

# A COMPARATIVE CLINICAL TRIAL OF ALBENDAZOLE VERSUS METRONIDAZOLE IN CHILDREN WITH GIARDIASIS

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## ABSTRACT

*The adverse effects and treatment failures to some of the currently recommended drugs for giardia infection have given rise to the need for alternative anti giardial agents. In an open, randomized parallel group study, the safety and efficacy of albendazole was compared with metronidazole for the treatment of giardiasis in children. Sixty four children of age ranging from 2-12 years was randomized to receive either albendazole suspension 400 mg daily for 5 days or metronidazole suspension 7.5 mg/kg thrice daily for 5 days. The mean days required for cure, as evident by absence of cysts and/or trophozoites in the stool specimen, were  $3.7 \pm 1.4$  and  $4.5 \pm 1.1$  days, respectively for children on albendazole and metronidazole therapy. Six children on metronidazole therapy developed anorexia 2 to 4 days after the treatment. Albendazole proved as effective as metronidazole in the treatment of giardia infection in children with the added advantage of the absence of anorexia.*

Key words: Albendazole, Metronidazole, Giardiasis.

Infection with *Giardia lamblia*, a flagellated protozoa, is responsible for a wide spectrum of gastrointestinal manifestations such as asymptomatic excretion of cysts, acute infectious diarrhea, chronic diarrhea with failure to thrive and persistent gastrointestinal tract symptoms with varying degrees of malabsorption(1). Metronidazole, tinidazole, furazolidone and quinacrine are the currently recommended drugs for the treatment of giardiasis. The unacceptable toxicity of quinacrine, particularly in children, and reported drug resistance against furazolidone and metronidazole(2,3) have given rise to the need for search of alternative anti giardial agents.

Albendazole is a well known broad spectrum anthelmintic. An *in-vitro* study reported albendazole to be a more effective anti giardial agent as compared to metronidazole or tinidazole(4). Hall and Nahar(5) treated giardia infection in children with varying doses of albendazole and reported cure rates of 62% and 75% with single daily doses of 600 mg and 800 mg, respectively. This cure rate increased to 81% and 95% when albendazole was used in daily doses of 400 mg for 3 and 5 days, respectively; the latter was comparable to metronidazole which cured 97% of the giardial infections. The present

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study was conducted to assess the clinical efficacy and safety of albendazole as compared to metronidazole in the treatment of giardiasis in children.

### Material and Methods

An open randomized parallel group study was conducted over a period of 8 months from April to November 1993 in the Department of Pediatrics, King George's Medical College, Lucknow. The study was approved by the local ethical committee of the College. Children in the age group of 2 to 12 years with proven *giardia* infection, as demonstrated by the identification of trophozoites and /or cysts of *Giardia lamblia* in stool specimens entered this study. Those suffering from acute febrile conditions, diarrhea, severe malnutrition or receiving long term therapy were excluded from the study. None of the children entering this study had received medication for treatment of *giardia* or intestinal helminthic infection in the previous 7 days. After an informed parental consent, 64 hospitalized children, who met the selection criteria, were randomly allocated to, receive either albendazole suspension (Zentel) in a single daily dose of 400 mg for 5 days or metronidazole suspension (Flagyl) in a dose of 7.5 mg/kg thrice daily (22.5 mg/kg/day) for 5 days. A record of symptoms and physical signs was made daily for 7 days and on days 14 and 21 after starting treatment. Stool samples were also collected on the same days and examined microscopically for the presence of trophozoites and cysts of *giardia*, within 6 hours, in the wardside laboratory by making a direct smear of feces in normal saline and formal ether concentration tests. Blood

samples were collected for hematological (Hb and total RBC, leukocyte and platelet counts) and biochemical (serum creatinine, bilirubin, alkaline phosphatase and ALT) examination prior to the treatment and on days 7 and 14 post-treatment. Adverse experiences as reported by the parents were recorded. The time required (days) for the stool samples to be *giardia* and symptom free was also noted.

