

# Vancomycin utilization at a teaching hospital in Hong Kong

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In the past 15–20 years, the utilization of vancomycin has increased because of the dramatic increase in methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus epidermidis* and in ampicillin-resistant enterococci.<sup>1</sup> Inappropriate use of vancomycin may not only increase health care costs but also contribute to the emergence of resistant organisms. Vancomycin-resistant enterococci (VRE) were first isolated in 1988. The alarming increase in cases of infection with VRE prompted the Centers for Disease Control and Prevention (CDC) to publish recommendations for preventing and controlling the spread of vancomycin-resistant organisms in 1995.<sup>2</sup> Since the release of the CDC guidelines, clinical isolates of *S. aureus* with reduced susceptibility to vancomycin have been reported in Japan, the United States, and France.<sup>3-6</sup>

In Hong Kong, 30–40% of clinical isolates of *S. aureus* are methicillin resistant. Vancomycin-heteroresistant staphylococci (staphylococci with

subpopulations showing reduced susceptibility to vancomycin) have been reported in Hong Kong and may be associated with a poor outcome.<sup>7</sup> Prince of Wales Hospital (PWH), a public hospital managed by the Hospital Authority, Hong Kong, is also a teaching hospital with approximately 1300 beds. The frequency of MRSA at PWH increased from 36.7% (76 of 207 isolates) to 44.9% (120 of 267 isolates) over the 1996–1998 period, and three VRE isolates were first found in urine cultures in 1998. Before the implementation of recommendations for prudent vancomycin use, a drug-use evaluation (DUE) was performed to

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examine the use of vancomycin at PWH and to determine the associated cost. This article reports the DUE and its findings.

**Methods.** All patients who received vancomycin between January 15, 2000, and March 31, 2000, were evaluated. Information collected included demographic data, admission diagnosis, site of infection, history of present illness, allergies, concurrent antimicrobials and nephrotoxic drugs, vancomycin dosage, route of administration, duration of vancomycin therapy, vancomycin-related adverse reactions, culture and susceptibility test results, and results of laboratory tests associated with vancomycin therapy.

The 1995 CDC recommendations for vancomycin use described situations in which the use of vancomycin is appropriate or should be discouraged.<sup>2</sup> A pharmacist, with the help of a consultant microbiologist, evaluated the appropriateness of each course of vancomycin therapy on the basis of CDC's guidelines. Each complete course was categorized as empirical therapy, specific therapy, or surgical prophylaxis and as appropriate or "should have been discouraged." Vancomycin dosages were also evaluated with consideration of the results of renal function tests, if available.

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■ **NOTE Vancomycin utilization**

Direct costs associated with vancomycin use were estimated from the perspective of a public health organization. Sources of data for cost estimation included the *Hong Kong Gazette*, the pharmacy department at PWH, and the Hospital Authority Finance Office. Resource items included drug acquisition costs; ancillary costs, such as i.v. sets and infusion bags; the cost of nursing time; the cost of serum vancomycin level and renal function monitoring; and the cost of managing adverse reactions. The cost of pharmacy labor was not included, because vancomycin preparations were compounded by nurses.

Descriptive statistics were used, and continuous variables were re-

ported as means and standard deviations. Statistical analysis was performed with SPSS version 9.05 (SPSS Inc., Chicago, IL).

**Results.** During the 11-week evaluation period, 115 patients (72 males and 43 females) received a total of 144 courses of vancomycin. There were 77 adults (mean  $\pm$  S.D. age, 58  $\pm$  17 years) and 38 neonates and pediatric patients. The distribution of vancomycin use by service is shown in Table 1. Intravenous administration accounted for 136 (94%) of the 144 courses. Other routes of administration included intraperitoneal (1%), oral (1%), and topical (4%).

Vancomycin was prescribed for empirical therapy in 75 courses

(52%), specific therapy in 52 courses (36%), and surgical prophylaxis in 17 courses (12%). Vancomycin was considered appropriate in 66 courses (46%); its use in 78 courses (54%) should have been discouraged, according to the CDC recommendations (Table 2). Vancomycin was appropriate in 48 (92%) of 52 courses of specific therapy, 16 (21%) of 75 courses of empirical therapy, and 2 (12%) of 17 courses of surgical prophylaxis. The appropriate use of vancomycin for specific therapy was associated with infections with  $\beta$ -lactam-resistant gram-positive organisms, including enterococci, coagulase-negative staphylococci, and MRSA. The most common situation (55 courses, 71%) in which vancomycin use should have been discouraged involved continuing empirical use for presumed infections in patients whose cultures were negative for  $\beta$ -lactam-resistant gram-positive organisms. Of those 55 courses, 41 were prescribed for the treatment of neonatal sepsis; the other conditions included pneumonia, peritonitis associated with continuous ambulatory peritoneal dialysis, cellulitis, septic arthritis, urinary-tract infection, and infections presumed on the basis of spiking fever.

Table 1.

