**Vancomycin versus daptomycin for the treatment of confirmed gram-positive catheter-related bloodstream infections in oncology patients**

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**Objective:** To analyse the effectiveness and safety of daptomycin versus vancomycin on the management catheter-related bloodstream infections in oncology patients.

**Method:** A retrospective study was carried out including all patients admitted at the Medical Oncology Unit between 2010 and 2018 with positive blood cultures confirmed catheter-related bloodstream infections due to gram-positive microorganism, who were treated with either vancomycin or daptomycin. The primary end point was all cause 30-days mortality, 30-days hospital readmission and length of hospital stay (length of hospital stay).

**Results:** A total of 70 patients with catheter-related bloodstream infections were included in the present study: vancomycin was administered to 61.4% (n = 43) and daptomycin to 38.6% (n = 27) of patients. 78.5% (n = 55) of isolated bacteria showed a vancomycin minimum inhibitory concentration ≤ 1 μg/ml. No differences were observed between the two groups of patients regarding the 30-day mortality rate.

**Keywords**
Daptomycin; Vancomycin; Bloodstream infections; Central venous catheter.

**How to cite this paper**

**Resumen**
**Objetivo:** Analizar la eficacia y seguridad de la daptomicina frente a la vancomicina en el tratamiento de las infecciones del torrente sanguíneo asociadas a catéter vascular en pacientes oncológicos.

**Método:** Se realizó un estudio retrospectivo que incluyó a los pacientes ingresados en la Unidad de Oncología Médica entre 2010-2018 con infección del torrente sanguíneo asociada a catéter vascular confirmada por microorganismos gram-positivos, que fueron tratados con vancomicina o daptomicina. Como objetivos principales se determinaron la tasa de mortalidad por todas las causas a los 30 días, el reingreso hospitalario a los 30 días y la duración de la estancia hospitalaria.

**Resultados:** El estudio incluyó 70 pacientes con infecciones del torrente sanguíneo asociadas a catéter vascular: el 61.4% (n = 43) recibió vancomicina y el 38.6% (n = 27) daptomicina. El 78.5% (n = 55) de las bacterias aisladas mostraron una concentración mínima inhibitoria de vancomicina ≤ 1 μg/ml. No se observaron diferencias entre ambos grupos de pacientes en cuanto a la tasa de mortalidad a 30 días (32.6% [n = 14]).

**Palabras clave**
Daptomicina; Vancomicina; Bacteriemia; Catéter venoso central.
strains that show diminished susceptibility to vancomycin. treatment infections, in particular at hospital centres with a low prevalence of their safety and effectiveness. Therefore, vancomycin should continue Conclusions: Our results show that both antibiotics are equivalent in their safety and effectiveness. Therefore, vancomycin should continue being the treatment of choice for gram-positive catheter-related bloodstream infections, in particular at hospital centres with a low prevalence of strains that show diminished susceptibility to vancomycin.

Introduction

Central venous catheters (CVC) are frequently used to administer antitumor treatments in oncology patients. However, its usage is not without complications, mainly due to catheter-related bloodstream infections (CRBSI) which have associated mortality of approximately 1225%3,6. There are frequently produced by gram-positive bacteria (25%)1. Furthermore, since 80% of coagulase-negative Staphylococcus (CNS) strains are meticillin-resistant and the increase in the prevalence of resistant Staphylococcus aureus to meticillin (MSSA), vancomycin and daptomycin are the treatment of choice for CRBSI2,4,5. Even though both antibiotics have shown to be effective in the treatment of CRBSI, to date, there are only a small number of comparative studies addressing its effectiveness and safety6.

This study aims to analyse the effectiveness and safety of daptomycin versus vancomycin on CRBSI in patients with solid tumors in routine clinical practice.

Methods

Study design and patient selection criteria

This retrospective study evaluated the effectiveness and safety of vancomycin, compared with that of daptomycin in patients with solid tumors with gram positive CRBSI. Oncologist Subjects with gram positive CRBSI who were hospitalized over 6 years period (2010-2018) at a 822-bed tertiary care hospital in Tenerife, Spain, were eligible for inclusion. Eligible patients were aged ≥ 18 years with solid tumor with Gram-positive CRBSI, without a source for the bacteremia other than the CVC who were treated either vancomycin or daptomycin. Empirical therapy was considered when an antimicrobial regimen was administered within 24 hours of extraction of the blood sample, and before susceptibility was known. Patients received vancomycin or daptomycin according to treating clinician preference.

