

Vancomycin Susceptibility of Methicillin-Resistant *Staphylococcus aureus* in Siriraj Hospital : 1997-1998

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Abstract

Vancomycin susceptibility status of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in Siriraj Hospital during 1997-1998 was determined by E-test. Of 95 strains isolated, all had minimal inhibitory concentration (MIC) of $\leq 2 \mu\text{g/mL}$. The MIC₅₀ was $1.5 \mu\text{g/mL}$ and MIC₉₀ was $2 \mu\text{g/mL}$. Seventy-five percent of all the isolates of MRSA had the MIC of $1.5\text{-}2 \mu\text{g/mL}$. The findings in this study indicated the possibility of heterogeneous resistant strains whose MICs may appear between 1 and $2 \mu\text{g/mL}$. Ongoing surveillance for emerging vancomycin-resistant MRSA is warranted. (*J Infect Dis Antimicrob Agents* 1999;16:149-50.)

INTRODUCTION

In 1996, the first case of methicillin-resistant *Staphylococcus aureus* (MRSA) with reduced susceptibility to vancomycin was discovered in Japan.¹ A year later, 2 patients from the US were reported as being infected by MRSA strains with the same minimum inhibitory concentration (MIC) level of $8 \mu\text{g/mL}$.^{2,3} The first case infected with vancomycin-resistant *S. aureus* (VRSA) with an MIC of $16 \mu\text{g/mL}$ was reported soon afterward.⁴ We have performed a study to determine vancomycin susceptibility status of MRSA isolates collected during 1997-1998 in our hospital by looking at their MIC values for vancomycin.

METHODS

All the MRSA isolates from clinical specimens in Siriraj Hospital have been collected since 1997 for

the purpose of epidemiological study. MRSA was defined as *S. aureus* with resistance to oxacillin by disc diffusion test with a clear zone diameter of ≤ 10 mm. In this study, consecutive isolates of MRSA were tested for MIC of vancomycin by agar gradient diffusion method with a full 24-hour incubation at 37°C . The break points were determined according to NCCLS.⁵

RESULTS

Ninety-five isolates of MRSA collected between August 1997 and February 1998 were studied. The source of the isolates were : sputum for 59; blood, 20; and other body fluids, 16. All the isolates had MIC of $\leq 2 \mu\text{g/mL}$ (Table 1). The MIC₅₀ was $1.5 \mu\text{g/mL}$ and MIC₉₀ was $2 \mu\text{g/mL}$. Medical records of the twelve patients whose isolates showed the MIC of $2 \mu\text{g/mL}$ were reviewed. The isolates were unrelated

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Table 1. Vancomycin MIC level of MRSA isolates in Siriraj Hospital 1997-1998.

MIC ($\mu\text{g/mL}$)	N (%)
0.5	1 (1.1)
0.8	10 (10.5)
1.0	22 (23.2)
1.5	50 (52.6)
2.0	12 (12.6)
Total	95 (100)

due to different location of patient wards and completely different diseases and clinical status. However, 6 (50%) of the 12 isolates were obtained from patients aged older than 60 years old.

DISCUSSION

It is not unexpected that someday *S. aureus* will be resistant to vancomycin in Thailand. In *in vitro* experiments, vancomycin resistance was induced by serial passage of sensitive *S. aureus* in vancomycin containing media.^{6,7} Coagulase-negative staphylococci with reduced vancomycin susceptibility have been reported.^{8,9} Moreover, high-level vancomycin resistance was established in many enterococci via *VanA* and *VanB* resistant genes. The *VanA* gene is plasmid-mediated and can be transferred to *S. aureus in vitro*.¹⁰ All of the evidence alerted clinicians to await for VRSA, which has already arrived.⁴ However, the mechanism of resistance of VRSA is not mediated via *VanA* gene, but seems to be associated with accumulation of a cell wall component and increased vancomycin binding to the cell wall.¹¹ Molecular investigations suggest that VRSA are conceived from heterogeneous resistant strains with subsequent selective pressure.¹² Therefore, the use of vancomycin is probably the main factor in the development of VRSA. The heterogeneous resistant strains were found in 9-20 percent of isolates in university hospitals in Japan.

This report is a part of the efforts to study vancomycin susceptibility status. We did not perform screening tests for heterogeneous VRSA. Although heterogeneous VRSA has higher vancomycin MIC than vancomycin susceptible *S. aureus* (VSSA), both may have an overlapping MIC at 1-2 $\mu\text{g/mL}$.¹² This is of concern because 75 percent of isolates in this study had an MIC of 1.5-2 $\mu\text{g/mL}$

and some of them could be heterogeneous VRSA waiting to develop vancomycin resistance. There was no identifiable factors associated with the infections caused by clinical isolates with an MIC of 2 $\mu\text{g/mL}$. The findings in this study support on going close monitoring for vancomycin-nonsusceptible *S. aureus* which may possibly develop soon if vancomycin is used without precautions.

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