

# Efficacy of Albendazole and Two Different Doses of Paromomycin for Treatment of Naturally Occurring Giardia Infection in Lambs

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## Summary

*Giardia duodenalis* is a protozoan that infects a variety of vertebrates. It is a major cause of diarrhea in agricultural animals. There have been reports of clinical signs in cattle and sheep, which include diarrhea, dehydration and weight loss, however; there are limited drugs available for the treatment of giardiasis in animals. In this study, we compared the therapeutic effect of 20 mg albendazole, 50 mg and 100 mg paromomycin (kg body weight orally) for 3 successive days in lambs naturally infected with giardiasis. The efficacy of these drugs was evaluated based on reduction in cyst excretion. In the group treated with albendazole, no cysts were seen in the feces after treatment on D5 (day 5) in 7 lambs and on D8 in all animals. In the group treated with 50mg/kg of paromomycin, no cysts were seen in the feces after treatment on D2 in 3 lambs and on D6 in all animals. In the group treated with 100 mg/kg of paromomycin, there were no cysts after treatment on D2 in 5 lambs and on D6 in all of lambs. White blood cell (WBC) levels were high in all groups before treatment; paromomycin decreased the total leukocyte count more than albendazole. In the present study, we found paromomycin to be more effective than albendazole for the treatment of lambs with giardiasis for both treatment regimens mentioned above.

**Keywords:** Albendazole, Paromomycin, Giardiasis, Lambs

## Doğal İnfekte Giardiazisli Kuzuların Tedavisinde Albendazol ve İki Farklı Paromomisin Dozunun Etkisinin Karşılaştırılması

### Özet

*Giardia duodenalis* çeşitli omurgalılarda hastalık yapan bir protozondur. Çiftlik hayvanlarında oluşan ishalin önemli sebeplerinden biridir. Sığır ve koyunlarda ishal, dehidrasyon ve kilo kaybı gibi klinik bulgular bildirilmiştir fakat çiftlik hayvanlarında giardiazis tedavisinde kullanılan ilaçlar sınırlıdır. Bu çalışmada doğal infekte giardiazisli kuzularda 3 gün oral kullanılan 20 mg Albendazol, 50 mg ve 100 mg Paromomisin'in (kg canlı ağırlık) terapötik etkileri karşılaştırıldı. Bu ilaçların etkinliği kist atılımındaki azalmaya bakılarak değerlendirildi. Albendazol grubunda 5. günde 7 kuzuda ve 8. günde bütün hayvanlarda kist atılımı sıfırlandı. 50 mg/kg paromomisinle tedavi grubunda 2. günde 3 kuzu ve 6. günde bütün hayvanlarda kist atılımı sıfırlandı. 100 mg/kg paromomisinle tedavi grubunda ise 2. günde 5 kuzu ve 6. günde bütün hayvanlarda kist atılımı sıfırlandı. Tedavi öncesi lökosit değeri bütün gruplarda normalin üstünde tespit edildi. Paromomisin total lökosit sayısını albendazole göre daha fazla düşürdü. Sonuç olarak giardiazisli kuzuların tedavisinde paromomisin albendazole oranla etkili bulundu.

**Anahtar sözcükler:** Albendazol, Paromomisin, Giardiazis, Kuzu

## INTRODUCTION

*Giardia duodenalis* is a flagellate binucleated protozoan that infected a variety of vertebrate including mammals, reptiles, and birds. It is a major cause of diarrhea in humans

and has been suspected of causing diarrhea in agricultural animals, especially in young animals <sup>1</sup>. High excretion rates and excretion intensities in young animals result in



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the contamination of the environment and infection via formites<sup>2</sup>. Contact with farm livestock is one risk factor for disease in humans<sup>3</sup>. Giardial infections in agricultural animals have been successfully treated with dimetridazole and it is also susceptible to furazolidone; however both drugs are illegal for use in food animals in many countries<sup>1</sup>. Treatment with albendazole and nitazoxanide are effective against giardiasis but require multiple doses<sup>4</sup>. Lofmark et al.<sup>5</sup> found that metronidazole is considered a cost-effective drug because of its low cost, good activity against pathogenic anaerobic bacteria, favorable pharmacokinetic and pharmacodynamic properties, and minor adverse effects. On the other hand, Plumb<sup>6</sup> reported that in veterinary medicine, the side effects of metronidazole include anorexia, and diarrhea also, this drug is illegal for use in food animals too. Paromomycin is a wide-spectrum amino-glycoside antibiotic, with well-known efficacy against several protozoan parasites like *Cryptosporidium parvum*<sup>7</sup>, and *Giardia duodenalis* in calves<sup>8</sup>. Paromomycin is poorly absorbed from the gastrointestinal tract and is therefore well tolerated by calves<sup>7</sup>.

