TREATMENT OF EXPERIMENTAL PARACOCCIDIOIDOMYCOSIS WITH THE ANTI-FUNGAL DRUG ITRACONAZOLE: IMMUNOPAPTHOLOGICAL STUDIES

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Introduction: Paracoccidioidomycosis (PCM) requires long, complicated treatment, justifying studies to broaden therapeutic options. Itraconazole is the drug of choice because it is effective, requiring shorter therapy than other drugs; but there is still much to be studied on the fungus/drug/immune response interactions.
Materials and Methods: We constituted 5 experimental groups with 10 mice each infected (intraperitoneally with $20x10^6$ viable Pb18 yeast cells/mL) and untreated, infected and treated orally, on alternate days with 3 mg/mL, 10mg/mL or 50mg/mL Itraconazole and non-infected controls. These mice were weighed on the day of infection, and after 2, 3 and 6 months when they were sacrificed, and morphological and weight alterations on the organs caused by the presence of the fungus were analysed. Seric antibody titers to *Pb* were determined by ELISA at 4 months of infection.
Discussion of Results: Significant differences in ELISA were found between infected mice treated with 10mg/mL in relation to those treated with 3mg/ml and also between the group of infected mice treated with 50mg/mL and the group of infected, untreated mice. Differences in the presence of the fungus in the groups treated with various doses of Itraconazole were observed by morphological analysis. Lesions consistent with presence of *Pb* were regularly observed in omentum, spleen, lungs, spleen of *Pb*-infected mice, in loads inversely proportional to the Itraconazole doses employed, as opposed to the observed in the non-infected group. As to organs weight, all groups had significant differences compared to the uninfected group. Lung presented significant differences between the infected, untreated group and the uninfected group, and also between the groups treated with either 3mg/mL or 10mg/mL and the untreated group. Omentum presented differences between the group treated with 3mg/mL and the groups treated with 50mg/mL, and with 50mg/mL and also with the non-infected group. Liver weight did not differ between groups and in the spleen lower weight of non-infected mice was a tendency.
Conclusion: Itraconazole treatment in experimental PCM is dose-dependent, reflecting in differences in the health of the mice, evaluated by their body weight. Increase in organs weight can be attributed to fungal load. Specific antibody levels are also altered by the treatment, a fact that can be interpreted as variations in the protective immunity developed after Itraconazole treatment.

Key words: *P. brasiliensis*, Itraconazole, ELISA

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