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National and regional susceptibility of gram-negative organisms to extended-spectrum cephalosporin and fluoroquinolone antibiotics: results of the Antimicrobial Resistance Management (ARM) program

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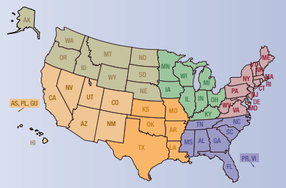
What is the Antimicrobial Resistance Management (ARM) Program?

Purpose

- The Antimicrobial Resistance Management (ARM) Program is an ongoing study to document trends in antimicrobial susceptibility patterns in inpatient and outpatient isolates and to identify relationships between antibiotic use and resistance rates
- Hospitals can delineate if and when antimicrobial resistance occurs
  - Allows strategic intervention
  - Provides data for local, regional, national benchmarks
  - Has potential to reduce costs of antibiotics associated with inappropriate use
- A total of 115 hospitals have enrolled to date
  - 85 (74%) nonteaching
  - 30 (26%) teaching
- For the purposes of comparison, US hospitals are grouped in 6 geographic regions (see map, below)
- The number of hospitals included from each region is as follows:



- North Central: 18 (16%)
- Northeast: 27 (22%)
- South Central: 9 (8%)
- Southeast: 56 (49%)
- Southwest: 5 (4%)

Data Collection

- Each hospital provides a minimum of 3 years of antibiogram or sensitivity report data
- Individual antibiotics and organisms are captured in the database
  - 46 antibiotics
  - 19 organisms
- A Web-based analysis tool allows comparisons between antibiotic use and resistance rates for any number of parameters
  - One year with another year
  - Groups of years to other groups of years
  - Hospital to hospital
  - Hospital to hospital system
  - Hospital to state
  - Within a state
  - Hospital to region
  - Hospital to national
  - State to state
  - State to region
  - State to national
  - Region to national

Abstract

OBJECTIVES: The ongoing ARM program was developed to document susceptibility patterns, including for gram-negative organisms, in both inpatient and outpatient isolates. Since 1987, more than 10 million isolates have been collected on 19 organisms and 46 antibiotics from 103 US hospitals in the Northeast, North Central, Southeast, South Central, and Southwest.

METHODS: Antibiograms and sensitivity reports of isolates for *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Serratia marcescens* were reviewed for susceptibility to extended-spectrum cephalosporin (cefuroxime, cefoxitin, cefotetan, cefotaxime, ceftazidime, ceftriaxone, and cefepime) and fluoroquinolone (ciprofloxacin, levofloxacin, ofloxacin, and trovafloxacin) antibiotics.

RESULTS: Total number of isolates and percentage of isolates susceptible to the antibiotics were determined for each organism. Nationally, *E coli* isolates had greater susceptibility to ceftriaxone (n=318,802) than fluoroquinolones (n=571,551). This was also seen for *K pneumoniae*, except in Southwest, where isolate susceptibility to ciprofloxacin (98.5%) differed from ceftriaxone (98.0%). Isolate susceptibility of ciprofloxacin and levofloxacin to *P mirabilis* was suppressed, specifically for ciprofloxacin in South Central (70.6%); cross-resistance is suggested by similar increases and decreases in susceptibility to these agents within regions. Isolate susceptibility differed nationally between ceftriaxone (99.4%, n=58,422) and ceftazidime (96.5%, n=29,344); especially in the Northeast (98.9% vs 86.8%). For *P aeruginosa*, national susceptibility to ciprofloxacin (73.6%, n=141,034) and levofloxacin (67.3%, n=41,673) was similar, except in Southwest, where levofloxacin was more susceptible (64.3% vs 77.0%); nationally, greater susceptibility was seen for ceftazidime (88.1%; n=159,066) vs cefepime (78.4%, n=10,052), a difference present within each region. For *S marcescens*, 94.4% of isolates nationally were susceptible to ceftriaxone (n=16,960), compared with 87.6% to ceftazidime (n=9799), also seen in North Central (94.8% vs 89.2%) and Southeast (93.7% vs 85.0%); a difference was noted between ceftriaxone and cefotaxime in Northeast (97.3% vs 92.3%) and North Central (94.8% vs 90.6%).

CONCLUSIONS: A greater percentage of gram-negative organisms remain susceptible to extended-spectrum cephalosporin than to fluoroquinolone antibiotics, a difference validated nationally and regionally within the US.

