

IN VITRO ACTIVITY OF AMPHOTERICIN B LIPID COMPLEX IN 2-DRUG COMBINATION WITH CASPOFUNGIN AGAINST ASPERGILLUS FUMIGATUS

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We investigated the in vitro susceptibility of *Aspergillus fumigatus* to a 2-drug combination of amphotericin B lipid complex (ABLC) with caspofungin (CFG), and the results were compared with those obtained for a pair-wise combination of conventional amphotericin B (c-AMB) with CFG. Conidial suspensions were prepared from 20 clinical isolates of *A. fumigatus* (Microbiology Laboratory, Detroit Medical Center, Detroit, Michigan) susceptible to ABLC (MIC, $1.26 \pm 1.14 \mu\text{g/mL}$), c-AMB (MIC, $1 \pm 0.0 \mu\text{g/mL}$), and CFG (MIC, $64 \pm 0.0 \mu\text{g/mL}$). The in vitro susceptibility of *A. fumigatus* to a 2-drug combination of ABLC or c-AMB with CFG was evaluated by the fractional inhibitory concentration index (FICI) method. The FICI was determined by a 2-dimensional checker-board using the M38-P broth microdilution technique proposed by the National Committee for Clinical Laboratory Standards for MIC testing of conidium-forming filamentous fungi except that the MIC was defined as the concentration of the drug that provided no visible growth. The FICI was calculated by the formula: $\text{FICI} = (A_c \div A_a) + (B_c \div B_a)$ where A_c and B_c are the MICs of drugs A and B in combination and A_a and B_a are the MICs of drugs A and B alone. The drug interactions were classified as synergistic (FICI ≤ 0.5), additive (FICI > 0.5 but ≤ 1), indifferent (FICI > 1 but ≤ 2), and antagonistic (FICI > 2). Combinations of c-AMB + CFG (FICI = 0.42 ± 0.12) and ABLC + CFG (FICI = 0.33 ± 0.15) provided synergistic interactions. These in vitro data suggest that ABLC and c-AMB in 2-drug combination with an echinocandin is synergistically active against *A. fumigatus*.