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Similarities and differences of Escherichia coli *and* Klebsiella pneumoniae *susceptibility to cephalosporins and fluoroquinolones from 1987-2001: results of the Antimicrobial Resistance Management (ARM) program*

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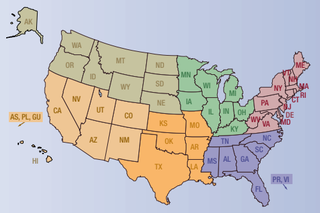
What is the Antimicrobial Resistance Management (ARM) Program?

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

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
  - 42 antibiotics
  - 16 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

PURPOSE: Using data from the ARM program, this study examined national and regional susceptibility rates of *E coli* and *K pneumoniae* to cephalosporin and fluoroquinolone antibiotics.

METHODS: Since 1987, more than 10 million US inpatient and outpatient isolates have been collected from 101 hospitals in 5 regions (Northeast, North Central, Southeast, South Central, Southwest). Antibiograms and sensitivity reports of isolates for *E coli* and *K pneumoniae* were reviewed for susceptibility to cephalosporins (cefazolin, cephalothin, cefuroxime, cefoxitin, cefotetan, cefotaxime, ceftazidime, ceftriaxone, cefepime) and fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin, trovafloxacin).

RESULTS: Nationally, *E coli* susceptibility to first-generation cephalosporins (n=402,596) ranged from 70.2% to 92.2%; second generation (n=368,877), 95.3% to 99.6%; third generation (n=568,828), 97.3% to 99.4%; cefepime (n=33,184) was 99.1%. Fluoroquinolone susceptibility ranged from 95.4% to 97.8%; n=562,693. *E coli* susceptibility was 99.4% to third-generation ceftriaxone and 95.4% for levofloxacin, a difference seen largely in Northeast (99.1%, ceftriaxone; 92.7%, levofloxacin). Nationally, *K pneumoniae* susceptibility to third-generation cephalosporins ranged from 94.1% for ceftazidime (n=46,899) to 98.2% for ceftriaxone (n=99,345); a range seen in every region except Northeast. *K pneumoniae* susceptibility to first-generation cefazolin (n=116,035) and second-generation cefuroxime (n=58,081) was equal (92.5%), an anomaly attributed to North Central differences (90.7%, cefazolin; 88.9%, cefuroxime). In Southwest, differences were seen between ciprofloxacin (91.1%) and ceftriaxone (98.7%) for *E coli* and between levofloxacin (91.6%) and ceftriaxone (98.0%) for *K pneumoniae*.

CONCLUSION: National and regional differences in *E coli* and *K pneumoniae* susceptibility were detected to cephalosporin and fluoroquinolone antibiotics; these differences were associated with an anticipated class/subclass effect.

PURPOSE

- Extended-spectrum beta-lactamase (ESBL)-producing organisms can mediate resistance to broad-spectrum beta-lactams, causing infectious outbreaks
- The two species in which ESBLs are most common are *E coli* and *K pneumoniae*
- 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]
- Using data from the ARM program, national and regional susceptibility rates of *E coli* and *K pneumoniae* to cephalosporin and fluoroquinolone antibiotics were examined

METHODS

- Antibiograms and sensitivity reports of *E coli* and *K pneumoniae* isolates were reviewed for susceptibility to:

Cephalosporins

First generation	*Second generation*	*Third generation*	*Fourth generation*
Cefazolin	Cefoxitin	Cefotaxime	Cefepime
Cephalothin	Cefotetan	Ceftazidime	
	Cefuroxime	Ceftriaxone	

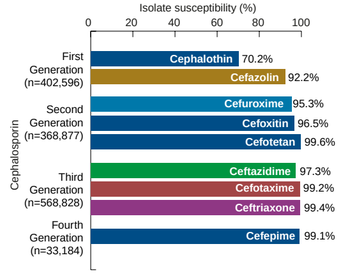
Fluoroquinolones

Ciprofloxacin	Ofloxacin
Levofloxacin	Trovafloxacin

RESULTS

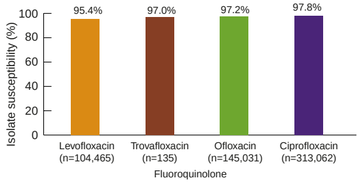
- Nationally, *E coli* susceptibility to first-generation cephalosporins ranged from 70.2% to 92.2%; second generation, 95.3% to 99.6%; third generation 97.3% to 99.4%; fourth-generation cefepime was 99.1% (Figure 1)

Figure 1.* E coli *susceptibility to cephalosporins (n=1,373,485)



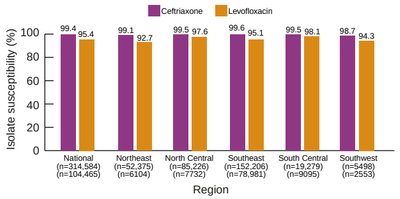
- Fluoroquinolone susceptibility ranged from 95.4% to 97.8% (Figure 2)

Figure 2.* E coli *susceptibility to fluoroquinolones (n=562,693)



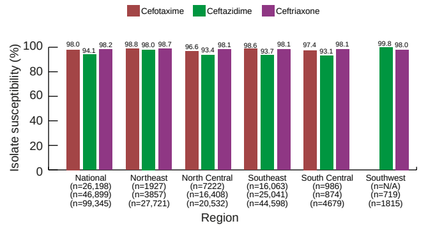
- Nationally, *E coli* susceptibility was 99.4% to third-generation ceftriaxone and 95.4% for levofloxacin, a difference seen largely in Northeast (Figure 3)

Figure 3.* E coli *susceptibility to ceftriaxone and levofloxacin



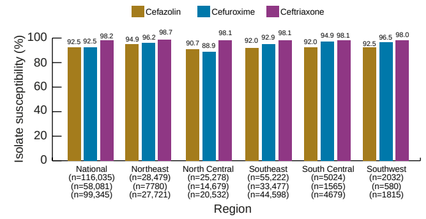
- Nationally, *K pneumoniae* susceptibility to third-generation cephalosporins ranged from 94.1% for ceftazidime to 98.2% for ceftriaxone, a range seen in every region except Northeast

Figure 4.* K pneumoniae *susceptibility to third-generation cephalosporins



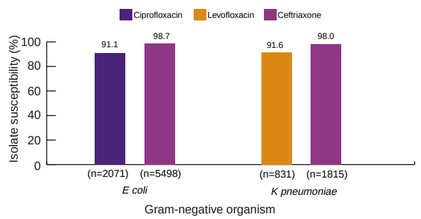
- *K pneumoniae* susceptibility to first-generation cefazolin and second-generation cefuroxime was equal, an anomaly attributed to North Central differences (Figure 5)

Figure 5.* K pneumoniae *susceptibility to first-, second-, and third-generation cephalosporins



- In Southwest, differences were seen between ciprofloxacin and ceftriaxone for *E coli* and between levofloxacin and ceftriaxone for *K pneumoniae* (Figure 6)

Figure 6. Differences between fluoroquinolone and ceftriaxone susceptibility in the Southwest



CONCLUSION

- National and regional differences in *E coli* and *K pneumoniae* susceptibility were detected to cephalosporin and fluoroquinolone antibiotics and were associated with an anticipated class/subclass effect
  - *E coli* and *K pneumoniae* susceptibility to third-generation cephalosporins remains high, suggesting no evidence of ESBL activity
  - In the North Central region, *K pneumoniae* susceptibility to first-generation cefazolin was greater than to second-generation cefuroxime
  - An association between fluoroquinolone resistance and ESBL production appears to exist
- 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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