The susceptibility to infection by *Toxoplasma gondii* ME49 and RH strains is dependent on cyclooxygenase-2 in brain and peritoneal macrophages of *Calomys callosus* rodents

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Toxoplasma gondii is an obligate intracellular protozoan parasite that infects a wide range of warm-blooded vertebrates, including humans. Many studies show that cyclooxygenase-2 (COX-2) is a potent modulator of immune response in multiple types of infection, favoring replication and dissemination of pathogens, as *Trypanosoma cruzi*. However, the role of COX-2 during an infection by *T. gondii* is still not clear. Therefore, the aim of this study was to investigate the functional role of COX-2 in *Calomys callosus* rodents infected with *T. gondii*, an excellent in vivo experimental model traditionally used for studies about toxoplasmosis. For this purpose, *C. callosus* females were infected with fifty cysts of *T. gondii* (ME49 strain), treated with COX-2 inhibitors (Meloxicam or Celecoxib) for 40 consecutive days, and evaluated every 72 h to check the body weight change and morbidity. After 40 days of infection and treatments, brain and serum samples were collected for detection of *T. gondii* or cytokines by real time PCR or CBA, respectively. Furthermore, peritoneal macrophages of *C. callosus*, uninfected or infected with *T. gondii* RH strain, were treated with Meloxicam or Celecoxib in order to evaluate the parasite intracellular proliferation by colorimetric assay and cytokine production by ELISA after 24 h of infection. The data showed that the body weight and morbidity of the animals changed after infection by *T. gondii*, regardless both treatments. Immunohistochemistry and real-time PCR performed on brain tissue showed a significant reduction of *T. gondii* in animals treated with both COX-2 inhibitors when compared to infected and untreated animals. In addition, it was observed that both COX-2 inhibitors were able to control the *T. gondii* intracellular proliferation in peritoneal macrophages. In the serum of *C. callosus*, the data showed that animals treated with all COX-2 inhibitors showed a upregulation of proinflammatory cytokines (IFN-γ, IL-17A, TNF and IL-6), while the supernatants of peritoneal macrophages demonstrated significant production of IL16, TNF and nitrite when treated with both COX-2 inhibitors. All these results indicate that COX-2 is important to facilitate the *T. gondii* infection in the brain and peritoneal macrophages of *C. callosus.* In conclusion, COX-2 is able to favor infection by *T. gondii*, since inhibition of this enzyme induced significant control of infection by upregulate proinflammatory cytokines and nitrite in rodent cells.

Keywords: *Toxoplasma gondii*, cyclooxygenase-2 and *Calomys callosus*

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