Evidence for Reduction in Breakpoints Used To Determine Vancomycin Susceptibility in Staphylococcus aureus

Questions regarding the prevalence and clinical significance of both vancomycin-intermediate Staphylococcus aureus (VISA) and, more importantly, heterogeneous VISA (hVISA) strains have been isolated from many areas of the world but are few in number (<30); however, hVISA strains appear more common. Current susceptibility techniques, along with CSLI (S/I/R-4/8-16/32) and EUCAST (S/R-4/8) recommended breakpoints, are generally inadequate for the identification of hVISA. VISA strains have been isolated from many areas of the world but are relevant, with patients with hVISA bacteremia more likely to have high-bacterial-load infections, vancomycin treatment failure, bacteraemia for >7 days, and a significantly higher mortality (63%) than those patients infected with vancomycin-susceptible methicillin-resistant S. aureus (VSSA) bacteraemia (12%). More recently, treatment failure in patients with infections caused by strains with MICs within the susceptibility range (≤2 mg/liter) has been reported (9). Also, current CDC guidelines for testing S. aureus with vancomycin recommend that strains exhibiting MICs of ≤2 mg/liter plus growth on vancomycin screening plates are possibly VISA (www.cdc.gov /ncidod/hip/vanco/vanco.htm). These data suggest that current susceptibility breakpoints for glycopeptides require review.

We used an international collection of VSSA, VISA, and hVISA strains with CSLI agar dilution techniques to determine vancomycin MICs (7). Each data set was compared with a view to recalculating a vancomycin breakpoint. VISA and hVISA phenotypes were identified by the more accurate modified population analysis method (population analysis profile-area under the curve) (14).

Of 106 glycopeptide-susceptible S. aureus strains, 10.4% had vancomycin MICs of 0.5 mg/liter, 85.8% had vancomycin MICs of 1 mg/liter, and 3.8% had vancomycin MICs of 2 mg/liter. The percentage of isolates classified as susceptible by the CSLI and EUCAST breakpoint (4 mg/liter) and a reduced breakpoint (2 mg/liter) was 100%, suggesting that no false positives would emerge from breakpoint reduction. Of 20 VISA strains, 55% exhibited vancomycin MICs of 4 mg/liter and 45% had vancomycin MICs of 8 mg/liter. Using the current breakpoint, 55% are classified as susceptible and 45% as intermediate. However, when using the reduced breakpoint, 100% are classified as intermediate (CSLI) or resistant (EUCAST). Of 157 hVISA strains, 2% exhibited vancomycin MICs of 1 mg/liter, 80.2% had vancomycin MICs of 2 mg/liter, and 17.8% had vancomycin MICs of 4 mg/liter. Using the current breakpoint, 100% are classified as susceptible; however, when using the reduced breakpoint, 82.2% would still be classified as susceptible but 17.8% would be classified as susceptible and 17.8% would be classified as intermediate (CSLI) or resistant (EUCAST).

The percentage of isolates classified as susceptible by the CSLI and VISA would increase from 45% and 0% to 100% and 17.2%, respectively. Distribution of vancomycin MICs in the different phenotypes shows that 2 mg/liter is the most predominant in hVISA (Fig. 1). The effect of a reduced breakpoint on the classification of coagulase-negative staphylococci would be minimal, with only 1.56% currently exhibiting a vancomycin MIC of 4 mg/liter (www .EUCAST.org). This evidence supports a modification of the contemporary interpretative guidelines for vancomycin susceptibility testing from ≤4 mg/liter for susceptible isolates to ≤2 mg/liter.

REFERENCES

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Evidence for Reduction in Breakpoints Used To Determine Vancomycin Susceptibility in *Staphylococcus aureus*

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Volume 49, no. 9, p. 3982–3983, 2005. Page 3982, column 2, line 22: “hVISA and VISA” should read “VISA and hVISA.”
Page 3982, column 2, line 23: “17.2%” should read “17.8%.”