Introduction

*Streptococcus pyogenes* (Group A streptococci) is the most common cause of bacterial pharyngitis. The organism is also frequently isolated in skin and skin-structure infections. Penicillin is generally considered the drug of choice for treatment of pharyngitis and other non-invasive streptococcal infections, with macrolides recommended as alternative agents in penicillin-allergic patients. While *S. pyogenes* remains uniformly susceptible to penicillin, there have been reports of increasing erythromycin resistance over the past decade. The ketolides, semisynthetic 14-membered ring macrolides, represent a new subclass of agents among the macrolide–lincosamide–streptogramin group. One of the newest agents, ABT-773, has demonstrated excellent *in vitro* activity against both erythromycin-susceptible and -resistant strains of *S. pyogenes*. While the MIC data look very promising, additional information is needed on the time–kill kinetics of these new agents. The purpose of this study was to compare the bactericidal activity of ABT-773 and amoxicillin against *S. pyogenes in vitro*.

Materials and methods

MIC and time–kill assays were performed on 10 clinical isolates of *S. pyogenes* (six erythromycin susceptible and four erythromycin resistant). The MIC ranges (mg/L) were 0.004–0.25 of ABT-773 and 0.015–0.12 of amoxicillin. At 24 h, ABT-773 concentrations of 2 × MIC and 8 × MIC were bactericidal against three and six organisms, respectively. In comparison, amoxicillin was bactericidal against all 10 organisms at both test concentrations.
Results and discussion

Independently of erythromycin susceptibility, both ABT-773 and amoxicillin were highly active against all *S. pyogenes* isolates. The MIC ranges (mg/L) were 0.004–0.25 of ABT-773 and 0.015–0.12 of amoxicillin. Based upon the proposed breakpoints for ABT-773 against non-pneumococcal *Streptococcus* spp. (≤0.5 mg/L for susceptible, 1 mg/L for intermediate and ≥2 mg/L for resistant), the 10 strains would be considered susceptible.\(^6\)

The results of the time–kill experiments are given in Figures 1 and 2. At 24 h, ABT-773 8 × MIC demonstrated bactericidal activity against six strains (four erythromycin susceptible and two containing the *mefA* gene). Bactericidal activity was observed at 24 h against three strains at an ABT-773 concentration of 2 × MIC (one erythromycin susceptible and two containing the *mefA* gene). In comparison, amoxicillin at concentrations of 2 × and 8 × MIC was bactericidal against all 10 isolates at 24 h. Both the rate and extent of killing were less for ABT-773 than amoxicillin against the 10 isolates.
Activity of ABT-773 against *S. pyogenes*

Limited data are available on the time–kill kinetics of ketolides against *S. pyogenes*.7,8 Odenholt *et al.*7 studied the bactericidal activity of telithromycin against one erythromycin-susceptible and two erythromycin-resistant strains. Similar to our results, the authors noted a slow rate of killing (<2 log₁₀ cfu/mL after 12 h) against the three isolates. The telithromycin concentration (0.6 mg/L) utilized in their study was reported to correspond to a 2 h free, unbound serum level following a 800 mg dose. Boswell *et al.*8 also performed time–kill studies with telithromycin against three isolates of *S. pyogenes*. At concentrations of 10 × MIC, bactericidal activity was reported with telithromycin in 2/3 strains at 24 h. Similar results were obtained in our study with 8 × MIC ABT-773. Organisms exposed to concentrations of telithromycin 2 × MIC demonstrated increased growth (1.51–4.17 log₁₀ cfu/mL), whereas in our study, ABT-773 2 × MIC demonstrated bacteriostatic activity against seven isolates and bactericidal activity against three isolates.

In conclusion, ABT-773 demonstrated in vitro activity against both erythromycin-susceptible and -resistant strains of *S. pyogenes*. Further in vitro and in vivo studies are needed to define further the role of ABT-773 in infections due to *S. pyogenes*.

**Acknowledgements**

This work was supported by a grant from Abbott Laboratories. This work was presented in part at the poster session of The 22nd International Congress of Chemotherapy, Amsterdam, The Netherlands, 2001.

**References**


Received 3 August 2001; returned 19 November 2001; revised 4 January 2002; accepted 14 January 2002