Reduced biofilm production associated with increasing linezolid MICs among linezolid-resistant staphylococci

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Sir,

To follow-up our previous finding of reduced polystyrene adherence accompanying the acquisition of linezolid resistance in a clinical bloodstream isolate of methicillin-resistant Staphylococcus aureus (MRSA),1 we evaluated the polystyrene adherence properties of linezolid-resistant staphylococci obtained from our institution as well as isolates obtained from multiple medical centres throughout the USA collected as part of the LEADER programme.2,3 Eleven coagulase-negative staphylococci from one medical centre identified by the Microscan susceptibility method (10 Staphylococcus epidermidis and 1 Staphylococcus haemolyticus) and 50 staphylococci identified from the LEADER programme (33 S. epidermidis, 7 S. aureus, 2 Staphylococcus caprae, 2 Staphylococcus capitis, 2 Staphylococcus warnerii, 1 Staphylococcus cohnii, 1 S. haemolyticus, 1 Staphylococcus saprophyticus and 1 non-specified) with linezolid MICs >4 mg/L were available for susceptibility testing by broth microdilution methods of the CLSI.4

The biofilm formation phenotype was assayed by polystyrene adherence assays as previously described.1 After approval was obtained from the internal review board for research, chart review of 13 patients at our hospital (11 cases whose isolates were used in the analysis plus 2 additional cases whose isolates were not available) with linezolid-resistant coagulase-negative staphylococci isolated from blood cultures was performed to determine patient age, sex, hospital ward, exposure to linezolid, hospital day at time of isolation, patient co-morbidities and whether the blood culture isolate fulfilled CDC criteria for catheter-related bloodstream infection.5 The patients had a median age of 60 years (range 18–78), 62% of the patients were male and the patients were hospitalized for a median of 37 days (range 6–217) at the time of isolation of the linezolid-resistant coagulase-negative staphylococci. Fifty-four percent received prior linezolid during the hospitalization but none of the patients was on linezolid at the time cultures were obtained. Of the 13 patients, 2 isolates (15%) were deemed clinically significant by fulfilling CDC criteria for catheter-related bloodstream infection. PFGE demonstrated a predominant clonal type, two closely related types and three unique clonal types.

Regression tree modelling revealed a dichotomous inverse relationship between polystyrene adherence and linezolid MIC for the 11 isolates from a single medical centre [P = 0.02, Kruskal–Wallis analysis of variance (ANOVA)]. This relationship was examined for reproducibility among the 50 isolates from the LEADER programme (Figure 1). The break occurred at a linezolid MIC of ≥32 mg/L, above which isolates showed significantly reduced polystyrene adherence (P = 0.004, Kruskal–Wallis ANOVA). Evaluation of the subset of 43 LEADER coagulase-negative staphylococci (excluding the 7 S. aureus) demonstrated consistency of this relationship (P = 0.02, Kruskal–Wallis ANOVA).

Linezolid resistance has until recently remained relatively uncommon among staphylococci. A recent report of a 4.4% prevalence of linezolid resistance among coagulase-negative staphylococci at a tertiary medical centre raises concern.6 In this report, we identified 13 patients from whom these isolates were obtained from blood cultures, although only 2 (15%) represented clinically relevant isolates as aetiologies in catheter-associated bacteremia. The majority of patients (54%) had received linezolid during the hospitalization, lower than the 76% seen in the prior report.6 This suggests that linezolid-resistant staphylococci may reside as part of the indigenous nosocomial flora that can subsequently colonize hospitalized patients. Further studies are required to examine the point prevalence of such isolates at individual centres and whether linezolid utilization can impact this prevalence.

An evaluation of 11 linezolid-resistant coagulase-negative staphylococci from a single institution and 50 linezolid-resistant staphylococci acquired from multiple medical centres around the USA demonstrated a dichotomous inverse relationship between linezolid MIC and polystyrene adherence. A linezolid MIC of >32 mg/L was associated with reduced polystyrene adherence when compared with linezolid-resistant staphylococci at the lower end of the resistant MIC range (MIC 8–16 mg/L). This finding may represent another example where a specific virulence property of bacteria may be attenuated by the acquisition of antimicrobial resistance, although the mechanism behind this observation is unknown and not immediately obvious. This relationship may provide at least a partial explanation as to why linezolid-resistant staphylococci remain relatively rare among clinical isolates.

This study provides a preliminary assessment of the epidemiological, microbiological and physiological features of linezolid resistance in staphylococci. A more thorough epidemiological evaluation and prevalence study of linezolid resistance among coagulase-negative staphylococci in hospitals is warranted. Studies evaluating the genetic background of these strains and their mechanisms of linezolid resistance are currently in progress in our laboratories. Because of potential future implications on the treatment of staphylococcal infections mediated...

Figure 1. Scatterplot demonstrating the relationship of linezolid MIC and polystyrene adherence measured by the optical density at 540 nm (a marker for biofilm formation) for 50 linezolid-resistant staphylococci collected from multiple centres throughout the USA via the LEADER programme. A dichotomous inverse relationship was noted between isolates with linezolid MICs of 8–16 mg/L (n=6) versus isolates with linezolid MICs ≥32 mg/L (n=44) and polystyrene adherence (P=0.004, Kruskal–Wallis ANOVA).

by the formation of biofilms, further work evaluating the relationships between mutation copy number in domain V of 23S rRNA and biofilm suppression as well as the mechanism by which linezolid interacts with the biofilm-producing machinery in staphylococci would be of interest.

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