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Comparative Clinical Trial of Mebendazole, Praziquantel and Metronidazole in Treatment of Human Giardiasis

Reza Imani[1], Abolfazl Khoshdel[*2], Hossein Yousofi Darani[3], Mahmoud Mobasheri[4]

Abstract

Background: Giardia lamblia is a common intestinal parasite associated with social or personal problems. Giardiasis is distributed all over the world; however, the infection is more prevalent in developing countries. Metronidazole is now considered as a drug of choice for giardiasis treatment. The increasing number of reports of refractory cases as well as side effects of this drug resulted in establishment of more investigation for new compounds.

Methods: In a randomized clinical trial, 90 Giardia lambilia infected cases, aged 2-30 years and each proven to be infected with Giardia lambilia by the microscopical examination of fecal sample, were randomly allocated to 3 groups. Group 1 was given metronidazole with three daily 20 mg/kg doses for 7 days. Group 2 and 3 were seperately given mebendazole and praziquantel, with single 60 mg/kg and 20 mg/kg doses, respectively, and Parasitological cure was documented when stool examination for Giardia lambilia was negative for 3 times within 7–10 days after therapy.

Results: Seventeen of 30 patients treated with praziquantel, 15 of 30 patients (50%) treated with mebendazole and 28 of 30 individuals (93%) treated with metronidazole had negative stool examination results. There was not a significant difference between cure rates of praziquantel and mebendazole ($P>0.05$), while this difference between these two drugs and metronidazole was significant ($P<0.05$).

Conclusion: Mebendazole and praziquantel were not as effective as metronidazole in the treatment of Giardiasis.

Keywords: Giardiasis, Praziquantel, Mebendazole, Metronidazole.

1. Infectious & Tropical Diseases Specialist, Associated Professor, Dept of Infectious Diseases, Shahrekord University of Medical Sciences, Shahrekord,Iran.
2. Pediatrics Infectious Diseases Specialist, Associated Professor, Dept of Pediatrics, Shahrekord University of Medical Sciences, Shahrekord, Iran.
3. Parasitologist, Professor, Dept of Parasitology, Shahrekord University of Medical Sciences, Shahrekord, Iran.
4. Epidemiologist, Assistant professor, Dept of Epidemiology, Shahrekord University of Medical Sciences, Shahrekord, Iran.

* **Corresponding Author**
Dr. Abolfazl Khoshdel, Pediatrics Infectious Diseases Specialist, Associated Professor, Dept of Pediatrics, Shahrekord University of Medical Sciences, Shahrekord, Iran.

E-mail: nikakhosh@gmail.com
Tel: +989133820659

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Introduction

Giardiasis caused by *Giardia lamblia* is a worldwide health problem. Although mortality due to Giardiasis is generally low, massive infections can lead to considerable morbidity. This infection is more endemic in regions with poor sanitation, e. g. developing countries. Different rates such as 10.9% in the whole country [1] 26.2% in Damghan[2] and 7% in Ardabil [3] have been reported for Giardiasis prevalence in Iran. Although giardiasis affects mainly children, it can also occur in adults of any age [4-6], and is one of the most important reasons for malnourishment [4-7]. The clinical manifestations range from acute stage, with steatorrhoea, diarrhea and weight loss to a chronic stage like a peptic ulcer disease which can lead to severe weight loss [8, 9].

The nitroimidazoles, metronidazole and tinidazole are conventional drugs of choice for treatment of Giardiasis with a cure rate of higher than 90%. All of these drugs may lead to numerous adverse reactions, require long duration therapy and none of them is absolutely safe for use during pregnancy [10, 11]. Furazolidone with efficacy of about 90% is often used in children [12]. Several clinical data have suggested that the anti helminthic compound of mebendazol, albendazole and praziquantel has anti giardial activity [11, 13-16].

In order to search for a safe and effective anti giardiasis drug in this clinical trial study, the effect of mebendazole and praziquantel in comparison with Methronidazole on Giardiasis has been investigated.

Methods

In this clinical trial study, the study population consisted of patients with gastrointestinal complaints, including diarrhea, weight loss, anorexia or fatigue, referred to rural Healthcare Centers of Kohrang, located in southwest of Iran and highly endemic in terms of Giardiasis. 600 people aged 2-30 years were subjected to stool examination using either wet smear or concentration methods in 2008. Parasite cyst or trophozoite was detected in 90 patients who were considered positive for Giardiasis and divided randomly into three equal groups. All these 90 patients were recruited for the study while the informed consent of their parents or themselves was provided. In addition, the investigation was approved by *Ethics Committee of Shahrekord University of Medical Sciences*.