**Distribution of Vancomycin Use by Service (n= 144)**

Service	No. (%) Vancomycin Courses
Neonatal ICU <sup>a</sup>	45 (31.3)
Medicine	33 (22.9)
ICU	22 (15.3)
Surgery	15 (10.4)
Burns	7 (4.7)
Oncology	6 (4.2)
Pediatrics	5 (3.5)
Orthopedics and trauma	4 (2.8)
Pediatric surgery	4 (2.8)
Obstetrics and gynecology	2 (1.4)
Coronary care unit	1 (0.7)

<sup>a</sup>ICU = intensive care unit.

Table 2.

**Appropriateness of Vancomycin Therapy<sup>a</sup> (n = 144)**

Clinical Situation	No. (%) Vancomycin Courses
<i>Vancomycin Use Is Appropriate</i>	
Treatment of serious infections caused by $\beta$ -lactam-resistant gram-positive organisms	48 (73)
Empirical use for presumed infections in patients yielding subsequent cultures positive for $\beta$ -lactam-resistant gram-positive organisms	8 (12)
Discontinued empirical use for presumed infections in patients yielding subsequent cultures positive for $\beta$ -lactam-susceptible gram-positive organisms	5 (7.5)
Discontinued empirical use for presumed infections in patients yielding subsequent negative cultures	3 (4.5)
Prophylaxis for surgical procedures involving implantation of prosthetic materials or devices	2 (3)
<i>Vancomycin Use Should Have Been Discouraged</i>	
Continued empirical use for presumed infections without culture support	55 (71)
Routine surgical prophylaxis other than in a patient who has a life-threatening allergy to $\beta$ -lactam antibiotics	10 (13)
Systemic or local prophylaxis for infection or colonization of indwelling central or peripheral intravenous catheters	5 (6.4)
Use of vancomycin solution for topical application or irrigation of wound	5 (6.4)
Treatment of infections caused by $\beta$ -lactam-susceptible gram-positive organisms in patients without serious allergies to $\beta$ -lactam antibiotics	2 (2.6)
Primary treatment of antimicrobial-associated colitis	1 (1.3)

<sup>a</sup>According to the recommendations of the Centers for Disease Control and Prevention.<sup>2</sup>

The mean  $\pm$  S.D. duration of vancomycin treatment was similar for specific therapy ( $9.9 \pm 8.2$  days) and empirical therapy ( $8.3 \pm 7.0$  days). The duration of courses for surgical prophylaxis was  $1.5 \pm 0.9$  days. Baseline assessment of renal function was done for 55 (40%) of the 136 i.v. courses, and 40 (73%) of these courses were for empirical or specific treatment in adults. Of these 40 courses, 16 (40%) were appropriately adjusted according to baseline renal function. During i.v. vancomycin therapy, renal function was monitored for 92 (68%) of 136 courses, and vancomycin levels were measured for 103 (76%).

A total of 111 dosage adjustments were done for 62 (46%) of the 136 i.v. courses. Ninety-eight dosage adjustments (88%) were done in response to measurements of vancomycin levels. The dosage adjustments resulted in achievement of therapeutic vancomycin levels (12%) and failure to achieve a therapeutic level (51%); follow-up measurements of levels were not performed in 37% of cases.

Red man syndrome was documented in 6 patients (4%) receiving i.v. vancomycin. Nephrotoxicity, defined as an increase in serum creatinine concentration of  $44 \mu\text{M}$  (0.5 mg/dL), was monitored in 38 patients who had renal function assessed at baseline and during i.v. therapy. Nephrotoxicity was observed in 3 (14%) of 21 of these pa-

tients who received vancomycin without other nephrotoxic agents and in 6 (35%) of the remaining 17 patients who received other nephrotoxic drugs (aminoglycosides, amphotericin B, and diuretics).

The total cost of vancomycin therapy during the study period was \$21,096.41; the cost per therapeutic course was \$146.54. The cost associated with situations in which vancomycin use should have been discouraged was \$8,972.95, or 43% of the total cost.

**Discussion.** In hospitals where MRSA is frequently isolated, prescribers face clinical dilemmas in managing high-risk patients with presumed infections requiring coverage against *S. aureus*; therefore, the institutional use of vancomycin for empirical therapy tends to be high. In this study, the most common situation in which the use of vancomycin should have been discouraged was continuing empirical use for presumed infections in patients whose cultures were negative for  $\beta$ -lactam-resistant gram-positive organisms. Sixty percent of initial vancomycin dosages were not adjusted for renal function, and only 12% of dosage adjustments achieved therapeutic levels. Inappropriate use of vancomycin is a major contributing factor in the emergence of VRE.<sup>2,4</sup> Prudent vancomycin use is strongly recommended by CDC to prevent the spread of resistance.<sup>2</sup>

Because of this DUE, institution-specific recommendations for the

empirical use of vancomycin and dosing and monitoring of vancomycin in patients with renal dysfunction were developed at PWH.

**Conclusion.** A substantial component (54%) of vancomycin use at a Hong Kong hospital should have been discouraged, according to CDC guidelines. Institution-specific guidelines on vancomycin use should specifically address (1) prolonged empirical therapy for presumed infections not confirmed by culture and susceptibility tests and (2) appropriate vancomycin dosing and monitoring.

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