Effectiveness of Linezolid, $^{127}$I-Linezolid and $^{131}$I-Linezolid Against Methicillin-Susceptible Staphylococcus Aureus by Time Kill Curve Methods

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Abstract

Objective: Linezolid (LNZ) is one of the most effective treatments against Gram positive bacteria. However LNZ resistant intermediate strains have recently emerged in worldwide. The aim of the study was to compare the minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC) and minimum biofilm inhibitory concentration (MBIC) of LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ against methicillin susceptible Staphylococcus aureus ATCC 35956 (MSSA) biofilms.

Methods: LNZ radiolabeled with $^{131}$I and cold labeling study with $^{127}$I was performed. Radiolabeling and inactive labeling quality-control studies of LNZ were carried out by using TLC (Thin Layer Radiochromatography) and HPLC (High Pressure Liquid Chromatography). LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ against biofilm-forming MSSA was investigated, using a twofold serial broth microtiter method, biofilm challenge, and bacterial count recovery.

Results: The binding yield was obtained to be about 86±2% for radiolabeled LNZ. Minimal inhibitory concentration (MIC) and minimal bactericidal concentration for LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ ranged from 1 to 2 µg/mL respectively. In time-kill studies LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ were bactericidal against staphylococci, producing ≥3 Log10 decrease in viable counts (cfu/mL) within 6 h at 2xMIC. Following the biofilm formation on polystyrene U-bottom microtiter plates to investigate the minimal biofilm inhibitory concentration (MBIC) of LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ was defined as the minimal concentration of antibiotic required to inhibit the biofilm. None of the LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ killed 100% of biofilm associated cells. Mean cell survival in biofilms treated with 64 µg/mL LNZ, $^{127}$I-LNZ and $^{131}$I-LNZ (64 µg/mL) was 48%, 49%, and 33%, respectively.

Conclusion: Our results show that radiolabeled Linezolid demonstrated that 24 h of exposure to 64 µg/mL, promise in treating biofilm producing Staphylococcus aureus.

Key words: Biofilm, iodine-131, linezolid, radiolabeling, staphylococcus aureus

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