

Rapid reinfection by *Giardia lamblia* after treatment in a hyperendemic area: the case against treatment

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عودة سريعة لعدوى الجيارديّة اللمبية بعد المعالجة في المناطق المفرطة التوطن: الحالة في مقابل المعالجة
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الخلاصة: قد قمنا باختبار 405 أطفال تتراوح أعمارهم بين عام وعشرة أعوام، مصابين بالعدوى، ولكن دون شكاوى بطنية أو معدية معوية خلال الشهر السابق. وعلى مدى 5 أيام تم إعطاء 204 منهم دواء المترونيدازول بجرعة 15 مغ/كغ/يوم بينما تناول 201 طفل شراب الفيتامين "ب" المركب. ثم فُحصت عينات من البراز بعد 2-3 أسابيع وكذلك بعد 3 أشهر من المعالجة، وتم اختبار النتائج باختبار خي مربع. وكذلك تمت مقارنة الطول والوزن بعد 6 أشهر من المعالجة، بالوزن والطول السابقين، وذلك باستخدام حُرَز Z واختبار t - ستودنت. وبلغت نجاعة المترونيدازول بعد 2-3 أسابيع 85.3%. وبعد مرور ثلاثة أشهر على المعالجة، عاودت العدوى ستين طفلاً (34.5%) وحدث شفاء تلقائي لواحدٍ وسبعين طفلاً (35.3%). ولذلك يوصي الباحثون بعدم معالجة الأطفال المصابين بعدوى الجيارديا العديمة الأعراض، نظراً لارتفاع معدل عودة العدوى، وإمكانية الشفاء التلقائي، ولارتفاع معدلات فشل المعالجة، فضلاً عن عدم تأثير العدوى على الوضع التغذوي أو النمو في هؤلاء الأطفال.

ABSTRACT We selected 405 children aged 1–10 years with *Giardia lamblia* infection but without abdominal or gastrointestinal complaints for the previous month. For 5 days, 204 received metronidazole 15 mg/kg/day and 201 received B-complex syrup. Stool samples were examined 2–3 weeks and 3 months after treatment and results were tested with chi-squared. Weight and height 6 months after treatment were compared with primary weight and height by Z-score and Student t-test. Metronidazole efficacy at 2–3 weeks was 85.3%. Three months after treatment, 60 were reinfected (34.5%) and 71 had spontaneously cleared (35.3%). Because of high reinfection, spontaneous clearing and treatment failure rates, and the lack of effect on nutritional status or growth, we do not recommend treatment for children with asymptomatic giardia infection.

Réinfection rapide par *Giardia lamblia* après traitement dans une zone hyperendémique : faut-il traiter ?

RÉSUMÉ Nous avons sélectionné 405 enfants âgés de 1 à 10 ans ayant une infection à *Giardia lamblia* mais n'ayant pas eu de troubles abdominaux ou gastro-intestinaux pendant le mois qui précédait l'étude. Pendant cinq jours, 204 enfants ont reçu du métronidazole à la dose de 15 mg/kg/jour et 201 enfants ont pris un complexe de vitamines B en sirop. Des échantillons de selles ont été examinés 2-3 semaines et 3 mois après le traitement et les résultats ont fait l'objet d'une analyse en utilisant le test du khi-carré. Le poids et la taille six mois après le traitement ont été comparés avec le poids et la taille initiaux à l'aide du test t de Student sur les scores Z. L'efficacité du métronidazole à 2-3 semaines était de 85,3 %. Trois mois après le traitement, 60 enfants étaient réinfectés (34,5 %) et 71 avaient éliminé le parasite spontanément (35,3 %). En raison des taux élevés de réinfection, d'élimination spontanée du parasite et d'échec thérapeutique ainsi que de l'absence d'effets sur l'état nutritionnel ou la croissance, le traitement pour les enfants ayant une infection à *Giardia* asymptomatique n'est pas recommandé.

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Introduction

Throughout the world, *Giardia lamblia* is often one of the first parasites to infect infants and children. Most human infections result from the ingestion of contaminated water or by direct fecal–oral transmission [1]. The prevalence of giardia in stool specimens submitted for ova and parasite examination has been reported to be 2%–5% in industrialized countries and 20%–30% in developing countries [2]. In the majority of infected individuals, or approximately 60% depending on the population, the infection remains asymptomatic. Asymptomatic infection may be more common in children and in people with prior infection [2–4]. Symptomatic patients have diarrhoea with loose, foul-smelling stool, flatulence, abdominal cramping, bloating, nausea, anorexia, malaise and weight loss. There is increased amount of fat and mucus in faecal samples, but blood is not present. Patients usually have no fever. Although giardia infection may resolve spontaneously, the illness lasts for several weeks and sometimes months if left untreated [5]. Patients with chronic giardiasis have profound malaise, diffuse epigastric pain and abdominal discomfort. Malabsorption of fats, carbohydrates, sugars and vitamins in cases of giardiasis has been well documented and may be responsible for substantial weight loss, even when the infection is apparently asymptomatic [5–7].