Objectives

- Extended-spectrum beta-lactamase (ESBL)-producing organisms can mediate resistance to broad-spectrum beta-lactams, resulting in an infection control problem
- Species in which ESBLs are most common are *K pneumoniae*, *E coli*, and other gram-negative aerobes
- Recent evidence suggests increasing frequency of an association between fluoroquinolone resistance and ESBL production, greatly limiting the role of this class of antibiotic against ESBL producers[1]

Methods

- Antibiograms and sensitivity reports of isolates for *E coli*, *K pneumoniae*, *P mirabilis*, *P aeruginosa*, and *S marcescens* in the ARM program database were reviewed for susceptibility to extended-spectrum cephalosporin and fluoroquinolone antibiotics.

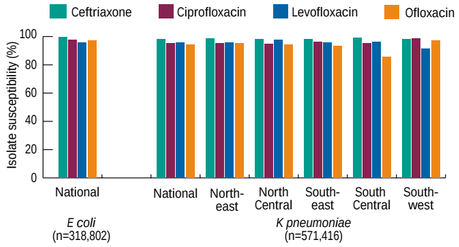
Results

- Total number of isolates and percentage of isolates susceptible to the antibiotics were determined for each organism

E COLI AND *K PNEUMONIAE*

- Nationally, *E coli* isolates had greater susceptibility to ceftriaxone than to fluoroquinolones (Figure 1)
- This trend was also seen for *K pneumoniae*, except in Southwest, where isolate susceptibility to ciprofloxacin was slightly greater than to ceftriaxone (Figure 1)

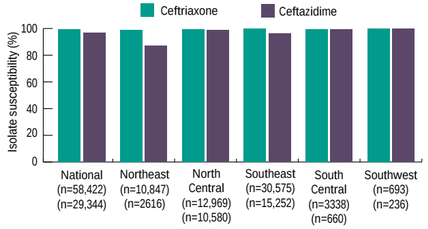
***Figure 1. Susceptibility trends for* E coli *and* K pneumoniae**



P MIRABILIS

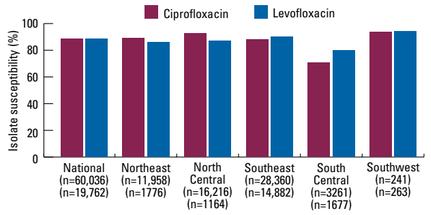
- *P mirabilis* isolate susceptibility differed nationally between ceftriaxone and ceftazidime, especially in the Northeast (Figure 2)

Figure 2.* P mirabilis *susceptibility to ceftriaxone and ceftazidime



- Nationally, *P mirabilis* isolate susceptibility to ciprofloxacin and levofloxacin was suppressed, specifically for ciprofloxacin in South Central; cross-resistance is suggested by similar increases and decreases in susceptibility to these agents within regions (Figure 3)

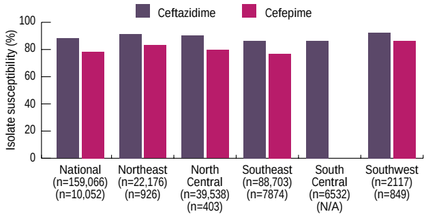
Figure 3.* P mirabilis *susceptibility to ciprofloxacin and levofloxacin



P AERUGINOSA

- Nationally, greater susceptibility was seen for ceftazidime vs cefepime to *P aeruginosa*, a difference present within each region (Figure 4)

Figure 4.* P aeruginosa *susceptibility to ceftazidime and cefepime

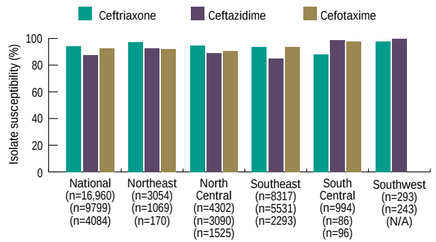


- For *P aeruginosa*, national susceptibility to ciprofloxacin (73.6%, n=141,034) and levofloxacin (67.3%, n=41,673) was similar, except in Southwest, where levofloxacin was more susceptible (64.3% vs 77.0%)

S MARCESCENS

- For *S marcescens*, 94.4% of isolates nationally were susceptible to ceftriaxone, compared with 87.6% to ceftazidime, also seen in the North Central and Southeast regions
- A difference was noted between ceftriaxone and cefotaxime in the Northeast and North Central regions (Figure 5)

Figure 5.* S marcescens *susceptibility to ceftriaxone, ceftazidime, and cefotaxime



Conclusions

- Within the USA, a greater percentage of gram-negative organisms remain susceptible to extended-spectrum cephalosporin than to fluoroquinolone antibiotics
- This difference is validated nationally and regionally
- These data suggest cephalosporin susceptibility has remained stable over time, whereas a role for fluoroquinolones in the treatment of gram-negative infections may increasingly be limited

References

1. Paterson DL. Recommendation for treatment of severe infections caused by Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBLs). *Clin Microbiol Infect.* 2000;6:460-463.

Acknowledgments

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