

## Albendazole and Mebendazole as an Alternative Therapeutic Agent for Adult Giardiasis

Seyyed Javad Hosseini Shokouh and Mossa Ahmadi\*

Infectious Diseases Research Center, AJA University of Medical Sciences, Tehran, IR Iran.

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We examined the therapeutic effects of albendazole, metronidazole and mebendazole in 183 patients with giardiasis in Tehran Province. Patients were randomized to receive albendazole (400 mg, once daily for 5 days) or metronidazole (250 mg, 3 times a day for 5 days) or mebendazole (200 mg, 2 times a day for 5 days). Demographic data of the patients, results of stool examination for *Giardia* (cyst or trophozoites) before and after treatment, and drug side effects were recorded. The final results showed that albendazole (93%) and mebendazole (89%) and metronidazole (95.5%) have similar therapeutic effects on giardiasis. Patients in the albendazole group (19.7%) had fewer side effects compared with metronidazole (39%) & mebendazole groups (27%). This difference is statistically significant ( $p < 0.01$ ). We offer the albendazole as a drug of choice for giardiasis.

**Key words :** Albendazole, Mebendazole, Metronidazole, Giardiasis, Therapy.

*Giardia lamblia*, also known as *Giardia duodenalis* or *Giardia intestinalis*, is one of the most common intestinal parasites world-wide and is a frequent cause of diarrhoeal illness<sup>1-3</sup>. It is estimated that about 300 million people annually are affected with the parasite all around the world and it is an important cause of morbidity in the developing world<sup>2,3</sup>.

Many drugs, including metronidazole and albendazole, mebendazole, furazolidone, tinidazole, ornidazole are used for the treatment of the disease. The most widely used treatment protocols employ metronidazole given 3 times per day for 3–5 days<sup>4-8</sup>. In one study, the therapeutic effects of mebendazole and metronidazole were compared on giardiasis. Mebendazole as 200 mg, 2 times a day for 5 days and metronidazole as 250 mg, 3 times a day for 5 days used in treatment of

giardiasis. In this investigation therapeutic effects of mebendazole was stronger than metronidazole<sup>5-13</sup>.

In another study, the therapeutic effects of albendazole and metronidazole were compared on giardiasis. Albendazole as 400 mg daily was effective on giardiasis (97%)<sup>6</sup>. In another study in India, average response to treatment, were faster with albendazole than metronidazole<sup>11</sup>.

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<sup>14-17</sup>.

### MATERIALS AND METHODS

In this study, we examined four groups of patients. The first group consists of high school students in Tehran (A). The second group consists of students of Tehran Teachers Training Center (B). The third group was patients admitted to the Infectious Diseases Clinics of Shahid Beheshti medical university (C), the fourth group consisted

\* To whom all correspondence should be addressed.  
Tel.: 00989125249008;  
E-mail: moses.ahmadi@yahoo.com

of patients attending private clinics (D) . 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. Stool samples were assessed for giardiasis by the saline–Lugol formalin ethyl acetate concentration and trichrome staining methods<sup>3</sup>. Only patients with *G.intestinalis* cysts or trophozoites in a sample were eligible for enrollment in the study. To evaluate the effectiveness of the therapy, 3stool samples from all cases were examined on 6 - 10 days following completion of treatment by the same laboratories. Clinical symptoms were also evaluated.

#### Study medication

The metronidazole and mebendazole and albendazole tablets were placed in separate packages. As none of the doctors were unaware of the type of pills in packages . Patients in each groups (A,B,C,D) were randomized to receive albendazole 400 mg/d for 5 d or metronidazole 250 mg thrice daily for 5 d. or mebendazole 200 mg twice daily for 5 d.

#### Cases

263 patients- aged 11– 47 years - participated in this study. Of these, 80 were excluded from the study for various reasons. 51 of these patients were high school students , 70 people were college students , 13 were employee and 30 were workers. 17 of these patients, were illiterate, 51 were elementary School ,115 were high school or higher. Of the 183 stool sample positive patients, 153 cases were positive for giardia cysts and 30 cases were positive for giardia trophozoites . Of these 70 cases were symptomatic (38/25% ) and 113 cases were asymptomatic (61/75%) . All trophozoite positive patients were symptomatic . These symptoms include : cramping , bloating, diarrhea , nausea , vomiting , foul smelling stool , weight loss .

