LETTER TO THE EDITOR

Continuous Infusion of Linezolid: Explaining the Discrepant Survival Outcomes between Two Studies

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A recently published study by Albadry et al. concluded that continuous infusion of linezolid was associated with a significantly higher clinical cure rate and shorter intensive care unit (ICU) and hospital stays compared with intermittent infusion ($p < 0.001$).[1] However, this study did not replicate the findings of De Pascale et al., who reported a significant reduction in ICU mortality with continuous infusion.[2]

After carefully reviewing both studies, we identified three major differences that may help explain this discrepancy in survival outcomes.

The first difference concerns dosing. In the Albadry et al. study, the continuous infusion group received a 300 mg loading dose, followed by 900 mg on the first day and 1200 mg/day from the second day onward. In contrast, De Pascale et al. used a higher 600 mg loading dose and gave 1200 mg/day from the 1st day. Although linezolid is a time-dependent antibiotic, the initial loading dose plays a crucial role in rapidly achieving plasma concentrations above the minimum inhibitory concentration (MIC).

Secondly, the patient profiles differed as patients were obese in De Pascale et al.'s study. In this context, a higher loading dose (600 mg instead of 300 mg) could have a much bigger impact.[3,4] The use of a full 1200 mg dose from day 1 might also ensure a higher alveolar penetration ratio.

A final key difference relates to the nature of the infection. De Pascale et al. treated patients with ventilator-associated pneumonia caused by methicillin-resistant *Staphylococcus aureus* (MRSA). In the context of more resistant bacteria, higher doses and continuous infusion are essential to reach pharmacodynamic targets.[4] In support of this, Albadry et al. quoted the findings of Adembri et al., who stated that linezolid being time-dependent, continuous infusion is better suited to maintain effective plasma concentrations—especially in septic patients with increased distribution volume.[5]

However, the original findings of Adembri et al. showed that patients receiving intermittent dosing often had concentrations (both total and free) below 4 mg/mL, and in some cases even below 1 mg/mL. On the contrary, all patients in the continuous infusion group had unbound and total linezolid concentrations above the susceptibility threshold. In the De Pascale et al. study, continuous infusion resulted in higher mean area under the serum concentration–time curve from 0 to 24 hours (AUC_{0-24}) compared with intermittent infusion (approximately 100 mg hour/L), although the difference was not statistically significant. Nevertheless, continuous infusion significantly improved both the time above the MIC (T > MIC) and the probability of target attainment. These benefits were less pronounced at the extreme ends of the MIC susceptibility range (0.5 and 4 mg/L).

In summary, several differences between the two studies, specifically in loading dose, early daily dosing, patient profile, and infection type may explain why De Pascale et al. observed a survival benefit while Albadry et al. did not.

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