Contemporary Causes of Skin and Soft Tissue Infections in Europe: Report from the SENTRY Antimicrobial Surveillance Program (2003)

C2-1895

ICAAC 2004

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AMENDED ABSTRACT

Background: Skin and soft tissue infections (SSTI) or wound infections in hospitalized patients were assessed by the SENTRY Program to detect resistance (R) variations and pathogen prevalence changes within various geographic areas (EU). Prior EU statistics were published for year 2000 from 11 countries (697 strains) [DMID 43:303-309, 2002]. The protocol was repeated in 2003 (1,319 strains).

Methods: 50 pathogens/site (106% compliance) were collected from 25 EU medical centers and susceptibility (S) testing was performed by reference broth microdilution methods and ESBL rates determined using NCCLS criteria and confirming tests. Possible epidemic clones were subjected to automated ribotyping and PFGE.

Results: SSTI pathogens by year.

	No/%		
Pathogen rank order	2003	2000	R patterns noted
S. aureus (SA)	550/42	216/31	21% MRSA, 3% mupirocin-R
P. aeruginosa (PSA)	131/10	97/14	21% ciprofloxacin-R
E. coli (EC)	119/9	94/14	12% ESBLs
Enterococci (ENC)	70/5	51/7	2% VRE, *E. faecium*
Enterobacter spp.	70/5	40/6	23% ceftazidime-R
CoNS	69/5	34/5	65% MR
ß-haemolytic streptococci (BHS)	65/5	12/2	10% erythromycin-R
Klebsiella spp. (KSP)	44/3	40/6	34% ESBLs
P. mirabilis (PM)	35/3	23/3	3% ESBLs
Acinetobacter spp.	31/2	21/3	19% imipenem-R

Two MRSA clones (200.2/A and 371.2/B) were detected in a UK medical center and one MDR-PSA clone (272.1/D) was widely disseminated in a Turkish site.

Conclusions: Pathogen occurrence in SSTI (EU) remains similar related to rank order over the last 4 years, but striking increases in *S. aureus* (+ 11%; but lower MRSA rate) and BHS (+ 3%) were observed, associated with significant decreases in Enterobacteriaceae, PSA and ENC isolations (-2 to -5%). R rates of most concern were the 1) ESBLs in EC, KSP and PM; 2) 19% carbapenem-R in PSA and 3) high-level R to the topical agent mupirocin (3%). Continued surveys appear to be prudent and at regular intervals.

INTRODUCTION

Complicated skin and soft tissue infections (SSTIs) are a major reason for hospitalization. Management of SSTIs requires a physical examination, a complete medical history of the patient and carefully selected diagnostic tests. Empirical antibacterial therapy should be based upon defined patient risk factors, expected pathogen(s) and rapid diagnostic reports, such as a Gram's stain result. Initial antimicrobial therapy remains empiric which requires knowledge of resistance trends in bacterial SSTIs at the local level, if possible.

Although improvements have been made to reduce the risks of infection, surgical site infections (SSIs) continue to be a major cause of hospitalized patient morbidity, mortality and hospital costs. CDC data estimates that 2.6% of operations are associated with SSIs, although it is believed by some that the rates are higher due to inadequate post-discharge surveillance. Due to overuse and misuse of antimicrobials, the prevalence of single- and multi-drug resistance continues to increase in some pathogens. This report from the SENTRY Antimicrobial Surveillance Program will demonstrate pathogen prevalence changes and resistance rate variations from geographic regions in Europe associated with SSTI and SSI.

MATERIALS AND METHODS

In 2000, the SENTRY Program tested 697 strains from 16 medical centers throughout Turkey, Israel and nine countries in Europe: Spain, Germany, Italy, Belgium, France, Switzerland, United Kingdom, Poland and Sweden. Results from that study were published in 2002 (Diagnostic Microbiology and Infectious Disease 43:303-309).

The year 2000 protocol was repeated in 2003 accumulating 1,319 strains from 25 medical centers. Three additional countries were included in the 2003 sample (Greece, Ireland, Russia). The medical centers collected 50 consecutive pathogens determined to be significant cutaneous wound infections by local criteria. The isolates were forwarded to the regional monitor (JMI Laboratories, North Liberty, IA, USA) along with clinical/patient demographics including nosocomial versus community-acquired origin. The isolates were subcultured, reviewed for identification accuracy, then stored at -80ºC. When necessary, species identification was confirmed by biochemical tests and/or the Vitek System (bioMerieux, Hazelwood, MO, USA). Reference broth microdilution was used for susceptibility testing. Quality control was performed using *Escherichia coli* ATCC 25922 and 35218, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *Streptococcus pneumoniae* ATCC 49619 and *Enterococcus faecalis* ATCC 29212.

