

# Albendazole versus metronidazole treatment of adult giardiasis: An open randomized clinical study

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## Abstract

**AIM:** To investigate the efficacy and tolerability of albendazole and metranidazole treatment in giardiasis.

**METHODS:** The open comparative randomized trial was carried out prospectively from December 1999 to July 2001 in Duzce City of Turkey. The diagnosis was based on the presence of signs and symptoms compatible with giardiasis including a positive stool examination of giardia cysts or trophozoite. Metranidazole group consisted of 29 patients and was given metranidazole 500 mg, three times a day for 5 d and albendazole group was consisted of 28 patients and was given albendazole 400 mg/d for 5 d.

**RESULTS:** There were no significant differences in demographical and therapeutical effects and patient's compliance between both groups. But side effects were seen more in metranidazole group than in albendazole group.

**CONCLUSION:** Albendazole is as effective as metranidazole in adults' giardiasis. Albendazole has less side effect potentials than metranidazole in the treatment of giardiasis.

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## INTRODUCTION

*Giardia intestinalis* is a protozoan parasite in the small intestine that causes extensive morbidity worldwide. Giardiasis is a hyperendemic disease in households lacking municipal sewer and water in the developing countries<sup>[1]</sup>. The life cycle of *G. intestinalis* has 2 forms: the trophozoite and the cyst. As few as 10 cysts may establish infection<sup>[2,3]</sup>. Giardiasis is currently treated with metronidazole, tinidazole and quinacrine<sup>[3]</sup>. The adverse effects and treatment failures to some of the currently recommended drugs (particularly 5-nitroimidazoles) for giardia infection have given rise to the need for alternative anti giardial agents. Albendazole is an important alternative drug for treatment of giardiasis. *In vitro* Albendazole inhibits the growth of trophozoites of *G. intestinalis* and their adhesion to cultured intestinal epithelial cells and disturbs the activity of microtubules

and microribbons in the trophozoite's adhesive disk. The results of giardiasis treatment with albendazole have been confused. A lot of trials were carried out for giardiasis treatment with albendazole in pediatric groups. Albendazole was found to be effective for pediatric giardiasis patients. Albendazole at a dose of 400 mg per day for 5 d, cured 97 percent of infections in children in Bangladesh<sup>[4]</sup>. A few studies were about the effects of albendazole on adult intestinal giardiasis. It was ineffective in a study of adult travelers returning from tropical areas<sup>[3,5]</sup>. In this study we aimed to investigate effect of albendazol on adult giardiasis compared with metronidazole treatment.

## MATERIALS AND METHODS

### Subjects

Adults with diarrhea at the outpatient clinic of the Department of Infectious Diseases of Social Security Hospital in Duzce/Turkey were screened for enrollment in the study. After informed consent was obtained, a detailed medical history was taken from each patient and physical examination was performed. For the demonstration of trophozoites or cysts in the stool, 3 stool samples were obtained. Patients with diarrhea and *G. intestinalis* cysts or trophozoites in a sample were eligible for enrollment in the study. Diarrhea was defined as more than 4 times of unformed stools per day. Giardia cysts were identified in fresh faecal material by direct faecal microscopic examination. A stool culture was carried out to identify bacterial causes of diarrhea. Patients with a positive coproculture for bacterial causes of diarrhea were excluded from analysis. All patients had a clinical response, recorded on d 7, 15, and a parasitological response recorded on the basis of examination of 2 stool samples between d 7 and 15 after initiation of treatment.

### Study medication

Patients were randomized to receive albendazole 400 mg/d for 5 d or metronidazole 500 mg thrice daily for 5 d.

### Treatment methods

Of the original 67 (38 female and 29 male) patients who were selected, 57 (24 males and 33 females) completed this study in the follow-up period (Figure 1). Twenty-nine patients who received metronidazole (Falgy1®) 500 mg 3 times daily for 5 d. Twenty-eight patients received albendazole (Andazol®) 400 mg /d for 5 d.

### Assessment of compliance

All patients were investigated for compliance to treatment, and one of the following requirements should be fulfilled in order to define a case as noncompliance to treatment, namely, failure to attend the controls, not use one or a few of the medicines at the instructed dose and the duration, not use the drug without taking the consent of the doctor.

