

Warifteine modulates experimental infection by *Trypanosoma cruzi*

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Introduction

The development of new agents capable of regulating infection diseases can uncover novel therapeutic approaches for the treatment. Warifteine is a majority alkaloid purified by *Cissampelos sympodialis* was previously shown to have anti-allergic and anti-inflammatory action (1). Recently our group demonstrated that warifteine modulates B cell response both *in vivo* and *in vitro*. Warifteine inhibit both proliferative response and immunoglobulin secretion induced by polyclonal stimuli. We also demonstrated that warifteine decreases the rise in intracellular calcium levels, phosphorylation of the mitogen activated protein kinase and the translocation of the transcriptional factor NFκB and also induced an increase in cAMP (2).

In the present study we investigated the effect of warifteine in *in vitro* macrophage infection with Dm 28c strain of *Trypanosoma cruzi* (*T. cruzi*) and the action of this alkaloid on infected mice. *T. cruzi* is the etiological agent of Chagas' disease that affects 20 million people in Latin America. Chagas' disease is an example of infection that results in immunological attack of host tissues (3). However, the pathogenic mechanisms involved remain unclear. Polyclonal B cell activation is detected during infection in both acute and chronic phase (4).

BALB/c mice were infected intraperitoneally with 10⁴ metacyclic forms of the *T. cruzi* clone Dm 28c. Some groups were additionally treated with warifteine. The parasitaemia was determined on blood samples obtained from tail vein and serum samples were collected to quantify the immunoglobulin levels by ELISA. Peritoneal macrophages were infected with 10⁵ chemically induced trypomastigote forms of the Dm 28c *T. cruzi* clone and some cultures were treated with warifteine. Supernatant trypomastigote numbers were determined by hemocytometer counting after 7 and 9 days of culture. The statistical analysis was performed using the Student t-test for independent samples, with the level of significance set at p<0,05.

Results and Discussion

Ours results demonstrated that warifteine was able to reduce the parasitaemia and to inhibit both IgM and IgG production in infected mice. We also observed that warifteine impaired the release of the trypomastigote forms from infected macrophages *in vitro*. Our results suggest that warifteine have a trypanocidal effect and can be able to modulate B cell activation during *T. cruzi* infection. Additional experiments will be performed to characterize the pathological aspects in acute and chronic infected mice after treatment with warifteine.

Conclusions

Take together ours results suggest that warifteine was not toxic to peritoneal macrophages in all concentration used in this work. The release of the trypomastigote forms from infected macrophages was impaired in the presence of warifteine 5 and 10 µg/mL *in vitro*. The infected mice treated with warifteine reduced trypomastigote forms in the peripheral blood. The production of IgM and IgG was modulated by warifteine in infected mice.

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