Giardia Antigen Detection in Patients with Chronic Gastrointestinal Disturbances

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Background. Giardia lamblia, a protozoan parasite, is transmitted by cysts in contaminated water or food or by person-to-person contact. The standard in diagnosis has been the microscopic demonstration of fecal cysts, which yields many false negatives due to high variability in cyst excretion. A new method that detects infection even when few parasites are present is now available. This immunodiagnostic test is rapid, sensitive, and specific, and typically requires only a single stool specimen. In this study patients with gastrointestinal (GI) complaints were screened for Giardia antigens, and the test results were compared to conventional microscopy. Costs incurred by patients with chronic GI problems were documented.

Methods. Twelve patients with GI complaints were tested for Giardia by microscopy and 13 patients by the immunodiagnostic test. Patient charts were evaluated for pertinent history and the diagnostic tests ordered before giardiasis was considered.

Results. For all patients, microscopy was uniformly negative, but 6 of 13 patients were antigen positive. Patients with chronic complaints, later found to test positive for Giardia, typically underwent five diagnostic tests at a cost of $338.

Conclusions. Giardiasis, an increasing problem in family practice, should be considered early in patients with GI disturbances. New, sensitive immunodiagnostic tests that usually require a single specimen are more useful than microscopy. Prompt diagnosis of giardiasis not only relieves patients of unpleasant symptoms, but can avoid unnecessary and costly evaluations.


Giardiasis is a disease of the small bowel caused by the protozoan parasite Giardia lamblia. In the past, Giardia infections acquired in the United States were typically associated with contaminated mountain streams and other untreated surface waters. For the past 10 years, Giardia has been the most common cause of waterborne outbreak of disease in this country. Aging and deficient water treatment facilities are, in part, to blame. Giardia cysts are unaffected by the usual chlorination procedures and must be removed from the water supply by filtration techniques that in many areas are antiquated or inadequate. Such systems were implicated in 9 outbreaks of giardiasis from 1986 to 1988 involving 1169 documented cases.1

During this same period, this protozoan pathogen was recognized as being effectively spread by the fecal-oral route. Specialized settings, such as day-care centers, have been the foci of recent attention. In one study of 239 toddlers in day-care centers, 16.3% were found to be infected.2 Similarly, in a 15-month, longitudinal study in a Houston day-care center, 48 episodes of Giardia infection were identified in 27 of 82 children (33%). Of the infected (cyst-passing) children, only 22% exhibited any symptoms.3 These results are typical of Giardia infection in children, which is often asymptomatic. However, the clinical picture can vary widely in character and severity. The manifestations of disease occur about 2 weeks after exposure and most often include anorexia, nausea, malaise, bloating, and diarrhea.4 Some individuals also report a lactose intolerance, an observation that has been documented in patients5 and in experimental infections.6-8 While most infections will resolve in about 2 months, there are individuals who will continue to pass cysts for long periods and may exhibit intermittent symptoms.4

When the initial episode of gastroenteritis due to Giardia does not prompt medical attention or is misdiagnosed, chronic symptoms may result. Intermittent
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symptoms of abdominal discomfort, diarrhea, or gas-
cousness may not be recognized as Giardia infection, and
patients may undergo expensive and time-consuming
diagnostic workups. In a recent presentation, Galland
tested 197 patients for Giardia who had been diagnosed
as having "irritable bowel syndrome." He found that 48%
(95 patients) were excreting Giardia cysts; in 72 of
the patients who tested positive, Giardia had not been
previously considered. When appropriate antibiotics
were administered, the symptoms resolved in more than
90% of these patients.

The present standard diagnosis of an active infection
is made by the microscopic identification of Giardia cysts
or trophozoites in stained fecal smears. Unfortunately,
cyst excretion is highly variable, and three to six stool
specimens may be required to produce positive results.
Detection of anti-Giardia antibody can sometimes be
helpful, especially in epidemiologic studies, but does not
distinguish between active and cured infections. The
most promising technique currently available is an im-
munodiagnostic method that detects cysts and soluble
parasite products (antigens) in stool specimens. To date,
sten studies using this technique with a single stool specimen
have shown a high degree of specificity (92.4%) and
increased sensitivity (90.5%) over conventional micros-
copy, Moreover, when conventional microscopic
methods are negative, antigen detection is recommended
as the most cost-effective approach.

