ORIGINAL ARTICLE

An outbreak of vancomycin-resistant Enterococcus faecium in an acute care pediatric hospital: Lessons from environmental screening and a case-control study

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Background: The present study describes a vancomycin-resistant enterococci (VRE) outbreak investigation and a case-control study to identify risk factors for VRE acquisition in a tertiary care pediatric hospital.

Objective: To report an outbreak investigation and a case-control study to identify risk factors for VRE colonization or infection in hospitalized children.

Methods: Screening for VRE cases was performed by culture or polymerase chain reaction. A case-control study of VRE-colonized patients was undertaken. Environmental screening was performed using standard culture and susceptibility methods, with pulse-field gel electrophoresis to determine relationships between VRE isolates. Statistical analysis was performed using SAS version 9.0 (SAS Institute Inc, USA).

Results: Thirty-four VRE-positive cases were identified on 10 wards between February 28, 2005, and May 27, 2005. Pulsed-field gel electrophoresis analysis confirmed a single outbreak strain that was also isolated from a video game found on one affected ward. Multivariate analysis identified cephalosporin use as the major risk factor for VRE colonization.

Conclusions: In the present study outbreak, VRE colonization was significantly associated with cephalosporin use. Because shared recreational items and environmental surfaces may be colonized by VRE, they warrant particular attention in housekeeping protocols, particularly in pediatric institutions.

Key Words: Cephalosporins; Outbreak; Pediatrics; Risk factor; VRE

The increasing emergence and spread of vancomycin-resistant enterococci (VRE) is a worldwide concern impacting health care-associated morbidity, mortality and the cost of care (1). VRE are relatively resistant to most currently used antibiotics and can be easily transmitted within the acute care hospital setting if infection control practices are suboptimal. Transmission of VRE to other patients usually occurs as a result of fecal contamination of the environment and subsequent spread via the hands of health care workers or others. Resistance to vancomycin is found primarily in Enterococcus faecium or Enterococcus faecalis; it is mainly transmitted by the vanA and vanB genes.

The control of VRE within acute care facilities requires an understanding of the selective forces driving the horizontal transmission of these organisms because most outbreaks have been shown to be clonally related. Several authors have found that risk factors for the acquisition of VRE include contact...
The Hospital for Sick Children (HSC) in Toronto is a 300-bed tertiary care pediatric hospital serving the Canadian province of Ontario (population 12.5 million); it admits referred patients with an emphasis on the identification of risk factors for vancomycin-resistant enterococci (VRE) colonization or infection in hospitalized children.

The primary aim of the present study was to describe an outbreak investigation and a case-control study with an emphasis on the identification of risk factors for VRE colonization or infection in hospitalized children.

**Table 1: Univariate analysis indicates multiple risk factors for vancomycin-resistant enterococci colonization**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>P</th>
<th>χ²</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic use</td>
<td>0.01</td>
<td>3.8</td>
<td>3.7 1.3–10.5</td>
</tr>
<tr>
<td>&gt;4 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End stage renal disease</td>
<td>0.12</td>
<td>2.4</td>
<td>6.0 0.6–57.7</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>0.05</td>
<td>4.0</td>
<td>3.5 1.0–11.0</td>
</tr>
<tr>
<td>Stay on ward X</td>
<td>0.03</td>
<td>4.8</td>
<td>6.0 1.2–29.7</td>
</tr>
<tr>
<td>Image-guided therapy</td>
<td>0.05</td>
<td>3.7</td>
<td>3.0 1.0–9.0</td>
</tr>
<tr>
<td>Use of any cephalosporin</td>
<td>0.01</td>
<td>7.3</td>
<td>3.5 1.4–8.8</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>0.16</td>
<td>2.0</td>
<td>0.5 0.2–1.3</td>
</tr>
<tr>
<td>Current length of stay</td>
<td>0.23</td>
<td>1.4</td>
<td>1.0 1.0–1.0</td>
</tr>
<tr>
<td>Aminoglycoside use</td>
<td>0.75</td>
<td>0.1</td>
<td>1.2 0.5–3.0</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>0.99</td>
<td>0.0001</td>
<td>1000 0.01–1000</td>
</tr>
<tr>
<td>Clinic visits</td>
<td>0.55</td>
<td>0.35</td>
<td>1.0 1.0–1.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.15</td>
<td>2.1</td>
<td>0.5 0.2–1.3</td>
</tr>
<tr>
<td>Immunosuppressive drug</td>
<td>0.37</td>
<td>0.8</td>
<td>1.5 0.6–3.7</td>
</tr>
<tr>
<td>Use of vancomycin</td>
<td>0.13</td>
<td>2.3</td>
<td>2.2 0.8–5.9</td>
</tr>
<tr>
<td>Use of piperacillin-tazobactam</td>
<td>0.53</td>
<td>0.4</td>
<td>0.7 0.3–1.9</td>
</tr>
</tbody>
</table>

