Abstract

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Therapy of Meningeal and Disseminated Cryptococcosis

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Key Words

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Abstract

Progressive meningeal and disseminated cryptococcosis can be obtained in normal and in immunodepressed guinea-pigs infected intravenously with an inoculum of *Cryptococcus neoformans*, 200 CFU/g body weight. Oral and parenteral treatment once daily for 35 days was started 3 days after infection. The animals were treated with oral or parenteral itraconazole and fluconazole, 5 and 10 mg/kg, alone or in combination, 5 mg/kg + 5 mg/kg, or with itraconazole, 5 mg/kg, combined with parenteral flucytosine, 10 and 40 mg/kg, or parenteral amphotericin B, 0.63, 1.25, or 2.5 mg/kg. Evaluation was based on behaviour, survival, skin cryptococ-comas, and cultures of brain and meninges and of 12 other organs. All drugs were active compared with the excipient-treated animals. Administration of itraconazole by the oral or the parenteral route was the most effective, followed by fluconazole. Combination therapy with lipophilic itraconazole and lipophobic fluconazole was no more effective than itraconazole alone, but a combination of itraconazole with flucytosine or with amphotericin B possessed additive or synergistic activity. No drug-related side-effects were observed with the azoles or with flucytosine at the tested doses. Amphotericin B produced side-effects proportional to the daily dose administered.