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

Oguz Karabay, Ali Tamer, Huseyin Gunduz, Derya Kayas, Huseyin Arinc, Harika Celebi

Abstract

AIM: To investigate the efficacy and tolerability of albendazole and metronidazole 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.

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[1]. The life cycle of G. intestinalis has 2 forms: the trophozoite and the cyst. As few as 10 cysts may establish infection[2,3]. Giardia is currently treated with metronidazole, tinidazole and quinacrine[3,4]. The adverse effects and treatment failures to some of the currently treated with metronidazole, tinidazole and quinacrine as 10 cysts may establish infection in the developing countries[5,6]. 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[6]. 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[10]. 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 (Flagyl® 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.
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, one patient in of albendazole group was found to be positive for giardia cyst, while none of the patients in metronidazole 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<0.001). Metal taste was determined in 18 patients of metronidazole group and in 2 patients of albendazole group (P<0.001). Metal taste was determined in 9 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).

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[6,7].

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[8]. Cedrallo-Rivera et al.[9] 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

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

| Parameter                                      | Metronidazol 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                    | 0                         | 0                       | NA   |
| for cysts or trophozoits on d 7                |                           |                         |      |
| Faecal examination positive for                 | 0                         | 1                       | NA   |
| cysts or trophozoits on d 15                   |                           |                         |      |
| Metal taste                                    | 9                         | 0                       | NA   |
| Anorexia +/-                                   | 18                        | 2                       | 0.0001|
| Abdominal pain                                 | 3                         | 1                       |      |
| After starting treatment healing of symptoms   | 83±39                     | 80±28                   |      |
| (h)                                            |                           |                         |      |
| 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.

**Figure 1 Flow chart of patients studied.**
tindazole, metronidazole, secnidazole were less active.

Various reports have published the effect of albendazole on giardiasis. Albendazole was found to be very effective on giardiasis. Misra et al. studied the effect of albendazole and metronidazole 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. 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 tindazole (50 mg/kg, as a single dose). They found that tindazole 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.

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. investigated the efficacy and tolerance of albendazol compared with metranidazol, furazolidone, tinidazol and secnidazol in the treatment of giardiasis in 79 children. They concluded that albendazol was as effective as metronidazol, furazolidone, tinidazol and secnidazol, but faster in eradicating Giardia lamblia in children and had a better tolerance than metranidazol, furazolidone and tinidazol.

The drug resistance was not an important problem for giardiasis. 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.

ACKNOWLEDGEMENTS
The authors would like to thank Dr. Gurhan Konački (Chief Manager of Social Security Duće Hospital) for providing his help.

REFERENCES
1. Redlinger T, Corellia-Barud V, Graham J, Galindo A, Avitia R, Cardenas V. Hyperendemic Cryptosporidium and Giardia in households lacking municipal sewer and water on the United States-Mexico border. Am J Trop Med Hyg 2002; 66: 794-798
2. Gardner TB, Hill DR. Treatment of giardiasis. Clin Microbiol Rev 2001; 14: 114-128
3. Liu LX, Weller PF. Antiparasitic drugs. N Engl J Med 1996; 334: 1178-1184
4. Hall A, Nahar Q. Albendazole as a treatment for infections with Giardia duodenalis in children in Bangladesh. Trans R Soc Trop Med Hyg 1993; 87: 84-86
5. Kollariotis H, Jeshko E, Wiedermann G. Albendazole is highly effective against cutaneous larva migrans but not against Giardia infection: results of an open pilot trial in travellers returning from the tropics. Trans R Soc Trop Med Hyg 1993; 87: 689
6. Vesy CJ, Peterson WL. The management of Giardiasis. Allment Pharmacol Ther 1999; 13: 843-850
7. Homan WL, Mank TG. Human giardiasis: genotype linked differences in clinical symptomatology. Int J Parasitol 2001; 31: 822-826
8. Tessler JL, Davies G. Giardiasis. Primary Care Update for OB/GYN 1999; 6: 8-11
9. Cedillo-Rivera R, Munoz O. In-vitro susceptibility of Giardia lamblia to albendazole, mebendazole and other chemotherapeutic agents. J Med Microbiol 1992; 37: 221-224
10. Misra PK, Kumar A, Agarwal V, Jagota SC. A comparative clinical trial of albendazole versus metronidazole in children with giardiasis. Indian Pediatr 1995; 32: 779-782
11. Escobedo AA, Nunez FA, MoreiraI, Vega E, Pareja A, Almirall P. Comparison of chloroquine, albendazole and tindazol in the treatment of children with giardiasis. Ann Trop Med Parasitol 2003; 97: 367-371
12. Chan Del Pino M, Cueva Cornejo L, Troyes Rivera L. Comparative study of albendazole versus nitrofurans and nitroimidazoles in the treatment of giardiasis in children. Rev Gastroenterol Peru 1999; 19: 95-108
13. Cruz A, Sousa MI, Azeredo Z, Leite E, Figueiredo De Sousa JC, Cabral M. Isolation, excystation and axenization of Giardia lamblia isolates: in vitro susceptibility to metronidazole and albendazole. J Antimicrob Chemother 2003; 51: 1017-1020
14. Wright JM, Dunn LA, Upcroft P, Upcroft JA. Efficacy of antigiardial drugs. Expert Opin Drug Sa 2003; 2: 529-541
15. Ali SA, Hill DR. Giardia intestinalis. Curr Opin Infect Dis 2003; 16: 453-460

Edited by Wang XL and Xu FM