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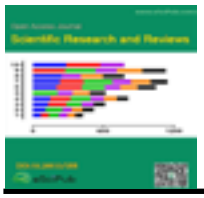

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in vitro EVALUATION OF ATOVAQUONE ON THE REPLICATION OF TOXOPLASMA GONDII TACHYZOITES STRAINS RH AND ME49

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ABSTRACT

Introduction: Since 1990 the standard treatment for toxoplasmosis has remained the same. The therapy is based on a synergistic combination of pyrimethamine and sulfadiazine, drugs that promote synthesis blockade and decrease of tachyzoite folic acid levels. This therapy acts only on the tachyzoite forms of the parasite, not affecting bradyzoites present in tissue cysts that persist in the individual during the chronic phase and not preventing possible disease reagudization even after treatment. Given the high seroprevalence of toxoplasmosis in the general population and the serious complications that this infection may bring to the patient, a safe and effective treatment against all morphological forms is necessary. The repositioning of drugs main objective is to use substances already marketed to treat other diseases. Thus, Atovaquone, which is an antimalarial of the naphthoquinone group recently accepted by the FDA and isn't yet part of the routine treatment protocols employed for toxoplasmosis, should be studied, as recent studies show its activity against tachyzoites and also against bradyzoites, representing a huge advantage over the drugs currently used. It also does not interfere with folic acid metabolism, proving to be a promising drug in the treatment of pregnant women. Objective: The present study aims to evaluate the effects of atovaquone on T. gondii strains RH and ME49 (type I and type II, respectively) in vitro. **Methodology**: In quintuplicate, murine RAW 264.7 macrophages were used in six-well culture plates with 3mL of supplemented RPMI medium, where 200.000 cells were seeded and incubated at 37°C, 5% de CO2 for 24 hours. After this period, the culture was infected with 1x106 tachyzoites/well of each strain analyzed and simultaneously treated with 100 nM Atovaquone. The parasites were analyzed by optical microscopy and quantified in a Neubauer chamber at 24h, 48h, 72h and 7 days. **Results**: For the RH strain, the control group showed steady growth, starting at 60.000 forms/mL within 24 hours, reaching 2.550.000/mL within 7 days. When treated with Atovaquone, within 24 hours the number detected was 30.000/mL, with decline in growth resulting in only 15.000/mL observed after the first week of cultivation. Similar results were observed with the Me49 strain, which at the beginning of the experiment had 150.000/mL tachyzoites in the untreated group and 90.000/mL in the treated group and, at the end of 7 days, 1.950.000/mL tachyzoites in the untreated group and 30.000/mL in the treated group. **Conclusion**: Atovaquone has shown great activity in controlling Toxoplasma gondii parasite replication in vitro.

Keywords: Toxoplasma gondii, atovaquone, drug repositioning.

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