TITLE: ANTIFUNGAL SUSCEPTIBILITY OF FUNGAL STRAINS ISOLATED FROM PATIENTS WITH TUBERCULOSIS

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ABSTRACT:

Tuberculosis is an infectious disease caused primarily by *Mycobacterium tuberculosis*, which still remains as one of the major challenges to public health. In the context of neglected diseases are also included fungal infections. The antifungal drug susceptibility was evaluated in samples of two patients attended at public hospitals in the State of Maranhão with co-infection: tuberculosis and invasive fungal infection. The protocol was approved by the *Comitê de Ética em Pesquisa* from *UNICEUMA* (Protocol: 1.570.408.). The sputum samples of two patients diagnosed with tuberculosis and suspected of co-infection were referred to the Central Laboratory of the State of Maranhão (LACEN-MA) for fungal diagnostic. The fungus research in the sample was carried out by direct examination, culture in Sabouraud-Dextrose Agar medium (28 ° C and 37 ° C for up to 20 days), and by the Vitek2 System (Biomerieux). The MICs for fluconazole (FCZ), intraconazole (ITZ), ravuconazole (RVZ), and amphotericin B (AMB) were determined by the microdilution method. The interaction between these antifungals was evaluated by determining the fractional inhibitory concentration (FIC). The interaction between these drugs was classified as synergism if FIC≤0.5; indifferent if 0.5<FIC≤4.0, and antagonism for FIC>4. The samples were positive for *Candida albicans* and *Cryptococcus laurentii*, that showed susceptibility to antifungals tested. The FIC for FCZ + AMB, ITRA + AMB, RAV + AMB against *Candida albicans* were 1.39, 0.64, and 0.22, respectively. The FIC data for *Cryptococcus laurenttii* in the FCZ + AMB, ITRA + AMB, and RAV + AMB combinations were 0.54, 0.68, and 0.43. Some studies emphasize that the combination of azole and polyene derivatives theoretically results in an antagonistic interaction. However, in this study it was found that the interaction between ravuconazole which is also an azolic derivative and amphotericin B may result in a synergistic interaction. Therefore, it is expected that these results contribute to the knowledge of the susceptibility of the fungi strains isolated from patients with co-infection. In this way, it is expected to reduce the period of initiation of treatment, as well as the side effects and costs treatment of tuberculosis and co-infections, reducing the high rates of morbidity and mortality.

Keywords: *Mycobacterium tuberculosis*, fungal pathogens, co-infection, diagnosis, treatment

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