In summary, the current study shows that ceftobiprole has good in vitro activity against E. faecalis and E. coli isolates from different human and animal origins and proved to be a potent antimicrobial agent against MRSA and MSSA irrespective of their susceptibilities to cefepime.

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Transparency declarations
None to declare.

References

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Antibiotic susceptibility profiles of European Bacteroides fragilis with reduced carbapenem susceptibility

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Sir,
Bacteroides fragilis usually causes infection together with other aerobic and anaerobic bacteria and is one of the most important anaerobic pathogens responsible for a variety of significant clinical infections including intra-abdominal infections, complicated skin and skin structure infections, bacteremia and deep abscesses. Antibiotic resistance in this important pathogen has been noted and is increasing in many parts of the world.1

The preferred agents of choice for B. fragilis infections include broad-spectrum penicillins, metronidazole, clindamycin, piperacillin/tazobactam, carbapenems, moxifloxacin and, more recently, tigecycline. Tigecycline was recently shown to exhibit promising activity against European isolates of various anaerobes, including Bacteroides spp.2 Today the majority of anaerobic infections are treated empirically and minimal, if any, antimicrobial susceptibility testing is performed. With the knowledge that antimicrobial resistance is increasing to many classes of antimicrobial agents used to treat anaerobic infections, active ongoing surveillance of resistance patterns of anaerobes is advantageous. The use of carbapenems as one of the preferred agents of choice has ultimately led to the development of carbapenem resistance and the recognition of the metallo-β-lactamase gene cfiA and its expression.3 This report documents the in vitro activity of six antimicrobial agents against B. fragilis isolates collected in Europe during 2007–08.

All isolates were derived from complicated intra-abdominal infections, gastrointestinal, wounds, blood and other body fluid sources. Isolates were identified to genus and species by the local laboratory and confirmed at a reference laboratory. Only one isolate per patient was accepted. There were 928 clinical isolates of B. fragilis collected between 2007 and 2008 from 20 unique laboratory sites in six European countries (Belgium, the Czech Republic, France, Germany, the UK and Hungary). All isolates were sent to a central laboratory in the USA (Laboratories International for Microbiology Studies, a subsidiary of International Health Management Associates, Inc., Schaumburg, IL, USA) for confirmation of identification and susceptibility testing. MICs were determined by agar dilution as specified by the CLSI.4 The following antimicrobial agents were tested with their dilution ranges (expressed in mg/L): tigecycline (0.06–32); clindamycin (0.25–8); metronidazole (0.12–16); piperacillin/tazobactam (0.06/4–64/4); meropenem (0.06–8); and cefoxitin (2–32). MIC interpretive criteria followed published breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) where applicable.5 Since no EUCAST guidelines were available for cefoxitin, CLSI breakpoints6 were used. FDA anaerobe breakpoints were used for tigecycline.7 Quality control testing was done following CLSI guidelines.4,6

