

Session: EP128 PK/PD in antifungal treatment

Category: 6c. Antifungal drugs & treatment

24 April 2017, 13:12 - 13:17
EP0632

Increase micafungin dose for patients under ECMO

Bruno Mourvillier^{*1}, Vincent Jullien², Jean-Louis Trouillet³, Stéphane Ruckly⁴, Gilles Capellier⁵, Michel Wolff⁶, Elie Azoulay⁷, Jean-François Timsit⁸

¹*Gh Bichat Claude Bernard; Reanimation Medicale ET Infectieuse*

²*Hôpital Européen Georges Pompidou*

³*Réanimation Médicale-Institut de Cardiologie; Gh Pitié-Salpêtrière*

⁴*Inserm Umr 1137, Iame*

⁵*Critical Care and Emergency Department; University Hospital, Research Center Ea3920*

⁶*Bichat-Claude Bernard Hospital; Medical Intensive Care Unit*

⁷*Hopital Saint Louis; Intensive Care*

⁸*Inserm Umr 1137*

Background: Micafungin is an antifungal drug belonging to the echinocandin class which are recommended in ICU patients for the treatment of candidemia. ECMO is a life support technique which was associated to modified PK/PD parameters for some antimicrobial drugs. In a post hoc analysis of the Empiricus prospective randomized trial (1) we compared the PK of the first dose of micafungin between patients treated with or without ECMO.

Material/methods: of the 97 patients in whom PK of the first dose of micafungin was available, we performed a matched-cohort (1:n) study of 11 patients treated with ECMO and 28 controls. Matching criteria were center, need for cardiac surgery, SOFA score ± 5 points and weight ± 25 kg. Each patient was matched to a maximum of three controls.

A negative binomial regression was used to model the value of the AUC according to ECMO and other confounding factors.

Results:

In the cohort, the AUC of micafungin was similar according to ECMO use [No ECMO: 71.6 [56.5 ; 93] vs ECMO 74.7 [56.5 ; 80.6]; p=1]. Patients with ECMO significantly differed according to SOFA score and use of cardiac surgery.

Characteristics of the matched population are on table 1. Matching was perfect for cardiac surgery.

	All patients (n=39)	Controls (n=28)	ECMO patients (n=11)
Age	60.3 (30,7-82,2)	63.9 [52.5 ; 69.4]	
Weight (kg)	89.6 (18.4)	88.4 [76 ; 100]	88.9 [80 ; 105]
SAPS2	46 [41;57]	46 [41;57]	45 [37;55]
SOFA	9 [7;11]	8.5 [6.5;11]	9 [8;12]
Acute respiratory failure	5 (12.8)	5 (17.9)	
Septic shock	17 (43.6)	16 (57.1)	0 (0)
Cardiogenic shock	10 (25.6)	2 (7.1)	
Hémodialysis	20 (51.3)	16 (57.1)	4 (36.4)
Albumin (g/l), median (IQR)	16.1 [0 ; 23.6]	16.1 [0 ; 23.6]	17 [0 ; 20]
AUC (mg.hr/L) median (IQR)	80.6 [57.7 ; 114.1]	101.2 [65.4 ; 116.1]	74.7 [56.5 ; 80.6]

AUC was lower in the ECMO group as compared to the matched controls (p=0.06).

In the negative binomial regression, adjusted for SOFA score, weight and albumin level, ECMO was associated in a 23% reduction of the AUC (p=0.029).

Conclusions: ECMO appeared to reduce micafungin AUC of ICU patients by 23%. This result suggests that micafungin dose may be increased for ICU patients treated with ECMO.

(1) Timsit JF et al, JAMA. 2016 Oct 18;316(15)