Curcumin enhances the anti-*Trypanosoma cruzi* activity of benznidazole-based chemotherapy in acute experimental Chagas disease

Rômulo D. Novaes[1]; Newmara Bianca F. Amaral[6]; Marcus V.P. Sartini[2]; João Paulo F. Rodrigues[1]; Reggiani V. Gonçalves[3]; Eliziária C. Santos[4]; Paulo Henrique F. Amaral[5]; Raquel L.M. Souza[2]; Ivo S. Caldas[2].

[1]Department of Structural Biology, Federal University of Alfenas, 37130-000 Alfenas, MG, Brazil. Email: romulo.novaes@unifal-mg.edu.br. [2]Department of Pathology and Parasitology, Federal University of Alfenas, 37130-000 Alfenas, MG, Brazil. [3]Department of Animal Biology, Federal University of Viçosa, 36570-000 Viçosa, MG, Brazil. [4]School of Medicine, Federal University of Jequitinhonha and Mucuri Valleys, 39100-000 Diamantina, MG, Brazil. [5]Escola de Enfermagem, Curso de Graduação em Medicina, Federal University of Alfenas, 37130-000 Alfenas, MG, Brazil. [6]Faculdade São Lucas,76805-846 Porto Velho, RO, Brazil.

Curcumin has emerged as a potentially useful natural resource in the treatment of parasitic diseases. Although curcumin can increase the effectiveness of drugs against malaria, combination therapies using this molecule have never been investigated in Chagas disease (ChD). Thus, we evaluated the efficacy of curcumin as a complementary strategy to benznidazole (Bz)-based chemotherapy in mice acutely infected with a virulent strain of *Trypanosoma cruzi*. Eighty-four 12-week-old Swiss mice were equally randomized into seven groups: uninfected (NI); *T. cruzi* (Y strain)-infected and non-treated (INF), infected and treated with 100 mg/kg Bz (B100), 50 mg/kg Bz (B50), 100 mg/kg curcumin (C100); 100 mg/kg Bz + 100 mg/kg curcumin (B100+C100); 50 mg/kg Bz + 100 mg/kg curcumin (B50+C100). After microscopic identification of blood trypomastigotes (4 days after inoculation), both drugs were administered by gavage once a day for 20 days. Curcumin showed limited antiparasitic, anti-inflammatory and antioxidant effects when administered alone. When curcumin and Bz were combined, there was a increased parasitemia clearance and drastic reduction in parasitemia, mortality, anti-*T. cruzi* IgG reactivity, myocardial inflammation, morphological and oxidative cardiac injury. These results exceeded the isolated effects of Bz. After immunosuppression by cyclophosphamide and hemoculture we identified that the combination of Bz and curcumin was also effective in preventing infection recrudescence, even when the animals were treated with 50% of the recommended therapeutic dose of Bz. By enhancing the antiparasitic efficiency of Bz, the concomitant curcumin administration may be a relevant therapeutic strategy in ChD treatment compared with Bz-based monotherapy. This strategy seems to be more tolerable than Bz alone considering that curcumin exhibits low toxic potential as well as antioxidant and anti-inflammatory properties.

Palavras-chave: Chemoterapy, experimental parasitology, Chagas disease.

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