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Short Communication

Efficacy of albendazole and fenbendazole against *Giardia* infection in cattle

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Abstract

Efficacies of albendazole and fenbendazole in suppressing *Giardia* cyst output of infected calves were evaluated in two clinical trials. In the first trial, 18 naturally infected calves were allocated to an untreated control group ($n=9$) and an albendazole-treated group ($n=9$). Calves in the treated group were given 20 mg kg^{-1} oral albendazole once daily for 3 days. Compared to controls, treated calves showed 98.5%, 97.6% and 90.8% reductions in cysts per gram of feces (cpg) 1, 2 and 6 weeks respectively after the start of treatment. In a second trial, 13 infected calves were allocated to an untreated control group ($n=6$) and a fenbendazole-treated group ($n=7$). Calves in the treated group were given 10 mg kg^{-1} fenbendazole orally twice daily for 3 days. Compared to the control group, treatments reduced cpg counts by 100%, 98.5% and 59.5% 1, 2, and 3 weeks respectively after the start of treatment. Both albendazole and fenbendazole appeared to be effective in suppressing cyst excretion by *Giardia*-infected calves.

Keywords: Cattle-Protozoa; *Giardia* sp.; Control methods-Protozoa; Albendazole; Fenbendazole

1. Introduction

Prevalence surveys in the last decade indicated that *Giardia* infection is prevalent in cattle in many areas of the world (reviewed by Xiao, 1994). Infection rates of calves varied from 1% to 100%. Some of these infections were associated with the occurrence of diarrhea and ill thrift (Deshpande and Shastri, 1981; Willson, 1982; Nesvadba et al., 1982; Pavlasek, 1984; St. Jean et al., 1987; Xiao et al., 1993). Therefore, *Giardia* infection is potentially pathogenic in calves and warrants the use of control measures under certain circumstances.

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Nitroimidazoles (metronidazole, dimetridazole and ipronidazole), quinacrine and furazolidone, which have been widely used in the treatment of giardiosis of humans and companion animals (Zimmer and Burrington, 1986; Zajac, 1992), have been used for the treatment of *Giardia* infection in calves (Deshpande and Shastri, 1981; Willson, 1982; Nesvadba et al., 1982; St. Jean et al., 1987; Xiao et al., 1993). Symptomatic improvement was achieved in all treated animals, although no control animals were used and parasitological cure was not evaluated in most cases. Adverse effects of drug treatment were not described in calves, but only limited numbers of animals were treated. It is well known that dogs and cats may develop toxic signs of drug treatment, including vomiting, diarrhea and neurologic symptoms (Zimmer and Burrington, 1986; Zajac, 1992). Because metronidazole and furazolidone are mutagenic and quinacrine easily crosses the placenta, these drugs have not been approved for use in food animals in most developed countries. Thus alternative drugs are highly desirable for the treatment of *Giardia* infection in farm animals.

Recent studies suggested that two benzimidazole drugs, albendazole and mebendazole, have clinical efficacy against human giardiosis (Zhong et al., 1986; Wang, 1988; Al-Waili et al., 1988; Al-Waili and Hasan, 1992). Although the claims for mebendazole were disputed (Gascon et al., 1989, 1990; Al-Waili, 1990; Gascon and Corachan, 1990), in vitro studies have shown that albendazole, mebendazole and fenbendazole are much more effective against *Giardia* trophozoites than metronidazole, tinidazole, or quinacrine (Edlind et al., 1990; Meloni et al., 1990; Cedillo-Rivera and Munoz, 1992; Chavez et al., 1992; Morgan et al., 1993). Benzimidazoles are well known as inhibitors of the polymerization of tubulin to microtubules. Because microtubules are major components of the four pairs of flagella, the median body, and the ventral disk of *Giardia* trophozoites, it is likely that these drugs exert their activities against *Giardia* through the inhibition of their attachment to the intestinal mucosa (Chavez et al., 1992; Reynoldson et al., 1992; Morgan et al., 1993). There have been several controlled studies in mice and dogs to evaluate the in vivo efficacy of albendazole (Reynoldson et al., 1991; Barr et al., 1993) and fenbendazole (Barr et al., 1994). The present study was designed to evaluate the clinical effect of both albendazole and fenbendazole in suppressing *Giardia* cyst excretion by infected calves.

