CONCISE COMMUNICATION

Vancomycin-Resistant Enterococci in Canada: Results from the Canadian Nosocomial Infection Surveillance Program, 1999-2005

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Surveillance for vancomycin-resistant enterococci (VRE) in sentinel Canadian hospitals has been conducted since 1999. From 1999 to 2005, the rate of VRE detection increased from 0.37 to 1.32 cases per 1,000 patients admitted, and the rate of VRE infection increased from 0.02 to 0.05 cases per 1,000 patients admitted. Thirty-three percent of all patients with VRE detected that were reported during 1999-2005 were identified in 2005, with increases seen in all regions of Canada. Although the incidence rate of VRE carriage in Canada is increasing, it remains very low.

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Since 1999, the Canadian Nosocomial Infection Surveillance Program (CNISP) has conducted surveillance for vancomycin-resistant enterococci (VRE). Although VRE is a rather low virulence pathogen, there is concern that vancomycin-resistance genes may transfer to *Staphylococcus aureus*.[1] Surveillance is one component of a strategy to identify and limit the spread of VRE in hospitals.

A 1996 CNISP VRE prevalence survey found a VRE infection rate of 0.1% among high-risk patients in hospitals where VRE is not endemic but a rate of 3.7% among high-risk patients in hospitals where VRE is endemic.[2] Compared with the 1999 US National Nosocomial Infections Surveillance summary, which reported that the mean annual incidence rate of VRE carriage was 25.9% in intensive care units,[3] the Canadian numbers were much lower. Therefore, CNISP implemented ongoing VRE surveillance to document trends, distribution, and the number of patients with carriage detected.

METHODS

Participating facilities. CNISP is a national surveillance program administered by the Public Health Agency of Canada (PHAC). CNISP is comprised of 48 hospital facilities, including 8 pediatric stand-alone facilities, providing primary to quaternary care services to 9 Canadian provinces. VRE surveillance is part of hospital quality-control activities for which Research Ethics Board approval is not required.

Case definitions. Any inpatient with *Enterococcus faecium* or *Enterococcus faecalis* having a minimum inhibitory concentration of vancomycin of $\geqslant 8$ μg/mL isolated from a clinical or screening specimen was enrolled. Infection was defined as the presence of an illness that met standard infection surveillance definitions.[4] Colonization was defined as the presence of VRE in surgical wounds, urine, stool (rectum), or other body sites in an individual not manifesting clinical signs and/or symptoms. To be defined as nosocomial colonization, there had to be no evidence that the organism was likely present at the time of admission. An epidemiological link was determined by the best judgment of the infection control practitioner (ICP) as to whether the patient could be linked to another patient carrying VRE.

Case finding. The hospital laboratory identified a VRE isolate and reported the patient's name to the ICP. Only incident cases were included. There is an active VRE case finding in most CNISP hospitals: 89% had policies for admission screening of patients deemed at high risk for VRE colonization, 36% conducted regular VRE prevalence surveys, and 96% obtained culture samples from inpatients identified as potential contacts of inpatients carrying VRE.[5] Stool or rectal swab specimens were obtained for screening purposes.[6] Clinical specimens were obtained at the discretion of the attending physician.

Data collection. A standardized nonnominal data extraction form was completed by the ICP for all incident cases. Data collected included hospital facility, patient demographic and clinical information, whether the patient was a known VRE carrier, whether the patient had been hospitalized within the past 12 months, the date the patient was first identified as carrying VRE, where the VRE was presumed to have been acquired, epidemiological links, the source of the culture-positive specimen, and whether the patient had concurrent infection or colonization with methicillin-resistant *S. aureus* (MRSA). Every year, data were collected from each facility on total vancomycin use (in grams), on the number of patients admitted, and on the number of enterococcal isolates identified.

