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ARTICLE

Comparison of Secnidazole and Fenbendazole for the Treatment of Asymptomatic Giardia Infection in Dogs

Jhon D Ruiz* **Gloria P Ramírez** **Ana M Múnera** **Carlos Arroyave** **Laura Castaño Pablo López**

Grupo de Investigación en Ciencias de los Animales. Facultad de Medicina Veterinaria y Zootecnia. Universidad CES. Medellín, Colombia

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ABSTRACT

The objetive of this study was to compare a single dose of secnidazole versus multiple doses of fenbendazole for the treatment of dogs with asymptomatic *Giardia* infection. Materials and methods: Twenty-four asymptomatic dogs with a positive test result for *Giardia* spp were randomized in two equal groups to receive a single dose of secnidazole at 30 mg/ kg PO, or fenbendazole at 50 mg/ kg PO q24h for 3 days. Hematological parameters were evaluated before and 8 days after treatment, and feces were re-examined at days 8, 15, and 30 post-treatment by fecal flotation and antigen test. Results: The number of positive dogs in the fenbendazole group was: 1 (day 8) and 3 (days 15 and 30). In the secnidazole group, the number of positive cases were: 4 (day 8), 3 (day 15), and 1 (day 30). Conclusion: Treatment with secnidazole or fenbendazole, were effective between 75% and 92% to eliminate the excretion of *Giardia* cysts in canines together with hygienic measures to control, like disinfection with quaternary ammonium of patients and their environment. Further studies that include more animals and multiple fecal exams on consecutive days would be necessary to confirm its efficacy in dogs.

1. Introduction

Giardia spp are flagellated protozoan parasites found in the intestinal tract of mammals, birds, and reptiles worldwide. *Giardia duodenalis (syn. G. intestinalis* or *G. lamblia*) inhabits the small intestine of humans, dogs, and cats, and is considered as a potential zoonotic risk [1]. In developing countries with a high prevalence and incidence of infection, some studies suggest that chronic *Giardia*sis causes delayed growth in children [2,3,4].

Although *Giardia* infection may be common, clinical signs of diarrhea are not always present and many dogs and cats are subclinical carriers [5,6,7]. The prevalence in dogs has been reported to vary from 1% to nearly 28%, with some predisposing factors being age and lack of hygienic conditions [8,9]. Although *G. intestinalis* is a species complex with a wide mammalian host range, including people, the role of pets as a source of human *Giardia*sis remains unclear and there are no current recommendations to test and treat healthy pets for *Giardia* spp infection [1,2,10].

**Corresponding Author:*
Jhon D Ruiz,
Grupo de Investigación en Ciencias de los Animales. Facultad de Medicina Veterinaria y Zootecnia. Universidad CES. Medellín, Colombia;
Email: jdruiz@ces.edu.co

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However, animals housed under conditions of stress or overcrowding may have high prevalences of *Giardia*, for this reason it is necessary to treat the infected animals in all cases.

Treatment of *Giardia*sis with fenbendazole at 50 mg/kg orally every 24 hours for 3–5 days has been reported to effectively eliminate infections in 86%–100% of dogs and cats [11,12]. An alternative treatment is metronidazole at 50 mg/kg q24h for 5 days, but it is only about 67% effective in eliminating *Giardia* spp from infected dogs and may be associated with adverse side effects such as development of anorexia and vomiting, which may progress to neurotoxicosis [13,14]. In addition, treatment for 5 days is impractical for some animals that are difficult to handle or for treating large populations (e.g., kennels, catteries). In these situations, the search for alternative therapeutic options, including single-dose treatments, could be quite valuable.

Secnidazole is an antiparasitic used in humans that it is administered as a single dose for the control and treatment of *Giardia*sis [15,16]. When a single oral dose of 30 mg/kg was used extralabel in 18 naturally infected cats it achieved a 100% efficacy to eliminate cyst shedding in the feces [17]. The aim of this study was to evaluate the use of a similar single oral dose of secnidazole for treating naturally acquired *Giardia*sis in dogs.

2. Materials and Methods

2.1 Ethics Committee

This study was approved by the Ethics Committee for Animal Experimentation of the University of Antioquia, Colombia, record No. 72.

2.2 Type of Study

A prospective positive-controlled study with dogs randomized to receive fenbendazole or secnidazole.

