Epidemiology, Appropriateness, and Cost of Vancomycin Use

William R. Jarvis

From the Investigation and Prevention Branch, Hospital Infections Program, Centers for Disease Control and Prevention, U.S. Public Health Service, Atlanta, Georgia

Pharmaceutical costs, which approach $40 billion annually, account for about 8% of health care costs. Prescription drugs represent 5% to 20% of the total hospital budget, and antimicrobials account for 20% to 50% of hospital pharmaceutical costs. At one university hospital, the percentage of patients receiving antimicrobials increased from 31.8% in 1988 to 53.1% in 1994. Receipt of vancomycin has been associated with the emergence of resistant enterococci and has resulted in Centers for Disease Control and Prevention (CDC) recommendations for its use. Studies show that vancomycin use is increasing, that dosing is often inappropriate, that certain populations (such as oncology, neurosurgery, and cardiovascular surgery patients) are more likely to receive vancomycin, and that often use is not consistent with CDC recommendations. Few studies have assessed the cost of vancomycin use; those that have show that it is costly. Further studies of vancomycin use are needed, so that use can be improved through focused educational programs.

It is estimated that $40 billion are spent annually in the United States for pharmaceuticals, representing nearly 8% of all health care costs [1]. Prescription drugs account for 5% to 20% of the total hospital budget in the United States, and antimicrobials account for 20% to 50% of hospital pharmaceutical costs. Some investigators [2] estimate that the worldwide market for pharmaceuticals will continue to increase. Costs were estimated at $75 billion in 1980 and at $150 billion in 1990 and are expected to rise to $270 billion by the year 2000 [2].

Expenditures on systemic antiinfectives in United States hospitals were estimated at $1,215,531,000 during January–July 1993 and at $1,165,489,000 during January–July 1994. These costs represent 21.2% and 19.9%, respectively, of the total expenditures for pharmaceuticals at these facilities [3]. During January–June 1994, antiinfective expenditures varied widely among health care settings. Nevertheless, these expenditures accounted for between 7.3% and 19.9% of the total drug budgets at these facilities (table 1).

Antimicrobial use in 1988 and 1994 was compared at the Latter Day Saints Hospital, a 520-bed teaching hospital in Salt Lake City (table 2) [4]. The percentage of all admitted patients receiving antimicrobials increased from just $<32\%$ to $>50\%$. In 1994, the percentage of pharmacy expenditures on antimicrobials was only about one-half of that in 1988. However, use of broad-spectrum antimicrobials was almost twice as high in 1994 as in 1988. Thus, there are greater numbers of patients receiving antimicrobials, particularly broad-spectrum agents. This practice could be enhancing the emergence of antimicrobial resistance in common pathogens.

Dramatically Increasing Use of Vancomycin

Because of the emergence of multidrug-resistant coagulase-positive or -negative *Staphylococcus, Enterococcus,* and *Streptococcus pneumoniae,* vancomycin use has dramatically increased during the last several years in the United States. For example, Ena et al. [5] retrospectively reviewed a 900-bed university hospital's pharmacy data for 1981–1991 (table 3). Vancomycin use increased 20-fold, from about 1,000 g (5.7 g per 1,000 patient-days) to about 20,000 g (121.25 g per 1,000 patient-days).

Ena et al. [5] also looked at data for patients receiving intravenous vancomycin (table 3). Overall, 35% of vancomycin use was prophylactic, 31.8% was empirical, and 33.2% was for treatment of specific infections. Univariate analysis of risk factors showed that organ transplant patients had a 29.86 times greater risk of receiving vancomycin, and oncology patients had a 10 times greater risk of receiving vancomycin. Patients with rapidly or ultimately fatal diseases were at higher risk of vancomycin exposure. The presence of a medical device or prolonged hospital stay also placed patients at increased risk of receiving vancomycin. However, when the independent importance of these various risk factors was determined by multivariate analysis, patients with intravenous devices, Hickman catheters, or other foreign bodies were found to be at significantly greater risk of receiving vancomycin.

Appropriateness of Vancomycin Treatment

How often is vancomycin used appropriately? Rodman et al. [6] prospectively surveyed all intravenous vancomycin use

---

This article is part of a series of papers presented at a satellite symposium of the 36th Interscience Conference on Antimicrobial Agents and Chemotherapy. The symposium was entitled ''Emerging Resistance with Gram-Positive Aerobic Infections: Where Do We Go from Here?'' and was held on 14 September 1996 in New Orleans.

Reprints or correspondence: Dr. William R. Jarvis, Investigation and Prevention Branch, Hospital Infections Program, Centers for Disease Control and Prevention, 1600 Clifton Road Northwest, MS-69, Atlanta, Georgia 30333.

