

COMPARISON BETWEEN EFFICACY OF A SINGLE DOSE OF TINIDAZOLE WITH A 7-DAY STANDARD DOSE COURSE OF METRONIDAZOLE IN GIARDIASIS

Mohammad Fallah¹, Soghra Rabiee², Ali Akbar Moshtaghi³

ABSTRACT

Objective: *Giardia intestinalis* is the most common intestinal protozoan in the under developed countries. Treatment of infection has some difficulties by metronidazole because of long course of therapy and various side effects. The objective of this study was to determine efficacy and side effects of tinidazole compared with metronidazole in the treatment of giardiasis in children.

Patients and Methods: A randomized controlled clinical trial, 106 subjects (69 males, 37 females) with *Giardia intestinalis* infection admitted to out patients or private clinics in Hamdan, West of Iran, was treated with tinidazole or metronidazole. The study period was May 2002 to January 2003. Tinidazole 50 mg/kg single dose and metronidazole 15 mg/kg three times a day for seven days were given orally to children. Parasitological cure was documented when there was 3 times negative stool examination for giardiasis at 1-2 weeks after therapy.

Results: Thirty-seven of 42 individuals (88.1%) treated with tinidazole and 43 of 64 children (67.2%) treated with metronidazole had parasitological cure. Cure rates between two groups were significant statistically ($P < 0.01$). No major side effect were observed except two cases in metronidazole group who had mild headache and abdominal pain for two days and some had metallic taste. Three cases in tinidazole group had nausea, dizziness and headache.

Conclusion: Tinidazole was more effective than metronidazole, produced fewer and mild side effects and is recommended as drug of choice in single dose therapy for giardiasis. Because of single dose administration, short course of therapy and good compliance of patients, this preparation is preferred to metronidazole in the treatment of giardiasis.

KEY WORDS: Giardiasis, Tinidazole, Clinical trial.

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INTRODUCTION

Giardia intestinalis is a protozoan parasite of the small intestine that causes extensive morbidity worldwide. Giardiasis is a cosmopolitan parasitosis. Diarrhea, abdominal colic and

flatulence are the main clinical symptoms, however, malabsorption, and impairment of growth of children may occur.¹ Despite the recognition of *G. intestinalis* clinical illness for the last 40 years, no definitive treatment protocols have been published. There is at present only a limited range of chemotherapeutic agents for the treatment of *Giardia* infection. These comprise metronidazole and related nitroimidazoles, quinacrine and furazolidone. The 5-nitroimidazoles are the drug of choice in the treatment of giardiasis. Metronidazole is not completely effective, exhibits undesirable side effects sometimes and, is carcinogenic in the laboratory animals.² In human giardiasis, therapeutic failure occurs more and more frequently, due to low compliance with drug therapy, reinfection or parasite resistance to

1. Dr. Mohammad Fallah
Department of Parasitology
 2. Dr. Soghra Rabiee
Department of Obstetrics & Gynecology
 3. Dr. Ali Akbar Moshtaghi
Department of Pediatrics
- 1-3: School of Medicine,
Hamadan University of Medical Sciences,
Hamadan - Iran.

Correspondences:

Dr. Mohammad Fallah
Email: mohfall@yahoo.com
fallah@umsha.ac.ir

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metronidazole.³⁻⁴ Treatment failures are common (5-20%), repeated courses of therapy are often required, and there is evidence of variable drug sensitivity between strains of Giardia.⁵ On the other hand, long period of therapy (7-10 days, three times a day) is a disadvantage for this drug. Therefore, the adverse effects and treatment failures of some of the currently recommended drugs for Giardia infection suggests need for alternative anti-giardial agents. Investigation for compounds with short course of therapy, single dose as far as possible, is a recent outstanding recommendation of the World Health Organization.⁶ A most attractive feature of tinidazole is that when used as single dose regimen according to some reports has produced excellent results.^{7,8} The aim of this study was to evaluate the efficacy of tinidazole, single dose, and standard therapy of metronidazole in giardiasis.

PATIENTS AND METHODS

The efficacy and tolerability of metronidazole and tinidazole were evaluated in a randomized, open-label, clinical trial performed with 106 Giardia intestinalis-positive children enrolled from public and private health centers by convenience sampling. The study period was nine months from May 2002 to January 2003 on patients admitted in Hamadan, West of Iran. The subjects (37 females and 69 males) were randomly allocated to two groups: experiment group (n=42) were given tinidazole and control group (n=64) were given metronidazole. In group one, metronidazole suspen-

Table-I: Comparison of the efficacy of tinidazole and metronidazole in giardiasis

Drug	Efficacy		
	Effective no. (%)	Non-effective no. (%)	Total no. (%)
Tinidazole	37(88.1)	5(11.9)	42(60.4)
Metronidazole	43(67.2)	21(32.8)	64(39.6)
Total	80(75.5)	26(24.5)	106(100)

sion as standard oral dose (15 mg/kg/day, three divided doses, for seven days), and in group two, tinidazole tablets, single dose (50 mg/kg of body of weight to a maximum 2 g, once a day) were prescribed respectively.⁹ Patients were followed for three weeks after the end of therapy for the presence of G. intestinalis in their stool. Clinical and parasitological follow-up was carried out before, and at 7, 14, 21 days after treatment and the outcome of treatment was noted. Stool examination was done by formalin ether concentration technique in the research laboratory of Department of Parasitology, School of Medicine Hamdan University Iran. Parasitological cure was documented when there were three consecutive negative stool examination for G. intestinalis at 1-3 weeks after therapy termination.¹⁰

