

In the Literature

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What Is the Linezolid Concentration?

Morata L, Cuesta M, Rojas JF, et al. Risk factors for a low linezolid trough plasma concentration in acute infections. *Antimicrob Agents Chemother* 2013; 57:1913–7.

The potential need for therapeutic drug monitoring of linezolid has previously been discussed here [1]. Using a target trough concentration of 2 mg/L, the minimum inhibitory concentration at which 90% of both *Staphylococcus aureus* and *Enterococcus* isolates are susceptible, Pea et al reported that, with standard dosing of 600 mg twice daily, this level was achieved or exceeded in only 71.4% of patients [2]. At the same time, values arbitrarily selected as potentially toxic—a minimum between-dose drug concentration (C_{\min}) of $>10 \mu\text{g/mL}$ and an area under the concentration-time curve of $>400 \text{ mg} \times \text{hour/L}$ over 24 hours—were found in 11.8% and 8.1% of measurements, respectively. These higher-than-expected drug exposures were associated with the coadministration of omeprazole, amiodarone, or amlodipine, each of which is a p-glycoprotein inhibitor.

Morata et al, in Barcelona, Spain, retrospectively reviewed linezolid C_{\min} results in 78 patients with acute infections who were receiving linezolid 600 mg every 12 hours and found that the concentration was $<2 \text{ mg/L}$ in 29.5%. Independent risk factors for a C_{\min} of $<2 \mu\text{g/mL}$ were an estimated glomerular filtration rate of $>80 \text{ mL/minute}$ and infection due to *Staphylococcus aureus*.

Marked interindividual variability in the pharmacokinetics of linezolid in severely ill critical care patients has been observed [3]. Although the data are somewhat contradictory, obese patients may require doses higher than that of the approved fixed-dose regimen. Coadministration of rifampin may significantly reduce linezolid exposure [4]. Each of these factors may put the patient at risk of treatment failure, and the risk of selection of resistant organisms may be increased.

On the other hand, excessive linezolid exposure may result in toxicity. Only 30% of linezolid is renally excreted, and no dose adjustment is recommended in patients with renal insufficiency, including those undergoing hemodialysis. Nonetheless, an increased risk of thrombocytopenia has been reported in patients with renal failure during receipt of this drug, and this complication has been associated with serum concentrations of linezolid that are higher than those observed in patients who did not develop thrombocytopenia [5]. Hiraki et al also reported that significant decreases in platelet count were associated with elevated C_{\min} values [6]. Besides renal insufficiency, elevated levels of linezolid may result from drug–drug interactions, as occurs with coadministration of clarithromycin [7].

It may be time to initiate routine therapeutic monitoring of serum linezolid concentrations in patients receiving this drug.

References

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