Clinical Infectious Diseases 1998;26:1200–3

Table 1. Antiinfective expenditures by practice setting during January–July 1994.

Setting	Expenditure	Percentage of total drug budget
Nonfederal hospitals	$1,165,489,000	19.9
Long-term-care facilities	$101,451,000	9.2
Health maintenance organizations	$74,703,000	7.4
Federal hospitals	$71,451,000	8.4

NOTE. Data are from [3].

at a community hospital during a 3-month period. The initial dose achieved the desired serum concentration in only 19 (39.6%) of the 48 patients who received vancomycin. Older patients were more likely to have been overdosed, and younger patients were more likely to have been underdosed. The investigators believed that use of a nomogram would have yielded the correct dose for 40 (83.3%) of the patients. Because inappropriate vancomycin dosing is common, these researchers recommended use of a nomogram.

Does vancomycin use comply with the recently reported recommendations from the Centers for Disease Control and Prevention (CDC) [7]? A prospective 1-month study [8] at a 461-bed university hospital evaluated all orders for vancomycin. Of the 101 orders, vancomycin use was in compliance with the CDC recommendations in 35 instances (35%) (table 4). For 65% of patients, vancomycin use was considered inappropriate because of various reasons.

Costs of Vancomycin Treatment

Very few studies evaluating the cost of vancomycin use have been conducted and reported. A prospective cohort study [9] performed at a community hospital reported that 100 infected adults received almost 1,400 doses of vancomycin. Duration of therapy (at a dosage of 2,000 mg/d) lasted a mean of 10 days. Phlebitis was the most common adverse reaction, occurring in 38 patients.

The investigators considered various costs, including pharmacy preparation, drug administration by nurses, monitoring serum concentrations, and, most important, treating adverse reactions. They found that the overall cost for preparation and administration was almost $24,000 (mean, $17.50 per dose), and the cost for monitoring serum concentrations was about $1,700 (mean, $15 per assay). Finally, the cost for treatment of adverse reactions was about $4,700 (mean, about $94 per adverse reaction). Thus, the total cost was about $30,000.

Table 2. Antimicrobial use at the Latter Day Saints Hospital, Salt Lake City, during 1988 and 1994.

	Finding	
Variable	1988	1994
No. (%) of patients receiving antimicrobials	8,051 (31.8)	11,624 (53.1)
Percentage of broad-spectrum antimicrobial use	24	47
Percentage of pharmacy expenditures on antimicrobials	24.8	12.9

NOTE. Data are from [4].

Table 3. The epidemiology of vancomycin use at a university hospital.

- Setting
  - 900-bed university hospital
- Study design
  - Retrospective pharmacy review, July 1981 to July 1991
- Study population
  - All patients receiving intravenous vancomycin
- Results
  - Vancomycin use increased 20-fold
    - 1981, 993 g (5.7 g per 1,000 patient-days)
    - 1991, 19,957 g (121.25 g per 1,000 patient-days)
  - Use significantly greater on hematology/oncology service
  - Uses
    - Prophylaxis, 35%
    - Empirical, 31.8%
    - Specific therapy, 33.2%
  - 63% of use judged inappropriate
    - Inappropriate selection, 10%
    - Inappropriate drug monitoring, 57%
- Univariate risk factors
  - Hematology/oncology patients (OR = 10)
  - Rapidly fatal disease (OR = 6.1)
  - Ultimately fatal disease (OR = 3.57)
  - Organ transplant (OR = 29.86)
  - Presence of medical device (OR = 13.36)
  - >14-day hospital stay (OR = 17.37)
- Multivariate risk factors
  - Intravenous devices (OR = 6.23)
  - Hickman catheter (OR = 76.12)
  - Other foreign body (OR = 10.50)

NOTE. Data are from [5].

Vancomycin Use for Pediatric Patients?

Most studies of vancomycin use have been conducted with adult populations. In 1996, Sinkowitz et al. [10] performed a retrospective study of vancomycin use and charges at a children's hospital during a 3-year period. Total vancomycin charges amounted to over $2 million for this one hospital (table 5). Over 98% of the charges were for intravenous vancomycin.

Vancomycin use varied widely by service, with cardiothoracic and neurosurgery services accounting for 34% and 45%, respectively, of the use on the pediatric surgery services and hematology/oncology and neonatology services accounting for 45% and 16%, respectively, of the use on the pediatric medical services; other than 12% of general pediatric patients using vancomycin, vancomycin was used by ⩽10% of the patients on all other services.

Overall rates of vancomycin use remained relatively stable over the entire study period. Annual rates of vancomycin use on the medical services ranged from three dose charges per 100 admissions on the general pediatric service to 34 dose charges per 100 admissions on the neonatology service. For the surgery services, rates ranged from five dose charges per 100 admissions for orthopedic and other services to 100 dose charges per 100 admissions for the cardiovascular surgery service.