E. coli, *Klebsiella* spp. and *Proteus mirabilis* isolates with ceftazidime or ceftriaxone or aztreonam MIC values of ≥ 2 µg/ml were screened for ESBL production by the disk approximation method. *P. aeruginosa* and *Acinetobacter* spp. resistant to carbapenems and ceftazidime were screened for metallo-ß-lactamase (MßL) enzymes also by a disk approximation method.

Phenotypically similar isolates from the same medical center and temporally related in time and location were compared by automated ribotyping and pulsed-field gel electrophoresis (PFGE).

RESULTS

- The rank order of pathogens for 2003 was: *S. aureus* (41.7%) > *P. aeruginosa* (9.9%) > *E. coli* (9.0%) > *Enterococcus* spp. = *Enterobacter* spp. (5.3%) > CoNS (5.2%) > ß-haemolytic streptococci (4.9%) > *Klebsiella* spp. (3.3%) > *P. mirabilis* (2.7%) > *Acinetobacter* spp. (2.4%). *S. aureus* remains the dominant pathogen of SSTI, increasing 10.7% when compared to the SENTRY Program report for 2000 (Table 1).
- There was also a significant increase in ß-haemolytic streptococci which was 1.7% in 2000, rising to 4.9% in 2003. This change may be due to an increase in community-acquired isolates collected by some medical centers.
- *E. coli*, *P. aeruginosa* and enterococci generally decreased (-2.0 to - 4.5%) in occurrence between 2000 and 2003.
- MRSA rates in Europe were documented at 20.7% with a 3.0% multi-drug resistant (MDR; resistant to ≥ five drug classes) rate. The MDR-MRSA were distributed among seven countries: United Kingdom (four), Turkey (three), Israel (two), Italy (two), France (two), Poland (two) and Russia (one). The cited MRSA rate was nearly identical to the latest EARSS report (2004) from 500 hospitals.
- The topical agent mupirocin was not effective (resistance in vitro) against some *S. aureus* (2.7%). CoNS resistance for oxacillin and mupirocin was 63.8 and 7.2%, respectively.
- In a United Kingdom medical center, two MRSA epidemic/endemic clones (riborpint number/PFGE pattern: 200.2/A and 371.2/B) were detected.
- There was only one *E. faecalis* isolate from Greece which was determined to be vancomycin-resistant (1.4% of enterococci).
- ß-haemolytic streptococci had resistance rates of 15.6% for erythromycin and 7.3% for clindamycin; 53.3% exhibited a *mefA* pattern.
- *P. aeruginosa* resistance to ciprofloxacin was 21.3%, ceftazidime was 15.3% and imipenem was 13.0% (Table 2). Five percent of *P. aeruginosa* isolates had a MDR pattern (piperacillin, imipenem, piperacillin/tazobactam, aztreonam, ceftazidime, gentamicin). The MDR strains were from Italy (three), Turkey (two) and Poland (two). Italy also had three *P. aeruginosa* expressing MßL enzymes, two of which were also MDR. One MDR-*P. aeruginosa* clone (272.1/D) was widely disseminated in a Turkish medical center.
- ESBL production in *Klebsiella* spp., *E. coli* and *P. mirabilis* remain significant in Europe (Table 3). Among all *Klebsiella* spp., the phenotypic rate was 23.7%. However, the *K. pneumoniae* ESBL rate was higher (34.0%), of which 90.0% were confirmed ESBL producers. The distribution of confirmed ESBL-positive strains was: Israel (six), Poland (two) and Turkey (one). *E. coli* ESBL phenotypic rates were 11.7% with 71.0% confirmed from five countries: Spain (three), Belgium (two), Turkey (two), Greece (two) and Poland (one). There was one *P. mirabilis* strain screen-positive for ESBL (2.8% of total) from Poland that was not shown to be an ESBL producer. The adjusted ESBL rate based on the disk approximation confirming method remains elevated for *Klebsiella* spp. (20.5%) > *E. coli* (8.4%) in Europe.
- Carbapenem resistance in *Acinetobacter* was: imipenem 12.9%. An *Acinetobacter* isolate from Turkey was positive for MßL-production.