2.3 Study Population and Treatment Protocols

This is a field study the owners maintained the dogs. Dogs eligible for inclusion in the study had owner consent as well as a positive test for *Giardia* cysts by fecal flotation with zinc sulfate solution on the day of examination. A total of 34 out of 250 clinically healthy dogs from the metropolitan area of Medellin met these criteria. The following hematological and biochemical parameters were analyzed on the day 0 of examination and at day 8 after treatment: complete blood count, BUN, creatinine, ALT, alkaline phosphatase, albumin, and direct and indirect bilirubin. Ten animals were excluded from the study due to concurrent illness, death, or being lost to follow-up. The study involved 24 dogs that were divided in 2 groups: secnidazole at 30 mg/kg PO single dose or fenbendazole at 50 mg/kg PO daily for 3 days. The secnidazole group was comprised of 4 females and 8 males with a mean age of 33 months (range 12–48 months). The fenbendazole group included 7 females and 5 males, with a mean age of 28 months (range 10–48 months).

2.4 Diagnostic Tests

Blood samples were collected on the day of examination (day 0) and at day 8 post-treatment. Stool samples were collected on days 0, 8, 15, and 30 post-treatment. The day of treatment (day 1), the perineal area was thoroughly bathed with a quaternary ammonium solution 0.05% to remove cysts from the hair coat and prevent reinfection from grooming. The owners were advised and trained to disinfect every day the premises where the dogs lived and to promptly remove feces to limit environmental contamination. They were also instructed to notify for any signs of vomiting, diarrhea, anorexia, or other abnormalities.

The diagnostic tests for *Giardia* included a direct smear examination for cysts following centrifugal fecal flotation with zinc sulfate, and multiple ELISA for the detection of *Giardia* antigens in feces (SNAP *Giardia* Test, IDEXX Laboratories) [18]. The sample was considered infected when resulted positive at least in one test. Statistical analysis was performed using SAS software with chi square analysis for qualitative variables (positive or negative infection) and Student's t for quantitative variables, and the level of statistical significance was set at $P<0.05$.

3. Results

A total of 250 stool samples from a random population of dogs from Medellin were processed by fecal flotation with zinc sulfate to detect *Giardia* cysts. There were 34 positive samples, giving a prevalence of 13.6% of the studied population. Some of these animals had to be removed from the study because they have clinical signs and a more complete treatment that included hydration, antibiotics and analgesics was required, leaving 24 suitable dogs that were equally divided in 2 groups to receive fenbendazole or secnidazole. This study did not include an untreated infected group, and effectiveness of treatment was determined by comparing the different evaluation days with day 0.

The number of positive and negative animals following treatment is shown in Table 1. In the group of animals that received secnidazole, there were 4, 3, and 1 dogs positive on days 8, 15, and 30, respectively, being always the

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same positive animals. In the fenbendazole group, only 1 of 12 animals had *Giardia* cysts on day 8; however, 3 dogs were positive at 15 days and the same 3 dogs were positive at 30 days after treatment. No statistical differences were observed in outcomes between the treatment groups ($p>0.05$).

With regard to the hematological and biochemical parameters analyzed, all values were within the normal range in every animal before treatment and on day 8 after treatment (Tables 2, 3, and 4). In addition, the owners did not report diarrhea or signs suggestive of adverse drug effects throughout the study period.

4. Discussion

Prevalence rates for *Giardia* infection in dogs have been reported to vary from 1% in fecal samples from well-managed pets to 28% in shelter dogs [5,8,9,19,20]. Typically, younger animals may show signs of infection, with adults being subclinical carriers [5,19,21]. In this study, 34 out of 250 (13.6%) dogs were positive by fecal flotation technique.

The classical treatment used in dogs and cats against *Giardia* has been fenbendazole (50 mg/kg/day for 3–5 days), and experimental infestations have shown its efficacy close to or at 100% [11,12]. Those studies are in accordance with the present results where only 1 of 12 animals was positive on day 8 following a 3-day treatment protocol with fenbendazole. The fact that a total of 3 animals in the fenbendazole group tested positive on days 15 and 30 suggests that re-infection occurred in 3 dogs.