The purpose of this article is (1) to illustrate that
Giardiasis is not always associated with diarrhea and may
persist for long periods, (2) to document the use of an
improved method to screen for Giardia infection in a
series of 13 patients with chronic GI disturbances, and
(3) to delineate the time and expense incurred when
Giardia is not considered early in the GI diagnostic
workup.

Materials and Methods

Stool Collection and Preparation

Patients in this study were drawn from the population of
the Family Practice Center (Baylor College of Medicine,
Houston, Tex), where approximately 2000 patients are
seen monthly. Over a 4-month period, 13 patients who
presented with acute or chronic gastrointestinal symp-
toms were included in the series. A single stool was
collected and kept at 4°C if stored longer than 3 to 4
hours prior to delivery to the laboratory. For direct
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Materials and Methods

Antigen Detection Assay

For evaluation of Giardia antigen in diluted stools, a
commercially available enzyme-linked immunosorbent
assay (ELISA) was employed as directed (GiardEIA,
Antibodies, Inc, Davis, Calif). Control and test tubes
coated with normal and anti-Giardia antibody, respecti-
vely, were incubated with 0.2 mL of diluted stool. A
matching set of tubes was incubated as above with 0.2
mL of "low positive control" solution provided in the kit.
After incubation for 15 minutes at room temperature,
tubes were washed four times with PBS, and 0.2 mL of
diluted horseradish peroxidase-conjugated anti-Giardia
antibody was added. The conjugate was incubated for 2
minutes, and tubes were again washed four times with PBS.

The control and test tubes incubated with the low positive
color in the test tube compared with the color in the
control tube. The set of control and test tubes incu-
bated with the low positive control solution provides
negative and positive quality control for assay reagents.
All specimens were tested in duplicate.

Treatment

Patients testing positive for Giardia by the immunoassay
were treated with 250 mg of metronidazole orally ad-
ministered three times per day for 7 to 10 days. In one
patient, whose symptoms recurred within a week of
completing this treatment, metronidazole (250 mg three
times daily) and quinacrine hydrochloride (100 mg three
times daily) were given for 14 days.

*Similar immunoassays are also commercially available from Trend Scientific Co (St
Paul, Minn), Aleson, Inc (Mountain View, Calif), Chemicon International (Temec-
ula, Calif), and LMD Laboratories, Inc (Carlsbad, Calif).
Table 1. Series of Patients with Gastrointestinal Complaints

<table>
<thead>
<tr>
<th>Patient No. and Condition</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Major Complaint</th>
<th>Duration of Symptoms</th>
<th>Number Ordered</th>
<th>Costs ($)</th>
<th>Ova and Parasite Examination Results</th>
<th>Immunoassay Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>9</td>
<td>Abdominal pain</td>
<td>NA</td>
<td>1</td>
<td>34</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>10</td>
<td>Diarrhea</td>
<td>1 wk</td>
<td>1</td>
<td>34</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>57</td>
<td>Diarrhea</td>
<td>2 wk</td>
<td>0</td>
<td>0</td>
<td>ND</td>
<td>+</td>
</tr>
<tr>
<td>Chronic symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>47</td>
<td>Bloating, abdominal pain</td>
<td>2 y</td>
<td>5</td>
<td>380</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>28</td>
<td>Abdominal pain</td>
<td>2 mo</td>
<td>5</td>
<td>372</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>76</td>
<td>Diarrhea, bloating</td>
<td>1 mo</td>
<td>2</td>
<td>49</td>
<td>-*</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>39</td>
<td>Abdominal pain</td>
<td>&gt;1 y</td>
<td>1</td>
<td>34</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>30</td>
<td>Diarrhea, abdominal pain</td>
<td>4 mo</td>
<td>7</td>
<td>189</td>
<td>-*</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>35</td>
<td>Diarrhea, lactose intolerance</td>
<td>&gt;1 y</td>
<td>7</td>
<td>219</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>NA</td>
<td>Diarrhea, bloating</td>
<td>1 mo</td>
<td>1</td>
<td>34</td>
<td>-*</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>1</td>
<td>Intermittent diarrhea</td>
<td>1.5 mo</td>
<td>2</td>
<td>68</td>
<td>-*</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>46</td>
<td>Abdominal pain, bloating</td>
<td>6 mo</td>
<td>3</td>
<td>338</td>
<td>-*</td>
<td>+</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>33</td>
<td>Intestinal diarrhea, abdominal pain, bloating, nausea</td>
<td>1.5 y</td>
<td>14</td>
<td>989</td>
<td>-*</td>
<td>+</td>
</tr>
</tbody>
</table>

