

**P0121 Synergistic activity of liposomal amphotericin B with posaconazole against *Lichtheimia corymbifera* biofilms**

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**Background:** Mucormycosis is an emerging life-threatening opportunistic fungal infection that affects patients with underlying immunosuppressive conditions, such as hematological malignancies, trauma, hematopoietic stem cell transplantation and diabetes mellitus. The ability of Mucorales to form biofilms (BF), structures with reduced susceptibility to antifungal agents, has recently been demonstrated. We investigated the damaging activities of deoxycholate amphotericin B (D-AMB), liposomal amphotericin B (L-AMB), posaconazole (POS) and of the combination of L-AMB and POS against mature BF of *Lichtheimia corymbifera*, a clinically significant *Mucorales* species.

**Materials/methods:** Three *L. corymbifera* clinical strains, were incubated at  $10^5$  cfu/ml in 96-well microtiter plates at 37°C for 48h. BF formation was assessed by 1% safranin staining and measured spectrophotometrically at 490 nm. For MIC determination, two-fold dilutions of D-AMB, L-AMB and POS (0.007-256mg/l) were incubated with BF or planktonic cells ( $2 \times 10^5$  cfu/ml) for 24h (n=9). The combinational activity of L-AMB (0.5-32mg/l) with POS (0.125-64mg/l) against biofilms at 37°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  $\geq 50\%$  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:** All *L. corymbifera* strains exhibited strong BF formation. BF MIC50 of D-AMB, L-AMB and POS were 2, 4 and  $>256$ mg/l, respectively, as compared to 0.007, 0.03 and 0.03mg/l for planktonic cells. Synergistic effects were observed at 1-2mg/l of L-AMB combined with 8-16mg/l of POS (mean  $\Delta E$  value of significant interactions: 19% [range: 17% to 21%]; mean SE: 1% [range: 1% to 3%]). None of the combinations exhibited antagonism.

**Conclusions:** *L. corymbifera* can produce strong biofilms that possess comparable susceptibility profiles to D-AMB and L-AMB, but are resistant to POS. The combination of L-AMB with POS at certain concentration ranges exhibits synergistic activity against mature *L. corymbifera* BF.