Enrofloxacin and toltrazuril are able to reduce *Toxoplasma gondii* growth in human BeWo trophoblastic cells by modulation of immune response and damages on tachyzoite structure

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Classical treatment for congenital toxoplasmosis is based on combination of sulfadiazine and pyrimethamine plus folinic acid. Due to teratogenic effects and bone marrow suppression caused by pyrimethamine, the establishment of new therapeutic strategies is indispensable to minimize the side effects and improve the control of infection. Previous studies demonstrated that enrofloxacin and toltrazuril reduced the *Neospora caninum* and *Toxoplasma gondii* infection. The aim of this present study was to evaluate the efficacy of enrofloxacin and toltrazuril in the control of *T. gondii* infection in human trophoblast cells (BeWo line). BeWo cells were analyzed by MTT in order to verify their viability after treatment with several concentrations of enrofloxacin, toltrazuril, sulfadiazine, pyrimethamine or association (sulfadiazine+pyrimethamine). Next, BeWo cells were infected by *T. gondii* (2F1 clone) and treated with the antibiotics and the *T. gondii* intracellular proliferation was analyzed by beta-galactosidase assay. ELISA was performed in the supernatants to measure the cytokine production. Finally, we evaluate the direct effect of treatments in tachyzoites by exclude trypan blue staining and transmission electron microscopy. Enrofloxacin and toltrazuril did not decrease the viability of cells in lower concentrations, and were able to reduce significantly the parasite intracellular proliferation in BeWo cells when compared to untreated conditions. Moreover, BeWo cells infected and treated with enrofloxacin or toltrazuril induced high levels of IL-6 and MIF, both proinflammatory cytokines. The production of proinflammatory cytokines represents a mechanism of immunological defense associated to the control of *T. gondii* infection. Finally, the drugs tested increased the number of unviable parasites and triggered damage on tachyzoite structure, especially during the cellular division into the host cells. Then, our data suggest that these drugs were able to alter the viability of *T. gondii* in a short time of treatment. Taken together, it can be concluded that enrofloxacin and toltrazuril are able to control the *T. gondii* infection in BeWo cells, probably by a direct action on the host cells and parasite, which leads to modifications in the cytokine release and tachyzoite structure.

Keywords: *Toxoplasma gondii*, trophoblast, enrofloxacin, toltrazuril and treatment.

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