Giardia lamblia in AIDS Patients with Diarrhea

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Abstract

Giardia lamblia, a flagellate protozoan is a protozoa, frequently associated with diarrhea in AIDS patients (adults and children). Transmission occurs *via* the fecal-oral route by ingestion of infectious cysts in contaminated food or drinking water. Giardia lamblia can cause diarrhea and intestinal malabsorption in both AIDS and non-AIDS patients. The prevalence rate of diarrhea caused by Giardia lamblia in AIDS patients is higher than in those without AIDS, due to humoral immune defect in AIDS patients. The most common symptoms are abdominal distress, watery diarrhea and weight loss. The clinical symptoms in AIDS patients are similar to those in non-AIDS patients. Diagnosis may be made by identifying either cysts or trophozoites in a stool sample, duodenal biopsy and aspirate. Metronidazole is the common drug of choice. Relapse may be found in AIDS patients. At present there is no vaccine. Prevention requires proper handling, good hygiene and treatment of water used for AIDS patients.

Key word : AIDS, *Giardia lamblia*, Diarrhea

Diarrhea is a frequent clinical manifestation in patients with acquired immunodeficiency syndrome (AIDS). The leading agents found in AIDS patients with diarrhea are Cytomegalovirus, Cryptosporidium, Microsporidium, Entamoeba histolytica, Giardia lamblia, nontyphoidal Salmonella and Shigella[1-8].

Giardia is a flagellate protozoan, Phylum Sarcomastigophora, Class Zoomastigo phorea, and Order Diplomonadida. It has two forms : the motile trophozoite and cyst forms. The cyst form is the infectious form[9]. Giardia lamblia is the species infecting humans (adults and children) and causes diarrhea and intestinal malabsorption. It also contributes to chronic diarrhea in developed and developing countries. Patients may be symptomatic or asymptomatic. Host immunity plays a role in providing protection from disease, in clearance of the

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parasite. Predisposition to giardiasis has been noted in patients with common variable immunodeficiency[8].

Pathogenesis and immune response

Infection occurs following oral ingestion of cysts, about 10-25 cysts may establish infection[10]. The incubation period of giardiasis after ingestion of cysts is 1-2 weeks. Trophozoites are destroyed by gastric acid. Following excystation, trophozoites colonize and multiply in the upper small bowel and attach the brush border of enterocytes by either a suction or clasping mechanism or involvement of specific receptor-ligand interactions[11,12]. Mucosal invasion is a rare occurence [13]. There is no evidence for production of an enterotoxin. Simultaneous colonization of the small bowel with Giardia spp. and Enterobactericeae or yeast may contribute to malabsorption in some patients by the deconjugation of bile salts[14]. Small bowel biopsy may demonstrate spruelike lesions or may be normal: two studies have correlated the severity of diarrhea with the degree of histologic abnormality on biopsy[15]. The histology of the small-bowel mucosa is inconspicuous in most subjects with giardiasis[16]. Gastric giardiasis can develop in the abscence of mucosal abnormalities during hypochlorhydria induced by treatment with a high dose of a prolong-pump inhibitor[17].

The host immune response is the other important component of the host-parasite relationship[18-20]. Host immunity plays a role in providing protection from disease, in clearance of the parasite. The components of host immunity are humoral and cellular including lymphocyte- and macrophage-mediated mechanisms[19,21]. The serum IgM and IgG antibodies develop and can be lethal to Giardia trophozoites. The studies in mice showed the possibly important role of IgA in clearance of the parasite and its abscence is associated with failure to resolve infection[21,22]. It remains unclear if selective IgA is a predisposing factor[23]. Failure to develop IgA against specific Giardia antigens has been suggested to correlate with chronic giardiasis in humans[24]. Predisposition to Giardiasis has been documented in patients with common variable immunodeficiency[25]. Patients with AIDS do not appear to have more severe illness with Giardia. However, they do exhibit impaired immune response to the parasite[26,27]. Humoral immune defect in the host was found to be the major determinant of whether the giardial infestation would be symptomatic or not, while associated bacterial infections and zymodeme patterns were not found to be important in determining the pathogenicity or presentation of giardiasis[28]. Oberhuber G et al showed evidence that intestinal intraepithelial lymphocytes are not activated in cytotoxic T cells in giardiasis but in celiac disease[29]. Several observations indicate that partially protective immunity may develop to Giardia.

Epidemiology

Giardiasis is the most common protozoal infection of the human intestinal tract and is found with increased frequency in homosexual men, children in day care centers and travellers to endemic areas. It can cause diarrhea in incompetent hosts and was once thought to be a harmless parasite but now it has a new meaning after the AIDS epidemic[30]. It is associated with symptomatic diarrhea and malabsorption in children. It has been found in 4 to 70 per cent of patients with AIDS in the United States[26,27,31,32] and in patients with AIDS from Europe[33]. Transmission occurs via the fecal-oral route by passage of infectious cysts from person to person or through ingestion of contaminated food or water[2,5]. Robertson LJ reported the epidemiology of severe giardiasis and cryptosporidiosis in Scotland, UK that the incidence of severe cryptosporidiosis was almost double that of severe giardiasis and the median duration of hospitalization was longer for cryptosporidiosis than giardiasis[34].

