Clinical Features, Epidemiology, and Treatment of Plesiomonas shigelloides Diarrhea

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Recent studies have suggested that Plesiomonas shigelloides is a cause of diarrhea. The present study addresses the clinical features, epidemiology, and response to antimicrobial therapy of P. shigelloides diarrhea. Thirty cases of P. shigelloides infection were defined by isolation of the organism from stool specimens, and 30 age-matched control patients were identified by detection of other enteric pathogens. Clinical and epidemiological information was obtained by interviewing the referring physicians and the patients. Of the P. shigelloides-infected patients, 71% had a history of recent tropical travel, but 29% acquired their infections locally in association with the consumption of seafood or untreated water or both. Seventy-eight percent of the P. shigelloides-infected patients had findings suggestive of colitis, and P. shigelloides-infected patients had a history of tropical travel, acute illness, abdominal pain, and prolonged symptoms significantly more often than did the control patients. Antimicrobial therapy significantly reduced the duration of illness in patients with Plesiomonas diarrhea. These results suggest that P. shigelloides is a significant cause of both locally acquired and traveler’s diarrhea that may respond to antimicrobial therapy.

Materials and Methods

Patient population. Patients submitting stool specimens to Metropolitan Clinical Laboratories between August 1986 and December 1987 were enrolled in the study if cultures yielded P. shigelloides. Additional isolates were identified from specimens submitted to the British Columbia Provincial Health Laboratories. During the same period, age-matched control patients were also identified. Stool cultures from these patients were negative for P. shigelloides but positive for other enteric pathogens. The clinical and epidemiological features of the illnesses in patients yielding P. shigelloides were compared with those in the control patients, who were infected with other recognized enteric pathogens.

Clinical and epidemiological information was collected by interviewing the patients or their referring physicians at the time of initial detection of an enteric pathogen and again at follow-up 1 to 12 months later. The information sought included age, sex, presence of diarrhea, nature of stools (volume, presence of blood or mucus), abdominal pain (location, intensity), urgency or tenesmus, fever, duration of symptoms before the patient presented to a physician (acute symptoms, <2 weeks; chronic symptoms, >2 weeks), total duration of illness, concomitant infection with enteric pathogens other than P. shigelloides, presence of fecal leukocytes, response to treatment (resolution of illness in <2 weeks), history of underlying disease, travel to tropical areas within 2 weeks of onset of illness, recent medications, and consumption of seafood or untreated water within 5 days of the onset of illness.

Stool cultures and identification of isolates. Stool specimens were cultured at the Provincial Health Laboratories were cultured on bismuth sulfite, deoxycholate-citrate-lactose-sucrose, Hektoen enteric, cefsulodin-Irgasan-novobiocin (Difco Laboratories, Detroit, Mich.), sorbitol-MacConkey, and campylobacter-selective agars. Stool specimens were cultured at Metropolitan Clinical Laboratories were cultured on Hektoen enteric, cefsulodin-Irgasan-novobiocin, sorbitol-MacConkey, campylobacter-selective, and MacConkey agars and on sheep blood agar (Prepared Media Laboratories, Tualatin, Oreg.). Specimens received in this laboratory during the last 6 months of the study period were also cultured on inositol-brilliant green-bile salts agar (16), which has been suggested as a selective-differential medium for the detection of P. shigelloides. Most specimens were examined for intestinal parasites by using permanent iron hematoxylin stain and Formalin-ethyl acetate concentration.

The enteric plating media and campylobacter-selective agar were screened for potential pathogens in accordance with standard procedures (8). Blood agar cultures were screened by flooding the plates with oxidase reagent and selecting oxidase-positive colonies for identification. Whitish or pinkish colonies on inositol-brilliant green-bile salts agar were subcultured to blood agar and tested for oxidase. Potential pathogens were identified by classical biochemical testing with serological confirmation of Salmonella and Shigella isolates. The following characteristics were required for identification of isolates as P. shigelloides: positivity for oxidase, indole, myoinositol, arginine, lysine, and ornithine; negativity for hydrogen sulfide, gas, urease, arabino-, mannitol, sucrose, and DNase; and a negative Voges-Proskauer test (15). P. shigelloides isolates were tested for antimicrobial susceptibility by using a standard disk-diffusion method (2).

