In vitro and intracellular activity of solithromycin (CEM-101) against clinical isolates of Legionella pneumophila

Abstract 1640

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Objectives: The goal of this study was to evaluate the in vitro and the intra-cellular activity of solithromycin, a fluoroketolide, against clinical Legionella pneumophila serogroup 1 (Lp1) strains collected in Ontario, Canada.

Methods: A total of 196 clinical Lp1 isolates collected from 1980 to 2008 and previously sequence-base typed at the Public Health Ontario Laboratories, Toronto, Canada, were studied. In vitro activity of solithromycin was compared to azithromycin using the broth microdilution method. To investigate the intracellular activity of solithromycin, in vitro invasion assays were performed using monolayers of NCI-H292 lung epithelial cells and 21 clinical strains displaying different azithromycin susceptibility profiles. Infected cultures were treated with solithromycin or azithromycin and the intracellular activity of each antibacterial agent was determined by counting viable intracellular bacteria after 24 and 48 hours of exposure.

Results: Solithromycin displayed a MIC_{50} of ≤0.015 mg/L and a MIC_{90} of 0.031 mg/L, respectively making its activity 4-fold and 32-fold higher than azithromycin. Most of the isolates presented MICs for solithromycin ranging from ≤0.015 mg/L to 0.031 mg/L whereas 83.6% of the isolates showed MICs for azithromycin ranging from 0.062 mg/L to 0.25 mg/L. Interestingly, most of the clinically prevalent L. pneumophila sequence type 1 isolates had higher MICs for azithromycin, ranging from 0.5 mg/L to 2 mg/L, compared to other sequence types. Both solithromycin and azithromycin inhibited growth of all Lp1 strains in lung epithelial cells at 4x or 8x MICs, displaying bacteriostatic effects rather than a bactericidal activity.

Conclusion: Solithromycin demonstrated the highest in vitro potency against all L. pneumophila isolates when compared to azithromycin. This new antimicrobial agent may prove to be an effective treatment option for L. pneumophila infections if clinical trials demonstrate efficacy and safety in patient indications. This is particularly relevant in times when strains resistant to macrolides and fluoroquinolones are emerging worldwide, complicating the antibiotic treatment of intracellular pathogen infections.

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