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Changing Patterns of Bacterial Pathogens and Their Antimicrobial Susceptibility Profiles in Patients Hospitalized with Pneumonia: Report from the SENTRY Antimicrobial Surveillance Program, 2002

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AMENDED ABSTRACT

Background: The emergence of resistance (R) among pathogens responsible for community-acquired and nosocomial pneumonia is changing approaches to empiric therapy, with increasing dependence on quinolones and ß-lactamase inhibitor combinations and less on cephalosporins, penicillin-derivatives and aminoglycosides. In this update, the frequency of occurrence of bacterial pathogens responsible for pneumonia and select susceptibilities (S) for 2002 were compared with the baseline 1997 SENTRY Program results in North America (NA).

Methods: 2,742 strains from patients with pneumonia were submitted in 2002 from medical centers in NA, and were analyzed using NCCLS broth microdilution methods and interpretive criteria. Results were compared with 2709 strains similarly collected in 1997.

Results: Rank order of principle pathogens and changes in select S are in the Table:

Species and frequency of occurrence (1997/2002 %)	Antimicrobial agent	MIC$_{50/90}$ in µg/ml (% S) 1997	2002
S. aureus (22.2/27.3)	Oxacillin	0.5/>8(60.6)	1/>8(54.1)
	Gentamicin	0.5/>16(83.2)	<2/<2(92.5)
P. aeruginosa (18.1/20.9)	Ceftazidime	4/>16(71.4)	2/>16(84.1)
	Imipenem	1/8(84.9)	1/8(82.5)
Klebsiella spp. (9.1/9.9)	Ceftriaxone	≤0.25/1(96.4)	≤0.25/32(84.9)[a]
	Gentamicin	0.5/1(95.5)	≤2/>8(82.4)[a]
H. influenzae (10.4/7.3)	Ampicillin	1/>8(58.9)	≤2/16(84.0)
	Amox/Clav	0.5/2(98.6)	≤2/≤2(100.0)
Enterobacter spp. (7.5/5.5)	Ceftazidime	0.5/>16(69.6)	≤1/>16(79.6)
	Gentamicin	1/4(90.2)	≤2/≤2(96.1)
S. pneumoniae (7.7/5.5)	Penicillin	0.06/1(58.0)	≤0.016/2(69.7)
	Erythromycin	≤0.25/2(83.6)	≤0.06/8(76.3)

a. Epidemic clone related to a single site.

S decreased for *Klebsiella* spp. whereas *Enterobacter* spp. and *H. influenzae* showed increased S. Other frequently isolated pathogens (*S. aureus*, *P. aeruginosa*, *S. pneumoniae*) contained elements of both.

Conclusions: Ongoing surveillance programs have established the baseline for longitudinal comparisons of emerging pathogens and changing susceptibility profiles. Modified demographics of patient populations and antimicrobial usage may be altering antibiograms that, in some cases, result in the re-establishment of more S strains.

INTRODUCTION

Pneumonia has a profound impact on the health care system, with community-acquired pneumonia accounting for approximately 10 million office visits each year in the USA. Hospital-acquired pneumonias, while being the second most common type of nosocomial infection, have the highest morbidity and mortality. The widespread usage of antimicrobial agents for all indications, coupled with the increasing medical complexity of hospitalized patients, are two factors that have contributed to the emergence of bacterial pathogens resistant to contemporary antimicrobial agents over the past two decades.

These changes in susceptibility profiles of the more common bacterial agents of pneumonia are challenging the usual approaches to empiric therapy, with increasing dependence on fluoroquinolones and ß-lactamase inhibitor combinations, and less on cephalosporins, penicillin derivatives, and aminoglycosides. While many studies have documented increases in resistance among the commonly occurring bacterial pathogens producing pneumonia, others are demonstrating the plateauing, and in some cases reduction in, resistance profiles to commonly used antimicrobial agents. These variations may reflect changes in prescribing practices, hospital infection control efforts and the use of targeted educational programs among other factors.

In this study, the frequency of occurrence of bacterial pathogens responsible for pneumonia and their current (2002) susceptibility profiles are presented and compared with the baseline 1997 SENTRY Antimicrobial Surveillance Program results for North America.

MATERIALS AND METHODS

Specimen collection. A total of 2,742 bacterial strains submitted from 34 medical centers in North America (2002) were included in the study and were recovered consecutively from patients hospitalized with pneumonia, including those with community-acquired and nosocomial infections. Isolates were determined to be clinically significant based upon participant criteria with only one isolate permitted from each patient. Bacterial identifications were performed by the submitting laboratory and confirmed by the monitoring facility (The JONES Group/JMI Laboratories, North Liberty, IA).

