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Keywords: Acinetobacter baumannii, glycyclines, resistance

Table 1. Comparison of susceptibility rates to tigecycline in MDR A. baumannii

<table>
<thead>
<tr>
<th>Isolates</th>
<th>TEST global</th>
<th>TEST Argentina</th>
<th>Navon-Venezia et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>377</td>
<td>48</td>
<td>82</td>
</tr>
<tr>
<td>TIG MIC ≥2 mg/L</td>
<td>20 (5.3%; 2.9–7.7%)</td>
<td>1 (2%; 0–7.16%)</td>
<td>64 (78%; 68.48–87.62%)</td>
</tr>
<tr>
<td>Method</td>
<td>microdilution</td>
<td>microdilution</td>
<td>Etest</td>
</tr>
<tr>
<td>IPM-R/I</td>
<td>178</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>TIG MIC ≥2 mg/L</td>
<td>10 (5.6%; 1.95–9.28%)</td>
<td>0 (0%; 0–1.78%)</td>
<td>21 (95%; 84.48–100%)</td>
</tr>
<tr>
<td>Method</td>
<td>microdilution</td>
<td>microdilution</td>
<td>Etest</td>
</tr>
</tbody>
</table>

MDR, multidrug-resistant; TEST, Tigecycline Evaluation and Surveillance Trial; TIG, tigecycline; IPM, imipenem; R/I, resistant/intermediate.

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Sir,

In the April 2007 issue of the Journal of Antimicrobial Chemotherapy, Navon-Venezia et al. reported high resistance rates to tigecycline in multiple clones of multidrug-resistant (MDR) Acinetobacter baumannii (n = 82). The authors found that 66% (54/82) were resistant to tigecycline (MIC ≥8 mg/L), 12% (10/82) were intermediate (MIC 4–6 mg/L) and 22% (18/82) were susceptible (MIC ≤2 mg/L). They used Etest to determine MICs and all the values correlated 100% with inhibition zone diameters using the disc diffusion method with tigecycline discs.

We agree with the authors that MDR in Acinetobacter spp. represents a global challenge to physicians; for this reason we will try to offer a wider point of view.

The Tigecycline Evaluation and Surveillance Trial (TEST) is a worldwide programme that includes, at the moment, 4247 isolates of Acinetobacter spp. of which only 2% have a tigecycline MIC ≥2 mg/L.

Based on this data, we compare the results of Navon-Venezia et al., with those of TEST, using the global data and the Argentinean sub-set data. We selected from the TEST database the isolates of MDR A. baumannii with the same resistance profile as those analysed by Navon-Venezia et al. (i.e. A. baumannii resistant to aminoglycosides, cephalosporins and fluoroquinolones) (Table 1).

In contrast with the 78% published by Navon-Venezia et al., only 5.3% of the global isolates and 2% of the Argentinean sub-set isolates of MDR A. baumannii in TEST had tigecycline MICs ≥2 mg/L. We asked ourselves what would be the probability of encountering such a difference if all the isolates belong to the same population. We performed a proportion test to do so. The probability was very low (P < < 0.0001).

Regarding the MDR A. baumannii isolates as previously defined, and additionally resistant or intermediate to imipenem, the resistance ratio to tigecycline showed important differences (95%, 5.6% and 0% for Navon-Venezia et al., TEST global and Argentinean sub-set, respectively).

Tigecycline has been approved for the treatment of complicated intra-abdominal infections and complicated skin and skin

References

structure infections. However, in Argentina, in the first month after launch, 61% of the tigecycline prescriptions were 'off label', especially for patients with ventilator-associated pneumonia (VAP) due to MDR Acinetobacter spp. (D. Curcio, F. Fernández and F. Duret, unpublished data). The high concentration in alveolar cells (77.5-fold higher than serum),3 the increase in carbapenem-resistant Acinetobacter spp. in Argentina (54%),4 the lack of medical evidence to use colistin in pulmonary infections and the association between inappropriate initial antibiotic therapy with mortality in patients with VAP (defined as the susceptibility of cultured organisms to the antibiotics used)5 seem to be the main reasons for using tigecycline in this indication.

Concerning tigecycline and Acinetobacter spp. several points should be taken into account: (i) definitive breakpoints of susceptibility are not available; (ii) results for Phase 3 clinical trials regarding clinical efficacy of tigecycline in nosocomial pneumonia and other infections produced by MDR microorganisms are not available; and (iii) we know that the overexpression of the intrinsic multidrug efflux pump (AdeABC) may decrease the susceptibility to tigecycline in Acinetobacter spp.6

However, at least in Argentina, some physicians consider this new antibiotic as a possibility to treat microbiologically documented severe infections caused by MDR A. baumannii, in order to improve the patient outcome when the therapeutic options are limited (i.e. isolates only susceptible to colistin).

Moreover, from a clinical point of view, until data on tigecycline clinical efficacy in severe Acinetobacter spp. infections become available, before treating a patient, physicians must consider the pharmacological and microbiological profile of tigecycline for each specific patient condition and carefully assess local susceptibility data to support its use.

Finally, we agree with the authors, that the high MICs for A. baumannii found by them is a worrisome local phenomenon and requires further investigation.

Transparency declarations

D. C. is a speaker for Wyeth SA (Argentina) for Tygacil®. F. F. does not have any conflict of interest.

References


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Rapid decrease in the prevalence of macrolide-resistant group A streptococci due to the appearance of two epidemic clones in Cantabria (Spain)

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Sir,

An increase in erythromycin resistance rates among group A streptococci (GAS) has been reported in some European countries, including Spain, where in some regions the level of resistance is very high (62.3%).1 Resistance to erythromycin is commonly caused by the presence of an active drug efflux pump (M phenotype) or due to target site modification by inducible or constitutive methylases (MLS\textsubscript{b} phenotype).

It is well established that the prevalence of resistance to antimicrobials depends in part on their use in the community.2 In the case of GAS, a nationwide study in Finland indicated that a reduction in macrolide use correlated with a decrease in macrolide resistance.3 In contrast with this idea, between 2002 and 2004 there were no relevant variations in the attended population or in the consumption of macrolides in Cantabria (Spain), however, we noted a marked decrease in macrolide-resistant GAS in January–April 2004. This study was undertaken to determine the reasons for this rapid decrease.

Antibiotic consumption data from January 2002 to April 2004 were obtained from SIFARCAN (Pharmaceutical Information System of Cantabria). All GAS collected from January 2002 to April 2004 at the Hospital Marques de Valdecilla of Cantabria (Spain) were identified by conventional methods. More than 95% of these isolates were from pharyngotonsillitis. Susceptibility of these isolates to macrolides during this period was routinely tested by disc diffusion according to the CLSI guidelines and phenotypes of resistance were evaluated as previously described.4

The prevalence of GAS resistant to macrolides in Cantabria was high from the second quarter of 2002 until the third quarter of 2003, when the percentage of the resistant isolates varied between 27.4 and 38.6, respectively, reaching a maximum of 53.6 between July and December of 2002 (Figure 1). The prevalence decreased rapidly in the last quarter of 2003, reaching a percentage as low as 3.7 in the first quarter of 2004. In parallel, the total number of GAS isolated from January 2002