Postantibiotic Effect (PAE) of linezolid on Staphylococcus aureus, Staphylococcus epidermidis and Enterococcus faecalis

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Abstract

Determination of PAE of linezolid has a great importance in extending its dosing interval. Linezolid MIC of clinical isolates and reference strains of methicillin-resistant and methicillin-susceptible S. aureus, S. epidermidis, vancomycin-resistant and vancomycin-susceptible E. faecalis were determined by agar dilution method. In-vitro PAE was determined by viable count method. All isolates were susceptible to linezolid. Resistance of S. aureus strains to methicillin does not seem to affect their PAE (p 0.05). Enterococci showed slightly longer PAE periods than staphylococci. The durations of PAE were directly proportional to linezolid concentration. Longer PAE periods were also observed at longer antibiotic exposure periods, lower bacterial inocula and in the presence of serum. However, PAE was markedly reduced in urine. In case of non-growing cultures of staphylococci a pronounced PAE was only observed at 4x MIC of linezolid. As revealed by transmission electron microscopy during the PAE period, cells of S. aureus ATCC 25923 and MRSA isolates were converted to oval shaped cells with thickening of the outer membrane, indentation and presence of multiple vacuoles in the cytoplasm. During PAE periods, significant reduction in the adherence properties of the tested bacterial cultures was observed to be directly proportional to increasing linezolid concentrations (p 0.05). A significant, concentration dependent, reduction in coagulase production by S. aureus ATCC 25923 and MRSA isolates during PAE period, especially at 4x and 8x MIC were also observed (p 0.05).

Linezolid appears to affect the expression of bacterial virulence factors as well as bacterial morphology during the PAE period.