According to clinical and epidemiological studies the effects of nondiarrhoeal or asymptomatic giardia infection on nutritional status are inconsistent. In New Delhi, asymptomatic infected children had lower weight and height than uninfected children of the same age [8]. In Guatemala, treatment of asymptomatic infection caused greater increases in weight and height than in a control group [9]. In other studies,

however, no adverse effects on growth or nutritional status were detected [3,10,11]. Because of differences in study designs, interpreting these findings is difficult.

There is general agreement that persons with symptomatic giardiasis should be treated, although the indications for treating children with asymptomatic giardia infection remain controversial [12,13]. Because diarrhoea is a common symptom of giardiasis, giardia infection in the absence of diarrhoea is often considered to be asymptomatic. However, other symptoms including flatulence, foul-smelling stool and abdominal pain may occur more frequently than diarrhoea and are often of more concern to parents and patients [14–16].

If many children who live in hyperendemic areas are rapidly reinfected after treatment and if their infections clear spontaneously without treatment, a policy of treatment for all infected children with giardia, with or without symptoms, may not be prudent where public health resources are scarce [13,17–19]. Our study aimed to determine the prevalence of asymptomatic giardia infection and its spontaneous clearing rate by evaluating the effect of metronidazole on carrier, growth and nutritional status of infected children and also to determine the rate of reinfection after effective therapy for children with asymptomatic giardia infection, i.e. without diarrhoea and without abdominal complaints, in Sari, Islamic Republic of Iran.

Methods

Our experimental study included children aged 1–10 years in day care centres and schools in Sari in the Mazandaran province in the northern part of our country. The children were without any abdominal or gastrointestinal complaints for the 1 month

prior to our study. Stool specimens were collected by the centres or the parents. Giardia infection was determined by 2 separate examinations of the specimen directly after emulsification in saline by 2 technicians in the Boalisina hospital laboratory. A portion of the stool specimen was preserved by emulsification in methiolate-iodine-formalin solution and processed by both formalin-ether sedimentation and zinc-sulfate flotation techniques.

We chose 405 asymptomatic children with giardia infections for our study. We then gathered from their parents informed consent and completed questionnaire about signs and symptoms related to giardia infection, educational level of the family, family size, water supply and sanitary conditions of the home. We measured weight and height and then charted and matched children in the case and control groups. Infected children in the case group received metronidazole at 15 mg/kg per day for 5 days and infected children in the control group received B-complex syrup also daily for 5 days. Children were followed for 6 months duration. Stool specimens from the children in the case group were examined 2–3 weeks after treatment to examine the efficacy of metronidazole. At 3 months after treatment, 3 stool samples from each child in each group were examined to de-

tect the rate of giardia infection. The results were compared with Student *t*-test. After 6 months, weight and height were charted again. *Z*-scores of weight and height of the 2 groups after treatment were compared by Student *t*-test.

Results

To identify the 405 asymptomatic giardia-infected children in our study, we examined 2500 stool samples from 2500 asymptomatic children, i.e. one sample from each child. Of these, 16.2% were positive. The rate of infection increased with increasing age. Table 1 shows that the infection rate was 10.0% for children attending day care centres, but was 17.7% for slightly older children in school.

Of the 405 children with asymptomatic giardia infection who were enrolled in our study, 204 children in the case group received 15 mg/kg per day of metronidazole for 5 days and 201 children in the control group received B-complex syrup only. To detect metronidazole efficacy, 2–3 weeks after treatment 3 stool samples from each child in the case group were examined. Table 2 shows that 30 of the 204 children in the case group (14.7%) were still infected, yielding an efficacy rate of 85.3%. To de-

Table 1 Asymptomatic *Giardia lamblia* infection among children aged 1–10 years in Sari