Table 1. Rank order of the 10 most commonly isolated SSTI pathogens from the SENTRY Antimicrobial Surveillance Program (Europe, 2000 and 2003).

	2000		2003	
Pathogen	Rank	No. tested (%)	Rank	No. tested (%)
S. aureus	1	216 (31.0)	1	550 (41.7)
P. aeruginosa	2	97 (13.9)	2	131 (9.9)
E. coli	3	94 (13.5)	3	119 (9.0)
Enterococcus spp.	4	51 (7.3)	4	70 (5.3)
Enterobacter spp.	5	40 (5.7)	5	70 (5.3)
CoNS	7	34 (4.9)	6	69 (5.2)
ß-haemolytic streptococci	10	12 (1.7)	7	65 (4.9)
Klebsiella spp.	6	40 (5.7)	8	44 (3.3)
P. mirabilis	8	23 (3.3)	9	35 (2.7)
Acinetobacter spp.	9	21 (3.0)	10	31 (2.4)
Total		628 (90.1)		1,216 (92.2)

Table 3. ESBL resistance rates among *E. coli*, *Klebsiella* spp. and *P. mirabilis* isolated from SSTI (SENTRY Program, Europe 2003).

Pathogen (no. tested)	Phenotype[a]	% Phenotype confirmed[b]	% of true ESBL producer[c]
E. coli (119)	11.7	71	8.4
Klebsiella spp. (44)	23.7	90	20.5
P. mirabilis (35)	2.9	0	0

a. Percentage based on ceftazidime or ceftriaxone or aztreonam MIC at ≥ 2 µg/ml [NCCLS, 2004].
b. The disk approximation method.
c. Percentage based on confirmed ESBL to total organism tested.

Table 2. Antimicrobial activity of skin and soft tissue pathogens from the SENTRY Program 2003 (Europe).

