Ten patients were receiving prophylaxis (5 fluconazole, 3 itraconazole, 1 posaconazole, 1 amphotericin), five were receiving empirical antifungal therapy (2 liposomal amphotericin, 3 echinocandin), while 11 were not receiving any antifungal therapy. Before the acquisition of the antifungal sensitivities, the antifungal treatment was revised in 22 patients (85%). After the acquisition, we concluded that 20 patients (77%) were receiving proper antifungal therapy. Five patients (19%), all with lymphoid malignancies, died due to the fungemia (2 C. parapsilosis, 1 C. inositis, 1 C. lusitaniae, and 1 Rhodotorula glutinis/C. lusitaniae). Two patients were not receiving proper therapy. DISCUSSION: Although fungal infections are very common in patients with hematological malignancies, proven fungemias are relatively uncommon, especially the breakthrough ones. It is notable that the incidence of C. albicans has decreased, with a relative increase of the other non-albicans species. Therapy according to species sensitivity results could improve the outcome, but unfortunately, due to the extended time necessary to acquire the antifungal sensitivities of the species, it is difficult to revise to a proper antifungal therapy on time, a fact that can be sometimes fatal.

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HUMAN RECOMBINANT LACTOFERRIN IS SYNERGISTIC WITH AMPHOTERICIN AND FLUCONAZOLE AGAINST PLANKTONIC CELLS AND BIOFILMS OF C. ALBICANS

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Candida is a common cause for neonatal sepsis and causes significant mortality, morbidity and health care costs. Lactoferrin, a component of milk and innate immunity, has broad-spectrum antimicrobial activity. Hypothesis: Talactoferrin (TLF, human recombinant lactoferrin) is synergistic with amphotericin and fluconazole, against planktonic and biofilm forms of clinical isolates of C. albicans.

Methods: C. albicans strains; ATCC® 32354, a human isolate, and C100 and M 101, blood isolates from septic neonates, were used to determine 50% minimum inhibitory concentrations (MICs) by the broth micro-dilution method for TLF, amphotericin and fluconazole as per CLSI guidelines, using XTT (tetrazolium salt) reduction to determine the endpoints. C. albicans (ATCC® 32354) biofilms were formed on 96 well microtiter plates for 24 hrs. Biofilm formation and the uniformity of formation in all wells were confirmed by inverted microscopy and XTT reduction assay. Minimum biofilm eradication concentration for 50% inhibition (MBECs) was determined for TLF, amphotericin and fluconazole. Combinations of TLF with amphotericin and fluconazole, for both planktonic and biofilms were tested by checkerboard method and XTT reduction. All experiments were done in duplicate on 2 days. Analyses: Combination indices (CI) were determined using the median effects equation using the software CalcuSyn at 3 different dose effects at 50%, 75% and 90% inhibition (ED50, ED75, and ED90) at equipotency ratios (ratios of MICs). CI < 1, >1, =1 denotes synergy, antagonism and indifferent effect respectively. Results: For planktonic C. albicans; ATCC # 32354, C100 and M101, the MICs of TLF were 62.5, 250 and 250, of fluconazole 0.032, 0.25 and 0.25, and of amphotericin 0.03, 0.0625 and 0.0625 respectively (in µg/ml). The C1 (in mean (SD) at ED50, ED75, and ED90) for combination of TLF + fluconazole; against ATCC® # 32354 were 0.47(0.021), 0.19(0.09) and 0.11(0.12), against C100 0.12(0.03), 0.06(0.05) and 0.04(0.04), and against M101 0.15(0.07), 0.06(0.04) and 0.03 (0.02) respectively. For TLF + amphotericin, C1 (mean (SD) at ED50, ED75, and ED90 were; for ATCC # 32354, 0.11 (0.08), 0.11(0.08) and 0.12(0.05), for C100 0.23(0.12), 0.15(0.03) and 0.11(0.03) and for M101 0.38(0.06), 0.26 (0.01) and 0.21 (0.02) respectively. C. albicans ATCC® # 32354 biofilms; MBECs of TLF, fluconazole and amphotericin were > 66400, 0.16 and 0.8 µg/ml respectively. The C1 (in mean (SD) at ED50, ED75, and ED90 for TLF + fluconazole were 0.25(0.01), 0.19(0.01) and 0.19(0.09) and for TLF + amphotericin combination 0.40(0.38), 0.28(0.21) and 0.25(0.12) respectively. Conclusion: TLF is synergistic with amphotericin B and fluconazole against planktonic forms and biofilms of C. albicans. We speculate that TLF may be used to enhance potency and fungal clearance in conjunction with antifungals against neonatal Candidiasis.

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CANDIDA ALBICANS AND CANDIDA DUBLINIENSIS CELL-CELL SIGNALING: NEW PLAYERS IN MORPHOGENESIS AND BIOFILM REGULATION

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Signaling among microbial cells is thought to be part of community dynamics. In Candida albicans, cell-cell communication molecules are beginning to be highlighted, with a special focus on farnesol and tyrosol. The aim of this study was to identify signal molecules produced by biofilm-grown Candida albicans and Candida dubliniensis, and to evaluate the impact of the production of signal molecules on cell morphogenesis and biofilm development. Biofilm supernatants, of both species, obtained at 24, 48, 72 and 96 h of biofilm formation, were analyzed by headspace-solid-phase microextraction and gas chromatography-mass spectrometry. It was found that supernatants fractions of C. albicans and C. dubliniensis contained isoamyl alcohol, 2-phenylethanol, 1-dodecanol, nerolidol, and farnesol. The physiological effect of the commercial (pro-analysis) formulation of these alcohols was evaluated on planktonic cell morphology and biofilm formation capability of both organisms. Treatment of planktonic cultures of both species with the tested alcohols revealed a role in morphogenesis control, inhibiting the transition of yeast to filamentous form by up to 50%. The ability of these compounds to regulate C. albicans and C. dubliniensis biofilm formation was assessed by adding the alcohols at 0h and 3 h of adherence and on 48 h biofilms. Biofilms were analysed in terms of total biomass by crystal violet staining and cellular activity by the reduction of a tetrazolium salt (XTT). The results indicate that besides farnesol other molecules regulate biofilm formation (at earlier stages) for both species, but not mature biofilms (48 h), which are not sensitive to any of the molecules assayed. Overall, the results show that C. albicans and C. dubliniensis tightly regulate their physiological behaviour through metabolites produced during growth, evidencing the complexity of C. albicans and C. dubliniensis signaling systems.

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CHANGES IN THE EPIDEMIOLOGY OF NOSOCOMIAL CANDIDIASIS FROM 2001 TO 2007 AT THE MAYO CLINIC JACKSONVILLE

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Background: Candida has emerged as one of the most important nosocomial pathogens and is associated with significant morbidity, mortality and cost to the health system. The epidemiology of fungal infections has dramatically changed over the last 20 years worldwide. Candida species are the fourth most common cause of nosocomial bloodstream infections and the third most common cause of these infections in the ICU setting. Methods: We conducted a retrospective review of all the episodes of Candidemia at the Mayo Clinic Jacksonville/St. Luke’s Hospital from 2001 to 2007 to determine the changes in epidemiology and clinical implications in our institution. Species identification, distribution and susceptibilities were reviewed, analyzed and compared for the period of 2001 to 2007. Results: We found 314 episodes of Candidemia for the study period. Candida glabrata (36%) was the most frequent species identified followed