Statistical analysis. The findings for P. shigelloides-in-
TABLE 1. Epidemiological and clinical features of P. shigelloides diarrhea

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control patients</th>
<th>P. shigelloides-infected patients</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Sex ratio (female/male)</td>
<td>19/11</td>
<td>14/15</td>
<td>NS</td>
</tr>
<tr>
<td>Age (median)</td>
<td>30 yr</td>
<td>30 yr</td>
<td>NS</td>
</tr>
<tr>
<td>Tropical travel</td>
<td>3/30 (10)*</td>
<td>20/28 (71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Seafood consumption</td>
<td>20/21 (95)</td>
<td>20/21 (95)</td>
<td></td>
</tr>
<tr>
<td>Untreated-water consumption</td>
<td>28/30 (93)</td>
<td>30/30 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Acute illness</td>
<td>11/28 (39)</td>
<td>21/27 (78)</td>
<td>0.004</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>17/19 (90)</td>
<td>30/30 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Bloody diarrhea</td>
<td>6/19 (32)</td>
<td>8/30 (29)</td>
<td>NS</td>
</tr>
<tr>
<td>Colitis</td>
<td>13/28 (54)</td>
<td>18/23 (78)</td>
<td>0.06</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>22/26 (79)</td>
<td>23/23 (100)</td>
<td>0.02</td>
</tr>
<tr>
<td>Fecal leukocytes</td>
<td>13/30 (43)</td>
<td>7/11 (64)</td>
<td>NS</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>9/27 (33)</td>
<td>10/25 (40)</td>
<td>NS</td>
</tr>
<tr>
<td>Fever</td>
<td>3/25 (12)</td>
<td>7/23 (30)</td>
<td></td>
</tr>
<tr>
<td>Illness lasting &gt;2 wk</td>
<td>6/19 (42)</td>
<td>19/25 (76)</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

* Calculated by chi-square analysis or the Fisher exact test (two tailed) by using Epic Analyst Software. NS, Not significant.

RESULTS

During the 18 months of study, 25 P. shigelloides isolates (from 22 patients), 677 Campylobacter isolates, 518 Yersinia isolates, 426 Salmonella isolates, 57 Shigella isolates, 49 enterohemorrhagic Escherichia coli isolates, 32 Aeromonas isolates, and 4 Vibrio isolates were isolated from 17,820 outpatient stool specimens cultured at Metropolitan Clinical Laboratories. All the P. shigelloides-infected patients were seen in the offices of physicians, and no isolates were detected in two hospital laboratories monitored during the same period. Another 12 P. shigelloides-infected patients were identified after analysis of stool specimens submitted to the Provincial Health Laboratories. Most of the strains were isolated from Hepcoen enteric and sorbitol-MacConkey agars; one strain was detected only on inositol-brilliant green-bile salts agar. Clinical and epidemiological information was available for 30 of the 34 P. shigelloides-infected patients and for 30 control patients. Of the P. shigelloides-infected patients, 27 underwent tests adequate for detecting other enteric pathogens, and 8 of these (30%) were positive for infection. The other isolates included Campylobacter sp. (three isolates), Shigella sp. (one), Salmonella sp. (one), Yersinia sp. (one), and mixed enteric pathogens (two). In 19 patients only P. shigelloides was isolated from stool specimens and no other enteric pathogens were found.

