ABSTRACT

Background. Linezolid resistance in Gram-positive isolates has been more closely associated with 23S rRNA mutations than with ribosomal proteins. Here, we assessed the molecular mechanisms associated with linezolid resistance in a worldwide collection of Gram-positive pathogens (2008-2009).

Methods. S. aureus (13,085), coagulase-negative staphylococci (CNS; 2,969) and enterococci (1,362) were collected from various cities within the United States, Europe, Asia, and Latin America.

Results. For linezolid, low-level resistance was noted in 1% of isolates. CoNS isolates displayed a broader range of linezolid susceptibility with a linezolid MIC of 8–16 µg/mL. CoNS strains (MIC values of 8–16 µg/mL) were screened for cfr−-presence of cfr- mutations in the 23S rRNA, L3 and L4 proteins by PCR/sequencing. Sequences were compared with those from linezolid-susceptible ATCC strains. DNA sequences with ≥128 µg/mL were subjected to partial 16S rRNA sequencing.

Conclusions. Linezolid is associated with a low incidence of resistance in a worldwide collection of Gram-positive pathogens. 

INTRODUCTION

Linezolid is approved for the treatment of complicated skin and skin-structure infections (cSSSI) and nosocomial pneumonia caused by Gram-positive pathogens, including methicillin-resistant staphylococci (MRSA) and vancomycin-resistant enterococci (VRE). Linezolid inhibits bacterial growth by interfering with the formation of the T75S ribosome, leading to the inhibition of protein synthesis.

Although linezolid resistance remains rare, molecular mechanisms underlying linezolid-resistant isolates have been identified. 

RESULTS

Materials and methods

Relevant isolates. S. auersus (13,085), coagulase-negative staphylococci (CNS; 2,969) and enterococci (1,362) were collected from various cities within the United States, Europe, Asia, and Latin America. 

These isolates were selected according to established institutions (JMI Laboratories, North Liberty, Iowa, USA) as part of the LEADER Program for 2008 (LEADER Program results for 2008 (2009). Zyvox Annual Appraisal of Potency and Spectrum program: Linezolid Dis program results for 2008 (LEADER Program for 2008). JMI Laboratories, North Liberty, Iowa, USA). 

Institutions included in the LEADER Program included several antimicrobial classes, including phenicols, macrolides, tetracyclines, and oxazolidinones linezolid and torezolid (TR-700).

The presence of linezolid resistance was suspected in the following organisms: S. aureus ICMP-200, Staphylococcus epidermidis ICMP-200, Enterococcus faecalis ICMP-200, and Staphylococcus epidermidis ICMP-200.

Detection of linezolid-resistant isolates. Isolates with elevated linezolid MIC values (≥16 µg/mL) were screened for cfr−-presence of cfr mutations in the 23S rRNA, L3 and L4 proteins by PCR/sequencing.

Sequence alignment and mutations. Sequences were compared with those from linezolid-susceptible ATCC strains. 

REFERENCES

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