Table 1 lists the susceptibilities of B. fragilis clinical isolates to the six antimicrobial agents. Isolates were generally susceptible to the antimicrobial agents with percentage susceptibilities of ≥87% with the exception of clindamycin for which 22.6% of isolates were resistant. The most active agents by MIC90 were meropenem (MIC90 0.5 mg/L), metronidazole (MIC90 1 mg/L) and piperacillin/tazobactam and tigecycline (MIC90 2 mg/L).
Table 1. *In vitro* activity of antibiotics against European *B. fragilis* clinical isolates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Isolates</th>
<th>Breakpoints (S</th>
<th>I</th>
<th>R)</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>%S</th>
<th>%I</th>
<th>%R</th>
<th>MIC range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tigecycline</td>
<td>all (n=928)</td>
<td>≤4</td>
<td>8</td>
<td>≥16</td>
<td>0.5</td>
<td>2</td>
<td>97.4</td>
<td>1.7</td>
<td>0.9</td>
<td>0.06 to 64</td>
</tr>
<tr>
<td></td>
<td>RS-MEM (n=32)</td>
<td>≤4</td>
<td>8</td>
<td>≥16</td>
<td>1</td>
<td>2</td>
<td>96.9</td>
<td>0</td>
<td>3.1</td>
<td>≤0.06 to 32</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>all (n=928)</td>
<td>≤16</td>
<td>32</td>
<td>≥64</td>
<td>4</td>
<td>32</td>
<td>87.4</td>
<td>7.9</td>
<td>4.7</td>
<td>0.25 to &gt;256</td>
</tr>
<tr>
<td></td>
<td>RS-MEM (n=32)</td>
<td>≤16</td>
<td>32</td>
<td>≥64</td>
<td>16</td>
<td>&gt;32</td>
<td>59.4</td>
<td>25</td>
<td>15.6</td>
<td>4 to &gt;256</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>all (n=928)</td>
<td>≤4</td>
<td>≥1</td>
<td>≥8</td>
<td>1</td>
<td>&gt;8</td>
<td>77.4</td>
<td>0</td>
<td>22.6</td>
<td>&lt;0.015 to &gt;256</td>
</tr>
<tr>
<td></td>
<td>RS-MEM (n=32)</td>
<td>≤4</td>
<td>≥1</td>
<td>≥8</td>
<td>2</td>
<td>&gt;8</td>
<td>65.6</td>
<td>0</td>
<td>33.4</td>
<td>0.5 to &gt;256</td>
</tr>
<tr>
<td>Meropenem</td>
<td>all (n=928)</td>
<td>≤2</td>
<td>4-8</td>
<td>≥16</td>
<td>0.12</td>
<td>0.5</td>
<td>96.6</td>
<td>2.8</td>
<td>0.6</td>
<td>0.015 to &gt;32</td>
</tr>
<tr>
<td></td>
<td>RS-MEM (n=32)</td>
<td>≤2</td>
<td>4-8</td>
<td>≥16</td>
<td>4</td>
<td>&gt;8</td>
<td>81.2</td>
<td>18.8</td>
<td>0.015 to &gt;32</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>all (n=928)</td>
<td>≤4</td>
<td>≥1</td>
<td>≥8</td>
<td>0.5</td>
<td>1</td>
<td>99.6</td>
<td>0</td>
<td>0.4</td>
<td>≤0.12 to &gt;256</td>
</tr>
<tr>
<td></td>
<td>RS-MEM (n=32)</td>
<td>≤4</td>
<td>≥1</td>
<td>≥8</td>
<td>0.5</td>
<td>1</td>
<td>96.9</td>
<td>0</td>
<td>3.1</td>
<td>≤0.12 to &gt;256</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>all (n=928)</td>
<td>≤8</td>
<td>16</td>
<td>≥32</td>
<td>0.25</td>
<td>2</td>
<td>96.7</td>
<td>1.7</td>
<td>1.6</td>
<td>≤0.015 to &gt;256</td>
</tr>
<tr>
<td></td>
<td>RS-MEM (n=32)</td>
<td>≤8</td>
<td>16</td>
<td>≥32</td>
<td>1</td>
<td>64</td>
<td>81.3</td>
<td>6.2</td>
<td>12.5</td>
<td>≤0.06 to 32</td>
</tr>
</tbody>
</table>

%S, %I and %R, percentage of isolates susceptible, intermediate or resistant, respectively. All MIC values are expressed in terms of mg/L. All (n=928) refers to all isolates tested in the study. RS-MEM refers to the 32 isolates exhibiting reduced susceptibility to meropenem. Breakpoints are defined by EUCAST<sup>5</sup> where available. Cefoxitin breakpoints are defined by CLSI.<sup>6</sup> Tigecycline breakpoints are defined by the FDA.<sup>7</sup>

(1). Although meropenem was the most active agent by MIC<sub>90</sub>, 3.4% (n=32) of all isolates exhibited reduced susceptibility to meropenem. An analysis of the activity of each antimicrobial agent against isolates with reduced susceptibility to meropenem revealed that the MIC<sub>90</sub> for meropenem was >8 mg/L (at least 16-fold higher than the MIC<sub>90</sub> for all isolates tested in the study) for which only 81.2% and 18.8% exhibited intermediate susceptibility and resistance to meropenem, respectively (Table 1). The MIC<sub>90</sub>s of tigecycline and metronidazole for isolates with reduced susceptibility to meropenem were within one dilution of their MIC<sub>90</sub> for all isolates (Table 1). By contrast, the MIC<sub>90</sub> of piperacillin/tazobactam for all isolates was 2 mg/L but was 32-fold higher for isolates with reduced susceptibility to meropenem, for which the susceptibility to this antibiotic combination was 81.3%. The only agents to which >90% of this subset of isolates were susceptible were tigecycline and metronidazole.

In summary, recent clinical isolates of *B. fragilis* from Europe included a sub-set of isolates with reduced susceptibility to meropenem. The carbapenem class has been a regular choice for the treatment of *B. fragilis* infections. Other choices include moxifloxacin; however, resistance to this agent has also become clinically important.<sup>8</sup> As the frequency of carbapenem non-susceptibility may eventually restrict the use of such agents against *B. fragilis*, monitoring of resistance trends in the carbapenem class is needed.

**Acknowledgements**

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**References**


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**Transparency declarations**

None to declare.