#### Statistical analysis

The data were evaluated by SPSS for Windows 6.1 . Differences between the ratios in qualitative variables were evaluated by Yates' corrected chi-square test . Differences with  $p < 0.05$  were considered to be statistically significant.

### RESULTS

In this study , 55 cases treated with mebendazole, 61 cases treated with albendazole and 67 cases treated with metronidazole . Eradication of the parasites (i.e., no *G. Lamblia* cysts and D or trophozoites present) was achieved in 49 cases treated with mebendazole, and 57 cases treated with albendazole and 64 cases treated with metronidazole (Table 2). The final results showed that albendazole (93%) and mebendazole ( 89% ) and metronidazole (95.5%) have similar therapeutic effects on giardiasis. By Using a Chi- square test that therapeutic success in each therapeutic groups was not statistically significant .

#### Therapeutic side effects

In this study, 26 cases of metronidazole recipients (39%) and 12 cases of albendazole recipients (19.7%) and 15 cases of mebendazole

**Table 1.** The age distribution of patients according to sex

Age in years	Male	Female	All
10 – 14	9	20	29
15 – 19	37	17	54
20 – 24	37	3	40
25 – 29	13	4	17
30 – 34	10	1	11
35 – 39	12	4	16
40 – 44	8	4	12
45 and above	3	1	4
All	129	54	183

**Table 2.** Parasite eradication following treatment with albendazole or metronidazole or mebendazole

Groups	Albendazole	Mebendazole	Metronidazole
parasite-free patients	57	49	64
parasite - positive patients	4	6	3
All	61	55	67

$\chi^2 = 1/9$

df =2

P = non significant

**Table 3.** Distribution of drugs side effects in each therapeutic groups

Groups	Albendazole	Mebendazole	Metronidazole
Complications-free patients	49	40	41
Complications-positive patients	12	15	26
All	61	55	67

$\chi^2 = 9/1$      $df = 2$      $P < 0/01$

**Table 4.** Percentage distribution of drug side effects in each therapeutic groups

Groups Side effects	Albendazole		Mebendazole		Metronidazole	
	Number	Percent	Number	Percent	Number	Percent
Malase	3	5	3	5.5	3	4.5
Nasea	3	5	3	5.5	11	16.4
Vomiting	0	0	0	0	9	13.4
Metallic taste	0	0	0	0	9	13.4
Dizziness	4	6.5	5	9	4	6
HeadacheOthers	2	3.3	2	3.6	3	4.5
	3	5	6	11	5	7.4

recipients (27.3%) had a drug side effects. By Using a Chi- square test that was statistically significant ( $P < 0/01$ ).

## DISCUSSION

The mainstay of treatment of giardiasis is metronidazole, It has been widely used to treat giardiasis in humans<sup>1,2</sup> and often causes side effects such as nausea, metallic taste, dizziness and headache<sup>8</sup>. In addition, this drug is a known mutagen in bacteria<sup>23,24</sup>, it is genotoxic to human cells<sup>25,25</sup> and it has been shown to be carcinogenic in animal models<sup>25,26</sup>. However, there is no evidence showing metronidazole is also carcinogenic in humans<sup>25</sup>. Typically, metronidazole is administered in doses of 250 mg 3 times a day for 5–7 days for adults and 15 mg/kg 3 times a day for 5–7 days in children. An extended period of time for the treatment of giardiasis may be associated with frequent side effects.

The other consideration when using metronidazole is the consumption of alcohol that may be associated with disulfiram-like reaction (nausea, vomiting, flushing, and tachycardia) and should be avoided by patients during systemic metronidazole therapy and for at least 24 hours

after completion of treatment.

Resistance of *G. duodenalis* strains to metronidazole has been reported both in vitro and in vivo. Misra *et al.*<sup>15</sup> reported a 100% cure rate in groups treated with either metronidazole or albendazole, while the other reports show an effectiveness of 72.7–100% for metronidazole and 77–97% for albendazole.

