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Albendazole as an alternative therapeutic agent for childhood giardiasis in Turkey

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ABSTRACT

The efficacy of albendazole for the treatment of giardiasis has been indicated by previous in-vitro and in-vivo studies. In order to compare the therapeutic efficacy of albendazole and metronidazole, 107 *Giardia*-positive children (aged 3–15 years), diagnosed by three consecutive positive stool examinations, were enrolled in the study. Of these children, 52 were given a single daily dose of albendazole 10 mg/kg for 5 days, and 55 were given metronidazole 20 mg/kg daily in three doses for 7 days. Parasite eradication was achieved in 47 (90.4%) of 52 children treated with albendazole and 49 (89.1%) of 55 children treated with metronidazole ($p > 0.05$). These results suggest that albendazole is an effective treatment option for childhood giardiasis.

Keywords Albendazole, *Giardia lamblia*, giardiasis, therapy

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INTRODUCTION

Giardia lamblia is a binucleate protozoan of the Mastigophora sub-phylum that parasitises the small intestines of mammals and causes intestinal infection [1]. This parasitic disease, known as giardiasis, is considered one of the most common causes of diarrhoea in the world today [2]. Giardiasis is endemic in areas of poor sanitation and is an important cause of morbidity in the developing world, where it is associated with infections in urban child care centres and residential institutions, as well as water- and food-borne outbreaks [3]. Although giardiasis affects mostly children, it can also occur in adults of any age [4]. The prevalence among children worldwide varies from 4% to 42%, but results from many surveys may be artificially low following examination of only one stool specimen [5]. Transmission of *Giardia* is common in certain high-risk groups, including children and employees in child care centres, consumers of contaminated water, travellers to certain areas of the world, male homosexuals, and persons exposed to certain animals [3]. The clinical manifestations of *G. lamblia* infection range from asymptomatic carriage to a transient or persistent acute stage, with steatorrhoea, intermittent diarrhoea and weight loss, or to a sub-acute or chronic stage that can mimic peptic ulcer disease [4].

Three major drug classes are of proven benefit in the treatment of giardiasis: the nitroimidazole derivatives, acridine dyes such as mepacrine, and the nitrofurans such as furazolidone [6]. The nitroimidazoles, metronidazole and tinidazole, are normally the drugs of choice, and are >90% effective. Furazolidone (*c.* 80% effective) is often used in children. None of these therapeutic alternatives is clearly safe for use in pregnancy; therefore, the poorly absorbed oral aminoglycoside paromomycin has been suggested for use in this clinical situation.

Limited clinical data have suggested that the anti-helminthic compound albendazole has anti-giardial activity, and its efficacy has been demonstrated in several in-vivo and in-vitro studies. In giardiasis, albendazole may act through tubulins and giardins located in the cell skeleton of *G. lamblia*. In addition, it has been shown that albendazole inhibits the growth of *G. lamblia*

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trophozoites and their adhesion to intestinal epithelial cells *in vitro*. The mechanism of this activity is damage to microtubule and microribbon function on the sucking discs of trophozoites [7].

Treatment failures may occur with any of the above therapies, consistent with in-vivo and in-vitro data suggesting that strain-dependent drug resistance not only exists, but may be induced during the course of therapy [8]. In addition, the widespread use of nitroimidazoles against *Giardia* in children in the highly endemic areas has been limited by poor patient compliance associated with the unpalatability of the drugs, varying sensitivity between *Giardia* isolates, and the potential carcinogenic effects of these compounds [8]. Thus, recent evidence for the anti-giardial activity of albendazole raises the prospect of safe and effective treatment of children in endemic areas if the drug is used with complementary health and hygiene education programmes [7].

MATERIALS AND METHODS

Cases

In total, 655 children, aged 3–15 years, were studied. These children were admitted to the Paediatrics Clinic of Celal Bayar University Hospital with gastrointestinal complaints, including diarrhoea, weight loss, anorexia and fatigue, and were examined for giardiasis between February and December 2002. Stool samples were assessed for giardiasis by the saline–Lugol, formalin ethyl acetate concentration and trichrome staining methods [4]. Of the 655 children, 107 (16.3%) were positive for *G. lamblia* cysts and/or trophozoites, and were treated according to the study protocols.

