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Increased *E faecium* Resistance to Vancomycin Correlates with Declining Susceptibility to Antianaerobic Antibiotics Among Gram-Negative Organisms: Results of the Antimicrobial Resistance Management (ARM) Program

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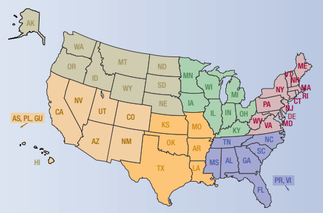
What is the Antimicrobial Resistance Management (ARM) Program?

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 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

BACKGROUND: A limited number of antibiotics have activity against vancomycin-resistant enterococci (VRE); in particular, vancomycin-resistant E faecium *(VREF). Treatment with antianaerobic antibiotic regimens such as piperacillin-tazobactam (PIP-TAZ) has been found to promote high-density colonization in patients with VRE in stool. The ARM program surveillance database was interrogated to determine whether there was a trend in* E faecium *isolate resistance to vancomycin and if a similar resistance trend existed among gram-negative organisms to PIP-TAZ and piperacillin (PIP).*

METHODS: The ARM program has collected data on more than 17 million inpatient/outpatient isolates representing 16 organisms and 44 antibiotics from 251 US hospital laboratories. Antibiograms and sensitivity reports from 1995-2002 for E faecium *isolates were reviewed for susceptibility to vancomycin.* Proteus mirabilis, Pseudomonas aeruginosa, *and* Serratia marcescens *isolates were reviewed for susceptibility to PIP-TAZ and PIP.*

RESULTS: From 1995-2002, E faecium *susceptibility to vancomycin (n=19,081) has decreased from 72.5% to 32.6%. Percentage of* P mirabilis, P aeruginosa, *and* S marcescens *isolates susceptible to PIP-TAZ and PIP have also decreased.* P mirabilis *susceptibility to PIP-TAZ (n=25,388) decreased from 100% to 99.3% and to PIP (n=72,495) from 95.4% to 89.2%. For* P aeruginosa, *susceptibility to PIP-TAZ (n=60,297) declined from 92.9% to 90.6% and to PIP (n=170,069) from 93.5% to 87.0%. For* S marcescens, *susceptibility to PIP-TAZ (n=7200) decreased from 95.9% to 82.8% and to PIP (n=20,946) from 90.7% to 86.0%.*

CONCLUSION: These data show that between 1995 and 2002, E faecium *isolates were increasingly resistant to vancomycin. A similar, albeit smaller, resistance trend was observed for the gram-negative isolates to the antianaerobic antibiotics PIP-TAZ and PIP; this correlation suggests use of these antibiotics may be one of the possible causes of an increase in VREF reported in institutions.*

BACKGROUND

- The Infectious Diseases Society of America, among other organizations, is working to call attention to the impending crisis with respect to the decline in availability of antimicrobials, including resistance to existing agents[1]
- Vancomycin-resistant enterococci (VRE) were first detected in France in 1986, with emergence observed in the United States in 1989; since then, VRE has become endemic at many US health care facilities[2]
- Few antibiotics are active against VRE; in particular, vancomycin-resistant *E faecium* (VREF)
- In a study of health care facilities in the Siouxland region of Iowa, Nebraska, and South Dakota, where VRE rapidly emerged in 1997, all isolates were VREF, with vancomycin MICs of at least 256 μg/mL[2]; risk factors for colonization with VRE were found to be use of antimicrobial agents and prior exposure to acute care facilities
- Treatment with antianaerobic antibiotic regimens such as piperacillin-tazobactam (PIP-TAZ), use of which has increased nationally, has been found to promote high-density colonization in patients with VRE in stool[3]; similarly, clindamycin use has been significantly correlated with VRE prevalence, suggesting restriction of antianaerobic agents may play an important role in future antimicrobial interventions[4]

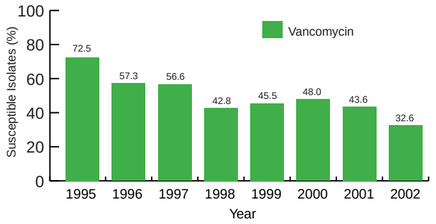
METHODS

- R-BUG Database-USA is one component of the ARM program, established in 1997 to document national and regional antimicrobial susceptibility trends among inpatient and outpatient isolates
- Antibiogram and sensitivity report data for *E faecium* isolates in the database were reviewed for resistance to vancomycin
- *P mirabilis, P aeruginosa,* and *S marcescens* isolates were reviewed for susceptibility to PIP-TAZ and PIP to determine if a similar resistance trend existed for these gram-negative organisms

RESULTS

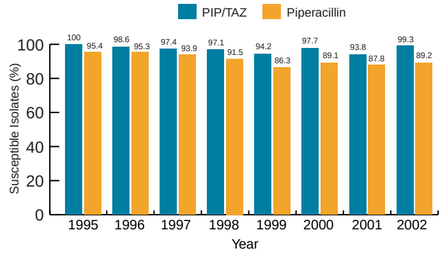
- Nationally, *E faecium* isolate susceptibility to vancomycin (n=19,081) has decreased from 1995-2002 (Figure 1)

Figure 1. National Decline in E faecium Susceptibility to Vancomycin, 1995-2002



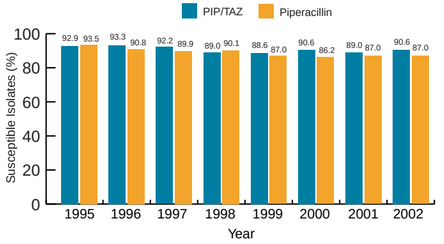
- A smaller decline in *P mirabilis, P aeruginosa,* and *S marcescens* isolates susceptible to PIP-TAZ and PIP was also observed nationally for the same years
- For *P mirabilis*, PIP-TAZ (n=25,388) and PIP (n=72,495) susceptibility decreased (Figure 2)

Figure 2. National Decline in P mirabilis Susceptibility to PIP-TAZ and PIP, 1995-2002



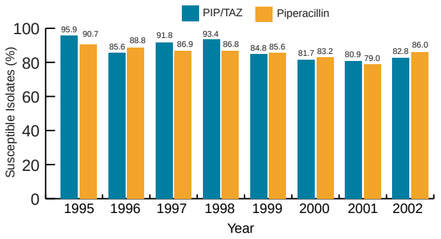
- From 1995-2002, *P aeruginosa* isolate susceptibility declined to PIP-TAZ (n=60,297) and PIP (n=170,069) (Figure 3)

Figure 3. National Decline in P aeruginosa Susceptibility to PIP-TAZ and PIP, 1995-2002



- Decreased susceptibility to PIP-TAZ (n=7200) and PIP (n=20,946) was also observed for *S marcescens* (Figure 4)

Figure 4. National Decline in S marcescens Susceptibility to PIP-TAZ and PIP, 1995-2002



CONCLUSION

- Data from the ARM program confirm that between 1995 and 2002, *E faecium* isolate susceptibility to vancomycin decreased from 75.2% to 32.6%
- A smaller decline in susceptibility was seen among the gram-negative isolates *P mirabilis, P aeruginosa*, and *S marcescens* to the antianaerobic agents PIP-TAZ and PIP, with the trend indicating resistance has increased annually
- Exposure to and use of PIP-TAZ and PIP may be one reason why VREF has become endemic so quickly in health care facilities

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