RESULTS

Thirty-seven of 42 children (88.1%) treated with tinidazole and 43 of 64 children (67.2%) treated with metronidazole had parasitological cure. Cure rate between two groups was significant statistically (P<0.01). No major side effect were observed except two cases in metronidazole group who had mild headache and abdominal pain for two days metallic taste

Table-II: Comparison of the efficacy of tinidazole and metronidazole in giardiasis in terms of weight of patients

Weight	Efficacy				Total n (%)
	Tinidazole		Metronidazole		
	Effective n (%)	No effective n (%)	Effective n (%)	No effective n (%)	
< 19 kg	10(31.25)	2(6.25)	13(40.62)	7(21.87)	32(30.2)
20-29 kg	15(39.5)	2(5.25)	15(39.5)	6(15.8)	38(35.8)
>30 kg	12(33.3)	1(2.77)	15(41.6)	8(22.22)	36(34)
Total	37(88.1)	5(11.9)	43(67.2)	21(32.8)	106(100)

Table-III: Comparison of the efficacy of tinidazole and metronidazole in giardiasis in terms of age of patients

Age	Efficacy				Total n (%)
	Tinidazole		Metronidazole		
	Effective n (%)	No effective n (%)	Effective n (%)	No effective n (%)	
< 8 years	9(26.5)	0(0)	16(47)	9(26.5)	34(32.1)
9-11 years	15(41.66)	2(5.55)	13(36.1)	6(16.66)	36(43)
>12 years	13(36.1)	3(8.33)	14(38.9)	6(16.66)	36(34)
Total	37(88.1)	5(11.9)	43(67.2)	21(32.8)	106(100)

after drug ingestion was more commonly reported in both groups and there was significant difference in both groups. No major side effect were observed except two cases in metronidazole group who had mild headache and abdominal pain for two days and three cases in tinidazole group who reported nausea, dizziness and headache.

Efficacy of two regimens in terms of weight, age, duration of symptoms and drug are presented in [Tables I-IV]. Tinidazole appears to be safe having a few ignorable side effects and produced a significant cure rate, more effective than metronidazole against *Giardia*, comparable with other anti-giardial agents used as a single dose therapy.

DISCUSSION

A single dose regimen of tinidazole had excellent effectiveness in treatment of giardiasis as compared with metronidazole. Introduction of nitroheterocyclic drugs in the late 1950s and the 1960s heralded a new era in the treatment of infections caused by a range of pathogenic protozoan parasites.¹¹ Metronidazole is

the drug now most widely used in the treatment of anaerobic protozoan parasitic infections caused by *G. intestinalis*, *Trichomonas vaginalis* and *Entamoeba histolytica*.^{12,13} Although various drugs have been available for several decades to treat this infection, none of them is entirely satisfactory due to high incidence of undesirable side effects and a significant failure rate in clearing parasites from the gastrointestinal tract.^{14,15} Some evidence suggests that drug resistance may be responsible for these failures.^{16,17}

Unfortunately, failures in treatment of giardiasis with standard metronidazole therapy have been reported in five to 20% cases.¹⁸ In the event of overt clinical resistance to metronidazole in *G. intestinalis* strains, tinidazole could be an alternative treatment. Unfortunately, this drug is not available in some countries, including Islamic Republic of Iran. A key issue should be keeping in mind the documented cross-resistance between currently used nitroimidazole drugs.⁴ As such the choice of drug will differ in each case depending on the local conditions and keeping in view the

Table-IV: Comparison of the efficacy of tinidazole and metronidazole in giardiasis in terms of duration of symptoms of patients

Age	Efficacy				Total n (%)
	Tinidazole		Metronidazole		
	Effective n (%)	No effective n (%)	Effective n (%)	No effective n (%)	
< 10 days	6(37.5)	0(0)	7(43.75)	3(16.75)	16(47.1)
11-20 days	1(16.66)	1(16.66)	3(50)	1(16.66)	6(17.6)
>21 days	4(33.3)	1(8.33)	5(41.76)	2(16.66)	12(35.3)
Total	37(88.1)	5(11.9)	43(67.2)	21(32.8)	106(100)

sensitivity of parasite strain. More ever, perhaps treatment of all asymptomatic *G. intestinalis* infections in developing countries hyperendemic for the disease is doubtful because of rapid reinfection.¹⁹

Clinical metronidazole resistance in *Trichomonas vaginalis* has also been documented previously.¹² Single dose therapy with tinidazole is effective in the metronidazole-resistant strains of *T. vaginalis* which could be another advantage of this drug.

CONCLUSION

Tinidazole was more effective than mertronidazole, produced fewer and mild side effects, and good compliance of patients. We recommend tinidazole as drug of choice for treatment of giardiasis because of its efficacy, desirable tolerance, single dose regimen and short course of therapy and good compliance of patients. This preparation is preferred to metronidazole in the treatment of *G. intestinalis* infection as a considerable advantage in low socio-economic communities. Moreover, this drug may be tried and used if other agents failed in the treatment of clinical giardiasis.

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