Data analysis. Incidence rates were calculated as the number of VRE isolates per 1,000 patients admitted. CNISP used 8 of the facilities that were able to report the number of nonduplicate enterococcal isolates to determine the proportion of enterococcal isolates that were resistant to vancomycin (number resistant per 100 enterococcal isolates). For reporting purposes, the provinces were divided into 3 regions: Western (British Columbia to Manitoba), Central (Ontario and Quebec), and Eastern (Nova Scotia, New Brunswick, and Newfoundland and Labrador). Data were entered into Office Access 2003 (Microsoft) and analyzed using EpiInfo, version 6.04d (Centers for Disease Control and Prevention), and SPSS

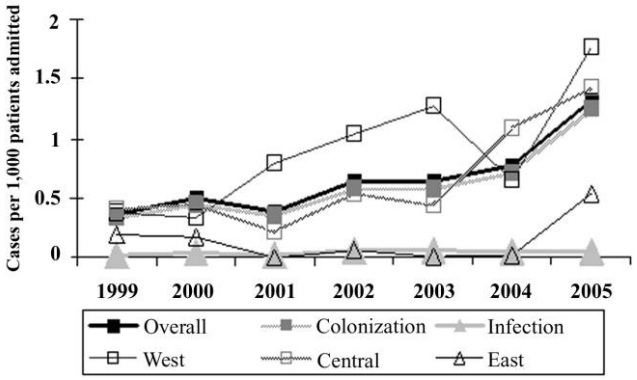

FIGURE 1. Rates of detection of vancomycin-resistant *Enterococcus* in the Canadian Nosocomial Infection Surveillance Program, 1999-2005.

software, version 11 (SPSS). The χ^2 test was used to analyze the linear trends in incidence rates. The Kendall tau-*b* test was used to quantify the correlation between MRSA and VRE rates and vancomycin use, ordered by years 1999-2005.

RESULTS

Between January 1, 1999 and December 31, 2005, there were 3,037 new patients carrying VRE reported. Colonized patients made up 2,848 (94%) of the total. Five facilities reported no patients with VRE detected (3 being exclusively pediatric facilities). The rate of VRE detection (Figure 1) increased 3.6-fold, from 0.37 to 1.32 cases per 1,000 patients admitted ($P < .001$). The rate of VRE infection also increased, from 0.02 to 0.05 cases per 1,000 patients admitted ($P = .004$). The increase in the rate was largely the result of an increase in VRE colonization, from 0.34 to 1.25 cases per 1,000 patients admitted ($P < .001$). Between 1999 and 2005, the percentage of enterococci that were vancomycin resistant increased 2.8-fold, from 1.16% to 3.25% ($P < .001$). The rate of VRE detection increased significantly over the 1-year period from 2004 to 2005: 1,001 patients with VRE detected (33% of the total) were identified in 2005 alone, and increases in the rate of VRE detection were seen in all regions (Figure 1). *E. faecium* accounted for 99% of VRE isolates.

The majority of patients (2,256 [74.3%] of 3,037 patients with VRE detected) had been hospitalized within the prior 12 months. For 2,460 patients (81%), the likely place of acquisition was an acute care facility; for 172 (5.7%), it was a dialysis unit. Most patients (2,096 [69%]) acquired VRE in their own hospital, and 1,551 (74%) of those 2,096 had an epidemiological link to another patient. Only 39 patients (1.3%) acquired VRE in a long-term care facility. Twenty-nine patients (1%) were 2 years of age or under, and 3 (10.3%) of these 29 had VRE infection. Forty-eight (1.6%) were between 3 and 18 years of age, and 4 (8.3%) of these 48 had VRE infection.

The vast majority of patients with VRE detected (2,843 [93.6 %] of 3,037) were identified by screening or surveillance. Only 189 (6.2%) had VRE detected in clinical specimens. Of these 189, there were 69 recovered from the urinary tract, 45 recovered from blood, 24 from skin and soft tissue, 28 from surgical wounds, and 23 from other sites. Of the 2,822 patients with VRE detected since 2000, there were 414 (14.7%) who had concurrent MRSA colonization or infection.

The total amount of vancomycin used at each facility (Figure 2) increased steadily from 1999 to 2005 ($P < .001$). Correlation coefficients from 1999 to 2005 for rates of MRSA and VRE detection and vancomycin use yielded an R of 0.961 ($P = .013$).

