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References


Comparison of the 5 \( \mu \)g disc and the NeoSensitab for determining the susceptibilities of \textit{Staphylococcus aureus} isolates to mupirocin

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Sir,

Mupirocin is a topical antibiotic that has excellent in-vitro activity against staphylococci (both methicillin-susceptible and -resistant) and streptococci. It is currently available in three formulations: a polyethylene glycol-based ointment for treating skin infections; a soft paraffin base for the eradication of \textit{Staphylococcus aureus} nasal colonization; and a cream formulation that has recently been licensed in the USA for the treatment of patients with infected traumatic skin lesions.

The susceptibilities of clinical isolates to mupirocin can be determined by a variety of methods, including disc

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diffusion, agar or broth dilution and the Etest, and interpretative criteria for defining the susceptibility categories of S. aureus strains causing infections, as determined by the National Committee for Clinical Laboratory Standards (NCCLS)-recommended disc diffusion method with a 5 μg disc, have been published. In addition, studies are currently under way to determine breakpoints for defining the susceptibility categories of isolates colonizing the nares; staphylococci with MICs up to 256 mg/L can be eliminated from these sites following the application of standard dosages of mupirocin.

Neo-Sensitabs are susceptibility test discs that are produced from compressed compound. The purpose of this study was to identify interpretative criteria for the mupirocin Neo-Sensitab and to compare the results of susceptibility testing with this disc with those obtained with the standard 5 μg mupirocin disc.

Ninety-seven S. aureus isolates with MICs ranging from ≤0.06 to >1024 mg/L were included in the study, although an effort was made to select strains with MICs close to the breakpoint for susceptibility to mupirocin (≤4 mg/L). Included amongst these were methicillin-resistant and -susceptible and β-lactamase-positive and -negative strains. Susceptibility was determined by the disc diffusion method with the 5 μg mupirocin disc (BBL, Cockeysville, MD, USA) and by an agar dilution method, in both cases according to recommendations of the NCCLS, and with Neo-Sensitabs containing 10 μg of mupirocin (Rosco, Taastrup, Denmark) which were used according to the manufacturer’s instructions. S. aureus ATCC 25923 was used as a control. Susceptibility was defined in terms of the following interpretative criteria: for the 5 μg disc, a zone of inhibition ≥14 mm; and for the Neo-Sensitab, a zone of inhibition ≥18 mm (as recommended by the manufacturer). The NCCLS guidelines for determining breakpoints with a scattergram specify that the proposed diameter of the zone of inhibition should be adjusted until results obtained with the disc diffusion method that are wrongly categorized as susceptible (very major errors) or resistant (major errors) are minimal. Very major errors should be detected with a frequency of <1.5% and major errors with a frequency of <3%.

The scattergram depicting the MICs of mupirocin as determined by the agar dilution method versus the zone diameters obtained with the Neo-Sensitabs is shown in the Figure. For the analysis of correlation, isolates with MICs ≤0.06 mg/L and those for which there were no zones of inhibition were eliminated from the calculations. For the remaining 49 isolates, the Pearson correlation coefficient was 0.927 for the Neo-Sensitab versus MICs.

Nine major errors were detected with the Neo-Sensitabs when the ≥18 mm breakpoint was used; this represents a major error rate of 9.3%. From the Figure, it can be seen that, if a breakpoint of ≥15 mm is used, the number of major errors would be reduced to two (2%) which is within the suggested limit.

The modified zone diameter breakpoints were used to compare the results obtained with the Neo-Sensitab and the 5 μg disc. There were four discrepancies: two isolates were susceptible according to both the Neo-Sensitab and the MIC, but resistant according to the 5 μg disc; one was susceptible according to both the 5 μg disc and the MIC, but resistant according to the Neo-Sensitab; and one was resistant according to both the Neo-Sensitab and the 5 μg disc, but susceptible according to the MIC. The MICs for all four of these isolates were 4 mg/L which places them in the susceptible range.