At the time of this study, we found only one report about therapeutic effect of paromomycin on giardial infection in calves at 3 different doses of 25, 50, and 75 mg/kg body weight. In this study, authors compared three different doses of paromomycin in calves<sup>8</sup>. This study demonstrated the good efficacy of this drug on giardial infection in calves, but we did not find any reports on the effect of paromomycin on giardial infection in lambs. For this reason we decided to compare two different doses of this drug in lambs by naturally giardial infection. The objective of this study was to evaluate the therapeutic effects of albendazole and different two doses of paromomycin in giardiasis in lambs.

## MATERIAL and METHODS

### *Sample Collection*

The materials used this study were obtained from a farm in Burdur Province, in the southwest of Turkey. A total of 38 housed lambs aged 1-3 months old, average body weight of 10-20 kg with diarrhea in 11 lambs, dehydration and naturally infected with giardia cysts were used. In order to count cysts in feces, fecal samples were taken from all of the lambs and 5 sheep daily for 8 days (the period of our study) directly from the rectum using sterile plastic gloves. The fecal samples were transported to the laboratory in a cool box and then stored for a maximum of 24 h before analysis.

Jugular blood was collected in ethylenediaminetetraacetic acid (EDTA) tubes before and after the treatments and an MS9 blood counting device was used for hematological analysis of the blood. For each animal, the sampling date, origin and age were recorded.

The clinical examination was conducted every morning by a veterinarian from the veterinary teaching hospital of the Faculty of Veterinary Medicine, University of Mehmet Akif Ersoy.

### *Microscopical Examination of Fecal Samples*

Microscopical examination of the fecal samples was conducted daily. Fecal samples were examined by using native methods that is based on the direct smear examination in drops of saline<sup>9</sup>. No giardia cyst was seen in 5 sheep.

### *Therapeutic Drugs*

The lambs used in the study were not allowed to graze to avoid reinfection. The lambs of every treatment groups were penned in 70-80 m<sup>2</sup> pens separately. Lambs were fed a Standard lamb diet and had free access to feed and water throughout the experiment. They were randomly allocated into 3 groups as follows: Group A was treated with albendazole (20 mg/kg BW - orally for 3 successive days, n = 13). Group PI was treated with paromomycin (50 mg/kg orally for 3 successive days, n = 13) and Group PII was treated with paromomycin (100 mg/kg orally for 3 successive days, n = 12). Eleven of 38 out of lambs had diarrhea. These 11 lambs randomly scattered to the treatment groups as 4 lambs for Group Albendazole, 4 lambs for Group Paromomycin I and 3 lambs for Group Paromomycin II.

### *Statistical Analysis*

All values were reported as mean and Standard Deviation (SD). Differences in the fecal samples among the groups were statistically analyzed using a one-way analysis of variance (ANOVA), and for hematological analysis a paired Student's *t* test. *P* < 0.05 or less was considered statistically significant.

## RESULTS

No adverse reactions were observed either during or after the treatments. The mean ( $\pm$  S.D.) of the fecal giardia cyst excretion on D0-D8 (day 0- day 8) for all groups are shown in the *Table 1*.

Treatment efficacy was measured by the reduction in cyst excretion for each treatment group. In the group treated with albendazole, no cyst was seen in the feces after treatment on D5 in 7 lambs and on D8 in all animals.

In the group treated with 50 mg/kg paromomycin, no cyst was seen in the feces after treatment on D2 in 3 lambs and on D6 in all animals.

In the group treated with 100 mg/kg paromomycin, no cyst was seen in the feces after treatment on D2 in 5 lambs and on D6 in all lambs.

Percentage reduction in the mean of daily cyst excretion compared to the first day (D0 = before treatment) for the 3 treatment groups are shown in *Table 2*.

Prior to treatment and on D1 all animals were excreting cysts and there was no significant differences in cyst excretion between groups.

On D2 and D3, the reduction in cyst excretion in Paromomycin I and Paromomycin II groups were higher than in the albendazole group ( $P < 0.001$ ,  $P < 0.05$ ). However on D4, D5, D7 and D8 were not seen significant differences between the groups. On D6, the reduction in cyst excretion nevermore in Paromomycin I and Paromomycin II groups were higher than in the albendazole group ( $P < 0.05$ ).