		% by category	
Organism/antimicrobial agent (no. tested)	$MIC_{50/90}$ (µg/ml)	Susceptible	Resistant
S. aureus (550)			
Ceftriaxone	4/>32	79.3[b]	20.7[b]
Ciprofloxacin	0.25/>4	78.5	20.6
Gentamicin	≤2/8	89.1	8.9
Linezolid	2/2	100.0	-[c]
Mupirocin	≤2/≤2	-	2.7
Oxacillin	0.5/>2	79.3	20.7
Quinupristin/Dalfopristin	0.5/0.5	99.6	0.2
Tetracycline	≤2/>8	88.0	11.3
Trimethoprim/Sulfamethoxazole	≤0.5/≤0.5	96.9	3.1
Vancomycin	1/1	100.0	0.0
P. aeruginosa (131)			
Cefepime	4/>16	83.2	10.7
Ceftazidime	4/>16	79.4	15.3
Ciprofloxacin	0.12/>4	75.6	21.3
Imipenem	1/>8	81.7	13.0
Piperacillin/Tazobactam	8/128	85.5	14.5
Polymyxin B	≤1/≤1	100.0	0.0
Tobramycin	0.5/>16	81.7	18.3
E. coli (119)			
Amoxicillin/Clavulanate	8/16	74.8	8.4
Cefepime	≤0.12/8	92.4	5.1
Ceftazidime	≤1/8	92.4	4.2
Ceftriaxone	≤0.25/8	90.8	8.4
Ciprofloxacin	≤0.03/>4	81.5	18.5
Gentamicin	≤2/8	89.1	8.4
Imipenem	≤0.5/≤0.5	100.0	0.0
Levofloxacin	≤0.03/>4	81.5	16.0
Piperacillin/Tazobactam	2/8	95.0	2.5
Enterococcus spp. (70)			
Ampicillin	2/>16	87.1	12.9
Ciprofloxacin	1/>4	54.3	37.1
Gentamicin (high-level)	≤500/>1000	74.3	25.7
Streptomycin (high-level)	≤1000/>2000	60.0	40.0
Linezolid	2/2	100.0	0.0
Quinupristin/Dalfopristin	>2/>2	14.3	75.7
Teicoplanin	≤2/≤2	98.6	1.4
Tetracycline	>8/>8	32.9	65.7
Vancomycin	1/2	98.6	1.4
Enterobacter spp. (70)			
Amoxicillin/Clavulanate	>16/>16	1.4	97.1
Cefepime	≤0.12/2	98.6	0.0
Ceftazidime	≤1/>16	77.1	18.6
Ceftriaxone	≤0.25/>32	81.4	12.9
Ciprofloxacin	≤0.03/4	88.6	11.4
Gentamicin	≤2/8	88.6	10.0
Imipenem	≤0.5/≤0.5	100.0	0.0
Levofloxacin	0.06/4	88.6	7.1
CoNS (69)			
Ceftriaxone	4/32	36.2[b]	63.8[b]
Ciprofloxacin	0.25/>4	65.2	29.0
Gentamicin	≤2/>8	78.3	14.5
Linezolid	1/1	100.0	-
Mupirocin	≤2/≤2	-	7.2
Oxacillin	1/>2	36.2	63.8
Quinupristin/Dalfopristin	≤0.25/0.5	100.0	0.0
Tetracycline	≤2/>8	69.1	30.9
Trimethoprim/Sulfamethoxazole	≤0.5/>2	82.6	17.4
Vancomycin	1/2	100.0	0.0
ß-haemolytic streptococci (65)			
Ceftriaxone	≤0.25/≤0.25	99.0	1.0
Clindamycin	≤0.06/≤0.06	92.7	7.3
Erythromycin	≤0.06/4	84.4	15.6
Levofloxacin	0.5/1	100.0	0.0
Penicillin	≤0.016/0.03	100.0	-
Tetracycline	4/>8	48.5	49.4
Klebsiella spp. (44)			
Amoxicillin/Clavulanate	2/>16	68.2	11.4
Cefepime	≤0.12/>16	79.5	20.5
Ceftazidime	≤1/>16	81.8	11.4
Ceftriaxone	≤0.25/>32	79.5	20.5
Ciprofloxacin	≤0.03/>4	84.1	15.9
Gentamicin	≤2/>8	79.5	20.5
Imipenem	≤0.5/≤0.5	100.0	0.0
Levofloxacin	0.06/>4	84.1	15.9
Piperacillin/Tazobactam	2/>64	77.3	13.6
Proteus mirabilis (35)			
Amoxicillin/Clavulate	≤1/16	82.9	5.7
Cefepime	≤0.12/0.25	100.0	0.0
Ceftazidime	≤1/≤1	97.1	2.9
Ceftriaxone	≤0.25/≤0.25	97.1	2.9
Ciprofloxacin	≤0.03/2	85.7	8.6
Gentamicin	≤2/>8	85.7	14.3
Imipenem	1/2	97.1	0.0
Levofloxacin	0.06/2	91.4	5.7
Piperacillin/Tazobactam	≤1/>128	77.1	20.0
Acinetobacter spp. (31)			
Ampicillin/Sulbactam	4/>32	64.5	16.0
Cefepime	4/>16	61.3	35.8
Ceftazidime	8/>16	61.3	29.0
Imipenem	≤0.5/>8	80.6	12.9
Levofloxacin	0.25/>4	67.7	29.0
Piperacillin/Tazobactam	4/>256	58.1	38.7
Polymyxin B	≤1/≤1	100.0[a]	0.0[a]
Tobramycin	1/>16	74.2	25.8

a. Susceptibility determined using NCCLS breakpoints, where available [2004]. Susceptible was defined at ≤ 2 µg/ml for polymyxin B, and resistance at the high-level for mupirocin was > 256 µg/ml.
b. Resistance rates based on oxacillin test results.
c. - = no interpretive criteria have been published.

CONCLUSIONS

- Pathogen occurrence rates among various wound infections in Europe remains similar over the past four years. Increases were detected for *S. aureus* (+10.7%) and ß-haemolytic streptococci (+3.2%).
- Although no dramatic increase in MRSA was observed, mupirocin and MDR-*S. aureus* are of greater concern.
- Resistance to carbapenems and the rise of MDR-*P. aeruginosa* pose serious therapeutic problems.
- ESBL producers among the Enterobacteriaceae should be closely monitored, especially in regions of higher occurrence.
- Continued surveillance of cutaneous or wound infections (SSI or SSTI) at regular intervals appears to be a prudent practice to monitor regional antimicrobial resistance and to guide empiric choices of antimicrobial agents.

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