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Imipenem dosing recommendations for patients undergoing continuous renal replacement therapy: systematic review and Monte Carlo simulations

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Abstract

Background: The appropriate dosing of imipenem for critically ill AKI patients undergoing CRRT remains scarce.

Purpose: This study aimed to (1) gather the available published pharmacokinetic studies conducted in septic patients receiving continuous renal replacement therapy (CRRT) and (2) to define the optimal imipenem dosing regimens in these populations via Monte Carlo simulations.

Methods: The databases of PubMed, Embase, and ScienceDirect were searched from inception to May 2020. We used the Medical Subject Headings of “Imipenem,” “CRRT,” and “pharmacokinetics” or related terms or synonym to identify the studies for systematic reviews. A one-compartment pharmacokinetic model was conducted to predict imipenem levels for the initial 48 h of therapy. The pharmacodynamic target was 40% of free drug level above 4 times of the MIC (40% fT > 4 MIC). The dose that achieved at least 90% of the probability of target attainment was defined as an optimal dose.

Results: Eleven articles were identified and included for our systematic review. The necessary pharmacokinetic parameters such as the volume of distribution and the CRRT clearance were mentioned in 100 and 90.9%, respectively. None of the current studies reported the complete necessary parameters. A regimen of 750 mg q 6 h was the optimal dose for the predilution-CVVH and CVVHD modality with two effluent rates (25 and 35 mL/kg/h) for the pharmacodynamic target of 40% fT > 4MIC.

Conclusions: None of the current studies showed the complete necessary pharmacokinetic parameters for drug dosing. Pharmacodynamic target significantly contributed to imipenem dosing regimens in these patients. Different effluent rates and types of CRRT had minimal impact on dosing regimens. Clinical validation of the recommendation is necessary.

Keywords: Imipenem, Drug dosing, AKI, CRRT, Critically ill patients

Introduction

In the critical care setting, both acute kidney injury (AKI) and critically ill are common complicating factors to therapeutic management. Anuric AKI patients may need therapeutic renal support by continuous renal

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