Background

- Vancomycin-resistant enterococci (VRE) account for approximately 30% of all enterococcal healthcare-associated infections.
- Patients with acute myeloid leukemia (AML) are at risk of colonization and infection with VRE.
- Additional risk factors for VRE colonization that are often present in patients with malignancies include: use of high-dose corticosteroids, carbapenem and cephalosporin antibiotics, diarrhea, and prolonged hospital length of stay.
- Vancomycin has not been consistently reported as a risk factor for colonization/infection with VRE, yet current Infectious Diseases Society of America guidelines recommend judicious use of vancomycin in patients with febrile neutropenia to curb the development of bacterial resistance.

Methods

Study Design

Retrospective cohort study

Study Population

Adult patients who received initial induction chemotherapy with cytarabine plus idarubicin in a 7+3 schema between 1 January 2012 and 31 December 2015 and who had at least two VRE rectal swabs or cultures taken during their admission, with the VRE rectal swab being the first one being negative.

Objectives

Primary: Evaluate potential risk factors associated with VRE colonization.
Secondary: Assess the impact of VRE rectal swab positivity on subsequent VRE infection.

Definitions

VRE colonization: discovery of VRE from any site in patients colonized with VRE, in the presence of clinical features of infection requiring treatment.

VRE colonization

- VRE rectal surveillance swabs per patient
- Time to VRE colonization
- Number of inductions
- Gender

Table 2. Risk Factors Associated with Faster Time to VRE Colonization

<table>
<thead>
<tr>
<th>Factor</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.002</td>
<td>0.811</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.922</td>
<td>0.049</td>
</tr>
<tr>
<td>Year of admission</td>
<td>0.964</td>
<td>0.651</td>
</tr>
<tr>
<td>Number of inductions</td>
<td>1.216</td>
<td>0.430</td>
</tr>
<tr>
<td>Positive Clostridium difficile nucleic acid test during admission</td>
<td>1.345</td>
<td>0.313</td>
</tr>
<tr>
<td>Cerillen neutropenia during admission</td>
<td>1.285</td>
<td>0.575</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>0.968</td>
<td>0.568</td>
</tr>
<tr>
<td>Vancomycin IV</td>
<td>1.567</td>
<td>0.021</td>
</tr>
<tr>
<td>Vancomycin PO</td>
<td>1.243</td>
<td>0.635</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>1.611</td>
<td>0.007</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>0.755</td>
<td>0.377</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>1.219</td>
<td>0.338</td>
</tr>
<tr>
<td>Carbapenem</td>
<td>1.437</td>
<td>0.439</td>
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</table>

Table 1. Characteristics of included patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>Overall (n=229)</th>
<th>VRE negative (n=195)</th>
<th>VRE positive (n=34)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60 (18-82)</td>
<td>61 (21-75)</td>
<td>59 (18-82)</td>
<td>0.660</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>117 (51)</td>
<td>104 (53)</td>
<td>13 (38)</td>
<td>0.022</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>4 (1-10)</td>
<td>4 (1-9)</td>
<td>4 (1-10)</td>
<td>0.415</td>
</tr>
<tr>
<td>Duration of neutropenia</td>
<td>3 (0-12)</td>
<td>3 (1-7)</td>
<td>7 (12-14)</td>
<td>0.151</td>
</tr>
<tr>
<td>Positive Clostridium difficile nucleic acid test during admission, n (%)</td>
<td>3 (0-12)</td>
<td>0 (0-0)</td>
<td>1 (29)</td>
<td>0.051</td>
</tr>
<tr>
<td>Length of stay, median (range)</td>
<td>33 (1-142)</td>
<td>31 (8-152)</td>
<td>33 (14-156)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Figure 1. Patient Sample

Adult patients admitted for intensive induction chemotherapy with 7+3 between January 2012 and December 2015, n = 296.

VRE colonization

- VRE rectal surveillance swabs per patient
- Time to VRE colonization
- Number of inductions
- Gender

Figure 2. Distribution of VRE colonization

Figure 3. Cumulative incidence of patients with VRE colonization

PRYMARY OBJECTIVE

- Overall, VRE infection developed in 14% (33/229) of patients; 82% (27/33) VRE bacteremia.
- Eleven percent (26/229) of patients received additional risk factors for VRE colonization that are often present in patients with malignancies.
- Time to VRE colonization: Alive with no evidence of leukemia.
- Acute myeloid leukemia (AML)*
- Other/unknown
- Ninety percent (96/229) of patients received metronidazole. The median duration was 13 (1-43) days.
- Six percent (14/229) of patients received a fluoroquinolone. The median duration was 6 (1-65) days.
- Forty-two percent (96/229) of patients received metronidazole. The median duration was 13 (3-94) days.
- Eleven percent (26/229) of patients received a carbapenem. The median duration was 9 (1-48) days.

Figure 5. Cumulative Hazard of becoming colonized with VRE calculated by the Nelson-Aalen Method

A. C. faecalis, B. W Vancomycin

SECONDARY OBJECTIVE

- Overall, VRE infection developed in 14% (33/229) of patients; 82% (27/33) VRE bacteremia.
- The incidence of VRE infection was 20% (25/126) in patients colonized with VRE, contrasted with 8% (8/103) in patients without prior VRE colonization, (p<0.01).

Figure 6. Cumulative incidence of patients with VRE infection

Conclusions

- Intravenous vancomycin utilization has important clinical implications on the development of VRE colonization, particularly given the confirmed association between VRE colonization and VRE infection.
- Judicious prescribing of intravenous vancomycin as outlined in IDSA guidelines should be practiced in an effort to reduce the development of VRE.

References