### Ethics

The study protocol was approved by the locally ethics committee. All patients were informed and agreed to participate in the study.

**Table 1** Demographical and clinical findings of treatment groups (mean±SD)

Parameter	Metranidazol Group (n=29)	Albendazol Group (n=28)	P
Female /Male	18/11	15/13	#
Age (yr)	38±14	41±12	#
Hemoglobin	13.2±1.5	12.7±1.5	#
Leukocyte count	7 996±2 668	8 225±3 016	#
Faecal examination positive for cysts or trophozoites on d 7	0	0	NA
Faecal examination positive for cysts or trophozoites on d 15	0	1	NA
Metal taste	9	0	NA
Anorexia +/-	18	2	0.0001
Abdominal pain	3	1	#
After starting treatment healing of symptoms (h)	83±39	80±28	#
Advers effects other than anorexia	8	6	#
Non-compliance to treatment	7	5	#

#:  $P>0.05$ , NA: Not applicable.

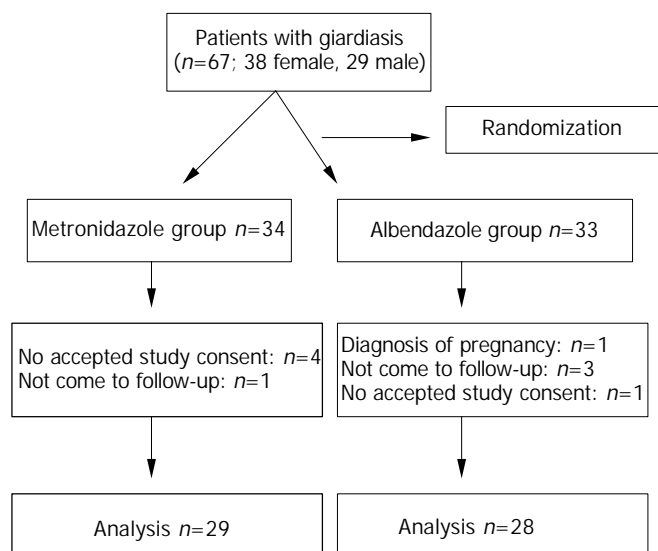
### Statistical analysis

Gender, age, mean hemoglobin concentration and leukocyte counts were compared between the 2 groups using non-parametric test (Mann-Whitney U test). Difference between the 2 groups was analyzed using chi-square test. We used Epi-info 6.0 (Centers for Disease Control, Atlanta) to perform the analysis and considered  $P<0.05$  as statistically significant.

### Criteria for exclusion

Patients receiving or having received antiparasitic drugs during the 10-d prior to commencing the study, patients with fever, pregnant women, mothers who were breast feeding, patients with known hypersensitivity to either albendazole or metronidazole, patients for whom any of the treatments used in the study were contraindicated.

one patient in of albendazole group was found to be positive for giardia cyst, while none of the patients in metranidazole group was positive for giardia cyst. Abdominal pain was found in 3 patients of metronidazole group and 1 patient of albendazole group ( $P>0.05$ ). Vomiting was seen in 1 patient of metronidazole group and none in albendazole group. Noncompliance to treatment was found in 7 patients of metronidazole group and in 5 patients in albendazole group ( $P>0.05$ ). Anorexia was found in 18 patients of metronidazole group and in 2 patients of albendazole group ( $P<0.001$ ). Metal taste was determined in nine patients of metronidazole group and none in albendazole group. Records associated with other (headache, abdominal pain, dazedness) adverse effects except anorexia and metal taste were not found to be significantly different between the 2 groups ( $P>0.05$ ).



**Figure 1** Flow chart of patients studied.

### RESULTS

The clinical and demographic findings in the albendazole group and metronidazole group are presented in Table 1.

