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Optimizing ceftolozane-tazobactam dosage during continuous renal replacement therapy: additional insights

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We read the recent report by Aguilar et al., who concluded that among patients with nosocomial peritonitis who are on continuous renal replacement therapy (CRRT), ceftolozane-tazobactam (C/T) at a dose of 3 g every 8 h is safe [1]. This finding was additional information following the notion that CRRT was an independent predictor of clinical failure when C/T was administered at 1.5 g every 8 h [2]. The Aguilar et al. protocol included a short infusion time, i.e., 1 h [1]. Previously described extended-infusion over 4 h was found to reach above the minimal inhibitory concentration (MIC), given that beta-lactam antibiotics exhibit time-dependent antibacterial activity [3]. This might prevent underdosing during CRRT [3]. Besides, the C/T elimination was explained by diffusion [1]. However, adsorption was not assessed. The acrylonitrile 69 Multiflow (AN-69-M) membrane, used in this study, has a lower adsorptive capacity compared with the AN69 surface-treated (AN69-ST) membrane, which is considered a highly adsorptive membrane (HAM). In a recent comparison of polysulphone versus AN-69-M for C/T extraction by CRRT in an ex vivo model [4], there was no difference in adsorption. In a case report, a continuous infusion (CI) of 6 g in 24 h of C/T was used in a cystic fibrosis patient with a multidrug-resistant (MDR) *Pseudomonas aeruginosa* and augmented renal clearance to optimize time-dependent antibacterial activity [5]. In this patient, therapeutic drug monitoring (TDM) confirmed adequate exposure [5]. CI and TDM are two critical parameters when using C/T for patients receiving CRRT especially when MICs of bacteria like MDR *P. aeruginosa* are considered very high.

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

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