

**P2805 *In vitro* activity of combinations amoxicillin-cephalosporins against endocarditis-associated *Enterococcus faecalis* isolates**Eléna Guillotel<sup>1</sup>, Nathan Peiffer-Smadja<sup>2</sup>, Xavier Lescure<sup>2</sup>, Vincent Cattoir\*<sup>1</sup><sup>1</sup> CHU de Rennes, Rennes, France, <sup>2</sup> AP-HP, Hôpital Bichat-Claude Bernard, Paris, France

**Background:** Enterococci (especially *Enterococcus faecalis*) are the third cause of infectious endocarditis (IE). Whereas the treatment of IEs due to *E. faecalis* is classically based on a combined therapy aminopenicillin-gentamicin, the combination aminopenicillin and third-generation cephalosporin (TGC) is increasingly used since it appears equally active and less toxic. It is also employed in case of high-level resistance to gentamicin. However, few data are available on the efficacy of combinations between aminopenicillin and other cephalosporins. The aim of the study was then to evaluate the *in vitro* activity of amoxicillin (AMX) combined with different cephalosporins against *E. faecalis* clinical isolates.

**Materials/methods:** A panel of 12 epidemiologically-unrelated *E. faecalis* strains were studied: 2 reference strains (ATCC 29212 and ATCC 51299) and 10 clinical isolates involved in IEs. The different cephalosporins tested were: cephazolin (CZ), ceftriaxone (CTO), cefotaxime (CTX), cefepime (FEP), ceftaroline (CPT) and ceftobiprole (CBP). MICs were determined by the broth microdilution reference method. Combinations between amoxicillin (at MIC x 1/4) and each cephalosporin (at the mean free plasma concentration) were studied in triplicates using time-kill curves. Bactericidal effect was defined as a  $\geq 3 \log_{10}$  decrease in CFU/ml after 24 h compared with the starting inoculum.

**Results:** MICs of AMX, CZ, CTX, CTO, FEP, CPT and CBP were 0.5-1, 16-64, 256-1,024, 256-1,024, 64-256 mg/L, 1-2 and 0.12-0.5 mg/L, respectively. A bactericidal effect was variably observed depending on the combination, the strain or the duration of exposure. Indeed, combinations AMX-CZ/AMX-FEP, AMX-CTO/AMX-CPT, and AMX-CTX/AMX-CBP were bactericidal at 24h against 9, 8 and 7 of the 12 strains, respectively. Note that a bacterial regrowth was observed between 12h and 24h for 3, 2 and 1 strains with combinations AMX-CTX/AMX-CTO, AMX-FEP and AMX-CZ, respectively. Finally, the reduction of the bacterial inoculum was slower for 8/12 strains with combinations AMX-CPT and AMX-CBP.

**Conclusions:** Cephalosporins other than TGCs exhibit an interesting *in vitro* activity against *E. faecalis* when combined with AMX. However, the bactericidal activity of each combination seems to be variable depending on the cephalosporin and the strain.

