sumed recurrent TB infection. He was treated with co-amoxiclav, and an intercostal drain was inserted to reduce the concomitant pleural effusion. He responded well to therapy, and an acid-fast smear of his sputum confirmed TB; TB therapy (rifampicin, isoniazid, ethambutol and pyrazinamide), as recommended by the South African Department of Health, was commenced. The patient was unable to recall prior fluoroquinolone use. N16 was isolated from a 55-year-old female, with previous renal impairment, admitted with pneumonia. She was treated with cefturoxime and responded well. She had received ciprofloxacin for a urinary tract infection within the previous 10 months of admission.

Emergence of these highly resistant *Haemophilus* species may be the result of several factors. Firstly, in the South African community, there is considered to be a relatively high use of fluoroquinolone antibiotics for the treatment—among other infections—of sexually transmitted diseases and urinary tract infections. Secondly, during the winter of 2001, two new fluoroquinolones (moxifloxacin and gatifloxacin) were licensed for use, widely advertised and recommended in the treatment of community-acquired pneumonia. It should be noted that both of the isolates described in this report were resistant to these new agents. Previous use of a fluoroquinolone has been associated with fluoroquinolone resistance in *H. influenzae*, and it is suggested that prior exposure to a quinolone selected the bacteria described. However, the high-level resistance of both these isolates has been considered previously to be extremely rare, and such strains have not been isolated easily in the laboratory after exposure to the older fluoroquinolones, such as ciprofloxacin and ofloxacin. Therefore, we caution the use of these newer fluoroquinolones, and emphasize the importance of vigilance and surveillance of bacterial species considered previously to be exceptionally susceptible to these agents, so that any changes in the population can be identified quickly and policies put in place to prevent transmission.

References


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Sir,

Portier et al. reported a multicentre, open-label, comparative study of 5 day clarithromycin modified release (MR) versus 10 day penicillin V in the treatment of pharyngitis due to group A β-haemolytic streptococci (GABHS), showing equivalence between both treatments.

In this study, Portier et al. provide the clinical and bacteriological results for the patients infected with clarithromycin-resistant strains, but there is no comparison with results of patients infected with susceptible strains. In fact, patients infected with a clarithromycin-resistant strain were excluded from the per protocol (PP) analysis. We have performed further analysis, using a Fisher two-sided test, to evaluate whether patients infected with a clarithromycin-resistant strain had different bacteriological and clinical results from patients infected with a clarithromycin-susceptible strain when treated with clarithromycin or penicillin V.

In the intention-to-treat analysis (ITT), in the group of patients treated with clarithromycin, clinical cure at visit three was obtained in 89.6% (146 of 163) of patients with susceptible strains, and in 71.4% (10 of 14) of patients with resistant strains (*P* = 0.066; odds ratio (OR) 3.4; 95% confidence interval (CI) 0.7–13.5), thus showing a better response in the former group. With respect to the bacteriological eradication at visit three (the principal criterion for efficacy analysis), the success rate was much higher in the group with susceptible strains than in the group with resistant ones (88.3% (121 of 137) versus 28.6% (4 of 14); *P* < 0.001; OR 18.9; 95% CI 4.6–89.4). When the comparison between patients infected with a clarithromycin-susceptible and those infected with a clarithromycin-resistant strain was performed in the group of patients treated with penicillin V, a statistically significant difference was found for bacteriological efficacy (86.1% versus 60%; *P* = 0.019; OR 4.14; 95% CI 1.07–14.66) but not for clinical efficacy (*P* = 0.31). Nevertheless, it should be taken into account that, in the bacteriological evaluation of the patients infected with a clarithromycin-resistant strain, five of 15 patients (five of six of those considered ‘not cured’) were classified as indeterminate (a much higher proportion than in the group of patients infected with a clarithromycin-susceptible strain). If the patients with indeterminate results are excluded from the analysis, then in the group treated with clarithromycin, differences between patients with a clarithromycin-susceptible and those with a clarithromycin-
Correspondence

Sir,

Ketolides are a new class of semisynthetic macrolide derivatives that show excellent activity against Streptococcus pneumoniae, even against erythromycin-resistant isolates. Previous investigators have not found any telithromycin-resistant isolates among S. pneumoniae with the constitutive macrolide–lincosamide–streptogramin B (cMLS5B) phenotype, even though staphylococci or Streptococcus pyogenes with the cMLS5B phenotype can develop resistance to telithromycin. The lack of induction of methylase production by this drug is one reason for such a difference.1,2

Recently, Hamilton-Miller & Shah3 reported that resistance to the ketolide cethromycin (formerly ABT-773) could be induced in S. pneumoniae with the cMLS5 phenotype by erythromycin or other related antibiotics. In this study, we examined whether 55 isolates of erythromycin-resistant S. pneumoniae (MIC ≥ 1 mg/L) carrying the mef(A) and/or erm(B) genes could develop resistance to telithromycin, a ketolide with different substitutions from cethromycin (ABT-773), when exposed to erythromycin.

Fifty-five clinical isolates of erythromycin-resistant S. pneumoniae (obtained from the sputum of patients with lower respiratory tract infections between 1998 and 2000) were used. These isolates were identified by their sensitivity to optochin and the bile solubility test, and by PCR amplification of the ftsA gene. S. pneumoniae ATCC 6305 was used as the quality control strain.

Reference samples of the following antimicrobial agents of known potency were kindly supplied in powder form by the indicated manufacturers: erythromycin (Shionogi Pharmaceutical Co., Osaka, Japan), clarithromycin (Kaken Pharmaceutical Co., Osaka, Japan), azithromycin (Tanabe Pharmaceutical Co., Osaka, Japan), telithromycin (Kissei Pharmaceutical Co., Nagoya, Japan), and cethromycin (Abbott Laboratories, North Chicago, IL, USA).

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Keywords: ketolides, inducible resistance, erythromycin-resistant Streptococcus pneumoniae

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References


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Induction of telithromycin resistance in Streptococcus pneumoniae

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