Daptomycin susceptibility of clinical isolates in invasive *Staphylococcus aureus* infections in Korean hospitals: can resistance to daptomycin occur without previous exposure to vancomycin?

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Abstract

**BACKGROUND**

It was suggested that daptomycin non-susceptibility in *Staphylococcus aureus* can be induced by vancomycin exposure in vitro and in vivo without daptomycin exposure. To prove this, we conducted a multicenter study in a large scale to evaluate whether daptomycin non-susceptibility can occur in the isolates from Korean patients with invasive *S. aureus* (ISA) infection who have never been exposed to daptomycin.

**METHODS**

We selected potential daptomycin-resistant isolates from *S. aureus* collection in the previous prospective study for ISA infections which was performed from July 2009 to June 2011 at 10 hospitals in Korea. Potential daptomycin resistant *S. aureus* isolates were defined as follows: 1) heteroresistant vancomycin-intermediate *S. aureus* (h-VISA) 2) S. aureus strain with vancomycin minimal inhibitory concentration (MIC) more than 1.5 μg/mL by Etest or brothmicrodilution (BMD); 3) persistent *S. aureus* bacteremia for 7 days or more. Vancomycin MICs were determined by the BMD and Etest, and daptomycin MICs by Etest. Clinical characteristics were collected and multicase sequence typing was performed for the daptomycin non-susceptible *S. aureus* strains.

**RESULTS**

A total of 208 non-duplicate *S. aureus* isolates from the cases of ISA infections, of which 171 was VISA were screened for daptomycin non-susceptibility by Etest. Among these, 124 showed vancomycin MICs more than 1.5 μg/mL, 93 persistent bacteremia, and 42 h-VISA with overlaps. Five *S. aureus* isolates with daptomycin non-susceptibility (MIC >1 μg/mL) were detected. These were isolated from patients without previous vancomycin exposure. All of them had healthcare associated (HA) infections and underwent surgery within recent one year. All but one of these patients had catheter associated bloodstream infections or surgical site infections (Table).

**CONCLUSION**

Daptomycin non-susceptible *S. aureus* is extremely rare in Korea where daptomycin is not commercially available yet. However, five *S. aureus* isolates with daptomycin non-susceptible (0.48%) were detected by Etest in our study. This showed non-susceptibility of these *S. aureus* isolates can develop without previous exposure to daptomycin or vancomycin.

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**Table. Clinical and microbiological characteristics of daptomycin non-susceptible invasive *Staphylococcus aureus* infections in Korea**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>H-VISA</th>
<th>Persistent bacteremia</th>
<th>Vancomycin MIC (μg/mL)</th>
<th>Daptomycin MIC (μg/mL)</th>
<th>ST</th>
<th>Location</th>
<th>Previous vancomycin exposure (&lt;1 m)</th>
<th>Underlying disease(s)</th>
<th>Primary foci</th>
<th>30-day mortality</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>39/M</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>2</td>
<td>3</td>
<td>1.5</td>
<td>HA</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>57/M</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>1.5</td>
<td>72</td>
<td>HA</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td>3</td>
<td>70/F</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>2</td>
<td>1.5</td>
<td>5</td>
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<tr>
<td>4</td>
<td>75/M</td>
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<td>No</td>
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</tr>
</tbody>
</table>

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**Figure 1. Distribution of invasive *Staphylococcus aureus* isolated from blood**

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**Figure 2. Percentage of discrepant Etest MICs stratified according to the MICs values**

- **-1**: 0-0.25
- **0**: 0.25-1.0
- **+1**: >1.0
- **-2**: >2.0

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**Results**

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