

Evaluating Linezolid Dose Based on Renal Function and Body Weight against Methicillin-Resistant Staphylococcus aureus (MRSA) by Monte Carlo Simulations

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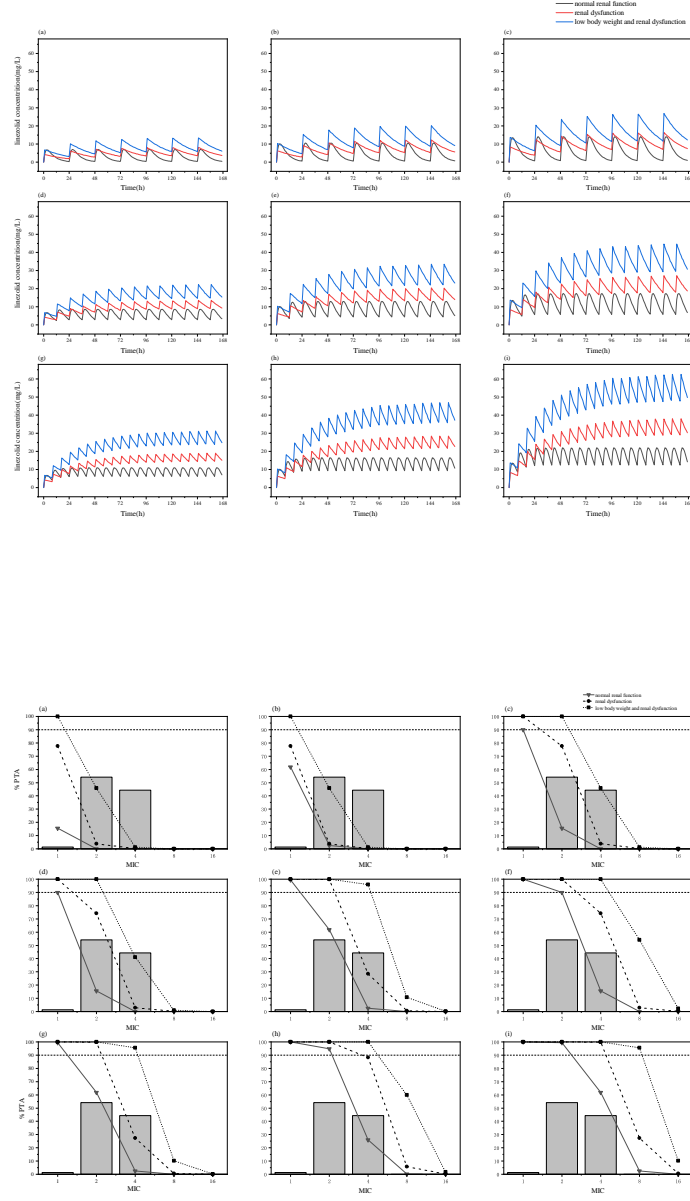
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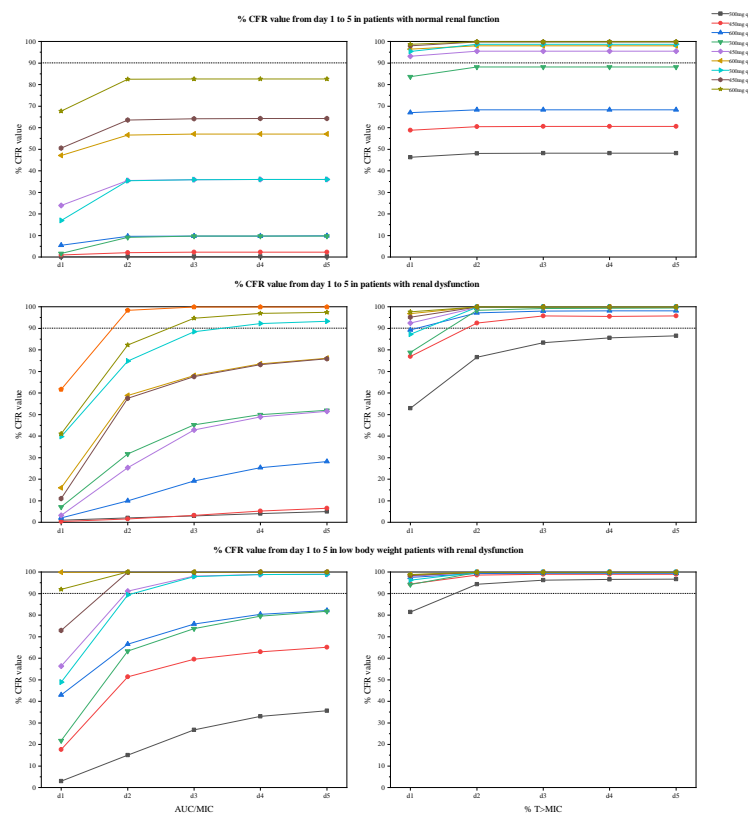
Abstract

Objective: To assess whether dose adjustments of linezolid were needed based on renal function and body weight against methicillin-resistant Staphylococcus aureus (MRSA) infections. **Methods:** Monte Carlo simulations (MCSs) were conducted to simulate pharmacokinetic/pharmacodynamic (PKPD) model. Area under the concentration time curve (AUC)/ minimum inhibitory concentration (MIC) ratio and percentage of time above the MIC (%T>MIC) were regarded as PKPD targets. The probability of target attainment (PTA) and cumulative fractions of response (CFR) were calculated to assess the efficacy. Regarding safety, trough plasma concentration (C_{min}) > 8 mg/L was used to target for toxicity. **Results:** Using AUC /MIC > 100 as the parameter, the CFR of linezolid at the standard dose [600 mg every 12 h (q12h)] were 57.01%, 93.22% and 99.93% in patients with normal renal function, patients with renal dysfunction and low body weight patients with renal dysfunction, respectively. Using 100%T > MIC as the parameter, all the CFR of three population groups were more than 90% at the standard dose. The percentages of C_{min} > 8 mg/L at the standard dose of linezolid were 24.16%, 53.24% and 90.10% in three population groups on day 7. **Conclusions:** The risk of thrombocytopenia of linezolid was extremely high in low body weight patients with renal impairment when receiving standard linezolid dose. 600 mg q12h might be effective and safe against MRSA infection in patients with normal renal function, while 450mg q12h and 300mg q12h in patients with renal dysfunction and low body weight patients with renal dysfunction, respectively.

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