Sadjjadi *et al.*<sup>21</sup>, who used 200 mg mebendazole thrice daily for 5 d -which resulted in somewhat higher cure rates [43 out of 50 (86%)] and found a frequency comparable to that obtained by using a 7-d course of metronidazole, it was 45 out of 50 (90 per cent) with no statistical difference between the two groups .

Roberto Cañete *et al.*,<sup>22</sup> also used 200 mg of mebendazole taken three times per day or quinacrine [2 mg/kg bodyweight] tid, both for five days . The frequency of cure was higher for quinacrine (83.6%) than for mebendazole (78.7%), the difference was not statistically significant ( $P > 0.05$ ). Adverse events were reported more in the quinacrine group ( $P < 0.05$ ), all of them transient and self-limiting. In most studies, albendazole was as good as metronidazole or better<sup>29</sup>.

Given the multiple side effects of metronidazole and some resistant *G. duodenalis*

strains to metronidazole and effective and with less side effects drugs other than metronidazole for treating *G. duodenalis*, using that drugs as an alternative would be reasonable .

In the present study, the final results showed that albendazole (93%) and mebendazole ( 89% ) and metronidazole (95.5%) have similar therapeutic effects on giardiasis . Advantage of this study is use of three anti-giardia drugs ( albendazole , mebendazole , metronidazole ) for the treatment of giardiasis and evaluation of their efficacies and side effects . There are some limitations in the present study. First, use of different laboratories, clinics and Colleagues can have undesirable Influence on the results. Second, Clinical and laboratory evaluation was performed on 6 - 10 days following completion of treatment only once. So after that, there was no data about symptoms and signs of patients (recurrent of diseases).

Considering the high rate of side effects from metronidazole therapy for giardiasis, combined with the global emergence of resistant strains of *G. duodenalis*, and similar therapeutic effects of these three drugs on giardiasis, we suggest effective alternative treatments such as albendazole for *Giardia* infections .

#### REFERENCES

- Adam RD, Biology of *Giardia lamblia*. *Clin Microbiol Rev* 2001; **14**: 447–475.
- Farthing MJ., Diarrhoeal disease: current concepts and future challenges. Pathogenesis of giardiasis. *Trans R Soc Trop Med Hyg* 1994; **3**: 17–21.
- Flanagan PA., *Giardia*—diagnosis, clinical course and epidemiology. A review. *Epidemiol Infect* 1992; **109**: 1–22.
- Gardner TB, Hill DR, Treatment of giardiasis. *Clin Microbiol Rev* 2001; **14**: 114–128.
- Liu LX, Weller PF. Antiparasitic drugs. *N Engl J Med* 1996; **334**: 1178–1185.
- Noori S, Dawood AL-Waili and Noori U. Hassan. Mebendazole in giardia infection a comparative study with metronidazole. *J Infectious diseases* 1992; **165**: 1170-1.
- Gardner TB, Hill DR, Treatment of giardiasis. *Clin Microbiol Rev* 2001; **14**: 114–128.
- Hall A, Nahar Q, Albendazole as a treatment for infections with *Giardia duodenalis* in children in Bangladesh. *Trans R Soc Trop Med Hyg* 1993a,b; **87**: 84-86.
- Bassily S, Farid Z, Mikhail JW, Kent DC, Lehman JS, The treatment of *Giardia lamblia* infection with mepacrine, metronidazole and furazolidone. *J Trop Med Hyg* 1970; **73**: 15-18.
- Jokipii L, Jokipii AMM, Comparison of four dosage schedules in the treatment of giardiasis with metronidazole. *Infection* 1978; **6**: 92–94.
- Kavousi S, Giardiasis in infancy and childhood: a prospective study of 160 cases with comparison of quinacrine (AtabrineH) and metronidazole (FlagylH). *Am J Trop Med Hyg* 1979; **28**: 19-23.
- Jokipii L, Jokipii AM, Comparison of four dosage schedules in the treatment of giardiasis with metronidazole. *Infection* 1978; **6**: 92–94.
- Rastegar-Lari A, Salek-Moghaddam A, Single-dose secnidazole versus 10-day metronidazole therapy of giardiasis in Iranian children. *J Trop Pediatr* 1996; **42**: 184-185.
- Bulut BU, Gu'lnar SB, Aysev D, Alternative treatment protocols in giardiasis: a pilot study. *Scand J Infect Dis* 1996; **28**: 493–495.
- Sadjjadi SM, Alborzi AW, Mostovfi H. Comparative clinical trial of mebendazole and metronidazole in giardiasis of child-dren. *Journal of tropical pediatrics*, 2001; **47**(3):176–8.
- Misra PK et al. A comparative clinical trial of albendazole versus metronidazole in children with giardiasis. *Indian pediatrics*, 1995; **32**(7):779–82.
- Baqai R, Zuberi SJ, Qureshi H, Ahmed W, Hafiz S, Efficacy of albendazole in giardiasis. *East Meditter Health J* 2001; **7**: 787–790.
- Alizadeh A, Ranjbar M, Kashani KM, Taheri MM, Bodaghi M, Albendazole versus metronidazole in the treatment of patients with giardiasis in the Islamic Republic of Iran. *East Meditter Health J* 2006; **12**: 548–554.
- Karabay O, Tamer A, Gunduz H, Kayas D, Arinc H, et al., Albendazole versus metronidazole treatment of adult giardiasis: An open randomized clinical study. *World J Gastroenterol* 2004; **10**: 1215–1217.
- Yereli K, Balciog'lu IC, Ertan P, Limoncu E, Onag'ç A, Albendazole as an alternative therapeutic agent for childhood giardiasis in Turkey. *Clin Microbiol Infect* 2004; **10**: 527–529.
- 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
- Sadjjadi SM, Alborzi AW, Mostovfi H. Comparative clinical trial of mebendazole and metronidazole in giardiasis of child-dren. *Journal*

