community at large—to move forward in their efforts to reduce multidrug-resistant organism transmission in health care facilities.

Acknowledgments

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References


The Activity of Daptomycin Against Wild-Type Staphylococcus aureus and Strains with Reduced Susceptibility to Vancomycin

To the Editor—Patel et al. [1] recently reported the antimicrobial susceptibility of 917 Staphylococcus aureus strains tested against vancomycin and daptomycin. The collection was described as “independent S. aureus isolates submitted to the Centers for Disease Control and Prevention (CDC) for antimicrobial susceptibility testing” [1, p. 1652]. The results showed an association between a vancomycin MIC of 4 μg/mL or 8 μg/mL and a daptomycin MIC of ≥2 μg/mL (P > .0001, by χ² test for trend) [1]. This association has been reported by other investigators [2, 3], and the authors speculated that some of the changes mediating reduced susceptibility to vancomycin may interfere with the antimicrobial action of daptomycin. However, the study of Patel et al. [1] contains some important limitations for determining relevance.

First, the authors’ collection of S. aureus was certainly biased toward a high prevalence of isolates with reduced susceptibility to vancomycin (MIC, ≥4 μg/mL; 8.2% of 917 isolates). It is very unlikely that this collection represents a typical sampling of S. aureus. Second, the occurrence of isolates with a daptomycin MIC reported at ≥2 μg/mL among those strains with vancomycin MIC ≤2 μg/mL is excessively high. We have been systematically following daptomycin activity against S. aureus isolates in the United States since 2002 [4]. In our surveillance program, the isolates are consecutively collected and are nonduplicate isolates obtained from patients with clinically significant infections (mainly bloodstream infections, skin and skin structure infections, and pneumonia in hospitalized patients). The isolates were susceptibility tested at a reference laboratory (JMI Laboratories; North Liberty, Iowa) by microdilution methods according to Clinical and Laboratory Standards Institute guidelines using validated panels manufactured by TREK Diagnostics and calcium-supplemented (50 mg/L) Mueller-Hinton broth for testing daptomycin. Among almost 10,000 S. aureus isolates tested, we detected only 4 (0.04%) with a reproducible daptomycin MIC of 2 μg/mL and none with a daptomycin MIC of ≥2 μg/mL (figure 1). All 4 S. aureus strains had a relatively high (but within the susceptible range) vancomycin MIC value (2 μg/mL). In addition, we observed only 2 isolates (0.02%) with vancomycin MICs of 4 μg/mL (i.e., vancomycin-intermediate S. aureus [VISA]), and these 2 isolates had a daptomycin MIC of 0.5 or 1 μg/mL (figure 1). No isolate with a vancomycin MIC of >4 μg/mL was found in this systematic surveillance. Thus, it is very important to emphasize that S. aureus with a daptomycin MIC of ≥2 μg/mL and/or a vancomycin MIC of ≥4 μg/mL is extremely rare in the contemporary clinical setting. In fact, only 70 (0.70%) of 9959 clinical strains exhibited a daptomycin MIC ≥1 μg/mL (figure 1) using Clinical and Laboratory Standards Institute methods with appropriate, monitored calcium medium content [6].

Patel et al. [1] also did not provide any details regarding the susceptibility methods used in the study, especially regarding the control of calcium concentration in the test media. Because it is well established that daptomycin potency is very sensitive to calcium concentration [6], we are concerned that low concentrations of calcium might have contributed to the tendency toward higher daptomycin MIC values (1 log, dilution step) observed in the study [1]. The aberrant results, reporting numerous isolates with daptomycin MICs ≥2 μg/mL and vancomycin MICs ≤2 μg/mL, support this concept.
Another important problem of the study [1] is the lack of information about the collection of organisms. The higher prevalence of isolates with decreased susceptibility to vancomycin clearly implies that these strains do not represent a normal population of clinical S. aureus strains, and it is possible that some of the strains were forwarded to the CDC because of suspected decreases in their susceptibility to vancomycin or daptomycin according to 1 or more susceptibility test methods.

Finally, we have recently evaluated the activity of daptomycin against a collection of VISA, hetero-VISA (hVISA), and vancomycin-resistant S. aureus (from the Network on Antimicrobial Resistance in Staphylococcus aureus collection). A tendency toward higher daptomycin MIC results, compared with results for the normal population of S. aureus (figure 1), was detected, but the tendency was not to the same degree as that reported by the CDC [1]. This study also demonstrated that vancomycin was only bacteriostatic against 69.3% of hVISA and all VISA strains, whereas daptomycin remained bactericidal against all hVISA and VISA strains [5]. In agreement with the results reported by Patel et al. [1], vancomycin-resistant S. aureus strains had very low daptomycin MICs (0.25–0.5 µg/mL), clearly inhibiting isolates that expressed a vanA resistance gene. Daptomycin retained potency and bactericidal activity against both vancomycin-resistant S. aureus and the more numerous hVISA isolates. We have shown that the very rare VISA isolates may present with a modest decrease in susceptibility to daptomycin (MIC, 2 µg/mL). The occurrence of strains with reduced daptomycin susceptibility is extremely rare (4 [0.04%] of our collection of 9959 strains) but can occur following long exposure to daptomycin therapy. Great care must be taken, however, to use appropriately supplemented Mueller-Hinton broth (50 mg/L calcium) to avoid over reporting or misrepresenting drug resistance and to assure the accurate assessment of this new bactericidal agent, daptomycin.

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References


Reply to Sader and Jones

To the Editor—In response to the letter by Dr. Sader and Dr. Jones [1], the isolates from our report [2] do not represent a normal distribution of Staphylococcus aureus isolates. Many of these isolates were sent to the Centers for Disease Control and Prevention to confirm an unusual susceptibility test result, such as reduced...