

MANAGEMENT OF VORICONAZOLE-INDUCED LIVER TOXICITY IN A PAEDIATRIC PATIENT

Martínez Suárez A, Merino Bohórquez V, Moñino Domínguez L, Aguado Paredes A, Castillejo García R, Calleja Hernández MA.
Clinical Pharmacy, Hospital Universitario Virgen Macarena, Sevilla, Spain

Voriconazole has variable pharmacokinetics linked to age, cytochrome CYP2C19, hepatic dysfunction and drug interactions. Children usually require higher doses to have voriconazole plasma concentrations (Cp_{vor}) within the therapeutic range (TR) and due to variability, close Cp_{vor} monitoring is recommended.

Objective:

To describe pharmacokinetic/pharmacokinetic (PK/PD) management, efficacy and safety of voriconazole-induced liver toxicity in a pediatric patient.

Design:

PK/PD management was performed by clinical pharmacists and the goal was to have Cp_{vor} within the TR (1.5-5.5 mg/L). Cp_{vor} were measured by a validated high-performance liquid chromatography method.

Efficacy → Analytical, clinical and radiographic improvement.

Safety → Absence of adverse reactions.

Results:

An 8-year-old pediatric patient undergoing active chemotherapy for acute myeloid leukemia.



2nd consolidation
probable invasive
aspergillosis

3rd consolidation
proven invasive
aspergillosis

Voriconazol- 20mg/kg/12h oral/IV
Cp_{vor}=1.5-5.5 mg/L

Hepatic toxicity

Close monitoring of Cp_{vor}
Close monitoring of liver function



2nd consolidation
Cp_{vor}=1.23mg/L
ALT=90U/L
AST=58U/L
GGT=430U/L
Mantain
20mg/kg/12h oral
Cp_{vor}=3.52mg/L
ALT↓
AST↓
GGT↓

3rd consolidation
Cp_{vor}=9.7mg/L
ALT=35U/L
AST=72U/L
GGT=569U/L
20 → 15mg/kg/12h IV
Cp_{vor}=1.58mg/L
ALT↓
AST↓
GGT↓

The patient was treated with oral and IV voriconazole, oral bioavailability was estimated to vary between 70-100%.

Conclusion:

- The patient required higher doses than those recommended in the data sheet to achieve TR.
- Voriconazole-induced liver toxicity is not dose-dependent.
- Treatment with voriconazole was effective in the treatment of probable and proven aspergillosis; she presented clinical, analytical and radiographic improvement.
- The patient had voriconazole-induced liver toxicity, resolved with PK/PD management.