The median age of patients infected with P. shigelloides was 30 years (range, 3 months to 70 years), and males and females were represented about equally (Table 1). Of P. shigelloides-infected patients for whom data were available, 71% reported a history of tropical travel within 2 weeks of the onset of their illness; in contrast, only 10% of the control patients had a history of tropical travel. Travel locations for patients with P. shigelloides included Southeast Asia (45%), Central America (45%), and Africa (10%). Eight patients acquired their infections locally in British Columbia, and all had a history of consumption of seafood or untreated water within the week preceding illness. Overall, 20 of 21 P. shigelloides-infected patients (95%) for whom information was available consumed seafood or untreated water within 5 days of the onset of symptoms. Infections with P. shigelloides in travelers were seen year-round, but locally acquired infections were detected only in July, August, and September.

Four P. shigelloides-infected patients had consumed codeine before their illness, but they were significantly less likely to have ingested this or other medication than were controls (4 of 22 patients versus 13 of 30 controls; P = 0.05). There were no significant differences between control patients and P. shigelloides-infected patients with respect to age, sex, or presence of underlying disease.

All patients yielding P. shigelloides were symptomatic and had diarrhea (Table 1). Seventy-eight percent of these patients sought medical attention within 2 weeks of the onset of illness, whereas only 39% of the control patients had such an acute illness. Plesiomonas diarrhea appears to involve predominantly the large bowel (colitis), and patients often had small-volume stools associated with lower abdominal pain, urgency, or tenesmus. Symptoms of colitis tended to be more common in P. shigelloides-infected patients (78%) than in control patients (53.6%), but the difference was not statistically significant (P = 0.06). Consistent with their symptoms of colitis, 27% of the P. shigelloides-infected patients experienced bloody stools, 30% had fever, 64% had fecal leukocytes, and 78% had often-severe left-lower-quadrant or hypogastric pain, and they were significantly more likely to experience abdominal discomfort than were the control patients. Forty percent of P. shigelloides-infected patients had nausea or vomiting, often early in the course of illness, and 3 of 27 (11%) experienced transient arthralgias.

Two patients with Plesiomonas infection underwent colorectal endoscopy and biopsy, and the results were abnormal for one of them. This biopsy was done during week 5 of illness, and the findings were interpreted as chronic nonspecific colitis. The symptoms of this patient subsequently resolved during week 7 of illness. Overall, the symptoms of Plesiomonas infection were of longer duration than those of the control patient infections.

Of the 30 Plesiomonas strains isolated from the study patients, 19 underwent antimicrobial susceptibility testing. Of the 19 strains, 2 (10.5%) were susceptible to all tested antibiotics, including ampicillin. Nine (47.4%) were resistant to ampicillin alone, and eight (42.1%) were resistant to ampicillin plus tetracycline. No isolate tested was resistant to co-trimoxazole or norfloxacin. No association was noted between the areas of presumed acquisition of Plesiomonas infections and antimicrobial susceptibility pattern. However, patients infected with strains resistant to ampicillin plus tetracycline took significantly longer to resolve their symptoms than did patients infected with more-susceptible strains (5 of 7 versus 2 of 11, respectively, took >2 weeks to resolve their symptoms; P = 0.04).

Of 24 P. shigelloides-infected patients for whom information was available, 9 were treated with an antimicrobial agent to which the isolate was susceptible in vitro and 15 had not been treated. Treated patients were significantly more likely than untreated patients to be asymptomatic within 2 weeks (8 of 9 versus 6 of 15 patients, respectively; P < 0.05). Treated patients were significantly less likely than untreated patients to have illness persisting longer than 4 weeks (1 of 9 versus 6 of 15 patients, respectively; P < 0.05). Illness...
lasting more than 4 weeks was not associated with any of the other factors examined, including age, underlying disease, foreign travel, or previous use of gastrointestinal medications.

The results presented above are from patients infected with *P. shigelloides* with or without other enteric pathogens. To more closely define the role of *P. shigelloides* in diarrhea, the results were reanalyzed for the 19 patients infected with *P. shigelloides* alone. No differences were found in the clinical features, epidemiology, or response to therapy when the results for these patients were compared with those for the 30 patients analyzed above.

