Evaluation of fenbendazole for treatment of *Giardia* infection in cats concurrently infected with *Cryptosporidium parvum*

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**Objective**—To determine whether fenbendazole effectively eliminates *Giardia* organisms from clinically infected cats that have a concurrent *Cryptosporidium parvum* infection.

**Animals**—16 clinically normal cats.

**Procedure**—Eight cats with chronic concurrent *Giardia* and *C parvum* infections received fenbendazole (50 mg/kg, PO, q 24 h) for 5 days (treatment-group cats). Feces from each cat were collected and processed 3 days weekly for 23 days after treatment. By use of an immunofluorescent assay for detection of *Giardia lamblia* cysts and *C parvum* oocysts, organism numbers were counted and scored. Fecal results from treatment-group cats were compared with those of 8 untreated cats with *Giardia* infection but no *C parvum* infection (control-group cats).

**Results**—Four of 8 treatment-group cats had consistently negative results for *Giardia* infection after treatment. These 4 cats had consistently positive results for *C parvum* oocysts prior to treatment and consistently negative results after treatment. One treatment-group cat had positive results for cysts on all fecal samples, and 3 treatment-group cats had 1 to 3 negative results and then resumed shedding large numbers of cysts; each of these cats had consistently positive results for *C parvum* oocysts. When compared with control-group cats, treatment-group cats shed less *Giardia* cysts during week 1 after treatment but not during week 2.

**Conclusions and Clinical Relevance**—Administration of fenbendazole decreases *Giardia* cyst shedding to less than detectable numbers in some cats. In our study, persistent *C parvum* infection may have been associated with failure of fenbendazole to eliminate *Giardia* infection. (Am J Vet Res 2003;64:1027–1029)

*Giardia* spp are flagellated protozoan parasites found worldwide that infect the intestinal tract of many animals and humans. Clinical signs of giardiasis in cats include acute or chronic diarrhea and weight loss; however, cats are often clinically normal while shedding *Giardia* cysts. In recent studies, *Giardia* spp were found to infect 7.3% of cats < 1 year of age in central New York State and 2.4% of cats with or without diarrhea in north central Colorado. These studies highlight the importance of testing for *Giardia* infection in all cats, as many cats shedding *Giardia* cysts had no signs of clinical illness.

Drugs that are reportedly effective for eliminating *Giardia* cyst shedding in cats or controlling diarrhea include metronidazole, quinacrine, and furazolidone, but numbers of cats treated in each report were minimal. Additionally, quinacrine is not currently available in the United States. Metronidazole and furazolidone are difficult to administer to some cats, and metronidazole has been associated with toxic effects on the CNS. Albendazole, a benzimidazole carbamate derivative, was effective in a short-term study in dogs with experimentally induced giardiasis. However, albendazole causes bone marrow suppression in some dogs and cats and was ineffective for the treatment of giardiasis in a group of cats. The related drug, fenbendazole, is apparently safer than albendazole and effective for the treatment of giardiasis in some experimentally and naturally infected dogs. To our knowledge, fenbendazole has not been evaluated for the treatment of *Giardia* infection in cats. The purpose of the study reported here was to determine whether fenbendazole would limit *Giardia* cyst shedding in cats with chronic subclinical *Cryptosporidium parvum* and *Giardia* infections.

**Materials and Methods**

**Animals**—Sixteen laboratory-reared male and female cats between 1 and 2 years of age were purchased from a commercial breeder for use in this study. Cats were individually housed and observed daily for attitude, appetite, stool consistency, and signs of drug toxicosis.

