286

Update on Resistance Among Respiratory Tract Infection Pathogens: Results of the Antimicrobial Resistance Management (ARM) Program

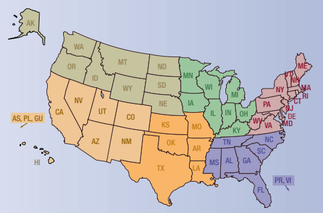
John G. Gums, PharmD, University of Florida, Gainesville, FL

John G. Gums, PharmD
625 SW Fourth Avenue
University of Florida, Gainesville, FL 32601 USA
Tel: +1.352-392-4541 Fax: +1.352-392-7766
E-mail: gums@chfm.ufl.edu

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 274 institutions have enrolled as of September 19, 2003
  - 220 (80.3%) nonteaching
  - 54 (19.7%) 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: 50 (18.3%)
  - Northeast: 71 (25.9%)
  - Northwest: 7 (2.5%)
  - South Central: 51 (18.6%)
  - Southeast: 80 (29.2%)
  - Southwest: 15 (5.5%)

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
  - 44 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: Streptococcus pneumoniae *and* Haemophilus influenzae *are the primary bacterial etiologic pathogens identified in respiratory tract infections, with* S pneumoniae *causing the greatest morbidity and mortality, especially among the elderly, and having the most significant resistance profile. The ongoing ARM program documents resistance patterns in US inpatient and outpatient isolates and includes data from 251 US institutions on more than 17 million isolates.*

METHODS: Antibiograms and sensitivity reports of S pneumoniae isolates collected in the ARM database from 1995-2002 were reviewed for resistance to penicillin, erythromycin, clindamycin, cefotaxime, and ceftriaxone; H influenzae *isolates were reviewed for resistance to cefotaxime and ceftriaxone. Comparisons were conducted using a Web-based analysis tool.*

RESULTS: Nationally, S pneumoniae *resistance to penicillin was 37.4% (n=37,688); to erythromycin, 29.6% (n=18,774); and to clindamycin, 9.9% (n=5510). Resistance to cefotaxime was 25.5% (n=10,527) and to ceftriaxone, 16.8% (n=26,594).* S pneumoniae *isolates in North Central and Northeast remained more susceptible to penicillin and erythromycin than in South Central and Southeast. Across all regions,* S pneumoniae *was more resistant to cefotaxime than to ceftriaxone, with the difference greatest in the Southeast and least in North Central. For* H influenzae*, resistance to cefotaxime was 4.3% (n=4927) and to ceftriaxone, 1.0% (n=10,353), a difference seen largely in the Northeast.*

CONCLUSIONS: Resistance rates from the ARM program showed pneumococcal and H influenzae *isolates to be more susceptible to ceftriaxone and cefotaxime, suggesting these third-generation cephalosporins may not be therapeutically equivalent. This disparity is believed to be due to clonal variations. In addition, data through 2001 do not reflect the new NCCLS breakpoints, artificially suppressing sensitivity numbers.*

CLINICAL IMPLICATIONS: Within each antibiotic class, agents vary significantly with respect to susceptibility to S pneumoniae*; use of the more active agent (ie, ceftriaxone) may delay emergence of resistance.*

BACKGROUND AND RATIONALE

- The elderly comprise the majority of the 1.7 million annual US hospitalizations for community-acquired pneumonia (CAP), with costs estimated at $23 billion[1,2]
- Treating patients with CAP requires ongoing surveillance of drug susceptibility patterns to determine the most effective agent
- *S pneumoniae* and *H influenzae* are the primary bacterial etiologic pathogens identified in respiratory tract infections
- Respiratory isolates of *S pneumoniae* and *H influenzae* have shown increasing resistance to a number of antimicrobial agents
- For the empiric treatment of adults with CAP, cefotaxime and ceftriaxone have historically been regarded as therapeutically equivalent; however, given the reduced susceptibility of pneumococcal isolates to cefotaxime when compared with ceftriaxone previously reported,[3] we investigated resistance rates between these two third-generation cephalosporins among *S pneumoniae* and *H influenzae* isolates in the ARM database

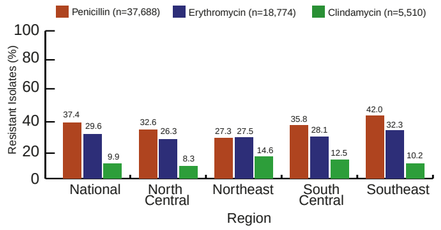
METHODS

- Using a Web-based analysis tool, antibiograms and sensitivity reports of *S pneumoniae* and *H influenzae* isolates in the ARM database were compared for the years 1995-2002
  - Pneumococcal isolates were reviewed for resistance to penicillin, erythromycin, clindamycin, cefotaxime, and ceftriaxone
  - *H influenzae* isolates were reviewed for resistance to cefotaxime and ceftriaxone