Patients were ineligible if they had any one of the following: patients with hematologic malignancies, neutropenic patients, no etiological agent identified or confirmed Gram-negative CRBSI. Patients in whom the antibiotic treatment was modified were excluded.

Because of the retrospective observational design of the study, neither patient consent nor ethics approval was required at the time the study was carried out.

Clinical variables evaluated

The study outcome was evaluated considering: demographic data and Charlson Comorbidity Index, which provides a general measure of severity of disease7. Antibiotic dose, frequency, and duration were recorded. To evaluate safety, nephrotoxicity was defined as an increase in the serum creatinine level of 0.5 mg/dl or 50%, whichever was greater, on at least two consecutive measurements from the initiation of antibiotic to 3 days after treatment8. Creatine phosphokinase values were evaluated in daptomycin treated subjects. A clinically significant elevation was defined as 5 times the upper limit of normal (ie, 0 850 U/L).

Antibiotic sensitivities were confirmed by broth microdilution, according to the Clinical and Laboratory Standards Institute (CLSI) guidelines9. Clinical categories were determined according to the breakpoints defined by the European Committee on Antimicrobial Susceptibility testing (EUCAST) criteria10 and CVC were removed in patients documented CRBSI due to S. aureus.

Definitions and outcome assessment

CRBSI was classified according to the current Infectious Diseases Society of America (IDSA) criteria guidelines11. The primary end point, was defined as a composite of 30-day mortality rate (M30), the re-admission rate at 30 days (R30) and the length of hospital stay (LOS). 30-day mortality was defined as mortality occurring in the 30-day period following index culture, and the R30 as the re-admission of the patient caused for any reason within the 30 days of index culture.

Statistical analysis

Statistical analysis was conducted using the Chi-squared test for the comparison between M30 and R30 from both therapeutic groups with SPSS Statistics v. 25.0 software (IBM Corporation, Armonk, NY, USA). To study the nephrotoxicity from the different groups the Chi-squared test was also the comparison between M30 and R30 from both therapeutic groups with SPSS for the dichotomous variables and alternatively using a Chi-Squared for the dichotomous variables. The statistical significance was established as p < 0.05.

Results

Demographic characteristics of the study population

A total of 558 cancer patients with an episode of suspected of CRBSI were treated with either vancomycin or daptomycin. Among them, 70 met the inclusion criteria, 47.1% (n = 33) were male and their average age 579 years old (standard deviation [SD] = 11.5). The 61.4% (n = 43) of these patients received vancomycin and the 38.6% (n = 27) daptomycin as a treatment.

The baseline characteristics of the two groups are presented in table 1; there were no significant differences in baseline characteristics between the two groups, differing only in the percentage of infections caused by the meticillin-susceptible Staphylococcus aureus (MSSA) which was higher in the group of patients treated with daptomycin (33.3% [n = 9] versus 11.6% [n = 5]; p = 0.0271) (Table 2).

The pharmacokinetic monitoring of vancomycin plasma concentrations was determined only in the 23.3% [n = 10] of the patients (average dose: 1.41 mg/kg/12 h; interquartile range [IQR]: 1.819±6). The average daily dose of daptomycin was 568.7 mg (average dose: 7.43 mg/kg/day; IQR: 4.212±3).

Effectiveness evaluation

No differences were observed at the M30 between patients treated with vancomycin and daptomycin (32.6% [n = 14] versus 29.6% [n = 8], respectively [p = 0.797]) (Figure 1). Additionally, no differences were found
Vancomycin versus daptomycin for the treatment of confirmed gram-positive catheter-related bloodstream infections in oncology patients

Table 1. Patient demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Vancomycin group (n = 43)</th>
<th>Daptomycin group (n = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>58.1 (10.2)</td>
<td>57.5 (13.5)</td>
<td>0.604</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>21 (48.8)</td>
<td>12 (44.4)</td>
<td>0.720</td>
</tr>
<tr>
<td>Charlson comorbidity index, mean (IQR)</td>
<td>8.5 (2-12)</td>
<td>8.8 (3-16)</td>
<td>0.256</td>
</tr>
<tr>
<td>Acute kidney injury, n (%)</td>
<td>3 (7.0)</td>
<td>2 (7.4)</td>
<td>0.946</td>
</tr>
<tr>
<td>Duration of therapy in d, median (IQR)</td>
<td>11.12 (2-21)</td>
<td>8.41 (2-17)</td>
<td>0.060</td>
</tr>
<tr>
<td>Total hospital LOS in d, mean (SD)</td>
<td>18.9 (3-74)</td>
<td>16.5 (4-81)</td>
<td>0.562</td>
</tr>
</tbody>
</table>

Table 1: Number of days; IQR: interquartile range; LOS: length of stay; N: number of patients; SD: standard deviation.