No. of children	Attending day care centres	Attending school	Total
<i>Total</i>	490	2010	2500
Girls	215	921	1136
Boys	275	1089	1364
<i>Infected (%)</i>	49 (10.0)	356 (17.7)	405 (16.2)
Girls (%)	22 (10.2)	118 (12.8)	140 (12.3)
Boys (%)	27 (9.8)	238 (21.8)	265 (19.4)

fect reinfection and spontaneous clearing, 3 months after treatment 3 stool samples from each child in the case and control groups were examined. We found that 90 children in the case group were infected, i.e. 30 remaining infections from ineffective treatment and 60 reinfections (reinfection rate = 60 of 174, or 34.5%), and that 71 of the 201 children in the control group were clear of infection (35.3% spontaneous clearing). The relative risk for reinfection was 1.89 (95% confidence interval = 1.59–2.26); for spontaneous clearing, relative risk was 8.81 ($df = 1$, $P < 0.01$). After 6 months weight and height were charted again. Mean (standard deviation) Z-score for weight of the cases was 0.115 (0.78), and of the controls, 0.163 (0.576), $t = 0.7$. Mean Z-score for height of the cases was

0.52 (0.42), and of the controls, 0.46 (0.495), $t = 1.3$. Neither Z-score was statistically significant.

Discussion

In our study, the asymptomatic giardia infection rate was 16.2% among apparently healthy children aged 1–10 years in Sari, Islamic Republic of Iran. The prevalence rate was not significantly different between high and low socioeconomic classes and between sexes, but increased with increasing age (10% at ages 1–5 years to 17.7% at ages 6–10 years). This indicated that giardia infection was as common as in other parts of the country, e.g. 25.8% for children aged 1–10 years in Tehran and

Table 2 Outcomes for 405 children with asymptomatic *Giardia lamblia* infection treated with metronidazole (cases) or with B-complex syrup (controls)

Parameter	Time	Cases (n = 204)	Controls (n = 201)
Girls (No.)		62	78
Boys (No.)		142	123
S/E positivity ^a (%)	3 weeks after treatment	30 (14.7%) ^b	127 (37%) ^c
	3 months after treatment	60 (34.5%) ^d	130 (35.3%) ^c
Mean weight in kg (No.)	Before treatment	27.7 (204)	26.3 (201)
	6 months after treatment	30.7 (183)	29.2 (188)
Mean weight Z-score (SD)	6 months after treatment	0.115 (0.78)	0.163 (0.576), $t = 0.7$ (NS)
Mean height in cm (No.)	Before treatment	131.8 (204)	127.75 (201)
	6 months after treatment	138.6 (183)	132.96 (188)
Mean height Z-score (SD)	6 months after treatment	0.52 (0.42)	0.46 (0.495), $t = 1.3$ (NS)

^a3 stool samples were examined for each child.

^bMetronidazole efficacy rate = 85.3%.

^cSpontaneous clearing rate.

^dReinfection rate = 34.5% of the 174 cases that were effectively treated.

The number of children examined before and 6 months after differ as some were lost to follow-up.

NS = not significant.

SD = standard deviation.

26.79% for children aged 6–12 years in Shiraz (both examined 3 samples) [11,20]. It was also as common as in other countries, such as 21% for children in day care centres and 26% for children aged under 2 years in the United States of America and 95% for Peruvian children [17,18].

The children in our study did not have gastrointestinal complaints attributable to giardia infection for 1 month before and 3–6 months after treatment. This indicated that most children tolerated giardia infection well, especially in cases of reinfection, as in prospective studies of day care centre children, of rural Egyptian children and others [3,4,17,19]. Most new infections were not associated with diarrhoea and were well tolerated.

The reinfection rate 3 months after successful therapy was 34.5%. This was similar to Shiraz, a hyperendemic area similar to Sari, where 3 months after therapy the reinfection rate was 24.5% with a 1-year cumulative reinfection rate of 97.6% [11]. It was also similar to Lima, Peru, where 6 months after treatment the reinfection rate was 98% [18]. These studies indicate that the chance of reinfection for a child who has been successfully treated is high.

Spontaneous clearing of infection without treatment after 3 months was 35.3% in our study and was comparable to or higher than other studies [21,11]. These studies have suggested that many people with giardia infection will be cleared of infection spontaneously.

The positive effects of anti-giardia therapy on nutritional status and growth rates as in studies of Indian children and of

Guatemalan children were not seen in our study (the differences between our case and control groups were not statistically significant) [8,9]. It was, however, comparable with other studies that found no effect on the nutritional status of asymptomatic giardia-infected children [3,10,11].

In our study, the efficacy rate of metronidazole was 85.3%. Few drugs are available for the treatment of giardiasis and they include metronidazole, tinidazole, furazolidone, quinacrine hydrochloride and paromomycin and their efficacy rates vary from 60% to 100%. All occasionally have severe side-effects [12,22,23].

