occurrence:	
Organism	Urinary tract infections (n=774)	Blood stream infections (n=3,192)
E. coli	1/339/45.6	1/664/20.8
Enterococci	2/99/13.4	5/248/7.8
P. aeruginosa	3/70/9.4	6/195/6.1
Klebsiella spp.	4/65/8.7	4/281/8.8
P. mirabilis	5/53/7.1	11/60/1.9
Enterobacter spp.	6/31/4.2	7/140/4.4
Indole-positive Proteae	7/21/2.9	13/29/0.9
Citrobacter spp.	8/16/2.1	14/23/0.7
S. aureus	9/13/1.7	2/612/19.2
Acinetobacter spp.	10/12/1.6	9/106/3.3
CoNS[a]	11/9/1.2	3/443/13.9
Serratia spp.	12/8/1.0	12/56/1.8
Other streptococci	-	8/125/3.9
S. pneumoniae	-	9/106/3.3

a.CoNS = coagulase-negative staphylococci.

RESULTS

- Compared to 1997-99 UTI pathogen prevalence data, enterococci were isolated in significantly greater numbers ($p < 0.05$) in 2000 (13.4% versus 7.8%; Table 1).
- Rank order for the occurrence rates of 2,307 strains of organisms from year 2000 UTI isolates was: *E. coli* (45.6%) > enterococci > *P. aeruginosa* > *Klebsiella* spp. > *P. mirabilis* > *Enterobacter* spp. > indole-positive Proteae. These seven organisms comprised > 90% of UTI isolates (Tables 1 and 2).
- *E. coli*, enterococci, and *P. aeruginosa*, the three most prevalent UTI pathogens, represented approximately 70% of strains isolated compared to only 35% of BSI isolates (Table 2) in the same year.
- Rank order of susceptibility for antimicrobials (Table 3) was very similar between UTI and BSI isolates, respectively: imipenem (100%, 100%) > cefepime (99%, 99%) > ceftazidime (97%, 97%) > ceftriaxone (95%, 97%) > nitrofurantoin (91%, 94%) > gentamicin (90%, 94%) > gatifloxacin (86%, 87%) = BMS284756 = cefazolin > ciprofloxacin (85%, 86%) > amoxicillin/clavulanate (81%, 80%) > trimethoprim/sulfamethoxazole (66%, 68%) > tetracycline (60%, 62%) > ampicillin (48%, 48%).
- Extended-spectrum ß-lactamase phenotypes were present among *E. coli* isolates and demonstrated ceftazidime or ceftriaxone resistance (MIC, ≥ 2 µg/ml) rates of 5.9 - 6.5% within UTI isolates and 5.3 - 5.4% for BSI isolates (Table 3).
- For those antimicrobials tested against the enterococci from UTI isolates, nitrofurantoin (87%), amoxicillin/clavulanate (86%), ampicillin (84%), and BMS284756 (81%) demonstrated acceptable levels of susceptibility, while amoxicillin/clavulanate (75%), BMS284756 (74%), ampicillin (74%) and nitrofurantoin (73%, but not appropriate for therapy) had the highest susceptibility rates against BSI isolates. Vancomycin was effective against all UTI isolates, but 3.6% of BSI enterococci were VRE. (Data not shown.)
- Of those antimicrobials tested against *P. aeruginosa* from UTI isolates, imipenem (80%) and ceftazidime (73%) had the highest susceptibility rates, while imipenem (77%), ceftazidime (71%) and ciprofloxacin (71%) had the highest susceptibility rates against BSI isolates. Generally, UTI isolates were equally susceptible to ß-lactams compared to BSI isolates, but resistance was greater among UTI isolates for aminoglycosides and the tested quinolones.
- BMS284756 (now garenoxacin) showed a comparable spectrum of activity to other quinolones versus UTI pathogens in Europe, but was more potent versus enterococci. Greater activity has particularly been demonstrated for this desfluoroquinolone against pathogens causing community-acquired respiratory tract infections [Fung-Tomc et al., 2000].

CONCLUSIONS

- *E. coli* continues to demonstrate the high occurrence rates (45.6%, 20.8%) from European isolates obtained from UTI and BSI, respectively.
- BMS284756 or garenoxacin, the new desfluoroquinolone, demonstrated good activity against *E. coli* isolates from both UTI and BSI strains, less activity but greater than that of other quinolones against the enterococci tested, and modest activity against *P. aeruginosa*, regardless of the site of infection.

Table 3. Comparative antimicrobial susceptibility patterns for the three (3) most common causes of UTI versus BSI isolates of the same species (15 antimicrobials; SENTRY Program 2000).

	% susceptible by NCCLS criteria (2002):					
	E. coli (no. tested)		Enterococci (no. tested)		*P. aeruginosa* (no. tested)	
Antimicrobial agent	UTI (339)	BSI (664)	UTI (100)[a]	BSI (248)[b]	UTI (70)	BSI (195)
Ampicillin	48	48	84	74	0	0
Amoxicillin/Clavulanate	81	80	86	75	1	1
Cefazolin	86	87	1	4	0	0
Ceftazidime	97(6.5)[c]	97(5.4)	0	<1	73	71
Ceftriaxone	95(5.9)	97(5.3)	4	2	6	11
Cefepime	99	99	3	2	69	68
Imipenem	100	100	76	70	80	77
BMS284756 (≤4 µg/ml)[d]	86	87	81	74	51	66
Ciprofloxacin	85	86	47	44	54	71
Gatifloxacin	86	87	61	61	51	67
Gentamicin	90	94	70[e]	68	54	69
Streptomycin	NTf	NT	57[e]	52	NT	NT
Tetracycline	60	62	22	39	0	<1
Nitrofurantoin	91	94	87	73	0	0
Trimethoprim/Sulfamethoxazole	66	68	68	70	1	2

a. Includes no VRE isolates.
b. Includes nine VRE (3.6%), four strains having a *van A* pattern.
c. ESBL-phenotype resistance rate in parenthesis.
d. Indicates the proposed breakpoint for susceptibility [Fung-Tomc et al., 2000].
e. High-level resistance screen for synergy.
f. NT = not tested.

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