**DISCUSSION**

These findings suggest that *P. shigelloides* is a cause of both locally acquired and traveler’s diarrhea and that the organism occurs more commonly than is currently recognized. Thirty-four patients with *Plesiomonas* diarrhea were found, despite the fact that no media were used to enhance recovery of the organism during most of the study period. Twenty of the *P. shigelloides*-infected patients had a history of recent tropical travel, but eight patients had no history of recent travel outside British Columbia. Experience with other enteric pathogens suggests that additional cases of *Plesiomonas* infection will be recognized when a more effective medium for isolating the organism becomes available.

Little is known of the epidemiology of *P. shigelloides* diarrhea. Waterborne (1, 14) and oyster-related (13) outbreaks of *Plesiomonas* diarrhea have been reported, and a recent case-controlled study suggested that consumption of raw oysters and travel outside the United States are risk factors for acquiring the infection (7). In the present study, the organism was found to affect all age groups and both males and females, and *Plesiomonas* diarrhea was significantly associated with tropical travel and with consumption of seafood or untreated water.

The clinical features of *Plesiomonas* infection in previous uncontrolled studies have suggested that the organism causes either secretory or invasive diarrhea. In a recent review, it was concluded that *Plesiomonas* diarrhea is most often secretory in nature and that invasive diarrhea occurs less commonly (3). Our findings and the results of another recent study (7) indicate that most patients with *Plesiomonas* infection have an acute illness, with abdominal pain and colitis. These findings suggest that invasive rather than secretory diarrhea is most commonly associated with *Plesiomonas* infection.

The results of several recent studies support the role of *P. shigelloides* as an enteric pathogen, and the results presented here demonstrate that this organism produces symptoms of infection with a frequency comparable to or exceeding that associated with other recognized enteric pathogens. Although these findings indicate that *P. shigelloides* is an enteric pathogen, an understanding of the mechanism of pathogenesis of the organism has been elusive, and previous in vitro studies of *P. shigelloides* pathogenesis have been inconclusive (3–5, 7). Studies of the mechanisms of pathogenesis in the strains isolated in this study are under way.

Little information on the natural history of *P. shigelloides* diarrhea is available from previous studies, but the results of the present study suggest that the organism often causes prolonged illness. We found that 76% of the *P. shigelloides*-infected patients had symptoms lasting more than 2 weeks, and 32% had symptoms lasting more than 4 weeks. This duration of symptoms was significantly longer than that seen in patients infected with other organisms (*P < 0.05*) and is consistent with other reports of prolonged illness associated with *P. shigelloides* infection (3, 7, 12).

The results of several previous uncontrolled studies have suggested that *P. shigelloides* diarrhea responds to antimicrobial therapy (9, 11). Our findings suggest that *P. shigelloides*-infected patients treated with antimicrobial agents to which the organism was susceptible had a significantly briefer illness than untreated patients. Although this study was not randomized and the number of patients studied was small, our results suggest that antimicrobial therapy is beneficial in *P. shigelloides* diarrhea. Additional controlled studies are needed in this area.

In summary, the present findings support the role of *P. shigelloides* as a gastrointestinal pathogen and indicate that the organism may be a more common cause of diarrhea than is currently recognized. In British Columbia, *Plesiomonas* diarrhea may be locally acquired or associated with tropical travel and is often related to consumption of seafood or untreated water. Study patients with *Plesiomonas* diarrhea had a more acute illness, more often had abdominal pain, and had a longer duration of illness than did control patients, who were infected with other enteric pathogens. Our findings suggest that the organism produces a clinical illness that resembles invasive diarrhea and that may respond to antimicrobial therapy. *P. shigelloides* may be an important new enteric pathogen.

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**LITERATURE CITED**


