NOTES

Skin Colonization with Vancomycin-Resistant Enterococci Among Hospitalized Patients with Bacteremia

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To assess the prevalence of skin and rectal colonization by vancomycin-resistant enterococci (VRE) in hospitalized bacteremic patients and to determine the relation between colonization and bacteremia, we compared 14 case patients who had bacteremia due to VRE with 30 control patients who had bacteremia due to other pathogens. Rectal colonization and skin (inguinal area and/or antecubital fossa) colonization with VRE were common among both case patients (100% had rectal colonization, and 86% had skin colonization) and control patients (37% had rectal colonization and 23% had skin colonization). Among patients with rectal colonization, skin colonization was more common when diarrhea or fecal incontinence was present. The bloodstream cleared without appropriate antimicrobial therapy in nine of the 14 patients with bacteremia due to VRE. The high prevalence of skin colonization with VRE may increase the risk of catheter-related sepsis, cross-infection, or blood culture contamination (which may explain the frequent spontaneous resolution of bacteremia due to VRE).

Enterococci are a frequent cause of nosocomial bacteremia [1]. However, the clinical significance of this infection is sometimes uncertain. In two case series, as many as 50% of the episodes of enterococcal bacteremia were considered clinically insignificant, which suggests that the episodes of bacteremia were transient or that the blood cultures had been contaminated [2, 3].

Infections caused by vancomycin-resistant enterococci (VRE) pose a challenging problem because therapy is usually limited to investigational compounds or unproven combinations of antibiotics. To assure the appropriate use of new antibiotics directed against VRE, it is necessary to understand the natural history, clinical importance, and sources of bacteremia due to VRE.

The gastrointestinal tract is often considered the origin of bacteremia due to VRE [4]; however, little is known about colonization of other sites. The results of a prior study at our institutions suggested that VRE may colonize the skin during hospitalization and that skin colonization may be a source of bacteremia and blood culture contamination [5]. The purpose of the present study was to assess the prevalence of skin and rectal colonization by VRE among hospitalized bacteremic patients and to determine the relation between colonization and bacteremia due to VRE.

Methods

This study was conducted in Chicago at Cook County Hospital and Rush-Presbyterian St. Luke's Medical Center. Case patients included all patients with vancomycin-resistant enterococcal bacteremia who were seen at either institution between August 1994 and July 1995. Thirty control patients, including 10 patients each with aerobic gram-negative bacillary bacteremia, vancomycin-susceptible enterococcal bacteremia, or coagulase-negative staphylococcal bacteremia were selected during the same period. None of the control patients had a history of infection with VRE. The records of all patients were reviewed for demographic and clinical information.

Microbiological methods. To determine colonization with VRE, samples from the rectums, inguinal areas, and antecubital fossae of case and control patients were obtained for culture. The skin sites chosen were those most likely to be used for venipuncture; a 10 × 10-cm area of skin was sampled by using a sterile cotton swab moistened with modified Stuart's medium (Culturette System, Becton Dickinson Microbiology Systems, Cockeysville, MD). Surveillance swabs were inoculated onto Enterococcosel agar (Becton Dickinson) supplemented with vancomycin (6 μg/mL). Plates were examined after 48 hours of incubation at 37°C. Isolates of VRE were identified to the species level, and molecular typing was done with use of

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pulsed-field gel electrophoresis (PFGE), as previously described [6].

Definitions and statistical methods. Strain types were considered distinct if PFGE profiles differed by more than six bands. Clinically significant bacteremia was defined as two or more blood cultures from separate venipuncture sites that yielded VRE or as one blood culture that yielded VRE in the presence of a culture-confirmed source of bacteremia [3].

Statistical analysis was done by using the Student's *t*-test and the χ^2 test, Fisher's exact test, and the Mantel-Haenszel Stratified χ^2 test, as appropriate.

Results

The demographic and clinical profiles (including the presence of multiple underlying diseases) were similar for the 14 case patients with bacteremia due to VRE and for the 30 control patients (table 1). All patients with vancomycin-resistant enterococcal bacteremia had rectal colonization with VRE (table 2). In addition, skin colonization of the inguinal area and/or the antecubital fossa was found in 12 (86%) of 14 case patients. Eleven (37%) of the 30 control patients had rectal colonization with VRE, and seven control patients (23%) had skin colonization. Of the 25 case and control patients colonized with VRE, 19 had rectal and skin colonization, and six had rectal colonization alone. No patient had skin colonization alone.

Skin colonization by VRE occurred more often in patients who had diarrhea or fecal incontinence (68%) than in patients who did not (19%; $P < .01$) and more often in patients who had received vancomycin, a third-generation cephalosporin, or metronidazole and/or clindamycin (79%) than in patients who did not (28%; $P < .01$). The influences of the presence of diarrhea and use of antibiotics on the rates of colonization were independent ($P = .05$).