### Results

Of the 64 children enrolled in the study, 32 each were randomized to receive either albendazole suspension or metronidazole suspension. Of these 4 on albendazole and 3 on metronidazole therapy dropped out before 7 days of follow up and were excluded from the final analysis. All these children had responded to the therapy and parents did not want the children to be hospitalized any further. The different demographic characteristics in the albendazole and metronidazole groups, respectively were: males/females-18/10 and 20/9; nutritional status >80% of expected weight-23 and 25, between 70-80% of expected weight 4 and 2 and between 60-70% of expected weight 1 and 2. The age stratification in the albendazole and metronidazole groups, respectively was 2-4 years -14 and 14; 4-7 years -7 and 11; and 7-12 years-7 and 4.

Twenty three children reported for the 14th day follow up in both the treatment groups while 18 and 16 on albendazole and metronidazole, respectively reported on the 21st day. Diarrhea, abdominal pain, anorexia, nausea, and vomiting were the main presenting

**TABLE I-** Clinical Features of Patients Before Treatment and Mean Duration (Days) Required for Relief of Symptoms Following Treatment.

Clinical features	Before treatment (No. of patients)		Mean duration (days) for relief	
	Albendazole	Metronidazole	Albendazole	Metronidazole
Anorexia	13	15	2.6	4.5*
Nausea	3	6	1.6	2.6
Vomiting	5	10	1.6	2.6
Abdominal pain	7	16	2.3	3.0
Stools: watery	2	8	2.3	4.0
No. of stools/day				
2-3	10	8		
4-5	7	2	3.5	4.5
>5	3	10		
Parasites in stools				
Cyst &/or trophozoites	28	29	3.7±1.4	4.5±1.1
Cyst	19	20	3.8±1.5	4.7±1.1
Trophozoite	7	7	3.5±1.7	4.2±1.4
Cyst & trophozoite	2	2	3.7	4.4

\*Six additional children not anorexic prior to treatment developed anorexia after 2-4 days of therapy with metronidazole.

symptoms (Table I). The relief of these symptoms following treatment was a little earlier in children on albendazole therapy. This might be because of more severe presenting symptoms in children on metronidazole therapy. All the children in both the treatment groups were cleared of the *giardia* from the stools within 7 days of the treatment. The mean duration for the clearance of the *giardia* cyst and /or trophozoite was nearly a day earlier in albendazole group as compared to metronidazole group ( $3.7 \pm 1.4$  vs  $4.5 \pm 1.1$  days) though this difference was statistically insignificant. The stool samples of all the 23

children in both the treatment groups were negative for the *giardia* on day 14. *Giardia* cysts were identified again in the stool of a single child on albendazole therapy on day 21.

Anorexia persisted for a mean period of 2 days longer in metronidazole group and 6 additional children, who did not have anorexia prior to therapy, became anorexic 2 to 4 days after the initiation of the treatment and this persisted throughout the period of therapy. No other side effects were reported.

No significant difference was noted in the hematological or biochemical

parameters on the 7th and 14th day after treatment in both the treatment groups.

### Discussion

*Giardia latnblia* is a common cause of acute and chronic diarrhea around the world. The present therapeutic regimes are not completely effective and exhibit undesirable side effects(1,2). This study shows that albendazole in a dose of 400 mg daily for 5 consecutive days is as efficacious as metronidazole in a dose of 7.5 mg/kg thrice daily for 5 days in the treatment of *Giardia* infection in children. Hall and Nahar(5) have also reported that albendazole 400 mg given as a single dose for 5 days is as efficacious as metronidazole administered in three divided doses for 5 days. The recurrence of *giardia* cysts in one child on albendazole therapy on the 21st day was probably due to reinfection and not treatment failure. This is evident by the absence of the cyst/trophozolte in 5 consecutive stool samples before its reappearance.

Six children on metronidazole therapy, who were not anorexic prior to the treatment, developed loss of appetite after 2 to 4 days of treatment. No side effects were reported in children treated with albendazole. The absence of any

significant difference in hematological and biochemical parameters before and after treatment suggests that albendazole is safe in the dosage used.

We conclude that albendazole in a dose of 400 mg daily for 5 days is as effective as metronidazole in the treatment of *giardia* infection in children. Albendazole has the added advantage of the absence of anorexia which was reported with metronidazole.

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