Clinical presentation

The majority of persons infected with Giardia have no symptoms. Asymptomatic giardiasis did not affect iron absorption in children with iron deficiency anemia in a previous study[35]. Angarano G et al reported that Giardia intestinalis in HIV +, is not considered a major cause of enteritis but it is a frequent event among AIDS patients, especially in the most advanced stage of the disease[36]. Immunodeficiency states, particularly hypogammaglobulinemia and malnutrition, are apparently associated with increased susceptibility to giardiasis[8].

Clinical symptoms of giardiasis in AIDS patients with diarrhea are similar to those in non-AIDS. Symptomatic giardiasis is characterized by acute diarrhea, nausea, abdominal cramps or chronic illness manifested by a protracted, intermittent, frequently debilitating disease[9]. Giardia infection was

associated with a decrease in rate of weight gain and impairment in feed efficacy in a study by using growing lambs as a domestic remnant model[37]. Giardia lamblia causes diarrhea and intestinal malabsorption. The malabsorption and anorexia that occur can result in significant weight loss and failure to thrive in prolonged infection. Initially, stools may be profuse and watery but later are commonly greasy, foul-smelling and may float. Gross blood, pus and mucus are usually absent. The stool is found to be free of polymorphonuclear cells (PMN)[2].

Table 1 shows the prevalence and clinical manifestations of Giardia lamblia in AIDS and non-AIDS patients (both children and adults) at Bamrasnaradura Infectious Disease Hospital, a centre for treating AIDS and diarrhea in Nonthaburi, Thailand between January 1995 and December 1997 (Moolasart P, unpublished data) Giardia lamblia was detected in stool specimens from 19 (1.7%) of the 1,102 diarrheal patients with AIDS, whereas, it was detected in 43 (0.7%) of the 6,156 diarrheal patients without AIDS. The results suggest that the prevalence rate of diarrhea caused by Giardia lamblia in AIDS patients (1.7%) is higher than those without AIDS (0.7%) (children and adults). Previous studies reported that children appear to be more susceptible to Giardia than adults [2,27,38]. However, in this study it was observed in only a limited number of children in both groups. Probably, the nutrition and hygiene education efforts for school children and their parents in this area of Thailand are partially successful. Patients with AIDS did not appear to have more severe illness with Giardia lamblia in this study which is similar to previous reports[29,30]. Although the rate of fever and weight loss/malnutrition of the AIDS group was higher than the non AIDS group, it is not clear whether the findings were associated with Giardia infection or with HIV infection or other opportunistic infections. There were no cases of severe dehydration in this study. Gross blood and PMN were not found in their stool specimens. The overall prevalence rate of Giardia lamblia infection of both groups in this study was underestimated because it was not identified by the extensive method, concentration method, or enzyme immunoassays. In addition, only symptomatic diarrheal cases were examined. A previous study showed only 25-50 per cent symptomatic cases of giardiasis[2]. However, this study emphasizes the more common occurrence of Giardia lamblia in AIDS patients.

Diagnosis

Diagnosis of giardiasis may be made by the finding of either cysts or trophozoites on stool examination, duodenal biopsy and aspirate in AIDS - associated diarrhea. Specimens should be examined by direct wet mount and by a concentration method. The number of cysts that are excreted vary, so at least three stool examinations spaced 2 days apart are needed[2,5]. Duodenal aspiration, or small - bowel biopsy may yield trophozoites[39]. Sanad MM et al found Giardia in gastric biopsy, particularly those showing chronic atrophic gastritis and

Table 1. Prevalence and characteristics of diarrheal patients with *Giardia lamblia* infection in Bamrasnaradura Hospital, Thailand (1995-1997).

	Giardia lamblia in diarrheal patients				
	with AIDS		without AIDS		P value
Prevalence (+ve G. lamblia)	16 / 548	(2.9%)	25 / 3,586	(0.7%)	
Children	1 / 61	(1.6%)	4 / 1,479	(0.3%)	
Adults	15 / 487	(3.1%)	21 / 2,107	(1%)	
Sex M : F	12 : 4		19 : 6		
Mean age	32.6 yr		27.3 yr		> 0.05
Age range	4 - 55 yr		3 - 58 yr		
Days of ilness before presentation	10.5 days		6.4 days		< 0.05
Watery / loose stool	13 / 16	(81.3%)	22 / 25	(88%)	
Abdominal pain	3 / 16	(18.8%)	5 / 25	(20%)	
Weight loss / malnutrition	15 / 16	(93.8%)	2 / 25	(8%)	
Fever	3 / 16	(18.8%)	2 / 25	(8%)	
No dehydration	14 / 16	(87.5%)	24 / 25	(96%)	

we should be aware of gastric giardiasis as a possible cause of upper gastrointestinal symptoms[40]. Giardia can also be diagnosed by antigen assays which use immunofluorescence (IFA) or enzyme-linked immunosorbent assay (ELISA)[41,42]. The coinfection with Giardia lamblia and Enterocytozoon bieneusi was found in a patient with AIDS and chronic diarrhea[43]. Some have reported an enteropathy without identfiable pathogens and difficulty in eradicating Giardia[44,45].

