In vitro activity of combinations amoxicillin-cephalosporins against endocarditis-associated Enterococcus faecalis isolates

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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), ceftaroline (FEP), cefepime (CPT) and ceftobiprole (CBP). MICs were determined by the broth microdilution reference method. Combinations between amoxicillin (at MIC x ¼) and each cephalosporin (at the mean free plasma concentration) were studied in triplicates using time-kill curves. Bactericidal effect was defined as a ≥3 log₁₀ 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.