Other studies have used alternative drugs with more variable results, including metronidazole at 30–50 mg/kg q12h for 15 days with or without silimarin [14], and albendazole at 25 mg/kg q12h for 2 days [11]. Similar to the results of this study, these products have good effects on the control of *Giardia* in dogs, but none over 100% of treated canines at all assessment times.

Earlier studies in cats showed that a single oral dose of 30 mg/kg secnidazol reached 100% efficacy at days 6, 7, and 8 post-treatment [17]. In this study, only 8 of 12 dogs were negative on day 8 post-treatment, even though all animals, except for one, turned negative by day 30. It is possible that because of the intermittent nature of *Giardia* shedding (from undetectable to large concentrations in feces), the negative test results on day 30 coincided with a time of no shedding. Therefore, infection cannot be definitively ruled out in spite of the lack of cysts in the fecal samples.

The pharmacological treatment of *Giardia* infection in dogs and cats is very effective; however, there may appear cases of therapeutic failure, that are very likely due to re-infection phenomena through the ingestion of cysts from the environment [22,23]. Reinfection is a phenomenon that in this study probably occurred since the animals were all the time in their homes with their owners and the disinfection was in charge of these, with possible flaws in this process. In addition, this study did not have information on the coexistence of other animals or humans that could be able to favor reinfection.

Thus, besides the antiprotozoal treatment, accompanying measures such as post-treatment bath and sanitation of the environment have been recommended before considering resistance to treatment [23]. Therefore, in this study we used the combination of treatment with secnidazol or fenbendazol together with the disinfection of the quarters with quaternary ammonium and washing of the perineum of the study subjects, thus reducing the risk of recontamination with the cysts excreted by the parasite. The high resistance and ubiquity of the *Giardia* cysts also play an important role in the recontamination. Nevertheless, our results indicate that treatment with secnidazol or fenbendazol, together with hygienic measures like disinfection with quaternary ammonium of patients and their environment, may be effective to eliminate the excretion of *Giardia* cysts in canines.

The administration of nitroimidazoles in animals may cause adverse reactions such as anorexia, nausea, and diarrhea [23] and a study reported that in felines secnidazol may cause increase of liver enzymes [17]. In the present study, none of the animals treated, that were asymptomatic, showed alterations or changes in their laboratory parameters. Nonetheless, more studies are suggested to help confirm drug´s safety mainly, if second doses of treatment are employed to counter reinfections.

Supplement

Table 1. Number of dogs shedding *Giardia intestinalis* cysts before and after treatment with secnidazole or fenbendazole

	N° of positive animals/Total (%)*			
Day	**0**	**8**	**15**	**30**
Secnidazole 30 mg/kg PO once	12/12 (100%)[a]	4/12 (33.3%)[b]	3/12 (25%)[b]	1/12 (8.3%)[b]
Fenbendazole 50 mg/kg PO for 3 days	12/12 (100%)[a]	1/12 (8.3%)[b]	3/12 (25%)[b]	2/12 (25%[b])

Note: *A positive animal was diagnosed based on detection of cysts by fecal centrifugation-flotation technique using zinc sulfate, and/or a positive ELISA result (SNAP *Giardia* Test, IDEXX Lab).

[a,b] Numbers followed by different letters in each row are statistically different from each other ($P<0.05$). No differences were observed between groups at any given time.

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Table 2. Mean (±SD) of hematological parameters in dogs infected with *Giardia intestinalis*, before and after treatment with secnidazole and fenbendazole

Parameter*	Before treatment	After treatment
Erythrocyte (x10^6/ul)	Reference range (5.5-8.5)	
Secnidazole	6.87 ± 1.06	6.91 ± 0.95
Fenbendazole	6.63 ± 0.81	6.68 ± 0.79
Hematocrit (%)	Reference range (37-55)	
Secnidazole	45.02 ± 7.22	45.50 ± 8.11
Fenbendazole	43.50 ± 5.93	42.11 ± 5.99
Hemoglobin (g/dl)	Reference range (12-18)	
Secnidazole	14.84 ± 2.32	14.93 ± 2.36
Fenbendazole	14.23 ± 2.28	13.72 ± 2.09
MCV (fl)	Reference range (60-77)	
Secnidazole	63.17 ± 2.08	62.33 ± 3.06
Fenbendazole	64.25 ± 3.41	63.83 ± 4.04
MCH (Pg)	Reference range (21-27)	
Secnidazole	22.14 ± 0.74	22.09 ± 0.94
Fenbendazole	21.68 ± 1.29	21.01 ± 1.17
MCHC (g/dl)	Reference range (32-37)	
Secnidazole	35.14 ± 0.99	34.99 ± 2.69
Fenbendazole	33.67 ± 1.38	32.81 ± 1.22
RDW (%)	Reference range (12-16)	
Secnidazole	14.85 ± 0.64	15.03 ± 0.94
Fenbendazole	15.32 ± 1.26	15.45 ± 1.51
Platelets (x10^3/ul)	Reference range (190-500)	
Secnidazole	195.33 ± 56.70	220.08 ± 87.35
Fenbendazole	252.58 ± 77.75	248.08 ± 72.33

