Empiric Vancomycin Use in Febrile Neutropenic Oncology Patients

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Vancomycin is commonly added as empiric therapy for febrile neutropenia. A retrospective chart review was conducted at a large community teaching institution to evaluate vancomycin use in oncology patients. The results revealed that a majority of empiric vancomycin therapy was inappropriate, raising concern for antibiotic resistance and prompting opportunities for improvement.

Keywords. febrile neutropenia; oncology; vancomycin; empiric; antibiotics.

Vancomycin is a glycopeptide antibiotic that is one of the most widely used antibiotics in the United States for treatment of methicillin-resistant Staphylococcus aureus (MRSA) [1]. Neutropenic fever in oncology patients is a medical emergency in which Gram-positive organisms are the predominant bacterial pathogens. Febrile neutropenia (FN) requires rapid administration of empiric antibiotic therapy; however, studies do not support the addition of vancomycin to the initial antibiotic regimen in all patients [2]. The Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America (IDSA) stated 7 specific criteria for the appropriate use of empiric vancomycin, which include instances that a Gram-positive infection should be suspected. Despite this update, vancomycin use continues to be widespread and often inappropriate [3].

The results of a large, retrospective study assessing compliance with guideline-based recommendations for FN in cancer patients over the last decade indicated that patients at teaching hospitals that treat ≥14.6 cases of FN per year were more likely to adhere to guideline-based recommendations [4]. The authors also concluded that empiric vancomycin, administered in 36.9% of patients, did not improve patient outcomes, which is consistent with previous literature [2]. Likewise, the aim of this study was to assess the appropriateness of vancomycin therapy in oncologic FN patients at a large, community teaching hospital.

METHODS

Study Design and Patient Population

A retrospective, systematic review of patient medical records from November 1, 2010 to November 1, 2012 at a large, community teaching hospital was conducted to assess appropriateness of indication and duration of therapy according to current IDSA guidelines in adult cancer patients with a diagnosis of FN [3]. Patients included in the study were 18 years of age or older, and they had an inpatient stay ≥72 hours. These patients were also diagnosed with FN, and their initial empiric treatment included vancomycin. The IDSA definition of FN was used to identify patients: an absolute neutrophil count (ANC) <1000 cells/mm³ or expected to decrease to <500 cells/mm³ within 48 hours and a temperature >38.3°C (101°F) or a sustained temperature >38°C (100.4°F) for at least 1 hour [3]. The authors concluded that if patients required in-patient admission for their FN, their ANC would likely drop below 500 cells/mm³ if not already below 500 on admission.

We considered evidence of at least 1 of the following: hemodynamic instability or other evidence of severe sepsis, assessed according to the 2012 Surviving Sepsis Guidelines; pneumonia documented radiographically; positive blood culture for Gram-positive bacteria before final identification and susceptibility testing if available; clinically suspected, serious, catheter-related infection; skin or soft-tissue infections at any site; known colonization with MRSA or penicillin-resistant Streptococcus pneumoniae; or severe mucositis if fluoroquinolone prophylaxis had been given and cefazidime had been used as empirical therapy, as an appropriate indication for empiric vancomycin therapy [3, 5].

Of the patients determined to have an appropriate indication, as outlined above, appropriate duration of vancomycin was assessed, defined as either discontinuation of vancomycin within 3 days of therapy if the patient did not have evidence of Gram-positive bacteria in the blood or continuation with a “clinically appropriate” indication. Group consensus determined clinically appropriate indications and included cases of persistent fever, symptoms of...
Table 1. Distribution of Appropriate Vancomycin Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Hemodynamic instability or other evidence of severe sepsis</td>
<td>37%</td>
</tr>
<tr>
<td>Clinically suspected, serious, catheter-related infection</td>
<td>15%</td>
</tr>
<tr>
<td>Positive blood culture for Gram-positive bacteria before final identification and susceptibility testing if available</td>
<td>11%</td>
</tr>
<tr>
<td>Known colonization with MRSA or penicillin-resistant Staphylococcus aureus</td>
<td>11%</td>
</tr>
<tr>
<td>Pneumonia documented radiographically</td>
<td>8%</td>
</tr>
<tr>
<td>Skin or soft-tissue infections at any site</td>
<td>7%</td>
</tr>
<tr>
<td>Severe mucositis if fluoroquinolone prophylaxis had been given and ceftazidime had been used as empirical therapy</td>
<td>0%</td>
</tr>
<tr>
<td>Multiple indications</td>
<td>11%</td>
</tr>
</tbody>
</table>

Abbreviations: MRSA, methicillin-resistant Staphylococcus aureus.

Table: The table shows the distribution of appropriate vancomycin indications among oncologic FN patients at a large, community teaching hospital. The primary outcome was appropriateness of indication and duration, and the secondary outcome was appropriateness of initial dosing regimen.

Results: From November 1, 2010 to November 1, 2012, 128 adult cancer patients were evaluated. The secondary outcome was to evaluate appropriateness of the initial vancomycin-dosing regimen based on a dose of 15–20 mg/kg (actual body weight) given every 8–12 hours for patients with normal renal function. The purposes of data collection were to determine whether a patient exhibited hemodynamic instability or other evidence of severe sepsis. The distribution of appropriate indications across the study population is displayed in Table 1. Eighteen patients were found to have both appropriate indication and appropriate duration (27.3%) in accordance with IDSA guidelines. Results from the secondary outcome showed that the initial dosing regimen for vancomycin was appropriate in 40 patients (60.6%).

Discussion: We found that the majority of empiric vancomycin therapy in oncologic FN patients at a large, community teaching hospital was inconsistent with current IDSA guidelines because vancomycin use was appropriate in only 27.3% of cases. In comparison, the results of a similar study illustrated that empiric vancomycin was used appropriately in 67% of FN patients. In our study, we found a considerably lower rate of appropriate therapy, which is concerning. Consequently, inappropriate vancomycin use may have deleterious effects such as the development of vancomycin-resistant Enterococcus (VRE). Acquisition of VRE has been associated with prolonged or repeated hospitalization, repeat use of broad-spectrum antibiotics, and neutropenia. Vancomycin-resistant Enterococcus is an independent risk factor for mortality in neutropenic patients, thus prevention of VRE in oncology patients is important and can be decreased through judicious use of vancomycin.

One of the limitations of this study was that the data were collected from only 1 institution and is not representative of care across the country. The primary outcome was appropriateness of indication and duration, and the secondary outcome was appropriateness of initial dosing regimen. The primary outcome was appropriateness of indication and duration, and the secondary outcome was appropriateness of initial dosing regimen.
prematurely added onto empiric antibiotic therapy in FN patients. In light of acquiring VRE through repeated exposure to vancomycin and the increased mortality associated with VRE [11], vancomycin use should be reserved only in those patients who exhibit indications for its use according to the IDSA guidelines [3].

Notes

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Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References