No positive giardia cyst was found in the stool samples of both albendazole and metronidazole groups on d 7. But on d 15

### DISCUSSION

Infections with parasitic helminths and protozoa are important causes of morbidity and mortality worldwide. The protozoan parasite *Giardia intestinalis* (synonyms: *Giardia duodenalis* and *Giardia lamblia*) is recognized as a major cause of diarrheal illness in humans and livestock. It is one of the most important non-viral infectious agents causing diarrheal illness, the infection may be asymptomatic or present with a variety of symptoms such as diarrhea, weight loss, abdominal cramps and failure to thrive. *G.intestinalis* may attach to small bowel wall but not invade it. Trophozoites may be encysted and shed in faeces for future ingestion by other hosts. Whereas the organism can cause diarrhea and abdominal pain. Some people experienced only a mild self-limiting illness, while others developed a chronic illness lasting for several months. Furthermore, people might be infected without any symptoms, and it has even been suggested that some people could benefit from their carrier state<sup>[6,7]</sup>.

Although *Giardia* infections resolve spontaneously in 85% of patients within 6 wk, all patients with symptomatic giardiasis should be treated. Metronidazole and quinacrine are the first-line treatment options and are more than 90% effective. Tinidazole, furazolidone, paromomycin, mebendazole, and albendazole have been used as alternative anti-giardial drugs<sup>[8]</sup>. Cedillo-Rivera *et al.*<sup>[9]</sup> investigated the susceptibility of a strain of *Giardia lamblia* to benzimidazole carbamates, 5-nitroimidazoles, nitrofurans and other drugs. They found that albendazole was the most active compound among the 5-nitroimidazoles tested, ornidazole was the most effective, and

tinidazole, metronidazole, secnidazole were less active.

Various reports have published the effect of albendazole on giardiasis. Albendazole was found to be very effective on giardiasis<sup>[10]</sup>. Misra *et al.*<sup>[10]</sup> studied the effect of albendazole and metranidazole on giardiasis in 64 children aged 2-12 years. They concluded that albendazole was proved as effective as metronidazole in the treatment of giardia infection in children with the absence of anorexia. Similarly, another study found albendazole at dose of 400 mg/d for 5 d cured 97% of infections in children in Bangladesh<sup>[4]</sup>. But, Escobedo *et al.* investigated in a comparative trial. One hundred and sixty-five Cuban children with confirmed giardiasis were randomized to receive albendazole (400 mg/d for 5 d), chloroquine (10 mg/kg twice daily for 5 d) or tinidazole (50 mg/kg, as a single dose). They found that tinidazole and chloroquine appeared equally effective, curing 91% and 86% of the children treated, respectively, and were significantly better than albendazole, which only cured 62% of the children<sup>[11]</sup>.

In this study we investigated the effect of albendazole and metronidazole on symptomatic adult giardiasis. We did not find any significant difference in demographical properties (gender, age), mean hemoglobins, and mean leukocytes between the 2 groups. Giardia cysts were not found in faecal examination both groups on d 7. But on d 15 after starting treatment, one patient was found to be positive for giardia in albendazole group and none in metronidazole group. We thought that this patient might be reinfected. After starting treatment, 9 patients complained of metal taste in metronidazole group and no patient in albendazole group. Anorexia was found in 18 patients of metronidazole group but only 2 patients complained of anorexia in albendazole group ( $P < 0.01$ ). In terms of adverse effects, albendazole was found superior to metronidazole. Patients' compliance was found to be similar in both groups ( $P > 0.05$ ). We thought that it might be due to a short treatment period (five days). Similarly, Chan Del Pino *et al.*<sup>[12]</sup> investigated the efficacy and tolerance of albendazole compared with metranidazole, furazolidone, tinidazole and secnidazole in the treatment of giardiasis in 79 children. They concluded that albendazole was as effective as metronidazole, furazolidone, tinidazole and secnidazole, but faster in eradicating *Giardia lamblia* in children and had a better tolerance than metranidazole, furazolidone and tinidazole.

The drug resistance was not an important problem for giardiasis<sup>[13-15]</sup>. In our country cost of both drugs is similarly. We thought that both drugs can be used in the treatment of giardiasis, because according to our results albendazole is as effective as metronidazole in adult's giardiasis and albendazole treatment has also less side effects than metronidazole.

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