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Activity of six quinolones against 226 recent clinical isolates of *Streptococcus pyogenes* with reduced susceptibility to ciprofloxacin

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Sir,

β-Haemolytic streptococci (Lancefield groups A, C and G) are known to be highly susceptible to gemifloxacin, followed by moxifloxacin or trovafloxacin, then sparfloxacin and levofloxacin, and at least moderately susceptible to ciprofloxacin and ofloxacin.[1] None the less, a worrying trend in ciprofloxacin resistance (MIC ≥ 4 mg/L) has recently been described in pharyngeal isolates of *Streptococcus pyogenes* as part of the nationwide surveillance network SAUCE (Susceptibility to Antimicrobials Used in the Community in 'España'), from 1.9% in 1996–1997 to 3.4% in 1998–1999.[2,3] Our study was designed to assess the intrinsic activity of newer quinolones against *S. pyogenes* isolates with a reduced susceptibility to ciprofloxacin (MIC ≥ 2 mg/L).

The study was carried out by a single central laboratory (Instituto Valenciano de Microbiología, Valencia, Spain), which tested the strains of *S. pyogenes* collected during the last 4 years in the national surveillance programme SAUCE involving 21 centres; the organisms fulfilled the criterion of ciprofloxacin MIC ≥ 2 mg/L.

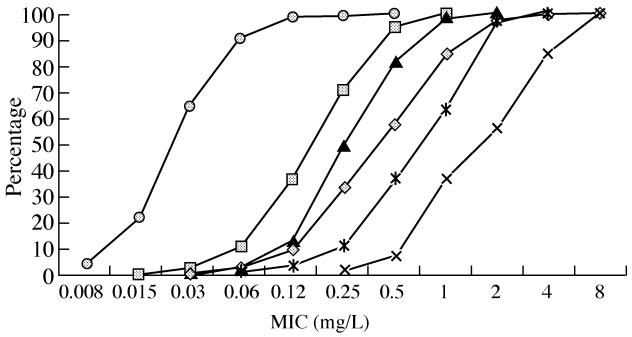

Figure 1. Cumulative percentage of clinical isolates of *S. pyogenes* with reduced susceptibility to ciprofloxacin that are inhibited by each antibiotic. Circles, gemifloxacin; squares, moxifloxacin; triangles, gatifloxacin; diamonds, sparfloxacin; asterisks, levofloxacin; crosses, ofloxacin.

The laboratory determined the MIC for every isolate with a semi-automated broth microdilution method with microtitre customized panels (Sensititre; Trek Diagnostics, Westlake, OH, USA) and NCCLS recommendations for testing ofloxacin, levofloxacin, sparfloxacin (0.004–64), gatifloxacin, moxifloxacin (0.004–16) and gemifloxacin (0.004–8).[4] Panels were inoculated with isolates suspended in cation-adjusted Mueller–Hinton broth with 3% lysed horse blood to achieve an inoculum of 5×10^5 cfu/mL. Incubation was carried out at 35°C in ambient air for 24 h before automated reading. *Streptococcus pneumoniae* ATCC 49619 was used as a control.

This study analysed 226 of 2830 (8%) *S. pyogenes* isolates collected in the SAUCE surveillance programme whose ciprofloxacin MIC was ≥2 mg/L.[2,3] The proportion of paediatric isolates was 79.6%. The cumulative percentage of strains within each MIC category for the agents is shown in Figure 1. The MIC_{50} was 2 mg/L of ofloxacin, 1 mg/L of levofloxacin, 0.5 mg/L of sparfloxacin and gatifloxacin, 0.25 mg/L of moxifloxacin and 0.03 mg/L of gemifloxacin. The MIC_{90s} were 8 mg/L of ofloxacin, 2 mg/L of levofloxacin and sparfloxacin, 1 mg/L of gatifloxacin, 0.5 mg/L of moxifloxacin and 0.06 mg/L of gemifloxacin. MIC ranges were 0.5–8 mg/L of ofloxacin, 0.06–4 mg/L of levofloxacin, 0.03–8 mg/L of sparfloxacin, 0.03–2 mg/L of gatifloxacin, 0.015–1 mg/L of moxifloxacin and 0.008–0.5 mg/L of gemifloxacin.

Except for ofloxacin (MIC_{90} 8 mg/L), all the other quinolones displayed an MIC_{90} within the susceptible range (2 mg/L of levofloxacin and sparfloxacin, 1 mg/L of gatifloxacin, 0.5 mg/L of moxifloxacin and 0.06 mg/L of gemifloxacin). The rank order of potency was ofloxacin

< levofloxacin < sparfloxacin < gatifloxacin < moxifloxacin < gemifloxacin. The comparison between the activity of gemifloxacin, in terms of MIC_{50} or MIC_{90}, was 60- to 120-fold higher versus ofloxacin, 30-fold versus levofloxacin and sparfloxacin, 17-fold versus gatifloxacin and 8-fold versus moxifloxacin.

Although the first marketed quinolones were most active against aerobic Gram-negative bacilli, particularly members of the family Enterobacteriaceae and *Haemophilus* spp., and against Gram-negative cocci such as *Neisseria* spp. and *Moraxella catarrhalis*, newer agents released recently are highly active against Gram-positive cocci. Regarding staphylococci and streptococci, the lowest mean MIC of ciprofloxacin is for coagulase-negative staphylococci. *S. aureus* comes next, followed by β-haemolytic streptococci (Lancefield groups A, C and G), *Streptococcus agalactiae* and enterococci, with α-, non-haemolytic streptococci and *S. pneumoniae* the least susceptible. Many of the newer agents can greatly exceed the activity of ciprofloxacin. However, the recent phenomenon of a sharp increase in ciprofloxacin resistance of *S. pneumoniae* has stirred up debate about a likely widespread loss of activity of newer quinolones in the near future if this trend continues.[3,5,6]

The data presented here resemble those already reported for *S. pneumoniae*, although the susceptibility of *S. pyogenes* to newer quinolones is higher despite a loss of susceptibility to ciprofloxacin. Likewise, isolates with very high MICs of other quinolones are found only occasionally even among this collection of highly selected isolates.

The increasing prevalence of erythromycin resistance in *S. pyogenes*,[2,3] coupled with its likely link with macrolide consumption,[7] could lead to the consideration of quinolones as second line therapy for mild infections in adults, at least in countries in which the MLS_B phenotype of resistance is significant, or more importantly, they might even deserve assessment in the setting of severe streptococcal infections such as necrotizing fasciitis, where β-lactam allergy could preclude treatment with the recommended combination of penicillin and clindamycin.[8]

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