Treatment

In patients with normal immune systems, infections with protozoal organisms including Giardia are generally of short duration and usually respond to therapy when available but in patients with AIDS, the clinical course may be protracted[4]. All patients with laboratory-confirmed clinical illness should be treated because it remains an important diarrheal agent that is curable. The regimens for treatment of giardiasis are shown in Table 2. Metronidazole, a nitroimidazole and quinacrine are drugs of choice in the treatment of giardiasis[46]. Many physicians have been treating giardiasis with metronidazole because of their familiarity with using it for other infections and its favorable side-effect profile and ready availability[2]. Treatment failure with nitroimidazole derivatives are common in giardiasis and may be resistant to these drugs. Quinacrine has frequent toxic side effects. Furazolidone, paromomycin and tinidazole may be used as alternative drugs. Furazolidone is the only drug available in liquid suspension for use in young children[6]. Doumbo O et al reported the effectiveness of nitazoxamide in the treatment of cryptosporidial diarrhea and other intestinal parasite infections including giardiasis associated with AIDS in tropical Africa[47]. Ornidazole 40 mg /kg as a single dose was used as an alternative protocol for treating giardiasis in a study[48]. Relapse is common in immunocom-promised patients and requires prolonged treatment[4].

Prevention

The prevention of giardiasis in AIDS patients requires proper handling, good hygiene, treatment of water and avoiding food or drinks that are likely to be contaminated[2]. Potentially contaminated water should be boiled or filtered. Chlorination is not effective. At present there is no vaccine or drugs for prophylaxis of giardiasis. Adequate sanitation should be provided for people, especially AIDS patients.

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Table 2. Treatment of *Giardia lamblia* that cause diarrhea in patients with AIDS.

Drug	Dosage
First drugs of choice	
Metronidazole	Adults : 250 mg tid x 5-7 days Children : 5 mg/kg tid x 7 days
Quinacrine	Adults : 100 mg tid x 5-7 days Children : 2 mg/kg tid x 7 days
Alternative drugs	
Furazolidone	Adults : 100 mg qid x 7-10 days Children : 1.5 mg/kg qid x 10 days (max. 400 mg/day)
Paromomycin	Adults : 10 mg/kg tid x 5-10 days
Tinidazole	Adults : 2 g x 1 dose
New recommended drugs	
Nitrazoxamide	Adults : 500 mg bid x 7 days
Ornidazole	Adults : 40 mg / kg IV x 1 dose

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เชื้อไจอาเดีย แลมเบลีย ในผู้ป่วยโรคเอดส์ที่มีอาการท้องร่วง

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Giardia lamblia เป็นโปรโตซัวชนิดหนึ่งที่เป็นสาเหตุของโรคท้องร่วงในผู้ป่วยโรคเอดส์ พบได้ทั้งในเด็กและผู้ใหญ่ การติดต่อเกิดจากกินซิสท์ของ *Giardia lamblia* ที่ปนเปื้อนกับอาหารและน้ำเข้าไป ทำให้เกิดอาการท้องร่วงและมีภาวะดูดซึมอาหารผิดปกติ การติดเชื้อนี้พบได้ทั้งในคนปกติทั่วไปและผู้ป่วยโรคเอดส์ แต่อัตราการเกิดจะพบมากในผู้ป่วยโรคเอดส์เนื่องจากภูมิคุ้มกันบกพร่อง อาการที่พบมากในผู้ป่วยเอดส์ที่ติดเชื้อนี้ คือปวดเบ่งในท้องและถ่ายเป็นน้ำ และน้ำหนักลด ซึ่งอาการและความรุนแรงจะไม่แตกต่างจากคนปกติที่ไม่เป็นเอดส์ การวินิจฉัยโดยการตรวจอุจจาระหาซิสท์หรือโทรโฟซ้อยท์ของเชื้อในอุจจาระ ชิ้นเนื้อ หรือสิ่งที่ดูดออกมาจากลำไส้ส่วนดูโอเดนัม ยาที่นิยมใช้รักษาได้แก่ เมโทรไนดาโซล การติดเชื้อซ้ำอาจพบได้ในผู้ป่วยเอดส์ ปัจจุบันยังไม่มีวัคซีนป้องกัน วิธีป้องกันที่ดีสุดสำหรับผู้ป่วยโรคเอดส์ในขณะนี้คือการล้างมือให้ถูกวิธี มีอนามัยดี และมีน้ำใช้ที่สะอาด

คำสำคัญ : โรคเอดส์, *ไจอาเดีย แลมเบลีย*, ท้องร่วง

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