O207
Oral Session
Bacterial pediatric infections

STAPHYLOCOCCUS CAPITIS IN NOSOCOMIAL BACTEREMIA IN INTENSIVE CARE NEONATES: WORLDWIDE DISTRIBUTION OF AN ENDEMIC METHICILLIN-RESISTANT CLONE (NRCS-A)

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Objective: Staphylococcus capitis pulsotype NRCS-A is involved in late-onset sepsis (LOS) in French neonatal intensive care units (NICUs) and showed to be multi-resistant (methicillin, aminoglycosides, vancomycin). We aim i) to investigate i) the worldwide distribution of NRCS-A clone by applying various molecular methods onto S. capitis isolates from several countries; ii) the specific *in vitro* ability of *S. capitis* NRCS-A to acquire vancomycin heteroresistance under selective pressure.

Methods: Twelve NICU S. capitis isolates from neonates septicemia (Australia, Belgium, France, United Kingdom, n=3 each) and 2 S. capitis isolates from adult patients were analyzed using PFGE (SmaI and SacII), SCCmec typing and dru-typing. A MLST-like analysis, based on 7 house-keeping genes, was also performed. After whole-genome sequencing of one of clinical NRCS-A strains, we performed a phylogenetic analysis with other publicly available S. capitis genomes to assess the evolutionary history. To explore impact of vancomycin selective pressure, after 15 daily iterative subcultures in presence of various vancomycin concentrations, the increase of voncomycin, daptomycin and linezolid MICs as well as their stability after subcultures without antibiotic were determined.

Results: All neonatal S. capitis (i) shared >80% similarity when characterized by SmaI and SacII PFGE and were similar to NRCS-A pulsotype, (ii) harbored a type V-related SCCmec element, (iii) exhibited the same dru-type (dt11c), and (iv) formed a monophyletic group using the 7 house keeping genes. The molecular profiles of both adult isolates differed from those of NICU strains. Unexpectedly, a CRISPR region was found within the SCCmec cassette and was detected by PCR, targeting the direct-repeats, in all NICUs isolates and one adult patient isolate. Finally, sequencing of the SCCmec element of one of the NICU isolates revealed the presence of a composite element including a SCCmec cassette and a second SCC carrying genes related to detoxification of heavy metals (SCCcad/ars). Phylogenetic analysis of all the 4 available whole-genome sequenced S. capitis strains suggests that the 2 SCC elements were acquired independently by the NRCS-A clone. An increase in vancomycin as well as daptomycin MICs (but not linezolid MICs) was observed for all tested strains. Increases were significantly faster ($p<0.05$) for S. capitis NRCS-A than for other tested strains (comparing the slopes of logarithmic curves MIC).

Conclusion: Our analysis demonstrates an unexpected worldwide distribution of the S. capitis NRCS-A clonal population involved in neonatal LOS. These results suggest that this multi-resistant clone is highly successful in the specific environment of NICUs. *S. capitis* NRCS-A is able to rapidly increase vancomycin MICs when in contact with vancomycin, giving a selective advantage to this clone in NICUs where vancomycin selective pressure is high. Further studies are underway to understand molecular mechanisms involved in both the way of spreading and glycopeptide adaptation of this clone.