Therapeutic efficacy of experimental Chagas disease treatment with low-doses of Benznidazole

Luísa H. P. Melo[1]; Paula M. A. Vieira[2]; Thaís V. Carvalho[2]; Kátia S. Fonseca[1]; Lívia M. Carvalho[2]; Beatriz C. Silva[1]; Luciana F. Medeiros[1]; Israel Molina[3]; Rodrigo Correa-Oliveira[1,5]; Cláudia M. Carneiro[1,4]

[1]Laboratório de Imunopatologia, Núcleo de Pesquisas em Ciências Biológicas, Instituto de Ciências Exatas e Biológicas, Universidade Federal de Ouro Preto, Ouro Preto, MG, Brazil. [2]Laboratório de Morfopatologia, Departamento de Ciências Biológicas, Núcleo de Pesquisas em Ciências Biológicas, Instituto de Ciências Exatas e Biológicas, Universidade Federal de Ouro Preto, Ouro Preto, MG, Brazil. [3]Tropical Medicine and International Health Unitat, Department of Infectious Diseases, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona, Barcelona, Spain. PROSICS Barcelona. [4]Departamento de Análises Clínicas, Escola de Farmácia, Universidade Federal de Ouro Preto,Ouro Preto, MG, Brazil. [5] Laboratório de Imunologia Celular e Molecular, Centro de Pesquisas René Rachou, Fundação Oswaldo Cruz, Belo Horizonte, Minas Gerais, Brasil

The Benznidazole in many countries is the only drug available to eliminate the protozoan parasite *Trypanosoma cruzi*, the etiologic agent of Chagas disease. However, it use was introduced empirically in therapy, the treatment has frequent and intense side effects and studies showed that Benznidazole treatment regimen might be overdosed. Believing that a reduction in the BNZ treatment dose can reduce side effects, which could increase treatment adherence maintaining therapeutic success, the aim of this study was to evaluate the efficacy of BNZ low-doses to induce a parasitological cure in mice. We investigated the *in vivo* activity of Benznidazole low-dose against *T. cruzi* Y strain, using swiss mice in the acute and chronic phase of Chagas disease. The animals were treated for 20 days with doses of 22, 40 and 100 mg/kg/day. The results showed that treatment in the acute phase with a dose of 22 and 40 mg/kg/day is able to suppress parasitaemia and preventing death in infected animals but do not exhibit parasitological cure capacity. However, in the chronic phase 100 % of the mice treated with BNZ 40 mg/ kg/day and 89% of animals treated with BNZ 100 mg/kg/day achieved parasitological cure. Thus, the experimental low-dose treatment of chronic Chagas' disease obtained better therapeutic success than acute phase and, apparently, a reduced dose of BNZ (40 mg/kg/day) is as effective as the usual dose of 100 mg/kg/day in treating mice. Our results demonstrate the importance of more studies on the treatment in the chronic phase of infection with *Trypanosoma cruzi*, and especially we should question us about therapy strategic currently in use.

Key Words: Chagas disease, low-dose, Benznidazole

Financial Support: FAPEMIG, CNPq, CAPES and UFOP.