**RESULTS**

Epidemiological and microbiological characteristics

Following the identification of the index case of VRE on a hematology-ondcology ward, 33 patients who had been hospitalized on 10 wards were further identified between February 28, 2005, and May 27, 2005 (Figure 1). No new VRE cases were identified in the last 30 days of the outbreak. Intensified outbreak screening and time-course analysis indicated that the majority of VRE-positive patients (29 of 34 [85%]) were identified between days 19 and 41 of the outbreak. Of the over 1800 potential contacts, most had already been discharged. The one-third remaining in hospital were screened for VRE colonization. There were no episodes of clinical infection in patients colonized with VRE, and all cases were identified as ‘VRE carriers’ from culture or, in cases of time constraint, by polymerase chain reaction of either rectal swabs or stool samples. All VRE isolates were identified as E faecium and were shown to carry the vanA resistance determinant. Strain typing of VRE by PFGE detected a single clone associated with all patients.
Environment findings

The only environmental site from which VRE were detected (one of 192) was the surface of a video game system in the playroom of an affected ward. The VRE strain isolated from the video game was indistinguishable from 29 patient strains by PFGE, and was closely related (two-band difference) to the remaining patient strains.

Case-control matching and univariate analysis

Case-control matching was possible for 33 of 34 cases of VRE colonization. Using univariate analysis, significant risk factors that were identified included the use of antibiotics for more than four days, the use of trimethoprim-sulfamethoxazole, stay on one ward which had the highest incidence of VRE cases, having undergone IGT and the use of any cephalosporin (Table 1).

Multivariate analysis

Multivariate ANOVA indicated that VRE colonization was predominantly associated with the use of any cephalosporin (P=0.03, $\chi^2=5.0$, OR=3.1, OR 95% CI 1.1 to 8.3). Multivariate ANOVA did not find an association between VRE and antibiotic use of more than four days (P=0.09, $\chi^2=2.2$, OR=2.6, OR 95% CI 0.7 to 9.3), or having undergone IGT (P=0.14, $\chi^2=2.2$, OR=2.6, OR 95% CI 0.7 to 9.3).

DISCUSSION

The present study is the first published description of a VRE outbreak investigation in a Canadian pediatric acute care institution, although reports in children’s hospitals have been reported worldwide. Similar to this outbreak, which was first identified in a hematology-oncology population, most previously described outbreaks and surveillance studies of VRE in pediatric hospitals have identified hematology-oncology patients as key reservoirs of VRE; reports of outbreaks in children in neonatal intensive care units have also been reported (4,5,11,12). For example, following the introduction of surveillance screening in the United Kingdom, Gray and George (4) found colonization with VRE in 38.3% of hematology-oncology patients and in 11.1% of hepatology-gastroenterology patients, but in only 2.3% of children in the pediatric intensive care unit and 1.5% of children in the renal unit. Other characteristics of the outbreak described here are similar to those previously reported in terms of risk factors, duration, number of patients involved and the use of control measures.

Pediatic VRE outbreaks in other institutions have been associated with antibiotic use; for example, one outbreak of 14 patients (19% of those screened) on an oncology ward was associated with prolonged treatment with cisplatin, ceftazidime or amikacin (5). In this report, the authors identified cephalosporin use as the key risk factor for VRE colonization. It is postulated that cephalosporin use may give VRE a selective advantage in the intestinal tract, thereby increasing the load of VRE that is transmitted between patients either by inanimate objects or the hands of health care workers (13). Findings like this have led to the idea that antibiotic stewardship may play a role in limiting the spread of VRE in hospitals by controlling antibiotic prescribing and/or the class of antibiotics used (13). However, this remains unproven, as does the hypothesis that certain antibiotics may actually be used to prevent a selective advantage for VRE colonization (14).

Other outbreaks in pediatric institutions have described much heavier environmental contamination than we observed in our outbreak (ie, 25% to 70% of samples testing positive) (4,5). If the environment was an important factor in transmission in our study, we might have missed the heavily contaminated areas due to the commencement of enhanced cleaning by the time environmental screening was performed. Alternatively, mobile or shared elements, such as the video game system, might have played a larger role in our outbreak than in others. Previous studies indicated that VRE can survive for prolonged periods of time on inanimate surfaces (15), and that occupancy of an environment previously used to house a VRE-positive patient is a risk factor for VRE acquisition (6). Thus, environmental decontamination is important in controlling outbreaks of VRE. In one study (5), the use of stringent infection control measures successfully reduced environmental contamination rates from 25% of samples in week 1 to none in week 11, which was the length of time it took to control the outbreak. Although the impact of individual control measures in our outbreak was not formally evaluated, the use of active surveillance, enhanced infection control measures and molecular testing were in line with previously reported efforts to control VRE outbreaks, and were clearly successful in ours (5,16,17).
Since our investigation, patients admitted to the hematology-oncology ward are actively screened for VRE and isolated with contact precautions if positive. We have had no evidence of further nosocomial spread of colonized patients admitted to hospital and no further outbreaks. Good antibiotic stewardship and judicious antibiotic use is reinforced by our institution’s antibiotic utilization committee. Currently, in the course of housekeeping and environmental disinfection, particular attention is paid to frequently touched surfaces and objects, including mobile toys and games. In a pediatric setting, the latter are of particular importance because despite policies to the contrary, it is hard to control access to these highly desired objects.

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