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 pharmacokineti 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)

**ISA dose reduction: 200mg/12-24h**

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

**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.