RESEARCH NOTE

Antimicrobial susceptibility of invasive isolates of *Streptococcus pneumoniae* in Ireland

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ABSTRACT

Between January 1999 and June 2002, 646 invasive isolates of *Streptococcus pneumoniae* were collected in Ireland. MICs of penicillin, ciprofloxacin, cefotaxime, moxifloxacin and linezolid were determined by Etest methodology. Eighty-seven (13.5%) isolates showed intermediate resistance to penicillin, while seven (1.1%) showed high-level resistance. Eighty-seven (13.5%) isolates were resistant to erythromycin, but all isolates were susceptible to cefotaxime, moxifloxacin and linezolid. The prevalence of pneumococcal isolates non-susceptible to penicillin in Ireland is worryingly high, but currently there are alternative agents available to treat invasive infection.

Keywords Antimicrobial susceptibility, penicillin, resistance, *Streptococcus pneumoniae*

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Streptococcus pneumoniae is a significant cause of bacteraemia and meningitis. In a recent UK study, the annual population incidence of bacteraemia was 9.8/100 000, with a mortality rate of 24% [1].

Increasingly, pneumococcal isolates are resistant to penicillin. The prevalence of non-susceptibility to penicillin in the UK increased from 1.5% in 1990 to 3.9% in 1995 [2], while in Quebec, Canada, the prevalence changed from 11% to 12% from 1996 to 1998 [3]. However, antibiotic resistance may not always correlate directly with an adverse outcome. Thus, a study comparing 22 meningitis patients from whom cefotaxime-non-susceptible pneumococcal isolates were obtained with 87 patients from whom cefotaxime-susceptible isolates were obtained revealed no difference in mortality or length of hospital stay [4].

The present study examined the susceptibility to newer antimicrobials of 646 invasive isolates of pneumococci, i.e., from blood (620 isolates) or cerebrospinal fluid (26 isolates), collected as part of the European Antimicrobial Resistance Surveillance System (EARSS). Isolates were submitted by referring laboratories participating in the EARSS project for further susceptibility testing between January 1999 and the end of June 2002. All isolates were tested for penicillin susceptibility by routine disk diffusion with an oxacillin disk (1 μg), and for erythromycin susceptibility according to the British Society for Antimicrobial Chemotherapy guidelines [5]. ATCC strains 49619 and 6306 were used as controls. MICs of penicillin, cefotaxime and ciprofloxacin were determined by Etests (AB Biodisk, Solna, Sweden) according to the manufacturer's instructions. In addition, MICs of moxifloxacin and linezolid were determined by Etest for 288 and 340 isolates, respectively. All plates were incubated in CO_2 5–10% v/v for 24 h at 37°C.

The 646 isolates were obtained from patients with a mean age of 50.8 years; 14.5% of the isolates were from patients aged ≤4 years, and 42.9% from patients aged ≥65 years. The male: female ratio was 1.18:1; 47% of patients were from general medical wards and 7% were from paediatric wards. Of the isolates tested, 94 (14.6%) were non-susceptible to penicillin, of which 87 (13.5%) showed intermediate resistance, i.e., with an MIC of 0.1–1 mg/L, while seven (1.1%) isolates showed high-level resistance, i.e., with an MIC of 2 mg/L (Fig. 1). Eighty-seven (13.5%) isolates were resistant to erythromycin, of which 62 (71%), 21 (25%) and four (4%) were susceptible, intermediately or highly resistant, respectively, to penicillin. All isolates had a cefotaxime MIC ≤1.0 mg/L, i.e., were susceptible. All but one isolate (MIC 4 mg/L) had a ciprofloxacin MIC <4 mg/L. The MIC_{90} of moxifloxacin was 0.094 mg/L, and no isolate had an MIC >1.0 mg/L; therefore, all isolates were suscept-

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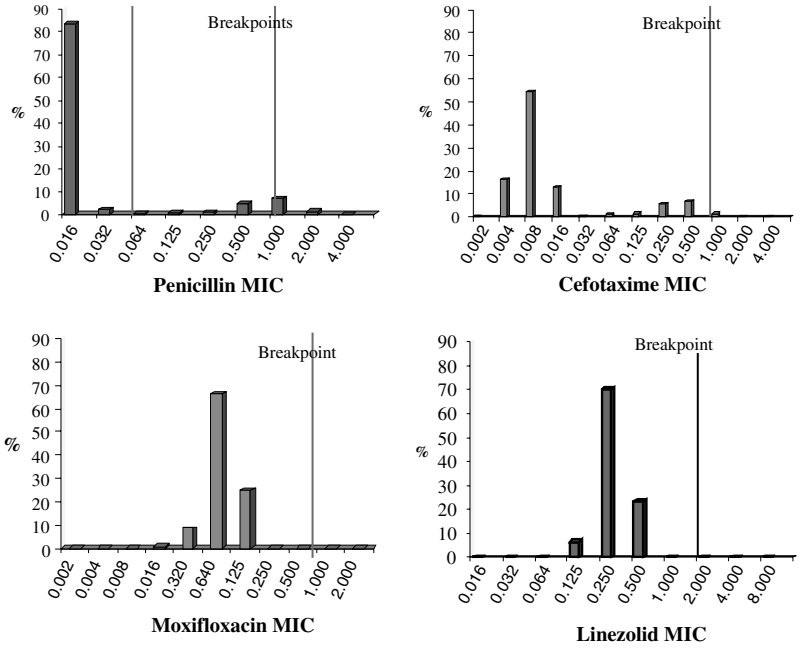

