Critical Care

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Optimizing ceftolozane-tazobactam dosage during continuous renal replacement therapy: some nuances

Gerardo Aguilar[1,2,3*] ⬛, Rafael Ferriols[2,3,4], Sara Martínez-Castro[1], Carlos Ezquer[3,4], Ernesto Pastor[1], Jose A. Carbonell[1], Manuel Alós[2,3,4] and David Navarro[2,3,5]

We have read the recent letter by Honore et al. [1] about our findings published in this journal regarding the influence of continuous renal replacement therapy (CRRT) on the pharmacokinetics of ceftolozane-tazobactam (C/T) [2]. In our report, we decided to administer a 3 g/iv dose every 8 h taking into account two previous studies referenced in our paper [2] and another one which showed CRRT to be an independent predictor of clinical failure (OR 4.5, 95% CI 1.18–17.39, $p = 0.02$) when C/T is administered at 1.5 g every 8 h [3].

As Honore et al. explain in their paper, the C/T elimination was assumed by hemodiafiltration and the adsorption was not assessed [1]. However, there is a misunderstanding in this letter [1], because we used a polysulphone membrane (Fresenius, Germany) instead of an acrylonitrile 69 Multiflow (AN-69-M). In contrast to highly adsorptive membranes (HAM; e.g., AN69 surface-treated, AN69-ST), the antibiotic adsorption with polysulphone ones is negligible, which facilitates antibiotic adaptation during CRRT [4].

Our data should not be extrapolated to other clinical scenarios, as noted by Honore et al. [1]. In our report, ceftolozane and tazobactam plasma concentrations remained above the minimal inhibitory concentration (MIC), for MICs of up to 8 μg/mL, but we estimated that the administration of standard doses of 1 g/0.5 g, even with polysulphone membranes, could compromise the effectiveness of C/T for not reaching adequate tazobactam concentrations. Thus, the use of HAM would represent a real risk factor of clinical failure when a C/T dose of 1.5 g every 8 h is administered, especially in

multidrug-resistant infections [3]. Therefore, we agree with Honore et al. [1] that therapeutic drug monitoring (TDM) is critical when using C/T for patients receiving CRRT, especially when MICs of bacteria like multidrug-resistant (MDR) *Pseudomonas aeruginosa* are considered very high. However, the recommendation of continuous (over 24 h) vs extended (over 2 to 4 h) or intermittent (over 30 to 60 min) infusion of beta-lactams is still under debate [5].

Abbreviations
AN-69-M: Acrylonitrile 69 Multiflow; AN-69-ST: AN69-surface treated; C/T: Ceftolozane-tazobactam; CRRT: Continuous renal replacement therapy; HAM: Highly adsorptive membranes; MDR: Multidrug-resistant; MIC: Minimal inhibitory concentration

Availability of data and materials
Not applicable.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Critical Care Unit, Anesthesiology and Critical Care Department, Hospital Clínico Universitario de Valencia, Valencia, Spain. [2]INCLIVA Health Research Institute, Avenida de Menéndez y Pelayo, 4, 46010 Valencia, Spain. [3]School of Medicine, University of Valencia, Avenida Blasco Ibáñez, 15, 46010 Valencia, Spain. [4]Department of Pharmacy, Hospital Clínico Universitario de Valencia, Avenida Blasco Ibáñez, 17, 46010 Valencia, Spain. [5]Department of

* Correspondence: gerardo.aguilar@uv.es
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[1]Critical Care Unit, Anesthesiology and Critical Care Department, Hospital Clínico Universitario de Valencia, Valencia, Spain
[2]INCLIVA Health Research Institute, Avenida de Menéndez y Pelayo, 4, 46010 Valencia, Spain
Full list of author information is available at the end of the article

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Microbiology, Hospital Clínico Universitario de Valencia, Avenida Blasco Ibáñez, 17, 46010 Valencia, Spain.

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