Targeting Education Programs

Examining the distribution of vancomycin use by service helps focus education and intervention programs. In the study by Sinkowitz et al. [10], hematology/oncology, neurosurgery, and cardiovascular surgery services used vancomycin the most. These results show that it is important to do service-specific evaluations of pharmaceutical use, so that educational programs can be targeted to the correct audience. It would be rather futile to try to get personnel of other services—such as critical care medicine, orthopedic surgery, pulmonary, and gastroenterology—to reduce their use of vancomycin, when it is very small to begin with.

Table 4. Appropriateness of vancomycin use at a university hospital.

Setting
461-bed university hospital
Study design
Prospective (1 mo)
Study population
All patients given vancomycin
Results
101 vancomycin orders written
35 (35%) of 101 uses were consistent with CDC recommendations*
66 (65%) of 101 uses were inappropriate
Empirical without positive cultures (n = 44)
Surgical antibiotic prophylaxis (n = 6)
Treatment of antibiotic-associated colitis (n = 3)
Convenience (hemodialysis) (n = 1)
Other (n = 12)

NOTE. Data are from [8]. CDC = Centers for Disease Control and Prevention.

* CDC recommendations are reported in [7].

Table 5. Epidemiology of vancomycin dose charges at a children's hospital from 31 October 1992 to 21 October 1995.

Setting
Children's hospital
Study design
Retrospective
Pharmacy and medical records database
Study population
All children for whom a vancomycin dose was charged
Results
25,738 total hospital admissions
105,704 vancomycin dose charges
3,589 patient hospitalizations with vancomycin dose charge
2,032 males (56.6%)
2,200 whites (61.3%)
Mean age, 5.9 y
3,326 inpatients (92.7%)
Mean hospital stay, 15.3 d
Mean ICU stay, 4.5 d
Mean mechanical ventilation duration, 2.8 d
Mean no. of vancomycin doses, 29.5
Vancomycin charges
Total, $2,009,746
Mean, $559.97
Median, $297.50

NOTE. Data are from [10]. ICU = intensive care unit.

Conclusions

Antimicrobial use is a major contributor to our health care costs. Clearly, these expenditures will be focused on more and more as health care costs and reimbursement are being evaluated. The appropriateness of antimicrobial use, including vancomycin, needs to be assessed in our hospitals, in health maintenance organizations, in outpatient settings, and in home therapy. Pharmacy databases, particularly in the inpatient setting, should be developed and used for monitoring antimicrobial use, not just for billing. Further studies of the epidemiology of antimicrobial use, especially vancomycin use, need to be conducted not only at the facility but at the service level if they are going to be useful. Comprehensive programs to improve the use of antimicrobials, including vancomycin, are needed.

References

1. Kunin CM, Johansen KS, Wornig AM, Daschner FD. Report of a symposium on use and abuse of antibiotics worldwide. Rev Infect Dis **1990**; 12:12–20.
2. Liss RH, Batchelor ER. Economic evaluations of antibiotic use and resistance—a perspective. Report of Task Force 6. Rev Infect Dis **1987**; 9(suppl 3):S297–312.
3. Santell JP. Projecting future drug expenditures—1995. Am J Health Syst Pharm **1995**; 52:151–63.
4. Pestotnik SL, Classen DC, Evans RS, Burke JP. Implementing antibiotic process guidelines through computer-assisted decision support: clinical and financial outcomes. Ann Intern Med **1996**; 124:884–90.

5. Ena J, Dick RW, Jones RN, Wenzel RP. The epidemiology of intravenous vancomycin usage in a university hospital. A 10-year study. JAMA **1993**;269:598–602.
6. Rodman DP, McKnight JT, Rogers T, Robbins M. The appropriateness of initial vancomycin dosing. J Fam Pract **1994**;38:473–7.
7. Centers for Disease Control and Prevention. Recommendations for preventing spread of vancomycin resistance. Recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). MMWR Morb Mortal Wkly Rep **1995**;44(RR-12):1–12.
8. Evans ME, Kortas KJ. Vancomycin use in a university medical center: comparison with hospital infection control practices advisory committee guidelines. Infect Control Hosp Epidemiol **1996**;17:356–9.
9. Garrelts JC, Worst WD, Silkey B, Gagnon S. A pharmacoeconomic model to evaluate antibiotic costs. Pharmacotherapy **1994**;14:438–45.
10. Sinkowitz RL, Keyserling HI, Walker TJ, Jarvis WR. The epidemiology of vancomycin usage at a children's hospital, 1993–1995. J Pediatr Infect Dis **1997**;16:485–9.