Therapeutic drug monitoring of vancomycin in a patient with Duchenne muscular dystrophy (DMD): A case report

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Vancomycin is widely used glycopeptide antibiotic that requires therapeutic drug monitoring (TDM) owing to its narrow therapeutic window. It is primarily eliminated by renal excretion; thus, estimating the renal function of a patient is vital in the TDM of vancomycin. In patients with Duchenne muscular dystrophy (DMD), it is difficult to estimate the glomerular filtration rate using the serum creatinine level owing to the pathophysiological nature of the disease. Here, we report a case of a patient in whom TDM of vancomycin was performed, and explore the appropriate methods for evaluating renal function in patients with DMD based on serum levels of creatinine and cystatin C.

CASE REPORT

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Case report

A 25-year-old male patient (height: 176 cm, body weight: 42 kg, body surface area (BSA): 1.43 m²) with a 5-day history of fever, sputum, and chest pain was admitted to Seoul National University Hospital (SNUH) for suspected ventilator-associated pneumonia (VAP).

A diagnosis of DMD was made in 2003, and the patient also had dilated cardiomyopathy. On admission, it was noted that he had been receiving enalapril, digoxin, carvedilol, and sildenafil.

On physical examination, the patient was found to have a fever (temperature of 38.1°C [100.6°F]), decreased lung sounds in the right lower lung field, and crackles in dependent lungs. Initial clinical laboratory tests results were as follows: WBC count, 8.67 × 10⁹/μL (77.4% neutrophils, 12.8% lymphocytes, and 0.6% eosinophils); blood urea nitrogen level, 7 mg/dL; serum creatinine level, 0.18 mg/dL; serum high-sensitive C-reactive protein level, 8.73 mg/dL; and serum albumin level, 3.3 g/dL. The results of
the urine and stool cultures were negative. The clinician began
the treatment with vancomycin 630 mg IV q6h and meropenem
800 mg IV q8h for VAP in the intensive care unit.

To prevent toxicity caused by vancomycin, TDM was con-
ducted. For TDM, a blood sample was obtained to measure the
serum vancomycin concentration just before the 5th dosing. The
observed serum vancomycin concentration was 20.4 μg/mL.
The estimated GFR calculated using the Cockcroft-Gault equa-
tion based on the initial serum creatinine level of the patient
(0.18 mg/dL) was 372.7 mL/min.[11] Based on this GFR, the
predicted trough serum vancomycin concentration at steady
state was 16.7 μg/mL, which was significantly lower than the
corresponding observed value. Owing to this discrepancy, an
inverse calculation was performed using the observed serum
vancomycin concentration value, and the calculated GFR value
was approximately 70 mL/min. Assuming that this inversely
calculated GFR was similar to the actual GFR of the patient,
to achieve a trough serum vancomycin concentration of 15.0 μg/
mL at steady state, the dosing regimen was adjusted to vanco-
mycin 630 mg IV q8h. The vancomycin treatment was stopped
two days after the TDM, and the patient was discharged because
of general condition recovery; hence, no further TDM was con-
ducted.

Pharmacokinetic calculations were conducted using the
ABBOTTBASE® Pharmacokinetic Systems software (version
1.10, Abbott Laboratories, Abbott Park, IL, USA).

Discussion

The estimated GFR of the DMD patient based on the serum
creatinine level was overestimated, and this overestimation
resulted in a significantly lower predicted serum vancomycin
concentration compared to the observed serum vancomycin
centration. This case indicates that the adjustment of the
vancomycin dose according to the estimated GFR using the se-
rum creatinine level may not be appropriate in DMD patients.
The ideal endogenous marker of GFR should be produced at a
constant rate, and be primarily eliminated by glomerular filtra-
tion and not reabsorbed or secreted.[3,6] Cystatin C has been
recognized as a promising endogenous marker of GFR. Cys-
tatin C is a non-glycated basic protein, which is produced by all
nucleated cells at a constant rate. It is freely filtered in the glom-
erulus, and does not undergo tubular secretion and undergoes
only limited extra-renal elimination.[7]

The equations most widely used to estimate the GFR using the

<table>
<thead>
<tr>
<th>Equation</th>
<th>GFR (mL/min)</th>
<th>Serum vancomycin concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cockcroft-Gault equation</strong>[11]**</td>
<td>372.7</td>
<td>16.7</td>
</tr>
<tr>
<td><strong>Schwartz equation</strong>[12]**</td>
<td>684.42</td>
<td>16.1</td>
</tr>
<tr>
<td><strong>Simplified MDRD equation</strong>[13]**</td>
<td>701.22</td>
<td>16.0</td>
</tr>
<tr>
<td><strong>CKD-EPI creatinine equation</strong>[14]**</td>
<td>229.22</td>
<td>17.8</td>
</tr>
<tr>
<td><strong>Larsson et al.[8]</strong></td>
<td>77.239</td>
<td>20.0</td>
</tr>
<tr>
<td><strong>Tan et al.[10]</strong></td>
<td>87.1</td>
<td>6.37</td>
</tr>
<tr>
<td><strong>Grubb A et al.[9]</strong></td>
<td>87.62</td>
<td>19.6</td>
</tr>
<tr>
<td><strong>CKD-EPI cystatin C equation</strong>[14]**</td>
<td>89.52</td>
<td>20.1</td>
</tr>
</tbody>
</table>

*GFR: Glomerular Filtration Rate, DMD: Duchenne Muscular Dystrophy. \(^{1}\)k = 0.33 if infant (low birth weight <1 year), 0.45 if (term <1 year), 0.55 if child or adolescent girl, and 0.70 if adolescent boy; 0.70 was used in this case. \(^{2}\)Unit: mL/min/1.73 m\(^2\).
serum creatinine level are the Cockcroft-Gault equation, the Schwartz equation, the simplified Modification of Diet in Renal Disease Study (MDRD) equation, and the Chronic Kidney Disease Epidemiology (CKD-EPI) creatinine equation.[11-14] Further, cystatin C-based equations have been applied to estimate GFR, such as those published by Larsson A et al., Grubb A et al., and Inker LA et al.[6,8-10,14] To determine appropriate methods for estimating renal function, GFRs were calculated using various equations by applying the initial serum creatinine level (0.18 mg/dL) and the latest measured serum cystatin C level (1.0 mg/L) of the patient. The corresponding predicted serum vancomycin concentrations of each estimated GFRs were compared with the observed serum vancomycin concentration (Table 1). All of the creatinine-based equations overestimated the patient’s renal function. On the other hand, the cystatin C-based equations allowed relatively closer prediction of the GFR compared to the corresponding values from the serum creatinine-based equations (Table 1).

In DMD patients, estimating the GFR using the serum creatinine level may be difficult owing to the muscle degenerative nature of the disease.[4] To conduct effective TDM of vancomycin in DMD patients, cystatin C can be considered as an alternative endogenous marker of renal function. It should be noted that our attempt to find an appropriate method to estimate the renal function of DMD patients, by comparing creatinine-based equations and cystatin C-based equations, was based on one patient. Further cases should be investigated to determine whether cystatin C-based equations are more appropriate in estimating renal function of DMD patients. Moreover, the use of cystatin C as an alternative endogenous marker of renal function in DMD patients should be investigated with other drugs that are also primarily eliminated via the renal route.

Conflict of interest

The that there is no conflict of interest regarding the publication of this paper.

References