2. Materials and methods

2.1. Albendazole trial

This trial was conducted on a commercial cattle farm. Eighteen Holstein male and female calves, 3–9 weeks of age and naturally infected with *Giardia* sp. without clinical signs, were divided into an albendazole treatment group and an untreated control group, each with nine animals. Albendazole (Valbazen; SmithKline Beecham Animal Health, Exton, PA) was given orally to animals in the treatment group at 20 mg kg^{-1} of body weight once daily for 3 days. Rectal fecal samples were taken from both groups shortly before treatment and 1, 2 and 6 weeks after the start of treatment. Calves from both groups were housed together until 2 weeks posttreatment, when they were pastured together until the end of the study.

2.2. Fenbendazole trial

This trial was conducted on a university research farm. Thirteen male Holstein calves, 8–10 weeks of age and asymptomatically infected with *Giardia* sp., were purchased from a commercial supplier. They were randomly allocated to a fenbendazole treatment group and an untreated control group, each with seven and six animals, respectively. Calves in the treated group were given 10 mg kg^{-1} fenbendazole (Panacur; Hoechst-Roussel Agri-Vet, Somerville, NJ) orally twice daily for 3 days. Rectal fecal samples were taken from all animals shortly before treatment and 1, 2 and 3 weeks after the start of treatment. Calves from each group were housed in different stalls during the entire experiment. Both stalls were cleaned and disinfected daily with Coverage Plus NPD (Calgon Vestal Laboratories, St. Louis, MO), an ammonium disinfectant.

2.3. Fecal examination

Fecal samples from both trials were examined for *Giardia* cysts with a quantitative immunofluorescence assay (Xiao and Herd, 1993), using a commercial kit (Merifluor Cryptosporidium/Giardia, Meridian Diagnostics, Cincinnati, OH). A 1% aliquot of fecal suspension obtained from 2 g of sample after filtering and washing was stained using the immunofluorescence kit. Thus the theoretical sensitivity of this test was 100 cysts g^{-1} of feces. The actual sensitivity of the test was above 1000 cysts g^{-1}, higher than those of the zinc sulfate flotation and sucrose gradient flotation (Xiao and Herd, 1993). Cysts in the aliquot were counted, and numbers of cysts per gram of feces were obtained by multiplying the total number of cysts by 100.

2.4. Percentage efficacy

Geometric means of cysts per gram of feces by groups at each sampling were calculated. They were compared between groups with a Student's *t*-test. Differences were regarded as significant when $P \leqslant 0.05$. The efficacy of drug treatment in suppressing cyst output of treated animals was calculated by the following formula:

$$\begin{aligned}\text{Efficacy } (\%) = &(\text{Geometric mean of the control group} \\ &- \text{Geometric mean of the treated group}) \\ &\times 100/\text{Geometric mean of the control group}\end{aligned}$$

3. Results

Results of the albendazole trial are shown in Table 1. Mean cyst counts of the control and albendazole-treated groups were similar before treatment. Treated calves had reduced excretion of *Giardia* cysts at 1, 2 and 6 weeks. Reductions in cysts per gram exceeded 90%, and differences between treated and control groups were significant ($P < 0.05$) at 1 week. Some animals in the albendazole treatment group, however, still had low *Giardia* cyst

Table 1
Giardia cyst output and percent reduction in nine albendazole-treated calves compared with nine control calves

Week	Control		Albendazole	
	No. positive	cpg*	No. positive	cpg
0	9	1119 ± 13^{a}	9	1009 ± 13^{a}
1	8	1041 ± 54^{a}	4	15 ± 26^{b} (98.6%)
2	6	225 ± 84^{a}	2	5 ± 61^{a} (97.8%)
6	5	22 ± 20^{a}	2	2 ± 8^{a} (90.9%)

*Geometric mean of cysts per gram of feces (cpg) ± standard deviation. Efficacies are in parentheses.
[a,b]Means with different superscripts in the same row are significantly different ($P < 0.05$).