DISCUSSION

Although the incidence rate of VRE carriage remains low in CNISP hospitals, there has been a small but steady increase over time. In particular, one-third of the cases in this study were detected in 2005, which cannot be attributed to a large outbreak in a single facility. However, this increase in the rate of VRE detection is lower than that noted for MRSA detection in the CNISP MRSA surveillance program,[7] and the number of cases of VRE carriage remains much lower than seen in the United States.[3] Additionally, VRE infection rates have not increased proportionately. Although it is reassuring that infection rates remain much lower than colonization rates, it is still of concern to see an increase in VRE carriage, given the ability of the genes encoding vancomycin resistance to be transferred to *S. aureus*. It should be noted that 14.7% of patients in this cohort were colonized with both VRE and MRSA.

Reasons for the recent increase in VRE detection cannot be identified from the present study. Associated with the increase in MRSA detection across Canada has been greater use

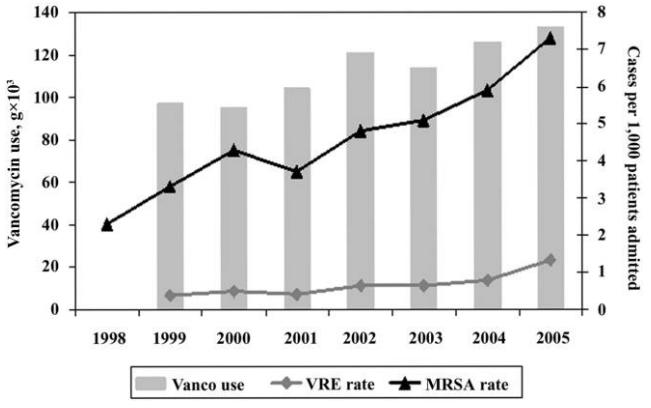

FIGURE 2. Overal rates of detection of vancomycin-resistant *Enterococcus* (VRE) and methicillin-resistant *S. aureus* (MRSA) in the Canadian Nosocomial Infection Surveillance Program and the mean amount of vancomycin used in each facility annually. Vanco, vancomycin.

of vancomycin (Figure 2), which may be contributing to the increased rate of VRE detection. This speaks to the importance of MRSA control as a measure to decrease the need for vancomycin. Oral vancomycin use is restricted at 61.9% of CNISP facilities,[5] and rates of *Clostridium difficile* carriage were the same in 2004-2005 as in 1997, with the exception of Central Canada.[8] Thus, changes in the rate of *C. difficile* carriage and oral vancomycin use are not likely to have contributed to the increase in VRE detection.

The aggressiveness of active case finding may have differed between facilities and over time. However, a survey of VRE screening practices in 1998 indicated that all 21 participating facilities had admission screening policies and that prevalence surveys were commonly performed at several centers.[9] The situation was much the same 7 years later. Thus, case ascertainment is unlikely to be a large factor leading to detection bias.

Several limitations should be considered when interpreting these data. CNISP hospitals may not be representative of all Canadian hospitals. Cases of VRE detection represent only the first occurrence. Patients with VRE carriage who would not be counted include those who are colonized and later become infected. Thus, the VRE infection rate may be underestimated. On the other hand, there may have been misclassification bias, because cases of urinary tract colonization may have been classified as infection, resulting in an overestimate of the number of infections. Also excluded from the reporting system are patients identified in an outpatient setting and not admitted to the hospital. However, it is expected that the number of such patients with VRE infection would be negligible, because VRE rarely causes infection (the stimulus for obtaining clinical specimens) and because most screening programs are focused heavily on inpatients (ie, those most at risk of VRE colonization and infection). It is therefore felt that the CNISP VRE surveillance program captures the majority of patients with VRE carriage that are detected in participating hospitals. However, hospitals may vary in their screening strategies, and this may affect the number of cases identified. For this reason, caution must be used when comparing rates between individual hospitals and regions without knowing the details of their screening strategies. Despite the limitations of the CNISP VRE surveillance system, the program gives an estimate of the impact of VRE carriage within Canada and provides a baseline for monitoring its occurrence.

CANADIAN NOSOCOMIAL INFECTIONS SURVEILLANCE PROGRAM

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