RESULTS

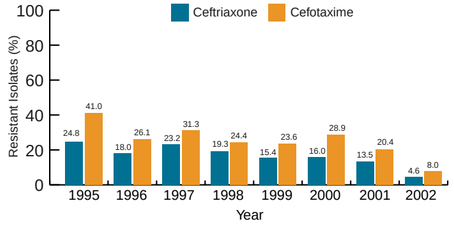
- Nationally, pneumococcal isolates were more susceptible to clindamycin than to penicillin or erythromycin (Figure 1)
- Pneumococcal isolates were more resistant to penicillin and erythromycin in the South Central and Southeast regions than in the North Central and Northeast regions (Figure 1)

Figure 1. National and regional S pneumoniae isolate resistance to penicillin, erythromycin, and clindamycin, 1995-2002



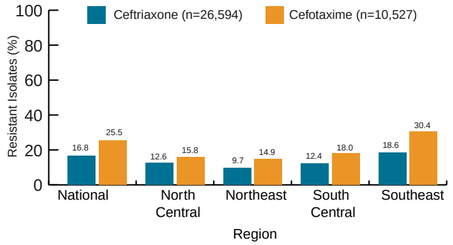
- Nationally, pneumococcal isolates were more resistant to cefotaxime than to ceftriaxone for each year from 1995-2002 (Figure 2)
- Data through 2001 do not reflect the new NCCLS breakpoints, artificially suppressing sensitivity numbers for the two agents

Figure 2. National S pneumoniae isolate resistance to ceftriaxone and cefotaxime, by year, 1995-2002



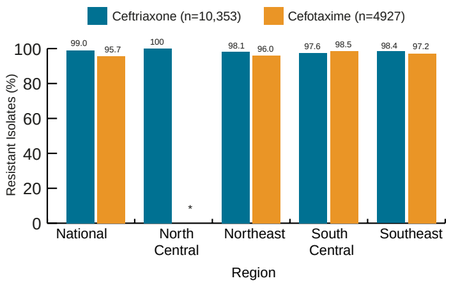
- Nationally and regionally, *S pneumoniae* isolates were more resistant to cefotaxime than to ceftriaxone, with the greatest difference between the two agents seen in the Southeast region and the least difference observed in the North Central region (Figure 3)

Figure 3. National and regional S pneumoniae isolate resistance to ceftriaxone and cefotaxime, 1994-2002



- *H influenzae* isolates were more resistant to cefotaxime than to ceftriaxone, a difference seen largely in the Northeast (Figure 4)

Figure 4. National and regional H influenzae isolate susceptibility to ceftriaxone and cefotaxime, 1995-2002



*Data not available

CONCLUSIONS

- Data from the ARM program show that nationally and regionally, *S pneumoniae* and *H influenzae* isolates are more resistant to cefotaxime than to ceftriaxone, suggesting these third-generation cephalosporins may not be therapeutically equivalent
- Sensitivity numbers for cefotaxime and ceftriaxone are artificially suppressed for 1995-2001, given that these isolates reflect breakpoints prior to January 2002, when NCCLS adopted an MIC ≥ 4 mg/mL for these two agents
- The clinical significance of the difference in resistance rates observed between cefotaxime and ceftriaxone is currently under investigation; the disparity is believed to be due to clonal variation
- Use of ceftriaxone for CAP may delay emergence of *S pneumoniae* resistance

REFERENCES

1. Sue DY. Community-acquired pneumonia in adults. *West J Med.* 1994;161:383-389.
2. Bartlett JG, Mundy M. Community-acquired pneumonia. *N Engl J Med.* 1995;333:1618-1624.
3. Gums JG. *Streptococcus pneumoniae* susceptibility to cefotaxime and ceftriaxone, 1994-2001: results of the Antimicrobial Resistance Management (ARM) program. Poster presented at the 2003 American Thoracic Society 99th International Conference, Seattle, WA, USA, May 19, 2003.

ACKNOWLEDGMENTS

The author would like to thank the participating institutions in R-BUG Database-USA, which make data collection possible, and Roche Laboratories, Inc., which financially supported the study.

Presented at CHEST 2003, the 69th annual international scientific assembly of the American College of Chest Physicians, Orlando, FL, USA, October 27-29, 2003.