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# P2285 Antagonistic activity of liposomal amphotericin B with voriconazole against *Fusarium* biofilms

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**Background:** *Fusarium* species are distributed worldwide and considered important emerging pathogens, as increasing number of fusariosis cases are diagnosed, especially among immunocompromised hosts. They are able to cause a broad spectrum of infections, including vision-threatening keratitis, as well as superficial, locally invasive or disseminated infections. The ability of *Fusarium* spp to form biofilms (BF) on contact lenses has been suggested as an important factor that contributes to *Fusarium* keratitis. Data on drug combinations against BF-derived *Fusarium* infections are, however, lacking. We investigated the *in* vitro damaging activities of deoxycholate amphotericin B (D-AMB), liposomal amphotericin B (L-AMB), voriconazole (VRC) and of the combination of L-AMB with VRC against *F. solani* mature BF.

**Materials/methods:** Two *F. solani* clinical strains were incubated at 10^5 cfu/ml in 96-well microtiter plates at 37$^{o}$C for 48h. BF formation was assessed by 1% safranin staining and quantitated spectrophotometrically at 490 nm. For MIC determination, two-fold dilutions of D-AMB, L-AMB and VRC (0.007-256 mg/l) were incubated with BF or planktonic cells (2x10^5 cfu/ml) for 24h (n=6). The combinational activity of L-AMB (0.5-32mg/l) with VRC (0.125-64mg/l) against BF at 37$^{o}$C for 24h was determined using a checkerboard microdilution method (n=10). BF damage compared to controls was assessed by XTT metabolic reduction assay. MIC50 was determined as ≥50% BF damage. Drug interactions were analyzed using Bliss independence model. The combination effect was defined as synergistic, antagonistic or indifferent when the observed BF damage was significantly higher, lower or equal to the expected damage, respectively.

**Results:** Both strains exhibited strong biofilm formation. Biofilm MIC50 of D-AMB, L-AMB and VRC were 0.5, 1 and >256mg/l, respectively, as compared to 0.125, 0.125 and 0.06mg/l for planktonic cells. Antagonistic effects were observed at 0.5-4mg/l of L-AMB combined with 0.125-16mg/l of VRC (mean ΔE value of significant interactions: -28% [range, -11% to -55%]; mean SE: 2%).

**Conclusions:** *Fusarium* biofilms are susceptible to D-AMB and L-AMB but resistant to VRC. The combination of L-AMB with VRC at certain ranges of concentrations exhibits antagonistic activity against mature biofilms. This finding may have important implications in the treatment of biofilm-related *Fusarium* infections.