Study protocols

The approval of the Ethics Committee of Celal Bayar University Medical School was obtained before the start of the study. All parents were informed and their written consent was obtained. The study group of 107 children with giardiasis determined clinically and parasitologically (71 asymptomatic and 36 symptomatic at that time) was divided into two random groups. In group I, 52 children were given single-dose albendazole tablets 10 mg/kg for 5 days. In group II, 55 children were given metronidazole in tablet or liquid form 20 mg/kg daily in three doses for 7 days. Albendazole and metronidazole are approved by the Ministry of Health in Turkey.

All children completed their treatment regimens. To evaluate the effectiveness of the therapy, stool samples from all cases were examined on the 7th, 10th and 14th days following completion of treatment by the same methods and the same microscopist. Clinical symptoms were also evaluated.

Statistical analysis

The data were evaluated by SPSS for Windows 6.1 (SPSS Inc., Chicago, IL, USA) and EPI Info 6.04b (WHO, Geneva, Switzerland). Differences between the ratios in qualitative variables were evaluated by Yates' corrected chi-square test (Fisher's absolute verified test in the presence of frequencies < 5). Differences with $p < 0.05$ were considered to be statistically significant.

RESULTS

In the overall study group, 64 (59.8%) children had diarrhoea and 87 (81.3%) had symptoms such as abdominal pain, anorexia, pruritis and foul-smelling greasy stools. The demographic and clinical features of treatment groups I and II are summarised in Table 1.

Eradication of the parasites (i.e., no *G. lamblia* cysts and/or trophozoites present) was achieved in 49 (89.1%) of 55 children treated with metronidazole, and 47 (90.4%) of 52 children treated with albendazole (Table 2). There was no statistically significant difference between albendazole treatment and metronidazole treatment ($p > 0.05$).

Table 1. General and clinical features of children with giardiasis in the two treatment groups

	Group I Albendazole 10 mg/kg/day (n = 52)	**Group II Metronidazole 20 mg/kg/day (n = 55)**
Age in years		
Mean	8.3	8.2
SD (range)	3.4 (3–15)	3.3 (3–15)
Sex		
Male	28 (52%)	23 (42%)
Female	24 (48%)	32 (58%)
Weight (kg)		
Mean	26.1	25.8
SD (range)	10.7 (12–61)	11.7 (16–59)
Stool frequencies		
≤ 10 stools/day	15 (29%)	15 (27%)
> 10 stools/day	37 (71%)	40 (73%)
Diarrhoea	30 (58%)	34 (62%)
Abdominal symptoms	44 (85%)	43 (79%)

Table 2. Parasite eradication following treatment with albendazole or metronidazole

Number of parasite-free patients						
Group I Albendazole (n = 52)			**Group II Metronidazole (n = 55)**			
Day 7	**Day 10**	**Day 14**	**Day 7**	**Day 10**	**Day 14**	**p**
30 (57.7%)	46 (88.5%)	47 (90.4%)	14 (25.5%)	28 (50.9%)	49 (89.1%)	0.92

Clinical symptoms disappeared in all parasite-free patients after treatment, and no side effects were reported for either albendazole or metronidazole during therapy.

DISCUSSION

The mainstay of treatment of giardiasis is metronidazole, but other treatment options are required because of occasional resistance. Metronidazole-resistant *Giardia* strains have been isolated from a number of patients who failed to respond to normal doses of metronidazole. Metronidazole is used extensively worldwide, not only for giardia infections but also for the treatment of *Trichomonas vaginalis*, *Entamoeba histolytica*, anaerobic bacteria and protozoa, and for pre- and post-surgical prophylaxis. Inappropriate dosing, poor compliance and other factors that may expose *Giardia* to doses of metronidazole of < 500 mg/day have been identified as potential factors that will facilitate the development of resistance in *Giardia*. A combination of metronidazole and quinacrine appears to be more effective than either drug alone for treating resistant giardia infections [8]; however, quinacrine is no longer manufactured in the USA.

