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Background: Solithromycin is in clinical development in adults and children. *Haemophilus influenzae* has intermediate susceptibility to macrolides and is known to persist in middle ear infections and in the lung of COPD patients. The purpose of this study was to determine MICs and MBCs of solithromycin and comparator drugs for nontypeable and typeable strains of *H. influenzae*.

Methods: Strains were obtained from a study of nasopharyngeal carriage of *H. influenzae* conducted in children by S. I. Pelton between July 1, 2010 and 2014. Serotypes were determined by slide agglutination using individual and poly antisera. MICs of solithromycin and comparator drugs were performed using broth microdilution in Haemophilus Test Medium as recommended by CLSI M7-A8. For determinations of MBCs of solithromycin and azithromycin, a total of 20 strains (14 nontypeable strains and 6 typeable strains) were selected from all strains tested to represent the range of observed MICs. MBCs were performed as recommend in CLSI M26-A.

Results: Of 210 clinical strains of *H. influenzae*, 165 strains were nontypeable and 45 strains were typeable. Of the typeable strains, 23 were serotype b, 13 were serotype d, 6 were serotype f, 2 were serotype e and 1 was serotype a. The range of MICs and MIC90 of solithromycin were 0.12-8 µg/ml and 2 µg/ml, respectively. The mode MIC of solithromycin for nontypeable strains was 0.5 µg/ml and for typeable strains was 1 µg/ml. Comparing MIC90s for non-typeable strains, solithromycin was (1) at least two twofold dilutions more active than ampicillin, erythromycin and trimethoprim/sulfamethoxazole, (2) as active as amoxicillin/clavulanate and (3) one twofold dilution less active than azithromycin and cefdinir. For 17 of the 20 strains selected to represent the range of observed MICs, the MBCs of solithromycin were either equal to the MIC or only one twofold dilution greater than the MIC.

Conclusion: Solithromycin was active against *H. influenzae* isolates and was equally active against typeable and nontypeable strains. For 17 of the 20 strains of *H. influenzae*, solithromycin could be considered bactericidal. These results, and those previously presented in the chinchilla otitis media model could support future testing of solithromycin against *H. influenzae*-related otitis media.