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Poster Session I

Animal models: treatment

ACTIVITY OF FLUCONAZOLE, AMPHOTERICIN B, CASPOFUNGIN AND ANIDULAFUNGIN AGAINST CANDIDA ALBICANS IN AN EXPERIMENTAL FOREIGN-BODY INFECTION MODEL

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Objectives: The optimal treatment against *Candida* biofilms is not defined. We investigated the infection profile of planktonic and biofilm *C. albicans* in untreated animals and the antifungal activity in an established foreign-body infection model.

Methods: Teflon cages were subcutaneously implanted and infected 2 weeks later by injection of low (3×10^4 CFU) and high (3×10^6 CFU) quantity of *C. albicans* (ATCC 90028) in the cage (day 0). For the infection profile, planktonic *Candida* was quantified in aspirated cage fluid on day 1, 2, 3 and 6 (in CFU/ml) and clearance rate (in %) in cage fluid was determined. On day 6, cages were removed and cultured in 5 ml Sabouraud dextrose broth (SDB) for 48 h to determine the spontaneous cure rate of *Candida* biofilm (in %). For treatment experiments with low inoculum (2×10^4 CFU), animals received intraperitoneally the following antifungal regimens 12 h after cage infection once daily for 4 days: saline (control), fluconazole (FZL, 16 mg/kg), amphotericin B (AMB, 2.5 mg/kg), caspofungin (CAS, 2.5mg/kg), anidulafungin (AFG, 20 mg/kg). Cage fluid was aspirated and plated for quantitative cultures of planktonic *Candida* before, during (before last dose) and 10 days after treatment. The biofilm cure rate was determined as described above.

Results: The quantity of planktonic *C. albicans* progressively decreased from 2.59 ± 0.49 CFU/ml to 1.82 ± 1.29 CFU/ml (low inoculum) and from 3.40 ± 0.52 CFU/ml to 2.28 ± 1.03 CFU/ml cage fluid (high inoculum) in 6 days. On day 6 (before explantation), *C. albicans* was cleared from 3/12 cage fluids (24%) with low inoculum and from 1/12 (8%) cage fluids with high inoculum. After explantation, *Candida* biofilm persisted in all 12 cages infected either with low or high inoculum. Before start of treatment, cage fluid contained 2.73 ± 0.68 log CFU/ml. Compared to untreated controls, FZL and AMB did not reduce planktonic *C. albicans* during and after treatment, whereas CAS reduced the numbers to 0.22 ± 0.51 and 0.0 CFU/ml and AFG to 0.11 ± 0.38 and 0.13 ± 0.46 CFU/ml cage fluid (Fig). FZL cured 2/12 cages (17%), AMB and AFG 1/12 cages (8%) and CAS 3/12 cages (25%).

Conclusion: In untreated animals, planktonic *Candida* progressively decreased in cage fluid and was cleared in 8% to 24% of cage fluids, however, *Candida* biofilm persisted on all cages, i.e. no spontaneous cure of cage-associated infections was observed. Against planktonic *C. albicans*, CAS and AFG showed better activity than AMB and FZL. Against biofilm *C. albicans*, CAS showed the highest cure rate (25%), whereas cure rates of other antifungals ranged between 8% - 17%, demonstrating the difficulty of eradicating *Candida* biofilms on implants.