Knowledge of the activity of other anti-giardial compounds relies mostly on clinical experience, as the routine reproduction, isolation and susceptibility testing of *G. lamblia* is difficult. In-vivo albendazole treatment of giardiasis has yielded variable results. Thus, while albendazole 400 mg was 95–97% effective when given as a single daily dose for 5 days to children with giardiasis, it was not effective in tourists returning from the tropics [9–11]. Similarly, albendazole was effective in only 50% of schoolchildren with giardiasis in Thailand [12]. In a study in Maryland, USA, resistance against albendazole developed easily *in vitro* [13]. Similarly, according to an Australian study, *G. lamblia* developed resistance easily against albendazole following modifications to the cell structure of *G. lamblia* [14]. Although more active benzimidazole derivatives have been tested recently [15], albendazole remains on the market as an alternative agent. In the present study, the therapeutic efficacy of albendazole was slightly higher (90.4%) than that of a conventional anti-giardial metronidazole regimen (89.1%). Since there was no significant difference between these two agents in terms of treatment efficacy, side effects and treatment procedure, it was concluded that albendazole was an effective and safe treatment choice for giardiasis in Turkey, particularly if used with complementary health and hygiene education programmes in endemic areas.

REFERENCES

1. Adam RD. The biology of *Giardia* spp. *Microbiol Rev* 1991; **55**: 706–732.
2. Pickering LK, Engelkirk PG. *Giardia lamblia*. *Pediatr Clin North Am* 1988; **35**: 565–572.
3. Larry K, Pickering L. Giardiasis and balantidiasis. In: Behrman M, ed. *Nelson textbook of pediatrics*, 16th edn. Philadelphia: WB Saunders, 2000; 1036–1039.
4. Markel EK, Voge M, John DT. *Medical parasitology*. Philadelphia: WB Saunders, 1992.
5. Strickland GT. *Hunter's tropical medicine*. Philadelphia: WB Saunders, 1991.
6. Davidson RA. Issues in clinical parasitology. The treatment of giardiasis. *Am J Gastroenterol* 1984; **79**: 256–261.
7. Liu LX, Weller PF. Antiparasitic drugs. *N Engl J Med* 1996; **334**: 1178–1185.
8. Upcroft JA, Upcroft P. Drug resistance and *Giardia*. *Parasitol Today* 1993; **9**: 187–190.
9. Dutta AK, Phadke MA, Bagade AC *et al.* A randomised multicentre study to compare the safety and efficacy of albendazole and metronidazole in the treatment of giardiasis in children. *Ind J Pediatr* 1994; **61**: 689–693.
10. 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.
11. Kollaristch H, Jeschko E, Wiedermann G. Albendazole is highly effective against cutaneous larva migrans but not against *Giardia* infection: results of an open pilot trial in travelers returning from the tropics. *Trans R Soc Trop Med Hyg* 1992; **86**: 418–420.
12. Pengsaa K, Sirivichayakul C, Pojjaroen-anant C, Nimnual S, Wisetsing P. Albendazole treatment for *Giardia intestinalis* infections in school children. *SE Asian J Trop Med Pub Health* 1999; **30**: 78–83.
13. Lindquist HD. Induction of albendazole resistance in *Giardia lamblia*. *Microb Drug Resist* 1996; **2**: 433–434.
14. Upcroft J, Mitchell R, Chen N, Upcroft P. Albendazole resistance in *Giardia* is correlated with cytoskeletal changes but not with mutation at amino acid 200 in beta-tubulin. *Microb Drug Resist* 1996; **2**: 303–308.
15. Navarrete-Vazquez G, Cedillo R, Hernandez-Campos A *et al.* Synthesis and antiparasitic activity of 2-(trifluoromethyl)-benzimidazole derivatives. *Bioorg Med Chem Lett* 2001; **11**: 187–190.