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Role of Artesunate and Ivermectin Used as Mono-therapeutic Agents or In-Combination with Triclabendazole against immature *Fasciola gigantica* worms

Abdel Hameed A Sabry[1], Eman M. H. Méabed[1], Maha K. Abd E l-Wahed[2]

[1]Department of Parasitology, Faculty of Medicine, Fayoum University, Egypt

[2]Department of Anatomy, Faculty of Medicine, Fayoum University, Egypt

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Abstract

There is a need to develop new fasciocidal drugs. Several studies have documented efficacy of artesunate and ivermectin against *Fasciola hepatica* infection particularly when used in combination with triclabendazole (TCBZ). However, there is lack of reports about *Fasciola gigantica* worms especially on the late immature stage of the worms.

The aim of this study is to evaluate the efficacy of each drug against the late immature stage of *Fasciola gigantica* worms, used either as monotheraputic agents or in combination with triclabendazole.

Materials and methods: Forty rabbits were allocated into eight groups, experimentally infected with *F. gigantica* encysted metacercariae. Treatment of seven groups was inducted at the 6th week post infection. The 8th group was kept as infected non treated control. The drug regimens used were single doses of (TCBZ 5 &10 mg/kg orally), (artesunate 100 & 200 mg/kg orally), (ivermectin 100 µg/kg intravenously iv). The combination regimens were TCBZ 5mg/kg used plus either artesunate 100 mg/kg orally or ivermectin 100µg/kg iv. Efficacy of different regimens was determined two weeks post treatment

by slaughtering animals, and careful inspection of their abdominal cavity and their liver for any gross pathological lesions. Also by extraction of all worms from the liver or the peritoneal cavity to determine the worm burden reduction rate (WBRR) in comparison with the control non-treated animals and estimation of the drug effect on the extracted worm size.

Results: Triclabendazole 10 mg/kg achieved significantly high WBRR up to 100% *($P \leq 0.001$)*, and few gross pathological changes. Combination between TCBZ and ivermectin resulted in a significant reduction rate up to 89.5% *($P < 0.01$)*, effectively decreased the size of the extracted worms and the animals showed few pathological changes. On the contrary, the used combination regimen between TCBZ and artesunate showed poor effect at this early stage of infection with 32.9% WBRR. Monotherapy using TCBZ 5 mg, artesunate 200, 100 mg and ivermectin 100 µg resulted in efficacy rates of 55%, 51.4% 28.5%, and 22.8% respectively in comparison with control group with concordance of WBRR results with the effect on the worm size and the degree of pathological changes.

Conclusion: Triclabendazole 10 mg/kg was the most effective regimen, followed by Combination between TCBZ and ivermectin. However, its combination with artesunate showed poor effect at this early stage of infection.