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Synergistic effect of doxycycline and fluconazole against Candida albicans biofilms and the impact of calcium channel blockers.

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Abstract

Candida albicans is a clinically important fungus and is capable of forming biofilms, which contributes to the emergence of fluconazole resistance. Here, sessile minimum inhibitory concentrations (SMICs) of fluconazole combined with doxycycline against biofilms of C. albicans were determined, and the results of SMICs were compared with minimum inhibitory concentrations (MICs) of planktonic cells. SMICs and MICs were determined by microdilution checkerboard method, and the interactions between two drugs were interpreted by two models of fractional inhibitory concentration index and the percentage of growth difference (ΔE). For the biofilms formed over 4, 8, and 12 h, synergism was displayed by the combination of doxycycline(1-64 mg L(-1)) and fluconazole, and the fluconazole SMIC reduced from 64-512 mg L(-1) to 1-16 mg L(-1) against all the tested isolates. Calcium homeostasis is an important factor in growth of C. albicans. In this study, the impact of calcium channel blocker on the drug combination was observed by plate streaking and determined by liquid methods quantitatively. Obvious enhancement of antifungal effect appeared by combination of three drugs. These results show us that fluconazole combined with doxycycline could be effective against C. albicans biofilm, and the combined antifungal mechanism is associated with calcium.

KEYWORDS: Candida albicans; biofilms; calcium channel blocker; drug interactions; drug resistance

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