Correspondence

In vitro activity of extended-spectrum cephalosporins against Streptococcus pneumoniae strains with reduced susceptibility to penicillin isolated from patients in Portugal between 1995 and 2000

Manuela Caniça*, Ricardo Dias, Deolinda Louro, Catarina Carvalho and the Multicentre Study Group†

Antibiotic Resistance Unit, National Institute of Health Dr Ricardo Jorge, Av. Padre Cruz, 1649-016 Lisboa, Portugal

*Corresponding author. Tel: +35-121-751-9246; Fax: +35-121-751-9246; E-mail: manuela.caniça@insa.min-saude.pt
†Members of the Multicentre Study Group are listed in the Acknowledgements

Sir,

The prevalence of serious infections (meningitis, pneumonia, respiratory tract infections) caused by strains of pneumococci with reduced susceptibility to penicillin is increasing throughout the world.1 Thus, the third-generation cephalosporins cefotaxime and ceftriaxone have become important drugs in the treatment of pneumococcal infections, particularly in cases of meningitis. However, pneumococcal strains exhibiting high levels of resistance to these β-lactams have been described,2–4 often associated with therapeutic failure. Furthermore, strains with diminished susceptibility to these two drugs have been observed in Portugal in the last few years.5

The Antibiotic Resistance Unit of the National Institute of Health, Lisbon, collected 384 penicillin-resistant isolates of Streptococcus pneumoniae between January 1995 and December 2000 during a multicentre study involving 23 different laboratories; 105 of the isolates were invasive, from blood, cerebrospinal fluid or pleura, 250 were isolated from the respiratory tract and 29 were of unknown origin.

The MICs of penicillin, cefotaxime and ceftriaxone for 384 S. pneumoniae isolates with reduced susceptibilities to penicillin are presented in Table 1. The MICs of penicillin, cefotaxime and ceftriaxone were determined by the agar dilution method, according to NCCLS protocols.6 Isolates were considered to be penicillin intermediate if the MIC of penicillin

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Penicillin-resistant (n = 79)</th>
<th>Penicillin-intermediate (n = 305)</th>
<th>Penicillin-susceptible (n = 384)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>7 (9.0)</td>
<td>50 (16.0)</td>
<td>56 (14.6)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>9 (11.7)</td>
<td>60 (19.7)</td>
<td>56 (14.6)</td>
</tr>
</tbody>
</table>

Table 1. MICs of penicillin, cefotaxime and ceftriaxone for 384 S. pneumoniae isolates with reduced susceptibilities to penicillin

© 2002 The British Society for Antimicrobial Chemotherapy
was between 0.1 and 1 mg/L, or to be penicillin resistant if the MIC of penicillin was ≥2 mg/L. Isolates were considered to be cefotaxime or ceftriaxone intermediate if the MICs of these two antibiotics were 1 mg/L and cefotaxime or ceftriaxone resistant if the MICs were ≥2 mg/L.

The in vitro activities of the three antibiotics against the isolates are shown in Table 1. Of the 384 isolates, 305 showed intermediate- or low-level penicillin resistance and 79 showed high-level penicillin resistance. The MIC\textsubscript{50} of both cefotaxime and ceftriaxone were the same for penicillin-resistant isolates (1 mg/L), but the MIC\textsubscript{50} of cefotaxime for penicillin-resistant isolates was higher (2 mg/L) than that of ceftriaxone (1 mg/L). The MIC\textsubscript{90} of the two cephalosporins were the same for penicillin-resistant isolates (1 mg/L), but the MIC\textsubscript{90} of cefotaxime for penicillin-resistant isolates was two-fold lower than those for penicillin-resistant isolates (1 mg/L). The MIC\textsubscript{90} of cefotaxime and ceftriaxone were the same for penicillin-resistant isolates (1 mg/L), but the MIC\textsubscript{90} of cefotaxime for penicillin-resistant isolates was higher (2 mg/L) than that of ceftriaxone (1 mg/L). The MIC\textsubscript{90} of two of the cephalosporins were the same for invasive and non-invasive isolates (data not shown). However, ceftriaxone had a higher in vitro activity against invasive isolates (MIC\textsubscript{90} 2 mg/L) than against non-invasive isolates (MIC\textsubscript{90} 1 mg/L). The percentage of penicillin-resistant isolates with intermediate resistance to cefotaxime (65.8%) was lower than the percentage of penicillin-resistant isolates with intermediate resistance to ceftriaxone (83.6%). Conversely, more strains were resistant to cefotaxime (30.4%) than to ceftriaxone (10.1%).

Comparison of these results with those of a previous study demonstrates that the percentage of clinical isolates of \textit{S. pneumoniae} with reduced susceptibility or resistance to third-generation cephalosporins has increased in Portugal. The resistance of clinical isolates to cefotaxime and ceftriaxone is related to the decreased affinities of PBP 1a and PBP 2x, due to genetic recombination events and the accumulation of point mutations in the mosaic forms of the \textit{pbp} genes. Thus, we emphasize the importance of monitoring the susceptibility to these drugs in Portugal, especially in cases of pneumococcal meningitis, where resistance to β-lactams may result in treatment failure.

Acknowledgements
The Multicentre Study Group consisted of: T. Afonso, Centro Hospitalar Funchal; J. Amorim, Hospital Geral S. António; R. Bento, Hospital José Joaquim Fernandes; R. Barros, Hospital D. Estefânia; L. Cabral, Hospital SAMS; J. Côrte, I. N. S. Dr Ricardo Jorge, Lisboa; A. Fonseca, Hospital Condes Castro Guimarães; F. Fonseca, Hospital S. Luzia; J. M. Marques, Hospital S. José; F. Martins, Hospital S. Francisco Xavier; A. Morais, Centro Saúde Oeiras; J. S. Moreira, Centro Hospitalar Coimbra; M. Pinto and J. Diogo, Hospital Garcia Orta; M. G. Ribeiro, Hospital Universidade Coimbra; M. J. Salgado, Hospital S. Maria; L. Sancho, Hospital Fernando Fonseca; J. M. Serra, Hospital Curry Cabral; M. L. Sobral, Centro Hospitalar Vila Nova Gaia; F. Teixeira, Hospital Central E. C. M. Pia; H. Troni, Hospital Pulido Valente; M. Vasconcelos, Hospital Reynaldo Santos; L. Bacteriologia, I. N. S. Dr Ricardo Jorge Porto; S. Microbiologia, IPOFG Centro do Porto. This work was presented in part at the 21st International Congress of Chemotherapy, Birmingham, UK, 1999. This work was supported in part by grant Comissão de Fomento da Investigação em Cuidados de Saúde/237/99 from the Ministério da Saúde, Portugal.

References