

## New approaches to therapeutic interventions on murine experimental schistosomiasis

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**Introduction:** *Schistosoma mansoni* infection triggers schistosomiasis, a serious public health problem especially in developing countries. In an infected person, after worms maturation, the deposited eggs enter the bloodstream and are trapped in the microvasculature of the liver, inducing the granulomatous response: a pathological element of chronic schistosomiasis. Also, the adult worms may clog the blood system, which induces circulatory congestion characteristic of the disease. One way of adult worms escape the immune system is related to the structure of the outer membrane of the parasite, which is comprised of host molecules, which mask antigenic epitopes present in the inner layer of the parasite. The chemotherapy with Praziquantel (PZQ), used to control the disease, induces disruption of the parasite outer membrane, exposing the antigenic molecules. Furthermore, studies suggest that leukotrienes are potent pro-inflammatory agents, protecting against various infectious agents. **Objective:** To evaluate whether the therapy using the association of PZQ and LTB<sub>4</sub> may increase the effectiveness of chemotherapy due to amplification of immune stimulation at the time of drug action on the parasite. **Methods:** Adult female C57BL/6 mice were infected subcutaneously with 80 cercariae of *S. mansoni*. After 32 days of infection, mice received the first dose of LTB<sub>4</sub> (0,14 µg/mL). Other LTB<sub>4</sub> doses were administered each 5 days after the first dose. After 42 days of infection mice were treated with PZQ (140 mg/kg). Mice were euthanized 49 days after infection, when adult worms were recovered from the hepatic portal system and the viability of eggs was evaluated in the gut wall. In addition, kidneys were kept in 10% formalin buffer for posterior histopathological analysis. **Results:** The treatments with PZQ or LTB<sub>4</sub> associated with PZQ induced decrease of egg numbers in the first stage and increased the number of non-viable eggs, comparing to the control group and the group treated only with LTB<sub>4</sub>. When PZQ treatment were compared to LTB<sub>4</sub> associated with PZQ treatment we do not observe reduction in the number of granulomas, but there was an apparent decreased in granuloma size. **Preliminary Conclusion:** Although there was an increase in the number of non-viable eggs and in the treatment with LTB<sub>4</sub> plus PZQ, our preliminary data don't allow us to affirm the specific role of LTB<sub>4</sub> therapy in this model. To determine whether or not the immune response is modulated by this treatment, we will evaluate cytokines produced at the site of infection. The apparent decrease in the size of granulomas after concomitant treatment with LTB<sub>4</sub> and PZQ needs to be confirmed, but appears to induce better control of tissue damage.

**Keywords:** *Schistosoma mansoni*, Praziquantel, LTB<sub>4</sub>.

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