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A nationwide susceptibility surveillance study of beta-hemolytic streptococcal isolates from pharyngeal swabs obtained in 11 Spanish hospitals between May 1996 and April 1997 against 12 antibiotics was carried out. Of the isolates 86% (786 of 914 isolates) were group A and 8% (77 of 914) were group C. No resistance was found to β-lactam antibiotics, but significant differences (P < 0.001) with respect to lack of susceptibility to macrolides were found between groups (27% for group A and 12% for group C) and between seasons (13.2% in summer and 31.7% in winter). Most of these isolates displayed the M phenotype (low-level resistance to erythromycin and susceptibility to clindamycin).

Penicillin remains the drug of choice in the treatment of streptococcal pharyngitis (3), although communications increasing report treatment failure frequencies of up to 30% (2, 4). This has been attributed to copathogenicity with beta-hemolytic streptococci (3), although communications increasing-
azithromycin, ceftriaxone, and cefotaxime, and 0.25 and respectively 0.5 and (of azithromycin). The MIC 90 of ciprofloxacin was 1 mg/ml from 4 activities, with MIC 90 so of resistance prevalence) to group A and 11.7% (9 of 77 isolates) for group C (that were nonsusceptible (intermediate strains plus resistant strains) to ciprofloxacin but not to macrolides. The percentages of isolates that were nonsusceptible (intermediate strains plus resistant strains) to macrolides were 27.1% (213 of 786 isolates) for group A and 11.7% (9 of 77 isolates) for group C (P = 0.001).

Table 1 shows the in vitro susceptibility of the 786 S. pyogenes isolates. All β-lactam antibiotics exhibited similar activities in vitro, with MIC<sub>C90</sub> of <1 μg/ml. The penicillins and parenteral cephalosporins exhibited similar activities with respect to MIC<sub>C90</sub>, MIC range, and resistance prevalence. With respect to oral cephalosporins, only cefixime showed MIC of >1 μg/ml (for 8 of 786 strains). Macrolides elicited resistance by around 27% of the isolates, as stated above, with MIC<sub>C90</sub> values ranging from 4 μg/ml (of erythromycin or clarithromycin) to 8 μg/ml (of azithromycin). The MIC<sub>C90</sub> of cipromoxacin was 1 μg/ml. This study reveals an increase in erythromycin resistance prevalence in Spain (27%) compared to the resistance rates of up to 10% found in previous studies (3, 6, 15), which is due in part to the use of different breakpoints for erythromycin in the present study and in the previous ones. Were the breakpoint (≥8 μg/ml) (12) employed in the previous studies (3, 6, 15) used, the erythromycin resistance prevalence in this study would be 6.1%.

When a cutoff value of ≥1 μg/ml was used for highly resistant strains (3, 13) resistance was found in only 3% of strains isolated in 1991 and 1992 (3) or 4.7% of those isolated in 1994 (13). The overall erythromycin resistance frequency of 27% is due in part to an increase in the isolation rate of very highly resistant strains; 6.1% of the isolates had MIC of ≥8 μg/ml, contrasted with 1% of those examined in 1991 and 1992 (3). This may be explained in part by the confirmed increase of macrolide-resistance exhibited a seasonal pattern, being 13.2, 25.0, 31.7, and 31.3% in summer, autumn, winter, and spring, respectively (P < 0.001). Antibiotic consumption patterns may contribute to resistance seasonality. In Spain community anti-biotic consumption accounts for 90% of total consumption, and 17% of it is consumption of macrolides (1). Another possible explanation is the existence of a seasonal clone variation of new phenotypes with respect to virulence and antibiotic susceptibility.

Figure 1 shows the erythromycin MIC distribution. With respect to S. pyogenes erythromycin resistance phenotypes (18), 93% (198 of 213 isolates) of strains belong to phenotype M (presumed efflux, with low-level resistance to erythromycin and susceptibility to clindamycin), as was found in previous studies in our country (6, 14), 6% (13 of 213 isolates) belong to the constitutive phenotype, and 1% (2 of 213 isolates) belong to the inducible phenotype. The increase in macrolide resistance observed is due to the M phenotype, with cross-resistance between C<sub>14</sub> (erythromycin and clarithromycin) and C<sub>15</sub> (azithromycin) macrolides.

Careful surveillance is required (8) for streptococcal isolates in countries where macrolide antibiotics are frequently prescribed (10) or high resistance rates for macrolides exist (as in Spain), as these antibiotics are the most widely used alternatives to oral β-lactams in the empiric treatment of streptococcal pharyngitis.

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Table 1. MIC<sub>90</sub> range of MICs, and susceptibility for 786 isolates of S. pyogenes obtained from pharyngeal exudate samples

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt; (μg/ml)</th>
<th>Range of MICs (μg/ml)</th>
<th>No. (% of strains)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>≤0.015, 0.015–0.06</td>
<td>786 (100.0)</td>
<td>0 (0) 0 (0)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>≤0.25, 0.25–0.25</td>
<td>786 (100.0)</td>
<td>0 (0) 0 (0)</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>≤1, 1–2</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cefixime</td>
<td>≤0.25, 0.25–0.25</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>≤0.1–0.16</td>
<td>573 (72.9)</td>
<td>3 (0.4) 210 (26.7)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>≤0.05–0.25</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> All the strains susceptible to penicillin can be susceptible to amoxicillin, amoxicillin-clavulanate, cefotaxime, and cefaclor (11). Amoxicillin-clavulanate was tested on a 2:1 basis.

<sup>b</sup> NA, not applicable. No breakpoint criteria have been established by the National Committee for Clinical Laboratory Standards.

<sup>c</sup> The breakpoints (μg/ml) for intermediate strains and resistant strains were respectively 0.5 and ≥1 for erythromycin and clarithromycin, 1 and ≥2 for azithromycin, ceftriaxone, and cefotaxime, and 0.25 and ≥4 for penicillin (11).

REFERENCES


