Antimicrobial activity of the fluoroketolide solithromycin (CEM-101) against L. pneumophila

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Abstract

Introduction and Objectives

Legionnaires’ disease is a major public health concern in industrialized countries. Morbidity and mortality of the disease ranges from a mild respiratory illness to a severe and rapidly fatal pneumonia. The case-fatality rate of legionnaires’ disease ranges between 40 to 80% in untreated immuno-suppressed patients, but can be reduced from 5 to 10% with appropriate case management.4 Macrolides and quinolones have become the preferred and recommended agents in the treatment of Legionnaire’s disease.4 However, development of resistance in L. pneumophila has been reported1-3 and only sporadically investigated.4,5 New therapeutic options are needed to counteract the emergence of resistance threatening the use of first-choice antimicrobials.5,6

Materials and Methods

Since 1976, the diagnosis of Legionnaires’ disease has been centralized at the Public Health Ontario Laboratory (PHO), which serves as the provincial reference laboratory and performs all testing for outbreak investigations and most testing of clinical specimens in Ontario. A total of 196 Legionella pneumophila clinical isolates collected from 1980 to 2011 in Ontario, Canada, were investigated. Isolates were stored in trypticase soy broth supplemented with 0.5% horse blood at -80°C. Cultures from the frozen stock were prepared by inoculating buffered charcoal yeast extract (BCYE) plates. Plates were incubated for 3 days at 37°C in 5% CO2.

Figure 1. In vitro activity and MIC distribution of solithromycin and azithromycin against Lp1 clinical isolates (n=196)


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Conclusions

Solithromycin has better in vitro activity than azithromycin against a variety of L. pneumophila clinical isolates displaying susceptibility levels ranging from ≤0.015 to ≥2 µg/ml. Solithromycin has a MIC50 of 0.015 µg/ml and a MIC90 of 0.031 µg/ml, making its activity 8-fold and 32-fold higher than azithromycin, respectively. 99% of the isolates presented MICs for solithromycin ranging from 0.015 µg/ml to 0.031 µg/ml whereas 83.0% of the isolates showed MICs for azithromycin ranging from 0.062 µg/ml to 2.0 µg/ml. Interestingly, 96.7% of the clinically prevalent L. pneumophila sequence type 1 isolates were ≥8-fold more susceptible to solithromycin compared to azithromycin.


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