Susceptibility testing. All strains were tested for susceptibility to a battery of more than 25 antimicrobial agents according to the NCCLS (2003) reference broth microdilution method using Mueller-Hinton broth (with the addition of 2 - 5% lysed horse blood for testing of streptococci) and Haemophilus Test Medium for testing of *H. influenzae*. Agents tested represented the most common classes and examples of drugs used in the empiric or directed treatment of pneumonia. Interpretation of quantitative MIC results was in accordance with current NCCLS criteria (2003). Quality control strains utilized included *Staphylococcus aureus* ATCC 29213, *Streptococcus pneumoniae* ATCC 49619, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922, and *Haemophilus influenzae* ATCC 49247 among others.

RESULTS

- While the top 10 bacterial pathogens associated with pneumonia in North America have not changed from 1997 to 2002, the prevalence and rank order has, reflecting an increase in opportunistic pathogens more commonly associated with seriously debilitated patients (*S. aureus*, *P. aeruginosa*, *S. marcescens*) and a decrease in infections caused by *H. influenzae* and *S. pneumoniae* (Table 1).
- *S. aureus* demonstrated a decrease in susceptibility to oxacillin (60.6 to 54.1%) and ciprofloxacin (59.5 to 48.9%) during this period, but a marked increase in susceptibility to gentamicin (83.2 to 92.5%) and erythromycin (29.4 to 40.8%; Table 2).
- Changes to the antibiogram of *P. aeruginosa* were also apparent with stable or decreased susceptibility rates to carbapenems and ciprofloxacin, and increased susceptibility rates to ceftazidime, cefepime, aztreonam, gentamicin and amikacin.
- By inference of phenotypic testing results for ampicillin and amoxicillin/clavulanate with *H. influenzae*, both ß-lactamase-producing strains and ß-lactamase-negative, ampicillin-resistant (BLNAR) strains have modestly decreased in prevalence from 1997 to 2002 (Table 2) in the population of hospitalized patients with pneumonia.
- *Klebsiella* spp. were found to be uniformly more resistant in 2002 to the commonly prescribed antimicrobial classes (ß-lactam/inhibitor combinations, third-generation cephalosporins, monobactams, aminoglycosides, fluoroquinolones) than they were in 1997. Increases in susceptibility rates were not noted for any agent.
- *S. pneumoniae* isolates displayed increased susceptibility to penicillin (58.0 to 69.7%; most change in 2002) during this time, whereas, decreased susceptibilities were detected for erythromycin (83.6 to 76.3%) and clindamycin (92.4 to 90.1%).
- Susceptibility rates increased among *Enterobacter* spp. when tested against piperacillin/tazobactam, third- and fourth-generation cephalosporins, aztreonam and gentamicin, and remained unchanged for other agents tested (Table 2).

RESULTS

Table 1. Frequency of occurrence of bacterial pathogens associated with patients hospitalized with pneumonia in North America for 1997 (2,709 strains) compared with 2002 (2,742 strains; SENTRY AntimicrobialSurveillance Program).

Organism	Rank (no.; % of isolates) 1997	2002
S. aureus	1 (602; 22.2)	1 (748; 27.3)
P. aeruginosa	2 (490; 18.1)	2 (572; 20.9)
H. influenzae	3 (282; 10.4)	4 (200; 7.3)
Klebsiella spp.	4 (247; 9.1)	3 (272; 9.9)
S. pneumoniae	5 (207; 7.6)	5 (152; 5.5)
Enterobacter spp.	6 (204; 7.5)	6 (152; 5.5)
E. coli	7 (128; 4.7)	9 (97; 3.5)
S. maltophilia	8 (102; 3.8)	8 (101; 3.6)
M. catarrhalis	9 (86; 3.2)	10 (97; 3.5)
S. marcescens	10 (69; 2.6)	7 (118; 4.3)
Others	(292; 10.8)	(233; 8.5)

Table 2. Comparison of activity of antimicrobial agents tested against the six most prevalent causes of pneumonia in hospitalized patients in North America for the years 1997 and 2002 (SENTRY Antimicrobial Surveillance Program).

