THERAPEUTIC DRUG MONITORING OF VORICONAZOLE

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BACKGROUND

Voriconazole presents a high pharmacokinetic variability that results in a significant variability in steady-state trough concentrations (C\textsubscript{trough}). Also, it shows a narrow therapeutic range. That’s why therapeutic drug monitoring (TDM) is recommended.

PURPOSE

1. To describe plasma voriconazole concentrations (PVC) of an adult cohort treated in a tertiary university hospital.
2. To identify potential causes of interpatient variability in C\textsubscript{trough} and find an association between PVC and clinical outcomes and/or adverse events (AE).

MATERIAL AND METHODS

- Observational retrospective study. All patients with an observed PVC during 2017 were included.
- Data was obtained from the electronic medical records.

RESULTS

PATIENTS
- 51 patients (60.8% men)
- Median age: 65.2 years (54.5-71.3)
- Median weight: 70.0 kg (62.0-81.0)
  - 19.6% BMI>30 kg/m\textsuperscript{2}
  - 11.8% with drinking history
  - 1 patient with liver failure

VORICONAZOLE
- 165 C\textsubscript{trough}
  - Median drug dose: 5.8 mg/kg (4.9-6.6)
  - Median duration: 62.0 days (20.5-141.5)
  - 45.0% cases co-medication with steroids
  - 1 drug-drug interaction (rifampin)

VORICONAZOLE TREATMENT INDICATION

<table>
<thead>
<tr>
<th>Indication</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Invasive aspergillosis</td>
<td>80.4%</td>
</tr>
<tr>
<td>Candidemia</td>
<td>9.8%</td>
</tr>
<tr>
<td>Prophylaxis of invasive fungal infections in high risk allogeneic hematopoietic stem cell transplant recipients</td>
<td>2.0%</td>
</tr>
<tr>
<td>Other indications</td>
<td>9.8%</td>
</tr>
</tbody>
</table>

REASONS FOR DISCONTINUATION

<table>
<thead>
<tr>
<th>Reason</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure</td>
<td>30.9%</td>
</tr>
<tr>
<td>Drug-related adverse events</td>
<td>16.4%</td>
</tr>
<tr>
<td>Exitus or limitation of therapeutic effort</td>
<td>14.5%</td>
</tr>
<tr>
<td>Negative culture in empiric therapy</td>
<td>12.7%</td>
</tr>
<tr>
<td>Switch to another antifungal due to therapeutic failure / poor adherence</td>
<td>9.1%</td>
</tr>
<tr>
<td>Other reasons</td>
<td>16.4%</td>
</tr>
</tbody>
</table>

We observed a trend towards higher PVC in patients reporting AE (p=0.177) and lower in alcoholic patients (p=0.053).
Within those cases with a C\textsubscript{trough}<1 µg/mL, co-treatment with corticosteroids and women showed significant lower plasma values (p=0.015 and p=0.052, respectively).

CONCLUSIONS AND RELEVANCE

- We confirm a high variability in voriconazole C\textsubscript{trough} in routine clinical practice.
- Co-treatment with corticosteroids, women and alcoholic patients were related to lower C\textsubscript{trough} values. Thus, in these patients, it might be especially suitable to perform therapeutic voriconazole monitoring in clinical practice to help us optimize antifungal treatment.

REFERENCE