Immunopathological response in mice with triple infection with *Trypanosoma cruzi* strains of different Biodemes submitted to treatment with immunosuppressor drugs

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**Introduction:** An important factor that contributes to the severity of Chagas disease in people living in endemic areas is the occurrence of multiple infections with *Trypanosoma cruzi*. Experimental studies have shown the increased morbidity due to successive reinfections with different strains, with the possibility of to evaluate the influence of multiple infections upon the tissue lesions. Multiple infections could also influence an activation of the disease in patients with HIV infection (AIDs) or immunosuppressed in cases of organs transplantation. In such cases, a reactivation of virulent strains could occur with aggravation of the disease. **Objective:** to evaluate the immunopathological response in mice triple infected with different *T. cruzi* strains and treated with immunosuppressor drugs. **Material and Methods:** Inbred Balb/c mice were successively infected with *T. cruzi* strains of different Biodemes: 1) Colombian strain (Biodeme Type III – *T. cruzi* I); 2) re-infections with 21SF strain (Biodeme Type II – *T. cruzi* II); 3) third infection with Y strain (Biodeme Type I, Z2b). For each *T. cruzi* strain a group of mice with a single infection was included as a control group. Twenty days after the last infection, groups of triple infected surviving mice were submitted to different schedules of treatment with immunosuppressor drugs: **Schedule 1** – Betamethasone (2mg/kg/day) plus Cyclophosphamide (250mg/kg/day), during four weeks; **Schedule 2** – Azathioprine (2mg/kg/day) plus Betamethasone (1mg/kg/day) and Cyclosporine (during 4 weeks). Results were evaluated by the evolution of parasitaemia and mortality, histopathology and serological specific responses. Evaluation of immunoglobulin isotypes (ELISA method) and skin test for delayed hypersensitivity (DTH). **Results:** A reactivation of *T. cruzi* infection in mice with triple infection and treated with Betamethasone and Cyclophosphamide was detected, with increased parasitaemia and mortality rates, macrophagotropism, arterites and peri-arterites intensification of perivascular mononuclear cells infiltration and of extracellular matrix deposits. Combined treatment with Azathioprine, Betamethasone, Cyclosporine in the triple infected mice did influence neither parasitaemia levels nor mortality rates. However the histopathological study demonstrated aggravation of the necrotic inflammatory lesion with the presence of arterites and peri-arterites in the myocardium and skeletal muscles. DTH cutaneous test, disclosed significant differences in the 48 hours point between untreated triple infected mice and the treated with either one of the treatment schedules. The immunosuppression with Betamethasone plus Cyclophosphamide determined reactivation of the acute phase of the infection with *T. cruzi*, comparable to that observed in immunosuppressed patients. Treatment with Azathioprine, Betamethasone and Cyclosporine determined aggravation of the immunopathological lesions, characteristics of DTH alterations, without re-agudization of *T. cruzi* infection. **E-mail:** sgandrade@bahia.fiocruz.br