**Treatment group cats**—Eight cats had been infected with a human isolate of *C parvum* 13 months previously. This genotype 2 strain of *C parvum* was purchased from a commercial vendor and is known to infect humans, mice, cats, and cattle. The *C parvum*-infected cats were clinically normal when it was discovered that they were coinfected with a *Giardia* strain that infects humans. It was assumed that contamination occurred via the adjacent room that housed cats, in which a *Giardia* vaccine study had just been completed. By retrospective evaluation of stored feces, it was determined that the *C parvum*-infected cats had been infected with the *Giardia* sp for approximately 3 months prior to being treated in this study. All 8 *C parvum*-infected cats had positive results for *Giardia* cysts in 5 or 6 fecal samples that were collected from 1 to 6 weeks prior to treatment; therefore, these cats were considered chronically infected. Fenbendazole (50 mg/kg, PO, q 24 h) was administered for 3 days to the 8 treatment-group cats that were coinfected with *Giardia* sp and *C parvum*. Feces were collected 3 days a week from all cats for 23 days after treatment began.
Control group cats—Fecal samples were collected during a similar period from 8 control-group cats that were experimentally inoculated with the same Giardia strain (1.0 X 10^8 cysts, PO) as the treatment-group cats. Control-group cats were infected for a similar period as the treatment-group cats, but they were not treated with fenbendazole. Cryptosporidium parvum oocysts were not detected in any fecal sample from the control group cats.

Fecal analysis—Fecal samples from cats were collected throughout the study. All feces were analyzed for the presence of Giardia cysts and C parvum oocysts by use of a commercially available direct immunofluorescence test. For each sample, 25 mg of feces was diluted in 1 mL of PBS solution and then processed and stained according to the manufacturer's instructions. The number of Giardia cysts per slide was counted by use of a fluorescence microscope. A cyst score was assigned from 0 to 4 on the basis of the following system: 0 = 0 cysts/slide; 1 = 1 to 250 cysts/slide; 2 = 250 to 500 cysts/slide; 3 = >501 cysts/slide; and 4 = "too numerous to count" (defined as >100 cysts/field, by use of the 10X objective field).

Statistical analysis—Two analyses were performed to compare the number of cysts shed by treatment- and control-group cats throughout the duration of the study. Because fecal samples were not available from all cats each day, samples from each of the 3 collection periods (ie, intratreatment and weeks 2 and 3) were broken into beginning, middle, and end, resulting in a total of 9 samples. From 3 to 7 fecal samples were available for evaluation each week from the treatment-group cats. An ANOVA, which was appropriate for a repeated measures experiment, and the Wilcoxon's rank sum test were used to assess the differences between groups by use of a software program. A value of \( P < 0.05 \) was considered significant.

Results
The 8 untreated control-group cats had Giardia spp positive results and C parvum negative results throughout the fecal sample collection period. After 5 days of treatment with fenbendazole, 4 of the 8 treatment-group cats had negative results for Giardia spp and continued to have negative results for the remainder of the study. These 4 cats had consistently positive fecal results for C parvum oocysts prior to fenbendazole treatment and consistently negative results after treatment. One of the 8 treatment-group cats had a transient decrease in the number of Giardia cysts shed but resumed shedding large numbers of Giardia cysts by day 9 of the study. This cat had positive results for C parvum throughout the duration of the study. The remaining 3 cats had negative results for Giardia spp a few days after treatment, then resumed shedding large numbers of cysts. These 3 cats that transiently had negative results for Giardia spp had negative results for C parvum oocysts for a few days after treatment with fenbendazole, then resumed shedding greater numbers of C parvum oocysts, as they did with the Giardia cysts.

When compared with results from control-group cats by use of an ANOVA, fenbendazole treatment-group cats began shedding significantly fewer Giardia cysts near the end of week 1, which continued until the start of week 3 (Fig 1). When evaluated by use of Wilcoxon's rank sum test, the fenbendazole treatment-group cats shed significantly fewer cysts in week 2, compared with control-group cats. In week 3, there was no significant difference in cyst numbers was detected between the treatment and control groups by use of either statistical method.

