

ISAVUCONAZOLE TREATMENT IN TWO PEDIATRIC PATIENTS DURING EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT: THE ROLE OF THERAPEUTIC DRUG MONITORING

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BACKGROUND AND IMPORTANCE


- Extracorporeal membrane oxygenation (ECMO) may lead to pharmacokinetic alterations of antimicrobials.
- Isavuconazole (ISA) is not approved in pediatric patients (off-label use) and data on pediatric ECMO are non-existent.


AIM AND OBJECTIVES

To describe two case reports using therapeutic drug monitoring (TDM) to optimize ISA dosage in pediatric patients during ECMO.

MATERIAL AND METHODS

Prospective study in critically ill pediatric patients → **ISA treatment + ECMO** (January 2021-August 2022)

 **Initial proposed dose: ISA base 5.4 mg/kg** (intravenous) first 48h q8h, followed by q24h (maximum 200 mg/dose)

 **TDM of ISA trough serum concentration (IsaCmin) → Therapeutic range: 2.5-5 µg/mL** (internal protocol)

Biodemographic, clinical and pharmacokinetic data were collected. Continuous variables were expressed as median (range)

RESULTS



2-year-old boy (11.5kg; 90cm)

Lung transplant (pulmonary capillary hemangiomatosis)

↓ 9 months after transplant

Tracheobronchitis caused by *Aspergillus flavus*

ISA treatment: 5.4 mg/kg (first 48h q8h → q24h)



IsaCmin in therapeutic range: 5.1 (2.5-5.5) µg/mL

*Secondary prophylaxis with isavuconazole was maintained

Severe respiratory failure
(multifactorial)



ECMO cannulation

ISA + ECMO support → 165 days

ISA dose increase to 16.5 (8.7-19.1) mg/kg/24h

↓ Achieve IsaCmin target

IsaCmin; 2.8 (1.3-6.5) µg/mL (24 blood samples)

- No new fungal infections were observed but sadly the patient died due to intracranial hemorrhage



11-year-old girl (70kg; 158cm)

Influenza A infection and necrotizing pneumonia (*S. aureus*)

↓ ECMO support

Positive galactomannan and tracheal aspirate

***Aspergillus niger* → Probable invasive fungal infection**
(EORTC criteria)

ISA + ECMO support → 30 days

Loading dose: 300mg/6h (suspected interaction with pentobarbital first 48h) → **TDM-guided maintenance therapy:**

900mg (12.9mg/kg)/24h (from 200mg/12h to 250mg/4h)

↓ **IsaCmin in therapeutic range**

IsaCmin: 4.0 (1.1-8.4) µg/mL (9 blood samples)



ECMO decannulation

ISA dose reduction: 200mg/12-24h



IsaCmin remained in therapeutic range: 3.9 (2.8-11.4) µg/mL

- She continues ISA maintenance treatment: partial response



CONCLUSION AND RELEVANCE

Pediatric patients on ECMO may require higher doses of ISA to achieve therapeutic concentrations, suggesting that TDM may be clinically useful.

Further studies in critically ill pediatric patients, especially those on ECMO, are necessary to confirm the optimal ISA dosage.