The two diffusion methods appear to be reliable screening tools for the detection of isolates resistant to mupirocin. However, for strains with inhibition zone

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Zone diameter (mm)</th>
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<tbody>
<tr>
<td>≤0.06</td>
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</tr>
<tr>
<td>0.12</td>
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<tr>
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<td>1</td>
</tr>
<tr>
<td>&gt;1024</td>
<td>1</td>
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</tbody>
</table>

Figure. Scattergram of mupirocin MICs versus inhibitory zone diameters obtained with the Neo-Sensitab (n = 97). The double horizontal line represents the MIC breakpoint for susceptibility, the double vertical line represents the susceptibility breakpoint recommended by the manufacturer (≥18 mm) for the Neo-Sensitab and the single vertical line represents the proposed breakpoint (≥15 mm).
diameters close to the breakpoint for resistance, MICs should be determined in order to avoid wrongly categorizing an isolate as resistant by the disc diffusion method and because this method does not differentiate between high- and low-level mupirocin-resistant isolates.

In conclusion, the mupirocin Neo-Sensitab is a reliable method of determining the susceptibilities of *S. aureus* isolates to this agent. The proposed breakpoints for strains causing infections are as follows: for the agar dilution test, susceptible \( \leq 4 \) mg/L and resistant \( > 8 \) mg/L; and for the Neo-Sensitab, susceptible \( \geq 15 \) mm and resistant \( \leq 14 \) mm.

**References**


**The in-vitro activities of co-amoxiclav and other oral antibiotics against *Streptococcus pneumoniae* isolates exhibiting intermediate susceptibility to penicillin**

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Sir,

The results of an ongoing, prospective, international, multicentre antibiotic susceptibility study (the Alexander Project), published in this Journal\(^1\) and elsewhere,\(^2,3\) have demonstrated that both amoxycillin and co-amoxiclav are more active *in vitro* than benzylpenicillin against strains of *Streptococcus pneumoniae* isolated from patients with community-acquired respiratory tract infections. The study also found that the activity of amoxycillin was greater than those of cephalosporins (cefaclor, cefuroxime and cefixime), macrolides, co-trimoxazole, ciprofloxacin and ofloxacin against *S. pneumoniae* strains exhibiting intermediate susceptibility to penicillin (Pen-I). As investigators participating in the Alexander Project, we report here recently compiled project data on the *in-vitro* activities of co-amoxiclav and other antibiotics used as oral therapy of patients with community-acquired respiratory tract infections against Pen-I strains isolated in the USA.

Between 1992 and 1996, 66 Pen-I strains recovered from either blood cultures or sputa were collected in five centres in the USA. On the basis of MIC susceptibility breakpoints recommended by the National Committee for Clinical Laboratory Standards (NCCLS)\(^4\) (or, in the case of ciprofloxacin, a breakpoint of \( \leq 1 \) mg/L recommended by the Food and Drug Administration), the susceptibilities of the isolates to various antibiotics were as follows: co-amoxiclav, 92%; amoxycillin, 89%; erythromycin, azithromycin and clarithromycin, 85%; ciprofloxacin, 85%; cefuroxime, 68%; and co-trimoxazole, 52%. The corresponding data for cefprozil, cefixime and cefaclor could not be determined as NCCLS breakpoints for these agents have not yet been published.

The high *in-vitro* activity of co-amoxiclav against Pen-I strains demonstrated here is in accord with the results of an earlier study undertaken by Korgenski *et al.*\(^5\) who found that, overall, the MICs of this agent were lower than those of benzylpenicillin against Pen-I strains isolated from patients with respiratory tract infections at a centre in the USA. Recent surveillance studies in the USA have shown that 25% of strains of *S. pneumoniae* causing lower respiratory tract infections in outpatients and 39-42% of those causing upper respiratory tract infections are resistant to penicillin;\(^6\) many of these strains, especially those causing infections that are usually associated with children, such as acute otitis media, exhibited intermediate susceptibility.\(^6,7\) The high activity of co-amoxiclav suggests that this agent may be the preferred oral antibiotic for use as empirical therapy of patients with acute otitis media or other community-acquired respiratory tract infections frequently caused by Pen-I strains and/or \( \beta \)-lactamase-producing strains of *Haemophilus influenzae* or *Moraxella catarrhalis*.

**References**