Some mean blood values are shown in *Table 3*.

hosts of this parasite<sup>11</sup>. However in recent studies domestic livestock (e.g., cattle, sheep, goats, pigs, horses) have been identified as major hosts. The disease is an also important parasite in human with high levels of infection<sup>12-14</sup>. In our region neonatal diarrhea is one of the most important cases and animal owner problems. For this reason we decided to do this study. The prevalence of Giardiasis in Turkey is unknown but some regional studies are available; Ozmen et al.<sup>14</sup> found the prevalence of Giardiasis in kids and lambs, as 36.6%, and Ozdal et al.<sup>15</sup> reported that Giardia prevalence in lambs as 48.48%. A limited number of drugs are available for the treatment of giardiasis in domestic animals. In the previous study Giardiasis in lambs and kids was treated with trimethoprim - sulfadoxine combination therapy<sup>14</sup>. In the present study, we compared the therapeutic effect of albendazole (20 mg/kg body weight

**Table 1.** The mean ( $\pm$  S.D.) of the fecal giardia cyst excretion on D0- D8 day for 3 treatment groups

**Tablo 1.** Gruplarda 0.- 8. Günler arasında dışkıyla ortalama giardia kist atılımı

| Groups                  | 0D             | 1D             | 2D              | 3D              | 4D              | 5D              | 6D              | 7D              | 8D |
|-------------------------|----------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|----|
| Albendazol (n = 13)     | 2 $\pm$ 0.19   | 0.9 $\pm$ 0.11 | 0.5 $\pm$ 0,1   | 0,3 $\pm$ 0.04  | 0.2 $\pm$ 0.04  | 0.1 $\pm$ 0.04  | 0.06 $\pm$ 0.03 | 0.02 $\pm$ 0.01 | 0  |
| Paromomycin I (n = 13)  | 1.5 $\pm$ 0.18 | 0.5 $\pm$ 0.06 | 0.13 $\pm$ 0.03 | 0.11 $\pm$ 0.04 | 0.07 $\pm$ 0.04 | 0.03 $\pm$ 0.03 | 0               | 0               | 0  |
| Paromomycin II (n = 12) | 1.1 $\pm$ 0.06 | 0.3 $\pm$ 0.03 | 0.09 $\pm$ 0.02 | 0.07 $\pm$ 0.03 | 0.03 $\pm$ 0.02 | 0.01 $\pm$ 0.01 | 0               | 0               | 0  |

**Table 2.** Percentage reduction in the mean of daily cyst excretion compared with day 0 (D0) in all of treatment groups

**Tablo 2.** Bütün gruplarda 0. gün ile karşılaştırıldığında ortalama kist atılımındaki yüzde azalış

| Groups                    | D0, D1 | D0, D2           | D0, D3       | D0, D4 | D0, D5 | D0, D6       | D0, D7 | D0, D8 |
|---------------------------|--------|------------------|--------------|--------|--------|--------------|--------|--------|
| Albendazole (a)           | 54.21  | 72.908           | 84.834       | 90.50  | 95.64  | 97.07        | 99.12  | 100    |
| Paromomycin I (b)         | 59.42  | 91.606           | 93.084       | 95.63  | 97.98  | 100          | 100    | 100    |
| Paromomycin II (c)        | 67.68  | 91.282           | 92.965       | 96.82  | 98.41  | 100          | 100    | 100    |
| Comparison Between Groups | -      | b>a***<br>c>a*** | b>a*<br>c>a* | -      | -      | b>a*<br>c>a* | -      | -      |

