In vitro Activity of Solithromycin (CEM-101) Against Macrolideresistant Streptococcus agalactiae (Group B Streptococcus)

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Introduction: Streptococcus agalactiae (Group B Streptococcus or GBS), now recognized as a qualified infectious disease pathogen (QIDP) by the FDA, remains the leading cause of morbidity and mortality among infants in the United States. Although the incidence of GBS in pregnancy has decreased, penicillin and ampicillin minimal inhibitory concentrations (MICs) for GBS have risen, requiring higher doses for maternal and intrapartum treatment. In addition, co-infections with Ureaplasma remain untreated with penicillin. We have determined the in vitro activity of solithromycin (CEM-101) against 60 macrolide-resistant and 10 macrolide–susceptible GBS strains compared to that of other macrolides and penicillin.

Methods: Phenotypic characterization of macrolide-resistant strains was performed by double-disc diffusion testing. Multiplex PCR was used to identify the ermB, ermTR, and mefA/E genes from the GBS strains. Determination of MICs was carried out using the broth microdilution method according to CLSI guidelines. The Etest method was used for penicillin, azithromycin, clarithromycin and erythromycin as routinely tested in the laboratory.

Results: CEM-101 had a MIC₅₀ of ≤0.008 mg/ml and a MIC₉₀ of 0.015 mg/ml against macrolide-susceptible GBS. These MICs were lower than those displayed by penicillin (MIC₅₀ of 0.032 and MIC₉₀ of 0.047 mg/ml), the antibiotic agent of choice for prophylaxis and treatment of GBS infections. Against macrolide-resistant GBS, solithromycin had a MIC₅₀ of 0.03 mg/ml and a MIC₉₀ of 0.125 mg/ml. Against ermB strains, CEM-101 had a MIC₅₀ of 0.03 mg/ml and a MIC₉₀ of 0.06 mg/ml, while against mefA strains it had a MIC₅₀ of 0.03 mg/ml and a MIC₉₀ of 0.125 mg/ml. Against ermB strains, erythromycin, azithromycin, and clarithromycin MICs were mostly >256 mg/ml, while against mefA strains, erythromycin MIC₅₀s and MIC₉₀s were 6 and >256 mg/ml, azithromycin’s MICs were 12 and >256 mg/ml and clarithromycin MIC₅₀s and MIC₉₀s were 1.5 and >256 mg/ml, respectively.

Conclusions: Overall, our results show that Solithromycin had lower or similar MICs compared to penicillin and good activity against macrolide-resistant GBS strains independent of their genotype or phenotype.