Group 1 cases were given metronidazole in tablet or liquid form with three daily 20 mg/kg doses for 7 days. Group 2 was treated with mebendazole in tablet form with a single dose of 60mg/kg and group 3 cases were given 20 mg/kg praziquantle as a single dose. To evaluate the effectiveness of the therapy, at least three stool samples from all cases were examined on the 7^{th}, 10^{th} and 14^{th} day after completion of the treatment by the same method of primary stool examination and also by the same microscopist. Clinical symptoms of the patients were also recorded in each group prior to and after treatment. Diarrhea was considered as defecation of watery stool and cases with many fatty bodies detected in stool examination were decided to be steatorrhea ones.

The data were analyzed by SPSS software. Differences in age between the three groups were analyzed using ANOVA and Chi-square test was employed to check the categorical variables between the three groups. *P* value <0.05 was considered as statistically significant.

Results

The demographic data and symptoms of the patients before and after treatment have been summarized in table1. In metronidazole group 28 out of 30, in mebendazole group 15 out of 30, and in praziquantel group 17 out of 30 patients were treated. Therefore in groups treated with metronidazole, Mebendazole or praziquantel the cure rate was 93%, 50% and 56.6%, respectively (table 2). No side effects were reported for either praziquantel or mebendazole by the patients or their parents.

Table 1: Demographic data and symptoms of *Giardia lambilia* infected patients treated with metronidazole, mebendazole or praziquantel

Characteristic		Metronidazol treated group	Mebendazol treated group	Praziquantel treated group	P
Age: mean [SD](range)		10.3[4.15] (2-18)	8.2[5.95] (3-32)	8.46[4.09] (2-22)	0.19
Sex(M:F)		10:20	15:15	16:14	0.249
Diarrhea	Before	20	22	23	
	After	0	5	4	
Constipation	Before	6	7	5	
	After	1	2	1	
Abdominal pain	Before	22	20	19	
	After	2	4	3	
Nausea and vomiting	Before	13	16	15	
	After	0	2	2	
Steatorrhea	Before	16	15	13	
	After	0	1	1	
Anorexia	Before	25	23	21	
	After	2	5	4	

Table 2: Cure rate of metronidazole, mebendazole and praziquantel in *Giardia lambilia* infected patients.

Stool examination results		Metronidazol group	Mebendazol group	Praziquantel group	P
At least one stool sample position	Before	30	30	30	
	After	2	15	13	0.001
Cure rate		93%	50%	56.6%	

Discussion

In this study aimed to find a safe and effective drug for giardiasis treatment, the effect of two anti helminthic drugs such as mebendazole and praziquanten, compared to a drug of choice with a wide range of side effects, i. e., metronidasole, on treatment of *Giardia lambilia* infection was investigated. In the present study cure rates of 93%, 50% and 56.6% were obtained for metronidazole, mebendazole and praziquantel, respectively. The effect of different drugs on treatment of giardiasis was investigated in previous works. Sadjadi et al. (2001) treated *Giardial lambilia* infected cases (7-12 years old) either with 200mg mebendazole three times a day for 5 days or metronidazole with a daily 15mg/kg for 7 days and reported cure rates of 86% and 90% for mebendazole and metronidazole, respectively[16]. Escobedo et al. (2003) also treated 146 *Giardia lambilia* infected children (5-15 years), with either three daily 200mg mebendazole for 3 days, or a single 30mg/kg secnidazole and obtained cure rates of 78.1% and 79.4% for mebendazole and secnidazole, respectively [14]. In another study Canate et al. (2006), treated 122 *Giardia lambilia* infected children (5-15 years old) either with 200mg mebendazole three times for one day or a single 50mg/kg dose of tinidazole. They reported cure rates of 63.9% and 81.97% for mebendazole and tinidazole, respectively [17]. In these three investigations cure rates of 86%[16], 78% [14] and 63.9% [17] were reported for mebendazole in treatment of *Giardia lambilia* infection. These results are not in agreement with what we reported as cure rate of mebendazole (50%). This difference may be related to our patients' age (2-30years) compared to age groups treated in those studies (5-15years).

Administration of praziquantel in combination with other drugs in treatment of animal giardiasis seems to be effective [13, 15] Pengssa et al. (2002) treated three groups of children with combination of albendazole and praziquantel, albendazole alone, and tinidazole alone. They reported cure rates of 74.2%, 50% and 92.6% for combined drugs, albendazole alone and tinidazole alone, respectively [18].

Conclusion

Here, cure rate of about 56% was achieved for praziquantel. It seems that this drug, if combined with other drugs, is more effective in treatment of giardiasis. Therefore, further researchis recommended investigating the effect of praziquantel in combination of other drugs in treatment of human giardiasis.

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Conflicts of interest

The authors declare that there is no conflict of interests.

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