Mebendazole as an Alternative in *Giardia duodenalis* Infection

The Editor,

Sir,

Pharmacological therapy remains an important component of *Giardia duodenalis* (*G duodenalis*) control both in industrialized and developing countries. However, treatment failures have been observed with all of the common anti-giardial agents, and drug resistance has been demonstrated in the laboratory (1). This situation has motivated researchers to search for new alternatives (2–4).

Mebendazole (MBZ) has been used worldwide because of its relatively poor absorption from the intestine, low level of adverse events and broad spectrum of action against soil transmitted helminthes (STHs), even in single doses. The low cost, effectiveness, lack of action on intestinal microbiota and the safety of this drug further enhance its therapeutic appeal. Mebendazole has been evaluated for its potential use against protozoan and helminth infections other than the common STHs, providing some evidence that could encourage scientists to use it in certain situations, such as for cases of treatment failure or resistance (5).

While investigating the activity of MBZ against intestinal nematodes, Hutchison *et al* noticed that the drug could cure some cases of Giardia infection (6). The results of subsequent in vitro studies confirmed that MBZ had considerable anti-giardial activity (7, 8). Edlind *et al*, for example, demonstrated that the drug not only had a static effect on parasite growth at low concentrations but also had a greater effect on trophozoite morphology, adherence and viability than two 5-nitroimidazoles [metronidazole and tinidazole] (7). Mebendazole and albendazole interfere with the growth of the protozoa, inducing trophozoite detachment and distortion of morphology and general structure through its anti-microtubule mode of action, as well as being able to resolve infections in a mouse model of *G duodenalis* infection (7–9).

Following previous findings, in 2002 our group studied the efficacy of MBZ 200 mg three times daily for three days compared to secnidazole in a single dose in 146 Cuban children aged 5–15 years (10). That study concluded that MBZ was as effective as secnidazole (78.1% vs 79.4%, respectively) and recommended this regimen for children infected by this protozoan in which first-line drugs failed or were not tolerated, with the additional advantage that MBZ could cure some of the common intestinal helminthes co-infections that are a frequent phenomenon in rural areas in different countries throughout the world.

Another trial was carried out in Cuba evaluating MBZ against *G duodenalis* infection in children in 2003 (11). One hundred and twenty-two Cuban children with confirmed giardiasis were randomized to receive MBZ (200 mg three times daily in a study group) or quinacrine (2 mg/kg body-weight three times daily in a control group), both for five days. The parasitological response was higher in the control group (83.6% vs 78.7%); however, it again confirmed the usefulness of MBZ for this parasite infection, which was similar in terms of efficacy to quinacrine. The results encouraged the authors to recommend the five-day regimen as it was similar in terms of efficacy to the three-day regimen used previously (10), although the three-day course seemed to be better in terms of cost and time taking the medication.

Considering the recommended doses of MBZ used by the World Health Organization to control STHs infections in different regions of the world, our group made another trial. One hundred and twenty-two children of both genders, aged from five to 15 years were included in this new study. One-day treatment with 600 mg of MBZ, compared to 50 mg/kg of tinidazole, was tested (12). The cure rate for the MBZ-treated group was 39 out of 61 (63.93%) and for the tinidazole treated group 50 out of 61 (81.97%). The difference was statistically significant in favour of the tinidazole.

The possible explanation about the results that emerged from these three studies carried out in Cuba could be found in the paper by Edlind *et al* (7). Those authors demonstrated that MBZ had a dramatic effect on *G duodenalis* morphology, beginning as early as three hours. After 36 hours, nearly all cells had assumed a grotesque appearance, with few recognizable structures. In addition, they proved that by increasing the concentration of MBZ and the length of the treatment period, the cells reached high levels of detachment until day three. These data justify why the single-day treatment using MBZ did not work and the three and five days did.

To demonstrate the usefulness of MBZ in adults, another trial was carried out in Cuba (13). To compare the efficacy and safety of MBZ and secnidazole in the treatment of giardiasis, a single-centre, parallel group, open-label, randomized non-inferiority trial was carried out. Mebendazole was used 200 mg every eight hours for three days because this was the best dose found in children and in vitro studies have shown that is the right time to this indication. One hundred and twenty-six participants who had symptomatic *Giardia* mono-infection took part in the study. The parasitological cure rate for the *per protocol* populations was 88.7% (55/62) for MBZ and 91.8% (56/61) for secnidazole. For the intention to treat populations, the cure rate at the end of treatment was 85.9% (55/64) for MBZ and 90.3% (56/62) for secnidazole. Both analyses showed there was not a significant statistical difference between MBZ and secnidazole treatment efficacy.

The management of *G duodenalis* infection has been considered by many clinicians as a problem, mainly in tropical and subtropical areas. Mebendazole has shown efficacy in its approved indications as an anthelmintic agent but seems to be also an excellent alternative in the treatment of...
giardiasis. The results that emerged from the studies referred here suggest that MBZ for three days is similar in efficacy to the first line drugs in the treatment of giardiasis, both in children and adult patients.

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REFERENCES