Safety assessment

Nephrotoxicity rate was similar in both groups of treatment: 7% (n = 3) of the patients treated with vancomycin versus 7.4% (n = 2) of the daptomycin group (p = 0.946) (Table 1). One patient treated with vancomycin suffered kidney failure and two developed kidney injury. In the case of dap-

Figure 1. All causes 30-day mortality vancomycin versus daptomycin.

Figure 2. Rate of 30-days hospital readmission.

Table 2. Characteristics of the microorganisms causing central intravascular catheter infections

<table>
<thead>
<tr>
<th></th>
<th>All (n = 70)</th>
<th>Vancomycin group (n = 43)</th>
<th>Daptomycin group (n = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative pathogen, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>4 (5.7)</td>
<td>4 (9.3)</td>
<td>0</td>
<td>0.103</td>
</tr>
<tr>
<td>MSSA</td>
<td>14 (20.0)</td>
<td>5 (11.6)</td>
<td>9 (33.3)</td>
<td>0.027</td>
</tr>
<tr>
<td>MR-CNS</td>
<td>30 (42.9)</td>
<td>18 (41.8)</td>
<td>12 (44.4)</td>
<td>0.832</td>
</tr>
<tr>
<td>MS-CNS</td>
<td>17 (24.3)</td>
<td>12 (27.9)</td>
<td>5 (18.5)</td>
<td>0.373</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>5 (7.1)</td>
<td>4 (9.3)</td>
<td>1 (3.7)</td>
<td>0.376</td>
</tr>
</tbody>
</table>

Table 2: Vancomycin MIC, n (%) |

<table>
<thead>
<tr>
<th></th>
<th>≤ 0.5 μg/mL</th>
<th>1 μg/mL</th>
<th>2 μg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin MIC, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 0.5 μg/mL</td>
<td>18 (25.7)</td>
<td>13 (30.2)</td>
<td>5 (18.5)</td>
</tr>
<tr>
<td>1 μg/mL</td>
<td>37 (52.8)</td>
<td>22 (51.2)</td>
<td>15 (55.5)</td>
</tr>
<tr>
<td>2 μg/mL</td>
<td>15 (21.4)</td>
<td>8 (18.6)</td>
<td>7 (27.9)</td>
</tr>
</tbody>
</table>

MIC: minimum inhibitor concentration; MR-CNS: meticillin-resistant coagulase-negative staphylococci; MRSA: meticillin-resistant Staphylococcus aureus; MS-CNS: meticillin-susceptible coagulase-negative staphylococci; MSSA: meticillin-susceptible Staphylococcus aureus; n: number of patients.
tomycina, dos pacientes presentaron lesión renal. No se presentó una significativa elevación de la creatinfosfokinasa en nuestro grupo de pacientes.

**Discusión**

Fue estudiada la comparación directa entre vancomicina y daptomicina en el tratamiento de bacteriemias. Además, se recogieron datos sobre las dosis terapéuticas de vancomicina en la mayor parte de los casos y se estableció que se puede utilizar un régimen terapéutico eficaz y seguro para la mayoría de los pacientes.

El objetivo principal de este estudio es demostrar la eficacia y seguridad de la daptomicina en el tratamiento de bacteriemias. En este estudio, se analizó la eficacia y seguridad de la daptomicina en un grupo de pacientes con bacteriemias. Se obtuvieron resultados controversiales, pero se consideró que la daptomicina es una opción viable para el tratamiento de bacteriemias.

**Funding**

No funding.

**Conflict of interest**

No conflicts of interest.

**Contribution to the scientific literature**

En este estudio, se analizó la eficacia y seguridad de la daptomicina en el tratamiento de bacteriemias. Se obtuvieron resultados controversiales, pero se consideró que la daptomicina es una opción viable para el tratamiento de bacteriemias.