

Publication

Activity of oxantel pamoate monotherapy and combination chemotherapy against *Trichuris muris* and hookworms : revival of an old drug

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BACKGROUND: It is widely recognized that only a handful of drugs are available against soil-transmitted helminthiasis, all of which are characterized by a low efficacy against *Trichuris trichiura*, when administered as single doses. The re-evaluation of old, forgotten drugs is a promising strategy to identify alternative anthelmintic drug candidates or drug combinations. **METHODOLOGY:** We studied the activity of the veterinary drug oxantel pamoate against *Trichuris muris*, *Ancylostoma ceylanicum* and *Necator americanus* in vitro and in vivo. In addition, the dose-effect of oxantel pamoate combined with albendazole, mebendazole, levamisole, pyrantel pamoate and ivermectin was studied against *T. muris* in vitro and additive or synergistic combinations were followed up in vivo. **PRINCIPAL FINDINGS:** We calculated an ED50 of 4.7 mg/kg for oxantel pamoate against *T. muris* in mice. Combinations of oxantel pamoate with pyrantel pamoate behaved antagonistically in vitro (combination index (CI) = 2.53). Oxantel pamoate combined with levamisole, albendazole or ivermectin using ratios based on their ED50s revealed antagonistic effects in vivo (CI = 1.27, 1.90 and 1.27, respectively). A highly synergistic effect (CI = 0.15) was observed when oxantel pamoate-mebendazole was administered to *T. muris*-infected mice. Oxantel pamoate (10 mg/kg) lacked activity against *Ancylostoma ceylanicum* and *Necator americanus* in vivo. **CONCLUSIONSIGNIFICANCE:** Our study confirms the excellent trichuricidal properties of oxantel pamoate. Since the drug lacks activity against hookworms it is necessary to combine oxantel pamoate with a partner drug with anti-hookworm properties. Synergistic effects were observed for oxantel pamoate-mebendazole, hence this combination should be studied in more detail. Since, of the standard drugs, albendazole has the highest efficacy against hookworms, additional investigations on the combination effect of oxantel pamoate-albendazole should be launched

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