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Toxoplasma gondii: anidulafungin activity against toxoplasmosis in a murine model

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Background: *Toxoplasma gondii* (*T. gondii*) is an important opportunistic pathogen for immunocompromised patients and responsible for toxoplasmic encephalitis, which is often lethal. The standart treatment for toxoplamosis is limiting due to toxic adverse effects, thus there is a need to identify new drugs that are less toxic. Anidulafungin is a semisynthetic echinocandin used as an antifungal drug. It also effective against the pneumocystis jiroveci. In this work we demonstrate the combination of anidulafungin with the current treatment for acute toxoplasmosis on the murine model in vivo.

Material/methods: For in vivo studies, mice were acutely infected intraperitoneally with 10^3tachyzoites of the virulent RH strain of *T. gondii* then treated for ten days from day one post-infection. Animals were distributed into four groups (20 mice for each group): Group 1: infected with *T. gondii*; Group 2: infected with*T. gondii* and treated with sulfadiazine (200 mg/kg, perorally) plus pyrimethamine (12. 5 mg/kg, perorally); Group 3: infected with *T. gondii* and treated with anidulafungin (16mg/kg, intaperitoneal); G4: infected with *T. gondii* and treated combinations of sulfadiazine (200 mg/kg, perorally) plus pyrimethamine (12. 5 mg/kg, perorally) with anidulafungin (16mg/kg, intaperitoneal). On the 5 th day, five mice from each group were selected and under anaesthesia, 1 ml normal saline was given into the peritoneum, drawn back later and number of trophozoites in 1 ml of perinoneal fluid was determined by counting them on the Thoma slide. The rest of the mice was used to monitor survival rate.

Results: The combinations of anidulafungin plus sulfadiazine and pyrimethamine was highly effective against *T. gondii in vivo*. After 10-day treatment with 0.5mg/day of anidulafungin combined sulfadiazine and pyrimethamine resulted in 73% survival of mice acutely infected with the highly virulent *T. gondii* RH strain, versus 61% of mice treated with just sulfadiazine and pyrimethamine. Combinations of anidulafungin with sulfadiazine and pyrimethamine was also effective in reducing the mortality rate of mice compared with the treatment without anidulafungin. The number of trophozoites in the Group 4 was found significantly lower than the other groups ($p<0.05$). The number of trophozoites in the Group 3 was found significantly lower than the group G1($p<0.05$).

Conclusions: The results obtained are promising for the treatment of human toxoplasmosis and point to the need to extend these studies to other murine models. The findings of our study the first study in which the effectiveness of the combination of sulfadiazine plus pyrimethamine with anidulafungin in

the treatment of acute toxoplasmosis. Anidulafungin may be a new supportive therapeutic option for toxoplasmosis.