

## **Assessment of linezolid resistance mechanisms among *Staphylococcus epidermidis* causing bacteraemia in Rome, Italy**

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**Objectives** To characterize linezolid resistance among blood cultured *Staphylococcus epidermidis* from patients at the Polyclinic Agostino Gemelli (2006-08). Isolates also showed elevated MICs of macrolide, lincosamide and streptogramin (MLS) compounds, which were investigated. **Methods** Ten *S. epidermidis* exhibiting linezolid MICs  $\geq 4$  mg/L were included. Isolates were screened for *cfr* mutations in 23S rRNA, L3, L4 and L22, and MLS genes by PCR/sequencing. Ribosomal proteins were compared with those from a linezolid-susceptible (MIC, 1 mg/L) clinical strain and ATCC 12228. *cfr* location was determined by Southern blot/hybridization. The *cfr* strain was submitted to plasmid curing. Epidemiology was assessed by PFGE and multilocus sequence typing (MLST). **Results** *S. epidermidis* displayed linezolid MICs of 4 or 8 mg/L, except for strain 4303A (MIC, 64 mg/L). These organisms and a linezolid-susceptible strain exhibited L3 Leu101Val compared with ATCC 12228. Isolates also showed L3 Phe147Leu and Ala157Arg, and L4 Asn158Ser. Strain 12375A possessed L4 Lys68Arg. Isolates were wild-type for 23S rRNA and L22. *cfr* was plasmid located in strain 4303A and the plasmid-cured strain exhibited a linezolid MIC (4 mg/L) similar to that for *cfr*-negative strains (4-8 mg/L). All organisms harboured *erm(A)* and *msr(A)*, while *vga(A)* was detected in several isolates. All isolates were clonally related and ST-23. **Conclusions** L3 Phe147Leu and/or Ala157Arg appeared responsible for the elevated linezolid MIC, since adjacent alterations have been associated with resistance. L4 Asn158Ser has been reported in a linezolid-susceptible isolate and Lys68Arg detected here did not seem to provide an additive effect. Acquisition of *cfr* markedly increased (8- to 16-fold) the linezolid MICs. *vga(A)* was associated with higher MICs of quinupristin/dalfopristin and retapamulin.

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