Discussion
Benzimidazole anthelmintics inhibit microtubule assembly in helminths and are thought to have the same effect in Giardia spp. The benzimidazoles, fenbendazole, albendazole, and febantel (a drug that is metabolized to fenbendazole) have been successfully used to treat giardiasis in dogs. Although benzimidazoles are widely used by veterinary practitioners for the treatment of giardiasis in cats, there has only been 1 published study in which albendazole treatment was reportedly ineffective. In our study, administration of fenbendazole (50 mg/kg, PO, q24 h) for 5 days lessened Giardia cyst shedding transiently, compared with untreated control-group cats, but only 4 of the 8 treatment-group cats had negative results for Giardia spp at the end of the 3-week study period. On the basis of retrospective evaluation of stored feces, we can be confident that the duration of infection of the treatment-group cats was 3 months. This Giardia sp causes a high degree of infection in cats for at least 6 months; it is unlikely that cats that had negative results for Giardia spp after treatment had spontaneous elimination of the infection. Our findings suggest that administration of fenbendazole will be effective for lessening Giardia cyst shedding and eliminating Giardia infection in some cats. Because Giardia infection was subclinical in cats of our study, it cannot be determined whether fenbendazole administration lessens the clinical signs of giardiasis.

When used with human feces, the detection limits of the direct immunofluorescence test used in our study are 100 C parvum oocysts/mL of feces and 100 Giardia cysts/mL of feces. Thus, it is also possible that the infections were not actually eliminated in the cats in our study but that oocyst and cyst numbers were just suppressed to below detectable limits of the assay. Future study in cats to determine drug efficacy should include more sensitive quantitative techniques, such as polymerase chain reaction.
There are potential explanations for the apparent fenbendazole treatment failures in our study. Of the treatment-group cats, 3 had transient negative results for Giardia spp. It is possible that fenbendazole lessened the infection in these cats to below detectable amounts, and cats were reinfeected from their environment. Another explanation is that the infection was temporarily suppressed by the fenbendazole, and when treatment ended, Giardia numbers increased again. Results also may have been affected by the coinfection with C. parvum. It was previously shown that C. parvum coinfection potentiated Trichomonas foetus infections in cats. Many Giardia spp exist and are hosted by a wide variety of mammalian species. One genotype specific to cats has been isolated. The Giardia strain used in our study was initially isolated from a human. It is possible that there are differences in benzimidazole susceptibility between isolates and that fenbendazole would be more effective against other strains.

Detection of C. parvum oocysts in the treatment group cats of our study appeared to parallel the detection of Giardia cysts. Cats that did not have detectable Giardia cysts after treatment also did not have detectable C. parvum oocysts. Over 100 compounds have been assessed for the treatment of C. parvum in vitro, none of which were found to be universally effective. Albendazole as well as several other benzimidazole derivatives were not effective in preventing C. parvum infections in a study in mice. In another study, assessing microsporidial β-tubulin DNA sequences as a predictor of benzimidazole sensitivity, C. parvum was shown to lack the appropriate microtubular structure on which these drugs act. Thus, our results suggest that as fenbendazole exerted an effect on the Giardia infection, there was an indirect effect on the C. parvum infection as well. This hypothesis is supported by a study of mice coinfected with Giardia spp and Cryptosporidium spp. In that study, ivermectin, which has no effect against C. parvum, was effective in decreasing shedding of both parasites.

Metronidazole is another drug frequently used but was less effective than albendazole in treating giardiasis in vitro. However, in a published case series of giardiasis in naturally-infected cats treated with metronidazole, 7 of 7 cats had positive responses. In addition, metronidazole benzoate (25 mg/kg, PO, q 12 hr, for 7 days) lessened cyst shedding to below detectable limits in 26 experimentally inoculated cats for at least 15 days. Because of the risk of neurotoxicity, care must be taken to avoid overdose or excessive duration of treatment, if metronidazole is used.

Further studies assessing the effect of benzimidazoles and other drugs for the treatment of giardiasis in cats are needed. However, as in humans and dogs, it is apparent that there is no single drug that will be universally effective for the treatment of this parasite in cats. Veterinarians should be prepared to attempt alternate treatment if the first choice fails.

References