EV0056

ePoster Viewing

Antimicrobials: antimicrobial PK/PD, pharmacogenomics, pharmacoeconomics and general pharmacology, drug interaction studies

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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Objective: FUS may constitute a useful alternative for treatment of MRSA infections (in regions with low resistance rates) but shows moderate activity against biofilms (ref. 1). Since FUS is commonly used in combination to avoid resistance selection, we examined which other antistaphylococcal antibiotics could at the same time improve its activity against mature biofilms in vitro.

Methods: ATCC25923 (reference strain) and 5 clinical isolates (infections on medical devices or chronic tissue infections) were used. Biofilms were grown for 24 h in 96-wells plates (ref. 1) 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 fC_{min} or the fC_{max} of the associated drug. Bacterial viability in biofilms was quantified using the redox indicator resazurin and biomass by crystal violet absorbance (ref. 1).

Results: See Table. At its human fC_{max}, FUS reduced viability of 19-75 %, while DAP, VAN, or LZD reduced it of < 20 % at their fC_{min}, and of 9-72 % at their fC_{max}. Combining FUS at its fC_{max} with each of these antibiotics improved efficacy, with reduction in viability reaching globally 40-96 % and 75-96 % when the associated antibiotic was used at its fC_{min} and fC_{max}, respectively. In contrast, combining FUS with clindamycin, moxifloxacin, doxycycline or rifampicin at either their fC_{min} or fC_{max} did not markedly improve activity on biofilms. Decrease of biomass was in all cases quite minimal.

Conclusion: Combining FUS with DAP, VAN, or LZD 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.

Ref 1: Bauer, Siala *et al*, AAC 2013; 57:2726-37

	% reduction in viability[a] within biofilms fur antibiotics alone or for FUS at fCmax combined with other antibiotics at their respective fC_{min}/fC_{max}						
Strains (origin)	**FUS at fC_{max}[b]**	**DAP at fC_{min}/fC_{max}[c]**		**VAN at fC_{min}/fC_{max}[d]**		**LZD at fC_{min}/fC_{max}[e]**	
	alone	**alone**	**+ FUS at fCmax**	**alone**	**+ FUS at fC_{max}**	**alone**	**+ FUS at fC_{max}**
ATCC25923 (reference strain)	25	0/52	96/94	5/20	94/94	15/45	96/94
2011S027 (chronic skin infection)	19	12/42	40/86	5/15	41/89	15/53	45/76
80224422456 (bone infection)	52	12/19	54/90	0/19	72/90	12/37	78/79
80124430375 (pacemaker)	52	0/9	83/89	16/65	78/89	20/33	86/87
80124432999 (knee joint prosthesis)	69	16/49	66/75	16/49	80/79	64/72	69/48
80124440624 (pacemaker)	75	12/57	80/75	13/18	75/74	29/38	94/93

[a] reduction in viability compared to untreated control [b] FUS MICs: 0.5-8 mg/L; fC_{max}: 35 mg/L; [c] DAP MICs: 0.5-1 mg/L; fC_{min}/fC_{max}: 0.7/9.4 mg/L; [d] VAN MICs: 1-2 mg/L; fC_{min}/fC_{max}: 2.5/20 mg/L;[e] LZD MICs: 1-4 mg/L; fC_{min}/fC_{max}: 9/17 mg/L