Macrolide Resistance Determinants of Invasive and Noninvasive Group B Streptococci in a Turkish Hospital

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Macrolide resistance in 156 consecutive group B streptococcal isolates was investigated. Thirty-five isolates (22.4%) had inducible (80%) or constitutive (20%) erythromycin resistance. The genes responsible were erm(B), erm(A) subclass erm(TR), and erm(B) plus erm(TR) in 62.9, 2.9, and 8.6% of isolates, respectively. Nine isolates (25.7%) harbored neither mef nor detectable erm genes.

Group B streptococci (GBS), namely, Streptococcus agalactiae, are one of the most important causes of neonatal meningitis and sepsis. GBS also cause other infections in pregnant women and the elderly. The treatment of choice for S. agalactiae infections is penicillin or its congeners. However, if there is a penicillin allergy or a lack of clinical response, macrolides are the major substitutes. Unfortunately, macrolide resistance determinants, as described elsewhere (2, 4), Two reference Escherichia coli strains carrying erm(A) and erm(BP) genes, respectively, and one S. pyogenes strain positive for mef(A/E) (kindly provided by Helena Seppälä, National Public Health Institute, Turku, Finland) were used as positive PCR controls. An S. pyogenes isolate harboring erm(TR) as confirmed by PCR and sequence analysis was used as the subclass erm(TR) control. For statistical analysis of the results, Fisher’s exact test was used and P values of <0.05 were considered significant.

All isolates were susceptible to penicillin, while 23 (26%) vaginal and 12 (20.9%) urinary isolates (total, 35 [22.4%]) (P = 0.6) were resistant to erythromycin. None of the resistant isolates harboring erm(TR) as confirmed by PCR and sequence analysis was used as the subclass erm(TR) control. For statistical analysis of the results, Fisher’s exact test was used and P values of <0.05 were considered significant.

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The high rate of tetracycline resistance (100%) that we observed among the erythromycin-resistant S. agalactiae isolates was also noted in some previous reports (>80% in Canada, 89.1% in France, 87% in Spain, and 99.2% in Taiwan). However, the mechanisms of this coexistence are yet not clear (5). On the other hand, the chloramphenicol resistance rate that we detected (44.2%) was considerably higher than those previously reported from Taiwan (20.3%) (13) and the United States (1%) (11). This rate was also considerably higher than that detected in Turkish S. pyogenes isolates (5.6%), in which tetracycline resistance was 39% (1). However, to assess the statistical significance of erythromycin-chloramphenicol coreistance detected in our isolates, the erythromycin-susceptible isolates should be compared with the resistant ones.

In conclusion, the MLSB resistance rate is high and accompanied by very high rates of tetracycline and chloramphenicol resistance in Turkish S. agalactiae isolates. Vancomycin and levofloxacin are the two reliable substitutes for erythromycin for GBS infections in patients with a penicillin allergy.

This study was supported by the Fatih University Research Project Fund. We thank Helena Seppälä from the National Public Health Institut, Turku, Finland, for providing the PCR control strains.

REFERENCES

<p>| TABLE 1. Distribution of MLSB resistance phenotypes according to genotype |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|</p>
<table>
<thead>
<tr>
<th>Phenotype</th>
<th>No. of isolates with genotype</th>
<th>erm(B)</th>
<th>erm(TR)</th>
<th>erm(B) + erm(TR)</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>cMLS</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>iMLS</td>
<td>15</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>28</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>35</td>
<td>35</td>
</tr>
</tbody>
</table>

The gene most frequently responsible for MLSB resistance was the erm(B) gene, a determinant commonly associated with high-level resistance. The M-phenotype prevalence rates reported from other countries are relatively low: 15% in Canada (3), 6 to 7.4% in France (6, 8, and 5 to 9.3% in Spain (5, 12), with the exception of Taiwan, where the M-phenotype prevalence was 37% (13). Interestingly, none of our isolates had the M phenotype. All the resistant isolates had iMLS or cMLS phenotypes; that is, none of the MLSB drugs can be used to treat the infections caused by these isolates.

erm(B) was the gene most frequently responsible for MLSB resistance, in agreement with prior studies, except for one from Canada in which erm(A) subclass erm(TR) was the most prevalent gene (3). All cMLS-expressing isolates had the erm(B) gene as expected. Coexistence of the resistance genes (erm with erm or erm with mef) in S. agalactiae is not uncommon (3, 5, 6, 12). Three of our isolates (8.6%) also harbored erm(TR) and erm(B) genes together and expressed the iMLS phenotype. Note that we did not detect the mef gene in any isolates. The isolates from which we could not amplify any of the resistance genes investigated might have harbored other erm genes not investigated or mutants of the investigated genes. Mutations of some ribosomal proteins such as L4 and L22 are other possible resistance mechanisms for the above isolates (10).

<p>| TABLE 2. MICs of erythromycin and clindamycin for the erythromycin-resistant isolates |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Phenotype, (n)          | Drug                      | MIC (µg/ml) |</p>
<table>
<thead>
<tr>
<th></th>
<th>MICc</th>
<th>MICg</th>
<th>MICc</th>
<th>MICg</th>
</tr>
</thead>
<tbody>
<tr>
<td>cMLS (7)</td>
<td>Erythromycin</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td></td>
</tr>
<tr>
<td>iMLS (28)</td>
<td>Clindamycin</td>
<td>16–&gt;128</td>
<td>1–&gt;128</td>
<td>1–&gt;128</td>
</tr>
<tr>
<td></td>
<td>2–128</td>
<td>0.06–128</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* MICc, MIC at which 50% of the isolates tested are inhibited.
* MICg, MIC at which 90% of the isolates tested are inhibited.

