In Vitro Activity of Tigecycline Against Methicillin-Resistant \textit{Staphylococcus aureus} Isolated from the Patients at Siriraj Hospital

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\section*{INTRODUCTION}
Methicillin-resistant \textit{Staphylococcus aureus} (MRSA) is one of the most common causes of infections in hospitalized patients. The prevalence of MRSA among \textit{S. aureus} isolates from hospitalized patients at Siriraj Hospital from January to May 2005 was 51.5 percent.\textsuperscript{1} The common sites of MRSA infections were the skin and skin structures, the lower respiratory tracts, and the blood stream. Antibiotics currently used for therapy of MRSA infections include glycopeptides, fluoroquinolones, co-trimoxazole, fosfomicin, fusidic acid, and linezolid. However, these antibiotics had considerable drawbacks including the possibility of toxicity, emergence of resistance, and high monetary cost. Therefore, a search for any new agents effective against MRSA is ongoing.

Tigecycline is a glycyclycline antibiotic that shows a promising activity against a wide range of organisms.\textsuperscript{2-4} Tigecycline is active against gram-positive cocci including methicillin-resistant staphylococci, penicillin-resistant \textit{Streptococcus pneumoniae}, and vancomycin-resistant enterococci.

The objective of the study was to determine an in vitro activity of tigecycline against MRSA clinical isolates from Thai patients.

\begin{abstract}
An in vitro activity study of tigecycline against 51 clinical isolates of methicillin-resistant \textit{Staphylococcus aureus} (MRSA) from different patients hospitalized at Siriraj Hospital, Bangkok, Thailand from 2002 to 2004 was performed by the disk diffusion method and E-test. All isolates had an inhibition zone of $\geq 20$ mm, with the MIC$_{50}$ and MIC$_{90}$ of 0.125 and 0.25 mg/L, respectively. The study results indicated that all MRSA isolates tested were susceptible to tigecycline. (\textit{J Infect Dis Antimicrob Agents} 2006; 23:1-4.)
\end{abstract}
MATERIALS AND METHODS

MRSA Isolates

Fifty-one clinical isolates of MRSA from different infected patients hospitalized at Siriraj Hospital, Bangkok, Thailand from 2002 to 2004 were included. They were isolated from the lower respiratory tract (N=15), the pus (N=16), the blood (N=10), and the other specimens (N=10). All isolates had oxacillin minimum inhibitory concentration (MIC) of >4 mg/L and vancomycin MIC of <4 mg/L. Forty-six isolates were vancomycin-susceptible MRSA, and 5 isolates were vancomycin-hetero-resistant MRSA. Vancomycin-susceptible MRSA and vancomycin hetero-resistant MRSA were determined by a one-point population analysis and confirmed by a population analysis.5,6

Tigecycline Susceptibility Study

The methodology for susceptibility testing was done by direct colony suspension according to the guidelines recommended by the Clinical and Laboratory Standards Institute (CLSI).7 The test isolate was grown overnight on blood agar at 35°C, and the colonies were picked and suspended in sterile normal saline equivalent to a 0.5 McFarland standard. The suspension was used to inoculate on Mueller-Hinton agar. The paper discs containing tigecycline 15 µg per disk (Becton Dickinson, USA) and E-test strips (AB BIODISK, Sweden) were placed according to manufacturer’s recommendation. The agar plates were incubated at 35°C for 18 hours before the inhibition zone and MIC results were read. Quality control was performed by testing the susceptibility of S. aureus ATCC 29213 as recommended by Wyeth Research, USA.

RESULTS

The MIC of tigecycline against S. aureus ATCC 29213 was 0.064 mg/L which was within the reference range of 0.03-0.25 mg/L. A distribution of inhibition zone diameters of tigecycline against 51 MRSA isolates by the disk diffusion method is shown in Table 1. The inhibition zone of tigecycline against all isolates of MRSA was > 20 mm. A distribution of MICs of tigecycline against 51 MRSA isolates by the E-test is shown in Table 2. The MIC50 and MIC90 values were

<table>
<thead>
<tr>
<th>Organism (No. of isolates)</th>
<th>Number of isolates with diameter of inhibition zone (mm)</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
<th>24</th>
<th>25</th>
<th>26</th>
<th>27</th>
<th>28</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>All MRSA (N=51)</td>
<td></td>
<td>4</td>
<td>7</td>
<td>9</td>
<td>11</td>
<td>2</td>
<td>13</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Vancomycin-susceptible MRSA (N=46)</td>
<td></td>
<td>2</td>
<td>7</td>
<td>9</td>
<td>8</td>
<td>2</td>
<td>13</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Vancomycin-hetero-resistant MRSA (N=5)</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Organism (No. of isolates)</th>
<th>Number of isolates with MIC (mg/L)</th>
<th>0.032</th>
<th>0.064</th>
<th>0.094</th>
<th>0.125</th>
<th>0.19</th>
<th>0.25</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>All MRSA (N=51)</td>
<td></td>
<td>2</td>
<td>6</td>
<td>12</td>
<td>17</td>
<td>7</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Vancomycin-susceptible MRSA (N=46)</td>
<td></td>
<td>2</td>
<td>6</td>
<td>12</td>
<td>15</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Vancomycin-hetero-resistant MRSA (N=5)</td>
<td></td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
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</table>
0.125 and 0.25 mg/L, respectively. Susceptibility profiles of tigecycline against vancomycin-susceptible MRSA and vancomycin-hetero-resistant MRSA were not significantly different.

**DISCUSSION**

According to the US Food and Drug Administration (FDA)-approved breakpoints of the inhibition zone of ≥19 mm and MIC of <0.5 mg/L indicating the susceptibility of *S. aureus* to tigecycline, all studied isolates of MRSA in one study were considered susceptible to tigecycline. These observations confirmed the worldwide data on in vitro susceptibility of tigecycline against MRSA. Tigecycline was found to be effective and safe for treating patients with complicated intra-abdominal infections and complicated skin and skin-structure infections. Tigecycline has been approved by the US FDA for treating patients with the aforementioned infections. However, the existing evidence proving the effectiveness of treating MRSA infections with tigecycline remains limited. Tigecycline may prove to be an important antibiotic for treatment of MRSA infections in Thailand in the near future once more clinical information on use of tigecycline in treating of MRSA infections becomes available.

**ACKNOWLEDGEMENT**

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**References**


