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Comparative in vitro activities of tigecycline and 11 other antimicrobial agents against 215 epidemiologically defined multidrug-resistant Acinetobacter baumannii isolates

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Sir,

Acinetobacter baumannii is a significant nosocomial pathogen, in particular in ICU patients. Their multidrug resistance, propensity for clonal spread and involvement in hospital outbreaks are a cause of concern. The carbapenems have been relied upon for treating infections caused by multidrug-resistant A. baumannii. Since the early 1990s, but more recently A. baumannii isolates with resistance to the carbapenems are increasingly reported. Tigecycline is the first glycycline and is one of the very few new antimicrobials with activity against Gram-negative bacteria encompassing not only most Enterobacteriaceae, but also—at least in vitro—multiresistant A. baumannii. Tigecycline has a distinct advantage over tetracycline and minocycline in that it evades acquired efflux and target-mediated resistance to classical tetracyclines. Several studies have tested the in vitro activity of tigecycline against A. baumannii and reported good bacteriostatic activity against strains with the wild-type susceptibility profile as well as those resistant to imipenem. However, clinical experience with this drug as well as with tetracyclines in the treatment of A. baumannii infections is still limited.

Current multicentre studies usually require that isolates are obtained from different patients. However, with highly epidemic microorganisms such as A. baumannii, isolates collected consecutively from different patients may nevertheless be clonally related. Antimicrobial susceptibility testing of isolates with the inclusion of multidrug-resistant epidemic strains tends to
overestimate the resistance of these microorganisms. Pachón-Ibáñez et al. \(^7\) recently reported on the activity of tigecycline against \textit{A. baumannii} bloodstream isolates. Forty-nine isolates were studied that predominantly represented two major epidemic clones. It is therefore not surprising that 78% of isolates were found to be resistant to imipenem, simply because their strain collection contained a large number of copy strains of an imipenem-resistant outbreak-strain. Conversely, this study design may have led to an overestimate of the activity of tigecycline against \textit{A. baumannii} because the major epidemic \textit{A. baumannii} strain may have exhibited a low tigecycline MIC.

The strength of the current investigation is that only \textit{A. baumannii} isolates were included that represented different strain types as assessed by molecular typing.

Our data support the findings of Henwood et al. \(^6\) who reported that tigecycline had good \textit{in vitro} activity (MIC\(_{50}\) and MIC\(_{90}\) 0.5 and 2 mg/L, respectively) against isolates of the \textit{A. baumannii} complex. Resistance to tigecycline was slightly higher in our study (6% versus 2.7%). Resistance to the carbapenems (3.3%) was still low in our study. The majority of imipenem-resistant isolates were still susceptible to tigecycline which is in keeping with previous reports. \(^7\)

In conclusion, tigecycline appears to be a promising agent adding to the small armamentarium of antimicrobials that remain active against \textit{A. baumannii}. Further clinical studies are urgently needed.

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**Transparency declarations**

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**References**


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Table 1. MIC distributions of tigecycline and other antimicrobials determined by broth microdilution for 215 \textit{A. baumannii} isolates

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC(_{50}) (mg/L)</th>
<th>MIC(_{90}) (mg/L)</th>
<th>MIC range</th>
<th>% Susceptible</th>
<th>% Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin/sulbactam</td>
<td>34 63 40 8 18 21 31(^b)</td>
<td>4 64 1/0.5–64/128</td>
<td>67.4 24.2</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>32 86 37 13 7 7 8 13</td>
<td>2 64</td>
<td>83.7 13.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefepime</td>
<td>4 31 33 28 55 24 40(^b)</td>
<td>16</td>
<td>44.7 29.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colistin</td>
<td>1 17 99 71 21 4 1 1</td>
<td>0.5 2</td>
<td>97.2 2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>62 44 18 17 22 15 13 5 19(^b)</td>
<td>1 32</td>
<td>75.8 17.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>21 47 31 15 8 15 20 14 44(^b)</td>
<td>2</td>
<td>56.7 36.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td>151 31 13 7 0 6 3 2 2(^b)</td>
<td>(\leq 0.125)</td>
<td>94.0 3.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>93 22 11 11 20 21 26 9 2(^b)</td>
<td>0.5 16</td>
<td>63.7 27.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin</td>
<td>1 1 4 25 52 37 7 88(^b)</td>
<td>32</td>
<td>38.6 40.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>1 43 166 4 1(^b)</td>
<td>8</td>
<td>ND(^a) ND(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tigecycline</td>
<td>46 36 36 25 40 19 4 2 7(^b)</td>
<td>0.5 4</td>
<td>85.1 6.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>60 67 32 13 11 12 8 6 6(^b)</td>
<td>0.5 8</td>
<td>85.1 9.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MIC\(_{50}\) and MIC\(_{90}\), MICs (mg/L) for 50% and 90% of isolates tested, respectively. Bold figures indicate CLSI breakpoints applied for susceptible isolates. Colistin, levofloxacin, tigecycline (FDA-approved breakpoint): 2 mg/L; doxycycline, gentamicin, imipenem, tobramycin: 4 mg/L; ampicillin/sulbactam, cefepime: 8 mg/L; amikacin, piperacillin: 16 mg/L.

\(^a\)ND, not determined, because no breakpoint is recommended for rifampicin versus Gram-negative microorganisms by the CLSI.

\(^b\)MICs of these isolates were greater than or equal to the indicated value.