Sir,

The BSAC Working Party on Sensitivity Testing has established MIC breakpoints (BPs) for many of the antimicrobials tested in the UK, and they were chosen based on pharmacokinetic and MIC distribution data. Methicillin is not used clinically and in this instance the MIC BP was based solely on MIC distributions for those staphylococci considered clinically significant and isolated most frequently. Since the publication of these guidelines the meCA gene, which confers resistance, has been identified and the presence or absence of this gene is now used as the definitive test for determining resistance to methicillin/oxacillin.

In the near future methicillin will be withdrawn from manufacture and it has been proposed that oxacillin be used as the agent to detect resistance. However, in a recent study, when MIC data for methicillin and oxacillin for 1694 coagulase-negative staphylococci (CNS) were used to determine rates of resistance, using the BSAC BP of 4 mg/L for methicillin and a BP of 2 mg/L for oxacillin (BP recommended by NCCLS and the Société Française de Microbiologie), statistically significant differences in the levels of resistance were observed for Staphylococcus epidermidis (P < 0.0001), Staphylococcus spp., 12 Staphylococcus hominis, seven Staphylococcus capitis, seven Staphylococcus warneri, six Staphylococcus simulans and three Staphylococcus lugdunensis), using methodology based on that described in the BSAC Guide to Sensitivity Testing published in 1991; with the results obtained using a commercially available rapid latex test which detects PBP2′ (Mastalex, Mast Diagnostics, Bootle, UK), in order to obtain an MIC BP for oxacillin. Any results not in agreement between the two methods were confirmed by PCR.

For the 200 strains tested there was disagreement between the latex and PCR results on two occasions, once with a strain of S. warneri and once with a strain of S. hominis. In both instances the latex test was positive and PCR was negative. A PCR was considered the definitive test, results for PCR were used for analysis. A disagreement between MIC BPs and the latex/PCR tests are shown in the Table. In the case of the latex/PCR-positive strains, agreement was similar for both agents (68.4% and 74.5% for methicillin and oxacillin, respectively). Of these strains, which were falsely interpreted as sensitive to both agents, most errors were seen with S. epidermidis where MIC values were equal to or one dilution below the MIC BP concentrations. For the latex/PCR negative strains there was a marked difference between the two agents used for detection, with agreement of only 49.5% for methicillin, yet agreement of 92.4% for oxacillin. The highest level of disagreement with methicillin was seen with strains of S. saprophyticus, where 47 strains with MICs of 8–16 mg/L (presumably the normal MIC distribution for the wild-type sensitive population) were falsely interpreted as resistant to methicillin.

When the same organisms were subjected to detection of methicillin/oxacillin resistance using the BSAC method of testing described in the BSAC Newsletter published in the Summer of 1998, that is, using Columbia agar supplemented with 2% sodium chloride, an inoculum equivalent to semi-confluent growth, a 1 μg oxacillin disc and incubation at 30°C for 24 h, the agreement between the latex/PCR

Table.

<table>
<thead>
<tr>
<th>Antimicrobial MIC BP</th>
<th>Latex/PCR negative agreement (A)</th>
<th>Latex/PCR positive agreement (B)</th>
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<tbody>
<tr>
<td>Methicillin (4 mg/L)</td>
<td>49.5% (52/105)</td>
<td>68.4% (67/98)</td>
</tr>
<tr>
<td>Oxacillin (2 mg/L)</td>
<td>92.4% (97/105)</td>
<td>74.5% (73/98)</td>
</tr>
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</table>
Correspondence

methods was 82% for the negative strains (compared with 96% for the positive strains, unpublished data).

It is clear from these data that the detection of methicillin/oxacillin resistance in CNS by MIC or abbreviated MIC methods may present problems because of the diversity of susceptibility amongst these species, and that the selection of one MIC BP may lead to false interpretation of sensitivity. Indeed, these data have shown that a single MIC BP of 4 mg/L for methicillin for all staphylococci was not appropriate for all CNS, especially for S. epidermidis and S. saprophyticus. In the case of oxacillin the problem seen for methicillin with S. saprophyticus was not observed. However, for S. epidermidis, a lower MIC BP of 1 mg/L might be more appropriate for detecting resistance. These data have also shown that the BSAC Standardized Disc Diffusion Method is reliable for detecting resistance in CNS.

In conclusion, an MIC BP for oxacillin of 2 mg/L correlates well with PCR/latex methods for detecting methicillin/oxacillin resistance in CNS, except for S. epidermidis where an MIC BP for oxacillin of 1 mg/L gave a more reliable interpretation.

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References


