

TITLE: SUSCEPTIBILITY EVALUATION OF ANTIFUNGAL DRUGS AGAINST *Cryptococcus gattii* e *Cryptococcus neoformans* var. *grubii* ISOLATED FROM PATIENTS WITH DIFFERENT CLINICAL-EVOLUTIVE ASPETS OF NEUROCRYPTOCOCCOSIS

AUTHORS: NASCIMENTO, E.1; VITALI, L.H. 1; VON ZESKA KRESS, M.R.2; MARTINEZ, R.1

INSTITUTIONS: 1.FACULDADE DE MEDICINA DE RIBEIRÃO PRETO – UNIVERSIDADE DE SÃO PAULO – BRASIL; 2 FACULDADE DE CIENCIAS FARMACEUTICA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO – BRASIL.

Cryptococcus neoformans is the main agente of cryptococosis in immunossupressed patients and *C. gattii* generally affects immunocompetent people. The mortality rate due cryptococosis is high, even with the clinically available treatment. Additionally, in the case of healing, neurological damage are frequent. In this study were analyzed the antifungal susceptibility profiles in clinical isolates of *C. neoformans* and *C. gattii* from immunocompromised patients and immunocompetent, co-infected with HIV and who had relapsed and refractory meningitis treatment. Thus, the main purpose was the determination and comparison of the minimal inhibitory concentration (MIC) with the susceptibility profile of *Cryptococcus* sp. isolates form patients with diferente clinical aspects of the fungal infection. The comparison beteen the species were additionally evaluated. 68 isolates of *Cryptococcus* were analyzes. The isolates were divided into 3 groups. Group 1 was evaluated with 55 isolates from 19 cases of patients co-infected with HIV and relapsed or refractory meningitis. Into the group 2, 30 patients (30 isolates) co-infected with HIV which presenting unique and limited episode of cryptococosis. Finally, into the group 3 the cryptococosis were evaluated in patients not co-infected with HIV apparently immunocompetent (7 cases) and immunossupressed (12 cases) totalizing 19 isolates. The isolates were genotyped by PCR and sequencing in which the majority is *Cryptococcus neoformans* var. *grubii*. Into the group 2 and 3 were identified 1 and 6 *C. gattii*, respectively. The sensitivity of *Cryptococcus* clinical isolates were obtained with microdilution broth method (CLSI MS27-A2). The analyzes between both species *C. neoformans* var. *grubii* and *C. gattii* presented similar MIC results. MIC50 and MIC90 were, respectvelly, amphotericin B 0.25 and 0.50 mg mL⁻¹, fluconazole 4.0 and 8.0 mg mL⁻¹, itraconazole 0.06 and 0.25 mg mL⁻¹, voriconazole 0.25 and 0.50 mg mL⁻¹ and 5-flucitosine 8.0 and 16.0 mg mL⁻¹. No statistical significance were observed. With these results it was concluded that all isolates of this study showed sensitivity to amphotericin B. The isolated from immunocompetent patients tended to be less sensitive to azoles and differences in the sensitivity profile of the isolates over the episodes of recurrent meningitis and / or refractory were not observed.

Keywords: Susceptibility to antifungal agents, cryptococcal meningitis, HIV, relapsed and refractory.

Financial Support: FAPESP