Conclusion

Considering the 15% failure rate and probable side-effects of therapy, the high rate of reinfection, the high rate of spontaneous clearing, the lack of effects on nutritional status and growth rate, the strong tolerance of reinfection by children, and the economic impact of treating all cases in developing countries with limited resources, we do not recommend the routine treatment of all asymptomatic giardia-infected children [9,23]. Treatment is required if an infected child exhibits persistent or intermittent, unspecific gastrointestinal symptoms, signs of malabsorption or impaired growth, poor weight gain, poor nutritional status and malnutrition even in the absence of other gastrointestinal symptoms. Treatment may also be indicated for prevention of transmission to close contacts who are at risk of developing severe giardiasis [13,16].

References

1. Keating JP. Giardiasis. In: Feigin RD, Cherry JD, eds. *Textbook of pediatric infectious diseases*, 4th ed. Philadelphia, WB Saunders, 1998:2400–3.
2. Ortega YR, Adam RD. Giardia: Overview and update. *Clinical infectious diseases*, 1997, 25:245–50.

3. Pickering LK et al. Occurrence of *Giardia lamblia* in children in day care centers. *Journal of pediatrics*, 1984, 104(4):522–6.
4. Rauch AM et al. Longitudinal study of *Giardia lamblia* infection in a day care center population. *Pediatric infectious disease journal*, 1990, 9(3):186–9.
5. Hill DR. *Giardia lamblia*. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas and Bennett's: Principles and practice of infectious diseases*, 5th ed. Philadelphia, Churchill Livingstone, 2000:2888–94.
6. Wolfe MS. Giardiasis. *Clinical microbiology reviews*, 1992, 5:93–100.
7. Hill DR. Giardiasis: Issues in diagnosis and management. *Infectious disease clinics of North America*, 1993, 7:503–25.
8. Gupta MC et al. Effect of giardia infection on nutritional status of preschool children. *Indian journal of medical research*, 1990, 92:341–3.
9. Gupta MC, Urrutia JJ. Effect of periodic antiascaris and anti giardia treatment on nutritional status of preschool children. *American journal of clinical nutrition*, 1982, 36:79–86.
10. Ish-Horowicz M et al. Asymptomatic giardiasis in children. *Pediatric infectious disease journal*, 1989, 8(8):773–9.
11. Alborzi A, Zerafati Z. Asymptomatic giardia infection in children in a hyperendemic area. *Iranian journal of medical sciences*, 1994, 19(1,2):1–6.
12. Nash TE. Treatment of *Giardia lamblia* infections. *Pediatric infectious disease journal*, 2001, 20(2):193–5.
13. Addiss DG, Juranek DD, Spencer HC. Treatment of children with asymptomatic and nondiarrheal giardia infection. *Pediatric infectious disease journal*, 1991, 10(11):843–6.
14. Spencer MJ et al. Parasitic infections in a pediatric population. *Pediatric infectious disease journal*, 1983, 2(2):110–3.
15. Hopkins RS, Juranek DJ. Acute giardiasis: an improved clinical case definition for epidemiologic studies. *American journal of epidemiology*, 1991, 133:402–7.
16. Katz M. Asymptomatic giardia infection: letters to the editor. *Pediatric infectious disease journal*, 1992, 11(3):248–9.
17. Bartlett AV et al. Controlled trial of *Giardia lamblia*: control strategies in day care centers. *American journal of public health*, 1991, 81(6):1001–6.
18. Gilman RH et al. Rapid reinfection by *Giardia lamblia* after treatment in a hyperendemic third world community. *Lancet*, 1988, 13:343–5.
19. Sullivan PS et al. Illness and reservoirs associated with *Giardia lamblia* infection in rural Egypt: the case against treatment in developing world environments of high endemicity. *American journal of epidemiology*, 1988, 127(6):1272–81.
20. Shirbazoo Sh, Aghamiri H. *Giardia lamblia* infection prevalence in Tehranian children. *Koosar medical journal*, 2000, 5(2):105–9 [in Persian].
21. Levi GC, De Avila CA, Neto VA. Efficacy of various drugs for treatment of giardiasis: A comparative study. *American journal of tropical medicine and hygiene*, 1977, 26:564–5.
22. Davidson RA. Issues in clinical parasitology: the treatment of giardiasis. *American journal of gastroenterology*, 1984, 79(4):256–61.
23. Murphy TV, Nelson JD. Five vs. ten days therapy with furazolidone for giardiasis. *American journal of diseases of children*, 1983, 137:267–70.