Organism/Antimicrobial agent (no. tested 1997/2002)	MIC$_{50/90}$ in µg/ml (% susceptible) 1997	2002
S. aureus (602/748)		
Penicillin	32/>32 (7.6)	16/>32 (9.1)
Oxacillin	0.5/>8 (60.6)	1/>8 (54.1)
Gentamicin	0.5/>16 (83.2)	≤2/≤2 (92.5)
Ciprofloxacin	0.5/>2 (59.5)	4/>4 (48.9)
Erythromycin	1/>8 (29.4)	>8/>8 (40.8)
Clindamycin	0.25/>8 (61.8)	0.12/>8 (58.4)
Rifampin	≤0.016/≤0.016 (96.0)	≤0.25/≤0.25 (97.7)
Trimethoprim/Sulfamethoxazole	≤0.5/>1 (85.7)	≤0.5/≤0.5 (96.0)
Vancomycin	1/1 (100.0)	1/1 (100.0)
P. aeruginosa (490/572)		
Piperacillin/Tazobactam	8/>64 (87.3)	8/>64 (87.6)
Ceftriaxone	>32/>32 (18.0)	>32/>32 (14.7)
Ceftazidime	4/>16 (71.4)	2/>16 (84.1)
Cefepime	8/>16 (67.8)	4/16 (82.0)
Aztreonam	8/>16 (59.8)	8/>16 (66.6)
Imipenem	1/8 (84.9)	1/8 (82.5)
Meropenem	0.5/8 (88.6)	0.5/8 (86.5)
Gentamicin	4/>16 (69.8)	≤2/>8 (83.7)
Amikacin	4/16 (91.0)	4/16 (95.1)
Ciprofloxacin	0.25/>2 (75.3)	0.5/>4 (67.3)
H. influenzae (282/200)		
Ampicillin	1/>8 (58.9)	≤2/16 (84.0)
Amoxicillin/Clavulanate	0.5/2 (98.6)	≤2/≤2 (100.0)
Ceftriaxone	0.016/0.06 (100.0)	≤0.25/≤0.25 (100.0)
Ciprofloxacin	≤0.016/≤0.016 (100.0)	≤0.03/≤0.03 (100.0)
Trimethoprim/Sulfamethoxazole	≤0.25/8 (75.9)	≤0.5/>2 (75.5)
Klebsiella spp. (247/272)		
Amoxicillin/Clavulanate	4/16 (85.8)	≤2/16 (82.3)
Ceftriaxone	≤0.25/1 (96.4)	≤0.25/32 (84.9)
Ceftazidime	0.25/1 (94.3)	≤1/>16 (82.7)
Cefepime	≤0.12/1 (98.8)	≤0.12/4 (98.2)
Aztreonam	≤0.12/4 (92.3)	≤0.12/>16 (81.3)
Imipenem	0.5/1 (100.0)	0.12/0.25 (99.6)

Table 2. Continued.

Organism/Antimicrobial agent (no. tested 1997/2002)	MIC$_{50/90}$ in µg/ml (% susceptible) 1997	2002
Klebsiella spp. (247/272) (Continued)		
Meropenem	≤0.06/0.12 (100.0)	≤0.06/≤0.06 (100.0)
Gentamicin	0.5/1 (95.5)	≤2/>8 (82.4)
Ciprofloxacin	0.06/0.5 (93.1)	≤0.03/1 (91.2)
Trimethoprim/Sulfamethoxazole	≤0.5/1 (90.7)	≤0.5/>2 (77.9)
S. pneumoniae (207/152)		
Penicillin	0.06/1 (58.0)	≤0.016/2 (69.7)
Cefotaxime	0.03/0.5 (97.6)	≤0.25/1 (95.4)
Levofloxacin	1/2 (99.5)	1/1 (99.3)
Erythromycin	≤0.25/2 (83.6)	≤0.06/8 (76.3)
Clindamycin	≤0.06/0.12 (94.2)	≤0.06/≤0.06 (90.1)
Vancomycin	0.25/0.5 (100.0)	0.5/0.5 (100.0)
Trimethoprim/Sulfamethoxazole	≤0.25/4 (77.3)	≤0.5/>2 (73.7)
Enterobacter spp. (204/152)		
Piperacillin/Tazobactam	4/>64 (72.1)	2/64 (81.6)
Ceftriaxone	≤0.25/>32 (77.0)	≤0.25/32 (84.2)
Ceftazidime	0.5/>16 (69.6)	≤1/>16 (79.6)
Cefepime	0.25/4 (98.0)	≤0.12/1 (99.3)
Aztreonam	≤0.12/>16 (72.1)	≤0.12/>16 (82.2)
Imipenem	1/2 (100.0)	0.5/1 (100.0)
Meropenem	≤0.06/0.12 (100.0)	≤0.06/0.12 (100.0)
Gentamicin	1/4 (90.2)	≤2/≤2 (96.1)
Amikacin	2/4 (99.5)	2/4 (97.4)
Ciprofloxacin	≤0.016/0.5 (92.6)	≤0.03/0.25 (92.8)
Trimethoprim/Sulfamethoxazole	≤0.5/>1 (87.3)	≤0.5/1 (94.7)

CONCLUSIONS

- A variety of factors have contributed to emerging resistances, including antimicrobial usage patterns, quality of hospital infection control programs, and the level of governmental commitment to public health infrastructure.
- Recent focused attention and proactive interventions to these problems, particularly in the hospital setting, may be having some positive effects with the stabilization of antibiograms in some areas and, in others, the reversal of emerging resistance (example: SENTRY Program medical centers).
- Global surveillance programs, including the SENTRY Program, provide critical data in helping identify those geographic regions with emerging antimicrobial resistance concerns, and in identifying the most active, often empiric, antimicrobial agents for the particular pathogens. This information is critical in the development of sound prescribing practices and in identifying appropriate targets for infection control and public health policy efforts.

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