

O0792 Synergistic activity of liposomal amphotericin B with voriconazole against *Scedosporium apiospermum* biofilms

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Background: *Scedosporium apiospermum* can cause a wide range of invasive infections. It can also chronically colonize airways of patients with cystic fibrosis impairing respiratory function. *Scedosporium* spp can grow in biofilms on both polystyrene and tissue culture surfaces; however, the correlation between biofilm formation and drug susceptibility has not yet been fully elucidated. The aim of this study was to investigate the antifungal activity of Amphotericin B (D-AMB), liposomal amphotericin B(L-AMB) and voriconazole(VRC) against *S.apiospermum* biofilms(BF) alone or in combination.

Materials/methods: Three *S.apiospermum* clinical strains, isolated from lung tissue and bronchial secretions of adult patients, were incubated at 10⁵ cfu/ml in 96-wellplates at 37°C for 48h. BF formation was assessed by 1% safranin staining measured spectrophotometrically at 490nm. Two-fold dilutions of D-AMB, L-AMB and VRC at 0.007 to 256 mg/l were incubated with BF for 24h (n=9).The combinational activity of L-AMB (0.5-32mg/l) with VRC (0.125-64mg/l) against BF at 37°C for 24h was determined using a checkerboard microdilution method (n=10).BF damage compared to controls was assessed by XTT reduction assay of metabolic activity. 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 than, lower than or equal to the expected damage, respectively.

Results: All strains exhibited strong BF formation. BF MIC50 of D-AMB, L-AMB and VRC were 1, 2 and 32mg/l, respectively, as compared to 0.25, 0.5 and 0.125mg/l for planktonic cells. Synergistic effects were observed at 2-4mg/l of L-AMB combined with 4-16mg/l of VRC. Mean ΔE value of significant interactions, 17% [range, 14% to 20%]; mean SE, 3.7% [range, 3.0% to 4.3%]. None of the combinations exhibited antagonism.

Conclusions: While biofilms of *S.apiospermum* show comparable susceptibility profiles to D-AMB and L-AMB, they appear to be relatively resistant to VRC. The combination of L-AMB with VRC at certain range of concentrations close to MIC exhibits synergistic activity against mature BF suggesting a potential role against this challenging pathogen