Note: MCV: Mean Corpuscular Volume.

MCH: Mean Corpuscular Hemoglobin.

MCHC: Mean Corpuscular Hemoglobin Concentration.

RDW: Red blood cell Distribution Width.

*No statistical differences were observed among groups or before and after treatment.

Table 3. Mean (±SD) of white blood cells in dogs infected with *Giardia intestinalis*, before and after treatment with secnidazole and fenbendazole

Variable*	Before treatment	After treatment
Total leukocyte count (/ul)	Reference range (100-1700)	
Secnidazole	11385.83 ± 3513.78	11764.17 ± 3165.25
Fenbendazole	18095.00 ± 5569.51	14962.50 ± 5660.67
Eosinophils (/ul)	Reference range (100-1700)	
Secnidazole	1624.61 ± 1551.33	1582.78 ± 1400.74
Fenbendazole	1669.04 ± 935.04	1599.68 ± 1775.98
Neutrophils (/ul)	Reference range (3300-12000)	
Secnidazole	6113.69 ± 2834.44	6952.72 ± 2805.93
Fenbendazole	11982.08 ± 5245.06	9444.13 ± 3895.04
Bands (/ul)	Reference range (0-300)	
Secnidazole	224.05 ± 340.88	84.87 ± 186.14
Fenbendazole	184.73 ± 220.34	32.14 ± 82.22
Lymphocytes (/ul)	Reference range (1000-4500)	
Secnidazole	3070.91 ± 971.06	2848.98 ± 1232.76
Fenbendazole	3856.25 ± 1563.57	3474.21 ± 1020.68
Monocytes (/ul)	Reference range (100-700)	
Secnidazole	314.91 ± 296.98	278.91 ± 211.43
Fenbendazole	402.91 ± 296.87	412.38 ± 245.09

Note: * No statistical differences were observed among groups or before and after treatment.

Table 4. Mean (±SD) of some clinical biochemistry in dogs infected with *Giardia intestinalis*, before and after treatment with secnidazole and fenbendazole

Parameter*	Before treatment	After treatment
ALT(UI/l)	Reference range (21-102)	
Secnidazole	47.20 ± 34.91	36.45 ± 11.29
Fenbendazole	43.42 ± 31.11	36.25 ± 9.09
Alkaline phosphatase (UI/l)	Reference range (10-73)	
Secnidazole	40.00 ± 17.26	27.75 ± 15.74
Fenbendazole	61.25 ± 37.77	58.09 ± 33.32
BUN (mg/dl)	Reference range (10-28)	
Secnidazole	25.60 ± 4.41	29.13 ± 4.76
Fenbendazole	26.26 ±5 .20	24.16 ± 7.25
Creatinine (mg/dl)	Reference range (0.5-1.5)	
Secnidazole	1.03 ± 0.14	1.05 ± 0.18
Fenbendazole	0.87 ± 0.13	0.92 ± 0.17
Total protein (g/l)	Reference range (54-71)	
Secnidazole	77.50 ± 12.48	79.50 ± 8.27
Fenbendazole	69.83 ± 5.56	69.33 ± 5.93
Albumin (g/l)	Reference range (26-33)	
Secnidazole	28.10 ± 4.56	28.08 ± 4.56
Fenbendazole	30.00 ± 3.77	31.58 ± 5.66
Total bilirubin (mg/dl)	Reference range (0.1-0.9)	
Secnidazole	0.72 ± 0.35	0.74 ± 0.55
Fenbendazole	0.94 ± 0.44	0.86 ± 0.71

Note: * No statistical differences were observed among groups or before and after treatment.

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