- oftropical pediatrics*, 2001; **47**(3):176–8.
22. Roberto Cañete, Angel A Escobedo, María E González and Pedro Almirall, Randomized clinical study of five days apostrophe therapy with mebendazole compared to quinacrine in the treatment of symptomatic giardiasis in children W Cantelli-Forti G, Aicardi G, Guerra MC, Barbaro AM, Biagi GL 1983.
  23. Mutagenicity of a series of 25 nitroimidazoles and two nitrothiazoles in *Salmonella typhimurium*. *Teratog Carcinog Mutagen* 2004; **3**: 51–63.
  24. De Meó M, Vanelle P, Bernadini E, Laget M, Maldonado J, *et al.*, Evaluation of the mutagenic and genotoxic activities of 48 nitroimidazoles and related imidazole derivatives by the Ames test and the SOS chromotest. *Environ Mol Mutagen* 1992; **19**: 167–181.
  25. Krause JR, Ayuyang HQ, Ellis LD, Occurrence of three cases of carcinoma in individuals with Crohn's disease treated with metronidazole. *Am J Gastroenterol* 1985; **80**: 978–982.
  26. Bendesky A, Mene´ndez D, Ostrosky-Wegman P, Is metronidazole carcinogenic? *Mutat Res* 2002; **511**: 133-144.
  27. Tillonen J, Va`keva`inen S, Salaspuro V, Zhang Y, Rautio M, *et al.*, Metronidazole increases intracolonic but not peripheral blood acetaldehyde in chronic ethanol-treated rats. *Alcohol Clin Exp Res* 2000; **24**: 570–575.
  28. Jang GR, Harris RZ, Drug interactions involving ethanol and alcoholic beverages. *Expert Opin Drug Metab Toxicol* 2007; **3**: 719–731.
  29. Chan Del Pino M, Cueva Cornejo L, Troyes Rivera L. Comparación de Albend-dazol con nitrofuranos y nitroimidazoles en el tratamiento de giardiasis en niños [Comparative study of albendazole vers-sus nitrofurazones and nitroimidazoles in the treatment of giardiasis in children.] *Revista de gastroenterología del Perú*, 1999; **19**(2):95–108.