NA denotes not available; ND, not done.
*Both tests were done on aliquots from a single specimen.

Results

Patient Population

Over a 4-month period, 13 patients reporting gastrointestinal disturbances with or without diarrhea were tested for the presence of *Giardia* antigen in stool samples (Table 1). All patients who were asked to enroll provided a specimen. Three patients presented with acute symptoms (<1 month duration); 10 patients had chronic complaints lasting from 1 month to 2 years (median duration, 5 months). The 6 female and 7 male patients ranged in age from 14.5 months to 53 years (median age, 34 years); only 3 of the patients were children. Among all patients, chronic or chronic intermittent diarrhea (62%) was the most common complaint, along with abdominal discomfort (54%) and bloating (38%).

Comparison of Tests

No empiric treatment was given before testing for *Giardia*. All except one severely ill patient had one or more examinations for ova and parasites at the time of the last examination. None of these tests were positive for *Giardia* cysts. In contrast, the *Giardia* antigen detection assay performed on the same sample or on a sample from the same symptomatic period revealed active infection in 6 of 13 (46%) patients. A direct comparison of the methods was carried out with seven stool samples; three were negative by both assays and four were negative by examination for ova and parasites but positive by antigen detection test. For the antigen detection test, duplicate assays done on each specimen were in agreement.

Response to Treatment

All of the six patients who were antigen positive were treated with metronidazole as described. Symptoms improved with initiation of treatment and were absent by the end of the course. In one case, however, symptoms returned and required treatment with two agents. A second patient reported that symptoms continued for 1 month following single-drug therapy and then resolved spontaneously. All other patients reported cessation of symptoms after completing the treatment regimen and remained free of further symptoms at 1 year post-treatment.

Cost of Additional Tests

Related diagnostic tests included ova and parasites, stool cultures, fecal leukocytes, fecal fat, sedimentation rate, chemistry panel, oral cholecystogram, gallbladder ultra-
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sonography, and gastrointestinal radiography, all of which were negative. Costs per patient for these tests are listed in Table 1. These costs do not include the antigen detection (immunoassay) method, which currently costs $54 in our area. As a point of comparison, the ova and parasite examination ($34 per test) must typically be done three or more times to document infection. The number of tests ordered for the five patients prior to the diagnosis of giardiasis ranged from one to five, with costs ranging from $34 to $989 (median cost per patient, $338). These costs are based solely on the tests and do not include the cost of patient time or office visits.

Discussion

Giardia cysts ingested as a result of contaminated water, food, or fingers undergo excystation after exposure to stomach acids. The excreted cysts can withstand a wide range of temperatures and remain viable in the environment for months. They are not adversely affected by usual chlorination techniques, but can be killed by temperatures exceeding 50°C or by exposure to 2% iodine.

Patients who present with acute symptoms of diarrhea and flatulence and who have a history of surface water exposure are usually promptly diagnosed and treated. However, patients whose symptoms are more chronic, atypical, or insidious in onset may pose more diagnostic difficulty. Of note is that 5 of 13 patients in the present series did not have diarrhea. It is increasingly common to acquire Giardia through inadequate public water systems or by direct fecal-oral contamination. Person-to-person spread is especially prevalent in nursing homes, day-care centers, and other institutionalized settings. Thus, lack of a history of surface water exposure no longer precludes the diagnosis of Giardia.