Fig. 1. Distribution of MICs (determined according to British Society for Antimicrobial Chemotherapy guidelines and breakpoints) of penicillin, cefotaxime, moxifloxacin and linezolid among invasive isolates of *Streptococcus pneumoniae* in Ireland between 1999 and 2002.

ible. The MIC_{90} of linezolid was 0.5 mg/L, and no isolate had an MIC >1.0 mg/L; therefore, all isolates were susceptible (Fig. 1).

The prevalence of isolates non-susceptible to penicillin among invasive strains of pneumococci is high in Ireland compared with many European countries [6,7]. The prevalence given in the EARSS data for 2002 is 11.5%, which is higher than in the UK (4.7%), The Netherlands (1.2%) and Germany (1.3%), but lower than in Spain (33.3%) and Portugal (19.7%) [6].

Overall, 13.5% of the isolates in the present study were resistant to erythromycin. In a study of 2586 invasive isolates from Germany, only 7.7% of isolates were resistant to erythromycin; of these, 12.1% were either intermediately or highly resistant to penicillin [8], compared with 29% in the present study. All isolates (100%) in the present study were susceptible to cefotaxime (MIC ≤ 1.0 mg/L), compared with 99.7% of the German isolates [8], but the German study was considerably larger. Of Irish pneumococcal isolates recovered from patients with lower respiratory tract infections between 1997 and 1998, 23% were either intermediately or fully resistant to cefotaxime according to the then British Society for Antimicrobial Chemotherapy guidelines, but the MIC_{90} was 1 mg/L [9]. However, these were non-invasive isolates, and non-susceptibility to cefotaxime may reflect exposure to previous antibiotics in patients with chronic pulmonary disease.

None of the present isolates had a ciprofloxacin MIC >4 mg/L, a breakpoint used previously [10]. One isolate had an MIC of 4 mg/L; i.e., it was resistant according to British Society for Antimicrobial Chemotherapy interpretive criteria [5] (there are no breakpoints provided by the National Committee for Clinical Laboratory Standards). In the USA, only 0.3% of isolates had a ciprofloxacin MIC ≥4 mg/L [10]. Many guidelines for the treatment of respiratory infection now include fluoroquinolones such as moxifloxacin. Only 0.9% of 807 isolates from sterile sites were resistant to moxifloxacin in a recent UK study; 8% were non-susceptible to penicillin, but 99% were resistant to ciprofloxacin, with a breakpoint of 1 mg/L [11]. All of the present isolates had a moxifloxacin MIC <1 mg/L, i.e., were susceptible. However, multidrug-resistant clones are prevalent in Hong Kong and Spain [12], and these could spread to Ireland.

Linezolid has an anti-Gram-positive bacterial spectrum, with little or no cross-resistance to other agents [13]. In a UK study of 374 Gram-positive isolates, the linezolid MICs were 0.5–2 mg/L for all except the enterococci; all pneumococci (41 isolates) had an MIC of either 1 or 2 mg/L [14]. With a breakpoint of 4 mg/L, all isolates (including those in the present study) were susceptible to linezolid.

Invasive infection can be prevented by vaccination. Irish EARSS isolates from 1999 comprised 25 capsular serotypes, with serotypes 14 (20.8%),

9V (15.3%), 4 (9%), 3 (6.9%), 8 (5.6%), 12B (4.9%) and 5 (4.9%) being the most common [15]. Only four serotypes were represented among the penicillin-non-susceptible isolates, namely 9V (74%), 14 (14.8%), 23F (7.4%) and 6B (3.7%). Only 11% of all isolates belonged to serotypes not included in the 23-valent non-conjugated polysaccharide vaccine, but some protection may be afforded by cross-reactivity between serotypes [15].

In conclusion, the prevalence of isolates non-susceptible to penicillin in Ireland is worryingly high, but all isolates are currently susceptible to cefotaxime, moxifloxacin and linezolid. Patients in Ireland with invasive pneumococcal infections should continue to receive cefotaxime as empirical treatment. Should cefotaxime resistance emerge, the extended-spectrum fluoroquinolones and linezolid may be useful alternatives.

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RESEARCH NOTE

High-level fluoroquinolone resistance in a clinical *Streptoccoccus pyogenes* isolate in Germany

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ABSTRACT

An isolate of *Streptococcus pyogenes* isolated from a 63-year-old woman with a serious wound infection was found to be highly resistant to fluoroquinolones (levofloxacin MIC ≥ 32 mg/L). DNA amplification and sequencing revealed a serine-81 to phenylalanine substitution in *gyrA* and three substitutions in *parC*: serine-79 to phenylalanine, aspartic acid-91 to

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