Table 1. Demographic characteristics of bacteremic patients with skin colonization by vancomycin-resistant enterococci.

Variable	Case patients ($n = 14$)	Control patients ($n = 30$)
Mean age (y)	50	61
No. (%) who were male*	7 (50)	20 (67)
Race		
Black	9 (64)	15 (50)
Other	5 (36)	15 (50)
Mean duration of hospitalization in d before first positive blood culture	17.0	14.2
No. (%) with nosocomial bacteremia	13 (93)	27 (90)
No. (%) with diarrhea or fecal incontinence	9 (64)	11 (37)

NOTE. Case patients had vancomycin-resistant enterococcal bacteremia; control patients had vancomycin-susceptible enterococcal bacteremia ($n = 10$), coagulase-negative staphylococcal bacteremia ($n = 10$), or gram-negative bacillary bacteremia ($n = 10$).

For all comparisons, $P > .05$.

Table 2. Rates of skin and rectal colonization by vancomycin-resistant enterococci among hospitalized patients with bacteremia.

Colonization site	No. (%) of case patients ($n = 14$)	No. (%) of control patients ($n = 30$)	*P* value
Rectum	14 (100)	11 (37)	<.001
Inguinal area	12 (86)	7 (23)	<.001
Antecubital fossa	8 (57)	2 (7)	<.001

NOTE. Case patients had vancomycin-resistant enterococcal bacteremia; control patients had vancomycin-susceptible enterococcal bacteremia ($n = 10$), coagulase-negative staphylococcal bacteremia ($n = 10$), or gram-negative bacillary bacteremia ($n = 10$).

Of 56 skin isolates of VRE from 19 colonized patients, 43 (77%) were *E. faecium,* 11 (20%) were *E. faecalis,* and 2 (3%) were *E. gallinarum.* Eight different strain types were identified on skin with use of PFGE. The strain type from upper-body skin was concordant with a strain type from the rectal or inguinal area for eight of 10 patients. Three of the 19 colonized patients carried two or three vancomycin-resistant *E. faecium* strain types on their skin. The distribution of species and strain types was the same for skin isolates as for rectal isolates.

For 13 of the 14 patients with bacteremia due to VRE, the bloodstream strain type was identical to that found in a culture of a skin or rectal sample or both. Bacteremia due to VRE was judged to be clinically significant for nine of 14 patients. Four of the nine bacteremias cleared without appropriate antimicrobial therapy and did not recur. None of the five patients with clinically insignificant bacteremia received appropriate antimicrobial therapy, and none had a recurrence of bacteremia due to VRE.

Discussion

We detected rectal colonization with VRE in all patients who had bacteremia due to VRE and in 37% of patients with bacteremia due to other microorganisms. This finding supports the widely held notion that the gastrointestinal tract is the most common site of colonization with VRE [4]. It was more surprising that we detected skin colonization by VRE in 12 (86%) of 14 patients with vancomycin-resistant enterococcal bacteremia and in 23% of patients with bacteremia due to other microorganisms. In fact, these percentages may be minimal estimates, since recovery rates may have been higher if other culture techniques, such as broth enrichment, had been used.

Skin colonization by VRE was associated with prior diarrhea or fecal incontinence. Yamaguchi and co-workers also noted

skin colonization by VRE among hospitalized patients that was associated with the presence of diarrhea [7]; this observation suggests that the skin colonization results from self-soiling. An additional risk factor for skin colonization in our study was prior therapy with vancomycin, a third-generation cephalosporin, and/or an antibiotic with activity against anaerobic bacteria; this finding supports the recommendations for prudent use of antibiotics as part of VRE control measures.

Skin colonization with VRE has several important epidemiological and clinical implications. First, the high prevalence of this condition may facilitate transmission of VRE from patient to patient and may help to explain the rapid dissemination of VRE in hospitals over the past several years. Second, the frequent spontaneous resolution of VRE bacteremia (nine [64%] of 14 cases in our study) suggests that some of the positive blood cultures may result from contamination of specimens via colonized skin. The hypothesis that VRE can behave as skin flora contaminants of blood cultures is supported by the results of a previous study that we conducted, in which it was noted that enterococci and coagulase-negative staphylococci were common coisolates in blood cultures [5]. Third, the skin colonization findings may explain the importance of VRE as a cause of vascular catheter–related bacteremia.

Whether VRE are only transient skin flora in colonized patients, especially those with diarrhea or fecal incontinence, and whether VRE can become resident skin flora must be evaluated. We caution that our study population was small and consisted primarily of patients with multiple underlying diseases who had been hospitalized for >2 weeks in institutions where VRE have been endemic for >5 years; the findings might have been different for a less debilitated group of patients or in a different setting. Nevertheless, skin colonization by VRE in hospitalized patients is an important potential source of blood culture contamination, bacteremia, and cross-infection.

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