In vitro activity of co-amoxiclav acid against clinical isolates of Escherichia coli

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Sir,

Strains of Escherichia coli have been reported to be increasingly resistant to co-amoxiclav (AMC). This may be due to overproduction of penicillinase, production of penicillinase resistant to inhibitors (IRT), production of cephalosporinase or to technical problems encountered whilst performing in vitro susceptibility tests. The aims of this study were, first to determine the frequency of \(\beta\)-lactam resistance phenotypes in the Franche-Comté region of France, and secondly to compare two susceptibility testing methods (disc diffusion and Etest) to determine how resistant \(E. coli\) was to co-amoxiclav, in vitro.

One-hundred and ninety-nine non-replicate clinical strains of \(E. coli\), isolated in 21 hospitals in the Franche-Comté region during one week (in November 1999), were included in the study. The urinary tract was the major site of isolation (64.3%). The isolates were equally distributed between community-acquired (50.2%) and hospital-acquired (49.8%) (strains acquired after at least 48 h hospitalization). Susceptibility to antibiotics was determined on Mueller–Hinton agar by the disc diffusion method. Strains were classified as susceptible, intermediate or resistant, according to the recommendations of the Antibiogram Committee of the French Society for Microbiology. The strains were classified into six phenotypes according to their susceptibility to \(\beta\)-lactams:

- wild-type (WT), susceptible to all \(\beta\)-lactams;
- low-level penicillinase (LLP), resistant to amoxycillin, but susceptible to the co-amoxiclav combination (AMX R, AMC S);
- high-level penicillinase (HLP), only partially susceptible to co-amoxiclav (AMX R, AMC I/R);
- inhibitor-resistant TEM IRT), resistant to amoxycillin and to co-amoxiclav but susceptible to cephalothin (AMX R, AMC R, CEF S);
- cephalosporinase (C), resistant to amoxycillin, co-amoxiclav and cephalothin, but susceptible to ticarcillin (AMX R, AMC R, CEF R, TIC S);
- extended-spectrum \(\beta\)-lactamase (ESBL), resistant or partially susceptible to all the \(\beta\)-lactams tested and detected by resistance to both co-amoxiclav and cefotaxime.

<table>
<thead>
<tr>
<th>Resistance to AMC determined by disc diffusion (number of strains)</th>
<th>Resistance to AMC determined by Etest (number of strains)</th>
<th>MICs determined by Etest (mg/L) (number of strains)</th>
</tr>
</thead>
<tbody>
<tr>
<td>resistant (5)</td>
<td>24 (5)</td>
<td></td>
</tr>
<tr>
<td>Resistant (13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>intermediate (8)</td>
<td>12 (5)</td>
<td>16 (2)</td>
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<tr>
<td></td>
<td></td>
<td>16 (1)</td>
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<tr>
<td>intermediate (27)</td>
<td></td>
<td>8 (10)</td>
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<td>Intermediate (36)</td>
<td></td>
<td>6 (15)</td>
</tr>
<tr>
<td>susceptible (9)</td>
<td>4 (8)</td>
<td></td>
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<td></td>
<td>3 (1)</td>
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The MICs of amoxycillin and co-amoxiclav were determined by the Etest method (BMD, Marne-la-Vallée, France) for amoxycillin-resistant strains. Sixty-one isolates (30.6%) were resistant to amoxycillin (seven LLP, 49 HLP and five C). All the amoxycillin MICs of amoxycillin-resistant strains were >256 mg/L. The disc diffusion method found that 9.0% of clinical strains were resistant to co-amoxiclav and that 18.1% were partially resistant. The Etest found a lower proportion of resistant and partially resistant strains: 5.0 and 17.6%, respectively. The MICs for high-level penicillinase-producing strains are shown in the Table. Of the 49 isolates identified as HLP by the disc diffusion method, the Etest found that only five were resistant to co-amoxiclav. Moreover, these resistant strains had relatively low MICs (24 mg/L).

The Etest found that fewer strains were resistant to co-amoxiclav than the disc diffusion method. Most of the isolates that were less susceptible were classified as intermediate, and those strains that were resistant had a relatively low MIC (24 mg/L). It is noteworthy that two-thirds of the *E. coli* strains were isolated from the urinary tract and that regardless of the method used to administer co-amoxiclav, the levels in the urinary tract were always substantially higher than the MIC measured by Etest. Thus despite the susceptibility results, co-amoxiclav probably acts on all urinary isolates of *E. coli*. Use of the Etest to determine the MIC of HLP *E. coli* may be an interesting way to limit the use of other broad-spectrum antibiotics, such as fluoroquinolones or third-generation cephalosporins for the treatment of urinary tract infection, thus preventing increasing antibiotic resistance in *E. coli* clinical isolates.

**References**


