



Experimental cystic echinococcosis therapy: In vitro and in vivo combined 5-fluorouracil/albendazole treatment

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Titre Experimental cystic echinococcosis therapy: In vitro and in vivo combined 5-fluorouracil/albendazole treatment

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Auteur Pensel, Patricia E [1], Elissondo, Natalia [2], Gambino, Guillermo [3], Ullio Gamboa, Gabriela Veroniva [4], Benoît, Jean-Pierre [5], Elissondo, María C [6]

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Human cystic echinococcosis is a zoonosis caused by the larval stage of the tapeworm *Echinococcus granulosus sensu lato* (s. l.). Although benzimidazole compounds such as albendazole (ABZ) and mebendazole have been the cornerstone of chemotherapy for the disease, there is often no complete recovery after treatment. Hence, new strategies are required to improve treatment of human cystic echinococcosis. The goals of the current study were as follows: (i) to evaluate the *in vitro* efficacy of the 5-fluorouracil (5-FU) and ABZ combination against *E. granulosus* s. l. protoscoleces and cysts, (ii) to compare the clinical efficacy of 5-FU alone or in combination with ABZ in infected mice. The combination of 5-FU +ABZ had a stronger *in vitro* effect against larval stage than that did both drugs alone. Even at the lowest concentration of 5-FU +ABZ combination (1 µg/ml), the reduction of the viability of protoscoleces and cysts was greater than that observed with drugs alone at 10 µg/ml. The results were confirmed at the ultrastructural level by scanning electron microscopy. These data helped to justify the *in vivo* investigations assessing the therapeutic potential of the combination of 5-FU and ABZ suspension in CF-1 mice infected with *E. granulosus sensu stricto* (s. s.) metacestodes. Treatment with 5-FU (10 mg/kg) or 5-FU (10 mg/kg) + ABZ suspension (5 mg/kg) reduced the weight of cysts recovered from mice compared with control groups. Interestingly, the effect of 5-FU given weekly for 5 consecutive weeks was comparable to that observed with ABZ suspension under a daily schedule during 30 days. Co-administration of 5-FU with ABZ did not enhance the *in vivo* efficacy of drugs alone calculated in relation to cysts weights. However, the combination provoked greater ultrastructural alterations compared to the monotherapy. In conclusion, we demonstrated the efficacy of 5-FU either alone or co-administrated with ABZ against murine experimental cystic echinococcosis. Since 5-FU treatments did not cause toxic effect in mice, further *in vivo* studies will be performed by adjusting the dosage and the frequency of treatments.

Résumé en anglais

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