PHARMACOKINETICS ALTERATIONS IN TWO CRITICALLY ILL PATIENTS ON EXTRACORPOREAL MEMBRANE OXYGENATION RECEIVING ISAVUCONAZOL

Doménech Moral L[1], García García G[1], Miarons Font M[1], Gomez Domingo MR[1], Riera del Brio J[2], Bonilla C[2], Gallart Vive E[2], Mateos C[1], M.Q. Gorgas Torner[1]. 1: Pharmacy Department. 2: Critical Care Department. Vall d'Hebron University Hospital
Contact: ldomenec@vhebron.net.

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BACKGROUND

Extra Corporeal Membrane Oxygenation (ECMO) can modify drug pharmacokinetics and pharmacodynamics.

We report two critically patients with known isavuconazole pharmacokinetics alterations induced by ECMO itself.

AIMS AND OBJECTIVES

- The main objective is to study the correlation between the dose of isavuconazole administered and its plasma drug concentrations (IsaPlasm).

- The secondary objective is to analize differences in IsaPlasm at different points in the circuit to study drug sequestration.

MATERIALS AND METHODS

Prospective study in patients treated with isavuconazole and receiving ECMO in the Intensive Care Unit (ICU) from August to October of 2021.

Isavuconazole area under the curve (AUCi) was calculated using the trapezoidal method.

Blood samples were drawn from an arterial catheter and from the ECMO circuit pre- and post-oxygenator at 0 (predose), 1 (end of infusion), 2, 4, 6 and 12 hours after isavuconazole infusion.

It was established a therapeutic goal of IsaPlasm though of 2.5 - 10µg/ml. The analytical method used was high-pressure liquid chromatography with fluorescent detector.

Differences greater than 10% on these sites were considered as a possible drug loss.

RESULTS

	Age (years)	Sex	Weight (kg)	Diagnosis	Treatment	Drug interactions	Justification	Outcome
Patient 1 (day 4)	61	Male	*65*	*COVID-19*	Isavuconazole 200 mg/8h during 48h, followed by 200 mg/24h.	No relevant drug interactions	Pulmonary aspergillosi	Isavuconazol dosage was increased to 200mg/12h.
(day 10)					Isavuconazole 200 mg/12h			Negative cultures and clinical improvement
Patient 2 (day 4)	65	Male	*84*	*COVID-19*	Isavuconazole 200 mg/8h during 48h, followed by 200 mg/12h.	No relevant drug interactions	Pulmonary aspergillosi	Died due to external causes.

	PATIENT 1		PATIENT 2
TIME (h)	Day 4 ISAPLASM (mcg/ml)	Day 10 ISAPLASM (mcg/ml)	day 4 ISAPLASM (mcg/ml)
0	1,39	2,16	2,00
1	2,83	3,17	3,01
2	2,28	3,10	3,00
4	1,60	2,67	2,44
6	1,61	2,41	2,34
12	1,06	2,24	3,09
AUC (mcg*h/ml)	36,80	144,30	125,20

isavuconazol dosage was increased to 200mg/12h

Patient 1 (day 4)	ARTERIAL (mcg/ml)	PRE-OX (mcg/ml)	POST-OX (mcg/ml)
C_0	1,39	1,36	1,34
C_1	2,83	2,64	3,02
Patient 1 (day 10)	**ARTERIAL (mcg/ml)**	**PRE-OX (mcg/ml)**	**POST-OX (mcg/ml)**
C_0	2,16	2,17	2,19
C_1	3,17	2,99	2,96
Patient 2 (day 4)	**ARTERIAL (mcg/ml)**	**PRE-OX (mcg/ml)**	**POST-OX (mcg/ml)**
C_0	2,00	1,96	1,86
C_1	3,01	3,34	3,21

CONCLUSION AND RELEVANCE

- **In our cases there was not a significant sequestration and loss of isavuconazole in ECMO circuit.**
- **However, patients required higher isavuconazole doses than described in the data sheet to achieve IsaPlasm therapeutic goals.**
- **Therapeutic drug monitoring during ECMO is appropriate to maximize therapeutic efficacy and security.**