Investigation of the linezolid resistance mechanisms in clinical isolates of coagulase-negative *Staphylococci* from Greece

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OBJECTIVES: Coagulase-negative staphylococci isolates resistant to linezolid (LZ-R) were isolated for the first time from ICU patients of Tzaneio General Hospital, Athens, in November 2008. The aim of this project was to investigate the resistance mechanisms and clinical and epidemiological aspects of this evolution.

MATERIALS AND METHODS: We studied the clinical characteristics of the patients, from whom LZ-R CoNS strains were isolated during one year (11/08-10/09) and the molecular characteristics of these isolates. The detection of mutations on the peptidyl-transferase center of the bacterial ribosome was performed in each of the 6 copies of the 23S rDNA by nested PCR and sequencing. The typing of the isolates was performed by PFGE. Environmental control and carrier control was performed among the staff of the ICU.

RESULTS: 46 LZ-R CoNS strains were isolated from 24 patients (16 male, average age 45±20.4 years). The majority of the isolates (41/46) was recovered from blood cultures. The dominant species was *Staphylococcus epidermidis* (38/46). The MIC to linezolid for 43/46 isolates was >256 μg/ml. All isolates were resistant to methicillin and susceptible to glycopeptides and daptomycin. The average time of hospitalization until the isolation of a LZ-R strain was 28±15.9 days. The study of the clinical characteristics of the patients proved that 7/24 had >2 underlying diseases, 9/24 reported previous hospitalization and 9/24 had foreign bodies. At the time of isolation of the LZ-R strain all patients had central lines, had already received multiple antimicrobials and 16/24 had mechanical ventilation. Average administration of linezolid was 11.2±7.5 days for 21/24 patients. 1/58 environmental samples developed LZ-R *S. epidermidis*, while the control of the staff for carriage of LZ-R S. epidermidis was negative. The molecular control of 30 isolates proved that 23/30 isolates bared simultaneously the characterized mutations T2504A and C2534T. The mutated copies of the 23S rDNA varied from 3 to 5 in each isolate. PFGE revealed clonal electrophoretic patterns indicating a clonal outbreak.

CONCLUSIONS: The clonal origin of the isolates demonstrates horizontal transmission and renders very important the application of intensive infection control measures in order to avoid further dissemination of these isolates.