Activity of fusidic acid (FUS) alone or in combination with daptomycin (DAP), vancomycin (VAN), or linezolid (LDZ) in an in vitro model of Staphylococcus aureus Biofilm

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Staphylococcus aureus is an important human pathogen causing chronic infections that are difficult to treat. Biofilm contributes to the persistence of infections, by protecting bacteria from immune system and antimicrobial agents. We showed that many antibiotics are poorly active on biofilms [1], especially when using clinical isolates from persistent infections [2]. Fusidic acid (FUS) may constitute a useful alternative for treatment of Staphylococcus aureus infections (in regions with low resistance rates) but shows moderate activity against biofilms [1]. Since FUS is commonly used in combination to avoid resistance selection, we examined which other antistaphylococcal antibiotics could at the same time improve, in vitro, its activity against mature biofilms of clinical isolates.

Materials and Methods

S. aureus reference strain ATCC25923 and 5 clinical strains isolated on medical devices or from chronic tissue infections were used. Biofilms were grown for 24 h in 96-wells plates and then exposed for 48 h to increasing concentrations (0.25-64 mg/L) of FUS (to obtain full concentration-response curves), combined with concentrations corresponding to the human Cmin or the Cmax of the associated drug. Bacterial viability in biofilms was quantified using the redox indicator resazurin (reduced to fluorescent resorufin by viable bacteria); biofilm biomass was evaluated using crystal violet absorbance.

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Conclusions

Combining FUS with DAP, VAN, or LDZ appears as a useful strategy to increase its antibacterial activity against biofilms. These data support the evaluation of these combinations in biofilm-related infections in vivo.