

In vitro activity of Solithromycin (CEM-101) against clinical *Neisseria gonorrhoeae* isolates displaying various types of antimicrobial resistance profiles

Abstract P1470

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Objectives:

Resistance in *N. gonorrhoeae* to penicillins, tetracyclines, fluoroquinolones, macrolides, and early-generation cephalosporins are today common worldwide. Recently, clinical resistance to the currently recommended cefixime and ceftriaxone has been reported. Accordingly, gonorrhoea may become untreatable and the search for new treatment options for gonorrhoea is essential. In this study, we investigated the efficacy of the newly developed fluoroketolide, solithromycin (CEM-101), compared to other antimicrobials previously recommended for treatment of gonorrhoea.

Methods:

The minimum inhibitory concentration (MIC) of solithromycin, azithromycin, erythromycin, telithromycin, spectinomycin, tetracycline, ciprofloxacin, ampicillin, cefixime, and ceftriaxone was determined using agar dilution method and Etest for a collection of 250 clinical *N. gonorrhoeae* isolates with various antimicrobial resistance genotypes and phenotypes. These included the recently described first extensively drug resistant (XDR) *N. gonorrhoeae* strain H041, other strains displaying clinical ESC resistance, and strains with other types of multi-drug clinical resistance.

Results:

The MIC range of solithromycin was 0.001-32 mg/L (MIC₅₀: 0.125 mg/L and MIC₉₀: 0.5 mg/L). Ninety-three isolates had an azithromycin MIC >0.5 mg/L. However, only six isolates had a solithromycin MIC >0.5 mg/L (1, 4, 4, 4, 16, and 32 mg/L). The corresponding MICs of azithromycin for these isolates were 2, 4, 4, >256, >256 and >256 mg/L, respectively. The antimicrobial activity of solithromycin was significantly superior to those of azithromycin, other macrolides, as well as other classes of antimicrobials.

Conclusions:

The present *in vitro* observations regarding the efficacy of solithromycin against *N. gonorrhoeae* suggest that this new fluoroketolide could be an appropriate alternative to the currently recommended ESCs for treatment of gonorrhoea. It is of great importance to perform further *in vitro* studies regarding, e.g., selection of resistance and mechanisms of solithromycin resistance in *N. gonorrhoeae*. Furthermore, previous small studies have indicated that solithromycin has high potency against mycoplasmas, ureaplasmas, and *Chlamydia trachomatis*, suggesting that solithromycin might be an appropriate option for treatment of several sexual transmitted infections (STIs). Nevertheless, larger, well-designed studies examining these STI pathogens are crucial.