culturable from cells 48 h after infection, suggesting that it is able to survive intracellularly, as previously demonstrated for GAS.\(^5\) The presence of the fnb gene, coding for Fn-binding protein FnB,\(^6\) was demonstrated in SdyIMR by PCR. As in GAS, multiple cocci were consistently found inside cells by microscopy and DNA sequences internal to fnb, and erm(A) continued to be amplified by PCR in infected cells until day 20 (both data not shown).

To our knowledge, this is the first report of a GCS S. dysgalactiae subsp. equisimilis isolate combining macrolide resistance and ability to enter human respiratory cells. As previously suggested for GAS, such a combination of resistance and virulence traits may confer an increased ability to propagate and spread, enabling escape from penicillin and other β-lactams (confined to the extracellular fluid) because of intracellular location and from macrolides (active in intracellular compartments) because of resistance.\(^3\)

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**Transparency declarations**

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**References**


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Keywords: glycyclcyclines, carbapenemases, susceptibility

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Sir,

Tigecycline is a new semi-synthetic derivative of minocycline and the first in the glycyclcline class of antibiotics. Its mechanism of action involves inhibition of bacterial protein synthesis by binding to the 30S ribosomal subunit and blocking the entry of tRNA into the A site of the ribosome, thereby preventing the elongation of peptide chains. Pre-clinical studies have demonstrated the potent in vitro activity of tigecycline against a wide range of aerobic Gram-positive and Gram-negative bacteria, including multidrug-resistant strains, anaerobic and atypical pathogens.\(^1,2\) Tigecycline circumvents the two most frequent mechanisms of tetracycline resistance, which are the active efflux of drug from the bacterial cell and ribosomal protection. In addition, it is not affected by β-lactamase production [extended-spectrum β-lactamase (ESBL) production and AmpC hyperproduction] or DNA gyrase alterations, defence mechanisms that are used by many microorganisms.\(^1,2\)

Even though many studies have demonstrated the activity of tigecycline against ESBL-producing Enterobacteriaceae, its activity is not well defined against microorganisms producing metallo-β-lactamases (MBLs) as there are only a few reports and the number of isolates tested is limited.\(^3\) The aim of the present study was to evaluate the activity of tigecycline against 109 MBL-producing Enterobacteriaceae.

A total of 109 non-duplicate MBL-producing isolates of the family Enterobacteriaceae collected from hospitalized patients from January 2004 to June 2007 were studied. The identification of microorganisms and susceptibility testing were performed using the Vitek 2 automated system (bioMérieux, France). The isolates included 4 *Escherichia coli*, 13 *Enterobacter* spp. (11 *Enterobacter cloacae* and 2 *Enterobacter aerogenes*), 4 *Serratia marcescens* and 88 *Klebsiella pneumoniae*. The isolates were recovered from the following sources: blood (34%), wounds (28%), urine (21%), central venous catheters (9%), sputum (7%) and cerebrospinal fluid (1%). All isolates were characterized as resistant or intermediate to imipenem and meropenem and gave positive results for the double-disc synergy test between imipenem and EDTA.\(^4\) The production of VIM-type MBL was confirmed by PCR using specific primers. PFGE of *Xba* I-digested genomic DNA indicated that most of the isolates were unrelated (data not shown). MICs of tigecycline were determined using the Etest, according to manufacturer’s guidelines. All isolates with tigecycline MICs of ≥1 mg/L were tested by the broth microdilution method using panels purchased from Microscan (Dade Behring, Sacramento, LA, USA). *E. coli* ATCC 25922 was used as quality control. MIC\(_{50}\) and MIC\(_{90}\) values were calculated for *Enterobacter* spp. and *K. pneumoniae* strains.

**In vitro activity of tigecycline against metallo-β-lactamase-producing Enterobacteriaceae**

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<https://academic.oup.com/jac/article-abstract/60/6/1406/824332> by guest on 03 January 2019
Our results are demonstrated in Table 1. *E. coli*, *S. marcescens* and *Enterobacter* spp. isolates were inhibited at MIC values of ≤1, 2 and ≤2 mg/L, respectively. For *K. pneumoniae*, MIC50 and MIC90 values of tigecycline were 0.25 and 2 mg/L, respectively. The Etest results were confirmed by the broth microdilution method. According to US Food and Drug Administration recommendation for tigecycline (susceptible ≤2 mg/L and resistant ≥8 mg/L), all isolates were susceptible and only one (1%) *K. pneumoniae* strain displayed an intermediate MIC of 4 mg/L. When the European Committee on Antimicrobial Susceptibility Testing breakpoint criteria (susceptible ≤1 mg/L and resistant >2 mg/L) were used, the percentage of tigecycline susceptibility decreased. Only 4 (31%) *Enterobacter* spp. and 78 (89%) *K. pneumoniae* isolates tested were susceptible. Furthermore, all *S. marcescens* were characterized as intermediate.

Currently, multidrug-resistant Gram-negative bacteria remain the most problematic pathogens worldwide, especially in intensive care units. Carbapenem antibiotics were important agents for the management of those infections. Over the past few years, the progressive increase in carbapenem-resistant Gram-negative non-fermentative bacilli as well as the spread of genes encoding carbapenem-hydrolysing enzymes in enterobacterial species is of great concern, leaving limited choices for therapeutic regimens. Our results confirm the in vitro activity of tigecycline against multiple-drug-resistant, including pan-resistant, Gram-negative and Gram-positive clinical isolates from Greek hospitals. *Antimicrob Agents Chemother* 2006; 50: 3166–9.


Invasive group B *Streptococcus* isolates showing reduced susceptibility to penicillin in Hong Kong

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Keywords: *Streptococcus agalactiae*, blood culture, penicillin G, benzylpenicillin

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Table 1. In vitro activity of tigecycline against 109 MBL-positive Enterobacteriaceae

<table>
<thead>
<tr>
<th>Organism (number of isolates)</th>
<th>MIC (mg/L)</th>
<th>Number of isolates with MIC (mg/L) of</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>range</td>
<td>MIC&lt;sub&gt;50&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>E. coli</em> (4)</td>
<td>0.03–1</td>
<td>NA</td>
</tr>
<tr>
<td><em>S. marcescens</em> (4)</td>
<td>2</td>
<td>NA</td>
</tr>
<tr>
<td><em>Enterobacter</em> spp. (13)</td>
<td>0.25–2</td>
<td>2</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> (88)</td>
<td>0.12–4</td>
<td>0.25</td>
</tr>
</tbody>
</table>

NA, not applicable.

<sup>a</sup>MIC<sub>50</sub> and MIC<sub>90</sub> at which 50% and 90% of isolates tested, respectively, are inhibited.

Transparency declarations

None to declare.

References


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