

TITLE: MOLECULAR IDENTIFICATION AND ANTIFUNGAL SUSCEPTIBILITY PROFILES OF CLINICAL STRAINS OF *FONSECAEA* SPP ISOLATED IN RIO DE JANEIRO, BRAZIL.

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ABSTRACT:

Chromoblastomycosis (CBM) is a chronic mycosis that affects the skin and the subcutaneous tissues. In Brazil, species of the genus *Fonsecaea* are the main agents of this disease. *Fonsecaea* spp. are phenotypically very similar, differing only by means of genotypic analyzes. The objectives of this study were to identify genotypically and to evaluate the *in vitro* susceptibility to antifungals of 20 *Fonsecaea* spp. strains obtained from patients with CBM in Rio de Janeiro, Brazil. Molecular characterization was performed through the amplification and sequencing of the ITS1-5.8S-ITS2 region of rDNA. The minimum inhibitory concentration (MIC) of amphotericin B (AMB), flucytosine (5FC), terbinafine (TRB), fluconazole (FLZ), itraconazole (ITZ), ketoconazole (KTZ), posaconazole (PSZ), voriconazole (VRZ), and ravuconazole (RVZ) or the minimum effective concentration (MEC) of caspofungin (CAS) and micafungin (MFG) were determined by the broth microdilution method, according to the Clinical and Laboratory Standards Institute M38-A2 protocol, with modifications. Three *Fonsecaea* species were identified: *F. monophora* (n = 10), *F. pedrosoi* (n = 5), and *F. nubica* (n = 5). Regarding the antifungal susceptibility test, TRB and VRZ were the antifungal drugs that yield the lowest MICs (geometric means: 0.09 and 0.14 µg/ml, respectively). On the other hand, FLZ, 5FC, AMB, and MFG showed high MICs/MEC (geometric means: 12.55, 6.28, 5.77, and 5.66 µg/ml, respectively). All patients presented mild, moderated or severe CBM, and none had cerebral involvement, including those infected with *F. monophora*. Antifungal therapy with ITZ was ineffective in most cases, regardless of strain MIC to this antifungal drug. These cases required cirurgical approaches during patient's management. These results point to a predominance of *F. monophora* in Rio de Janeiro, which is the second *Fonsecaea* species of South America. The absence of cerebral involvement in all patients infected with *F. monophora* suggests that neurotropism of this species must be strain dependent. TRB and VRZ should be better studied in the clinical context of CBM treatment due to their low MICs.

Keywords: Antifungal susceptibility; chromoblastomycosis; *Fonsecaea* species

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