Table 2
Giardia cyst output and percent reduction in seven fenbendazole-treated calves compared with six control calves

Week	Control		Fenbendazole	
	No. positive	cpg*	No. positive	cpg
0	6	81647 ± 13^{a}	7	15438 ± 11^{a}
1	6	16328 ± 3^{a}	0	0^{b} (100%)
2	6	4705 ± 9^{a}	4	72 ± 93^{a} (98.5%)
3	6	1277 ± 1^{a}	5	517 ± 150^{a} (59.5%)

*Geometric mean of cysts per gram of feces (cpg) ± standard deviation. Efficacies are in parentheses.
[a,b]Means with different superscripts in the same row are significantly different ($P < 0.05$).

excretion after treatment. Animals in the control group had a gradual reduction in cyst output during the experiment.

Results of the fenbendazole trial are shown in Table 2. Mean cyst counts of the control group were higher than those of the fenbendazole-treated group before the start of the experiment, but the difference was not significant ($P > 0.05$). All fenbendazole-treated calves became negative for *Giardia* cysts 1 week after treatment. Afterwards, some calves in the treated group started to excrete low number of cysts. The difference between the untreated control group and the fenbendazole treatment group was significant ($P < 0.05$) at 1 week. Calves in the untreated control group also showed reductions in cyst excretion as the experiment proceeded.

4. Discussion

Results of this study confirmed the antigiardial efficacy of albendazole and fenbendazole. Cyst output after treatments in both trials was reduced by more than 90%, although parasitological cure was not achieved in all treated animals. This is similar to results of controlled trials conducted in mice and dogs (Reynoldson et al., 1991; Barr et al., 1993, 1994). The dose of both drugs tested for *Giardia* treatment is much higher than for helminth treatment (20 mg kg^{-1} daily for 3 days versus 10 mg kg^{-1} once in calves). These dosages were empirically based on dose titration studies done with mice and dogs, in which doses required

for antigiardial treatment were much higher than those required for anthelmintic treatment (Reynoldson et al., 1991; Barr et al., 1993, 1994).

The antigiardial efficacy of albendazole and fenbendazole is somewhat different. In the albendazole trial, four of nine treated calves had low cyst excretion 1 week after the start of treatment. Because this was just 4 days after the administration of the last dose, it is unlikely that these cysts were from reinfection. Apparently, some *Giardia* trophozoites survived the treatment and continued passing cysts in feces. In the fenbendazole trial, no cysts were detected in treated animals 1 week after the start of treatments, but cyst excretion resumed at later samplings. Although treated animals were housed separately and daily cleaning and disinfection of stalls were undertaken, it is possible that some animals were reinfected shortly after the treatment. Thus, the cyst-suppressing effect of both drugs is probably short-lasting in field conditions despite the high efficacy of both drugs. This is in contrast to results of in vitro studies, in which the antigiardial effect of albendazole and fenbendazole was irreversible and long-lasting (Meloni et al., 1990; Morgan et al., 1993). The gradual reduction in cyst output seen in untreated animals in both trials probably resulted from acquired immunity (Xiao and Herd, 1994).

Comparison of the results of clinical efficacy of albendazole and fenbendazole with traditional antigiardial drugs (nitroimidazole derivatives, quinacrine and furazolidone) is not possible, because the latter were used in the treatment of only a few calves in uncontrolled studies. Albendazole and fenbendazole, however, have some advantages over these traditional antigiardial drugs. Both drugs have a higher safety margin (the safety index in cattle is 10 for albendazole and 50 for fenbendazole) and additional anthelmintic efficacy (Prichard, 1983). In contrast, the nitroimidazoles, quinacrine and furazolidone, are not approved for use in farm animals because of their mutagenic and teratogenic activities. They are known to cause toxicity in humans and companion animals and to disrupt the normal intestinal bacterial flora (Edlind et al., 1990). Thus albendazole and fenbendazole have the potential to become new antigiardial agents in farm animals.

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