

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_{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_{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/m²
- 11.8% with drinking history
- 1 patient with liver failure

START

VORICONAZOLE



- 165 C_{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)

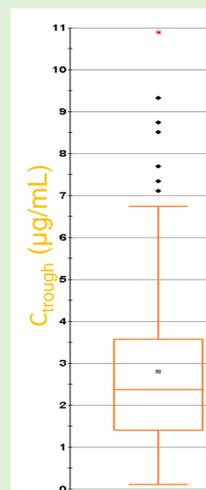


VORICONAZOL TREATMENT INDICATION

Invasive aspergillosis	80.4%
Candidemia	9.8%
Prophylaxis of invasive fungal infections in high risk allogeneic hematopoietic stem cell transplant recipients	2.0%
Other indications	9.8%

REASONS FOR DISCONTINUATION

Cure	30.9%
Drug-related adverse events	16.4%
Exitus or limitation of therapeutic effort	14.5%
Negative culture in empiric therapy	12.7%
Switch to another antifungal due to therapeutic failure / poor adherence	9.1%
Other reasons	16.4%



C_{trough} distribution

>4 µg/mL	20.6%
1-4 µg/mL	63.6%
<1 µg/mL	15.8%

- 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 $C_{\text{trough}} < 1 \mu\text{g/mL}$, 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_{trough} in routine clinical practice.
- Co-treatment with corticosteroids, women and alcoholic patients were related to lower C_{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

Int J Clin Pharmacol Ther. 2018; 56(5): 239-246

For more information: 