-  $P > 0.05$ , \*  $P < 0.05$ , \*\*\*  $P < 0.001$

**Table 3.** Mean blood values in all of the treatment groups before and after treatment

**Tablo 3.** Grupların tedavi öncesi ve sonrası ortalama kan değerleri

| Parameter           | Albendazole             |                         | Paromomycin I           |                         | Paromomycin II          |                         | Comparison Between Groups |
|---------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------------------------|
|                     | BT (a)<br>Mean $\pm$ SE | AT (b)<br>Mean $\pm$ SE | BT (c)<br>Mean $\pm$ SE | AT (d)<br>Mean $\pm$ SE | BT (e)<br>Mean $\pm$ SE | AT (f)<br>Mean $\pm$ SE |                           |
| WBC ( $10^3/mm^3$ ) | 15.17 $\pm$ 2.21        | 6.52 $\pm$ 0.78         | 9.75 $\pm$ 1.10         | 8.02 $\pm$ 0.81         | 10.64 $\pm$ 1.31        | 6.92 $\pm$ 0.54         | a>b**<br>e>f**            |
| RBC ( $10^6/mm^3$ ) | 11.90 $\pm$ 0.80        | 11.19 $\pm$ 0.40        | 11.71 $\pm$ 0.66        | 11.26 $\pm$ 0.41        | 11.31 $\pm$ 0.40        | 10.78 $\pm$ 0.29        | -                         |
| Hct (%)             | 35.09 $\pm$ 2.25        | 32.90 $\pm$ 1.32        | 35.18 $\pm$ 1.54        | 34.30 $\pm$ 0.93        | 35.77 $\pm$ 0.84        | 33.12 $\pm$ 1.09        | -                         |
| Hb (g/dl)           | 10.46 $\pm$ 0.52        | 11.72 $\pm$ 0.26        | 11.04 $\pm$ 0.57        | 11.76 $\pm$ 0.37        | 10.85 $\pm$ 0.43        | 11.27 $\pm$ 0.20        | a<b*                      |

-  $P > 0.05$ , \*  $P < 0.05$ , \*\*  $P < 0.01$ , BT: Before Treatment, AT: After Treatment

## DISCUSSION

The genus Giardia is known to infect a wide range of species, including mammals, birds, amphibians, and reptiles<sup>10</sup>. In the past, humans, dogs, cats, and certain species of wildlife have been described as the principal

orally for 3 successive days), paromomycin I (50 mg/kg body weight orally for 3 successive days) and paromomycin II (100 mg/kg body weight orally for 3 successive days) in lambs that were naturally infected with giardia cysts.

No adverse reactions were seen either during or after

after treatment. As shown in *Table 1*; in this study, cyst excretion began to decrease on D5 in the albendazole group, and D2 in the paromomycin I and II groups. Cyst excretion stopped totally on D8 in the albendazole group and on D6 in both paromomycin groups. These results indicated that paromomycin is more effective than albendazole for the treatment of giardiasis in lambs. Diarrhea recovered in two out of four animals on D3 and the other two lambs recovered on D4 in albendazole treatment group. Three out of four lambs with diarrhea in paromomycin I, and two out of three lambs in paromomycin II group recovered on D2. In another trial, experimental giardiasis infection in calves was treated with paromomycin for 5 days<sup>8</sup>. However in the present study we have demonstrated that 3 successive days of therapy is sufficient for the treatment of giardiasis in lambs.

Other authors have reported that fenbendazole and albendazole have similar effects on giardiasis in calves and cattle<sup>16-18</sup>. In the present study, the reduction in daily cyst excretion increased more rapidly in the paromomycin groups than the albendazole group based on the cyst count on the first day. These results shown that treatment with albendazole may require multiple doses<sup>4</sup>. Furthermore, were not seen significant differences between the treated group with paromomycin I and paromomycin II in terms of excretion cyst, for that reason, 50mg/kg doses of paromomycin can be sufficient for the treatment of giardiasis in lambs (*Table 2*). This result indicates that the effect of paromomycin is faster than that of albendazole. In particular, the short term cyst-suppressing effect of paromomycin was significantly better than that seen with albendazole.

WBC levels were high in all treatment groups in this study. In another study, Sahinduran et al.<sup>19</sup> reported that the leukocyte levels were also very high in lambs with coccidiosis. This was attributed to the severe tissue damage in the intestine. Furthermore, Radostits et al.<sup>1</sup> reported that tissue damage and fever can cause leukocytosis.

Treatment with paromomycin decreased the WBC levels more than albendazole (*Table 3*). This result accounted for the recovery of general symptoms in lambs with giardiasis. No reports are available on the effect of albendazole or paromomycin in blood values; however in the present study we found that paromomycin was more effective than albendazole in normalizing the blood values.

In our region neonatal diarrhea is one of the most important cases and animal owner problems. For this reason we decided to do this study. This study demonstrated the efficacy and safety benefits of paromomycin 50 mg/kg body weight orally for 3 successive days was significantly

higher than the efficacy of albendazole 20 mg/kg body weight orally for 3 successive days against naturally occurring giardiasis in lambs, but there was no significant difference between two different doses of paromomycin.

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