Detection of Giardia by microscopic evaluation of stool specimens usually requires several specimens. The mechanics of multiple collections and the time required for communication with the laboratory make compliance problematic. Even when Giardia ranks high in the differential diagnosis, patients may not want to endure the process of submitting one, two, three, or more specimens while waiting for effective treatment for their symptoms.17,18 The antigen detection test is especially useful since the commercially available kit is rapid (30 minutes), simple to carry out and interpret, and requires no instrumentation. Thus, the test is suitable for a hospital or office-based laboratory.

Our study, like others,2,10-15 suggests that the antigen detection test is more sensitive than the standard examination for ova and parasites, particularly on a single stool specimen. Earlier tests revealed no cross-reactivity with several other protozoan or helminthic GI parasites.19 However, like all tests, the antigen detection assay has limitations; it is not 100% sensitive or specific. To date, the lower level of sensitivity has not been defined. Thus, it may be possible to miss some Giardia-infected individuals (false negatives) because they are tested at an early point in the infectious process or because the infection has remained at a low level. Ova and parasite examination would very likely be negative in these situations as well. Likewise, false-positive results are also difficult to document since the increased sensitivity of the test may well surpass the reference standard of conventional microscopy. In the cases presented here, all but one of the patients who tested positive by the antigen test responded to treatment. This patient received a single course of metronidazole and reported that symptoms resolved 1 month later. Thus, it is unclear whether the immunoassay yielded a false-positive result or whether the therapy was inadequate, and the infection resolved spontaneously after a short time.

For some patients an empiric trial of therapy may be justified if giardiasis is suspected, even though ova and parasite studies are negative. The more sensitive immunoassay can be beneficial in this instance since a negative result might preclude an unnecessary course of medication and delay further diagnostic evaluation. Also the value of a definitive diagnosis rather than a “therapeutic trial” is demonstrated by studies that show a low response to standard therapy in some populations.20 As seen in one of our patients, some patients may require more than one course of therapy or more than one drug. If the antigen test had not been available to aid in interpretation of the recurrent symptoms, this patient would probably have undergone additional unnecessary tests.

An important consideration in obtaining an early diagnosis is cost, including the cost of the patient’s time off from work or for multiple office visits. To decrease these costs, the physician may choose to select several evaluative tests when the patient first presents rather than perform a stepwise assessment. In the cases presented here, costs for negative tests in patients with chronic Giardia infection ranged from $34 to $989, with a median cost of $338. Moreover, if the patients with negative ova and parasite examination had not been tested with the more sensitive immunoassay, the expenses for further evaluation would likely have been higher. The greatest savings, however, may be that obtained when much more costly radiologic or endoscopic studies prompted by the impatience of the physician or patient are avoided. A Giardia test that is sufficiently sensitive to reliably diagnose infection with only one specimen can be cost-effective, even though more expensive than a single.
conventional microscopic examination. Indeed, uniformly negative results on the examinations for ova and parasites for the patients in this series are typical of the findings when only a single stool specimen is examined and highlights the necessity of multiple specimens when microscopy is used to detect *Giardia* infection.

In summary, the results obtained from our study of 13 patients, although limited, confirm the observations of another investigator.\(^9\) While most of the patients studied had a history of gastrointestinal symptoms lasting more than 1 month, several had documented abnormalities lasting for years. During this time, patients often underwent one or more diagnostic tests at a median cost of $388, most of which failed to reveal abnormalities. However, 54% of patients in this series had detectable *Giardia* antigen in a single stool specimen, in contrast to uniformly negative results obtained by conventional microscopy. Multiple specimens, which are usually necessary for positive ova and parasite examinations, were not required for the immunoassay. Of the six antigen-positive patients, five were successfully treated, and their symptoms resolved.

These cases demonstrate the importance of considering giardiasis early in the workup of gastrointestinal complaints, and also substantiate the advantages of using the immunodiagnostic test for *Giardia* antigens over conventional methods of ova and parasite detection. Patients with diarrhea of more than 1 month’s duration or chronic abdominal discomfort should have a *Giardia* antigen test performed, even if microscopic examinations for ova and parasites have been negative. When an antigen detection test is performed before a more extensive workup is undertaken, the patient can save time, money, and the risk of unnecessary diagnostic procedures, as well as the discomfort of a chronic infection.

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**References**


