The Role of Diet in the Treatment of Travelers’ Diarrhea: A Pilot Study

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(See the editorial commentary by Steffen and Gyr on pages 472–3).

A pilot study was performed to compare the effects of a restricted physiologic diet in 48 subjects with those of an unrestricted diet in 57 subjects on the duration and symptoms of acute travelers’ diarrhea among US adults being treated with an antimicrobial agent in Mexico. Restricted physiologic diet was defined as the avoidance of certain foods during diarrheal illness, as specified in limited published literature. The mean duration of diarrhea (37 vs. 33 h) and clinical symptoms were similar between those practicing the restricted diet and those practicing unrestricted diets. These results suggest that restricting diet during treatment of travelers’ diarrhea with an antimicrobial agent is not associated with improvement of clinical symptoms or with decreased duration of diarrhea. However, a much higher number of subjects would need to be studied to prove this point statistically.

Travelers’ diarrhea is the most common health problem in persons traveling to developing countries. Diet (control of food intake), oral rehydration therapy, and symptomatic antidiarrheic drugs are options in the nonspecific treatment of travelers’ diarrhea. Of these, diet is an area that has not been well studied in individuals with acute travelers’ diarrhea. Controversies exist about the details of partial fasting, the resumption of solid food intake, and the role of dietary advice in individuals who develop diarrhea [1–3]. The present pilot study was designed to compare the effects of a restricted physiologic diet with those of an unrestricted diet on the duration of acute travelers’ diarrhea and the clinical symptoms associated with diarrheal illness in US students traveling to Guadalajara, Mexico, who were receiving antimicrobial treatment for their diarrhea.

PATIENTS AND METHODS

A total of 105 US college students (age range, 18–26 years) attending summer sessions during 2001 in Guadalajara participated in this study. The subjects were part of studies examining the role of antibiotic treatment (levofloxacin vs. azithromycin and rifaximin vs. ciprofloxacin) administered to patients with travelers’ diarrhea [4, 5]. Subjects had not taken any medication (e.g., aspirin, ibuprofen, bismuth subsalicylate, loperamide, or other antibiotics) that might have had activity against enteric infection in the 7 days prior to the onset of illness, nor did they take such medications during the 48 h of observation after the initiation of antimicrobial treatment for diarrhea. Acute diarrhea was defined as diarrhea of <14 days duration in which the subject had passed at least 3 unformed stools in the previous 24 h and had had at least 1 symptom of enteric disease, such as abdominal pain, excessive gas/flatus-
dient, the field investigators of this study were not blinded to the diet intervention of each subject. However, the investigator (M.W.D.) who assessed the daily diaries and determined the duration of diarrhea and clinical symptoms over time was blinded to the diet practiced by each subject. Patients in both groups were instructed to consume liberal amount of fluids during their illness to replace diarrheic losses.

The restricted diet intervention was based on limited dietary recommendations and on published physiological studies on certain food types [6–8]. Subjects assigned to the restricted diet were given the following instructions: While acute diarrhea continues, take clear liquids (e.g., mineral water, consomme, jello, sherbet, and Manzanilla tea) to match diarrhea losses, and limit solid-food consumption to salted crackers, tortillas, bread, and toast (jelly is OK but butter is not). As symptoms improve but stools remain unformed, add bananas, rice, potatoes, and baked chicken or fish to the diet. Until stools are formed and you feel well, avoid red meat, cheese, milk, butter, ice cream, vegetables, fried foods, coffee, alcohol, and fruit other than bananas. Subjects assigned to the unrestricted diet were given the following instructions: While acute diarrhea continues, take fluids to match diarrhea losses. Eat and drink whatever you wish.

Because several students might live in the same household, the diet to which the first ill person in the household was randomized determined the diet assigned to all subsequent ill persons in the same household. In this way, the señora in an affected household perceived that the diet requests were consistent; she was not inconvenienced or confused and was more likely to help enforce compliance with the dietary assignment.

In addition to maintaining a daily diary of clinical symptoms and stool passages, enrollees in the diet study also kept a daily log of food and beverage intake during the 48-h period after initiation of antimicrobial therapy. The primary study end point was duration of diarrhea (i.e., time from initiation of antimicrobial agent until passage of the last unformed stool [after which subjects were declared healthy] or “time to last unformed stool” [TLUS]). As defined by a US Food and Drug Administration subcommittee guideline, TLUS or cure was declared when there was passage of no unformed stools without fever during a 48-h interval or when there was passage of no watery stools and ≤2 soft stools and an absence of fever or other enteric symptoms during a 24-h interval [9]. Clinical symptoms that were measured included abdominal pain, gas, nausea, vomiting, fever, and tenesmus. These clinical symptoms were self-reported as “none,” “mild” (tolerable), “moderate” (interferes with activities), and “severe” (incapacitating). The daily diaries were checked regularly to ensure compliance with the recording of diarrheic and clinical symptoms and adherence to the assigned diet.

Participation in this study was voluntary and required the written informed consent of subjects prior to enrollment. This study was approved by the Committee for the Protection of Human Subjects of the University of Texas at Houston Health Science Center and by the Universities of San Diego (CA) and Arizona (Tuscon), whose programs the students were attending while in Guadalajara.

We performed an intent-to-treat analysis, in which subjects were analyzed in the group to which they were originally assigned. We also performed an efficacy analysis, in which subjects who did not conform to the assigned diet were reassigned for analysis purposes to the diet they actually practiced. In the efficacy analysis, subjects with any dietary noncompliance with the restricted diet intervention were switched to the unrestricted diet intervention group. If the subject practiced a restricted diet without any deviations from the restricted diet protocol, as documented by his or her food diary, the subject was counted as practicing a restricted diet intervention.

Differences in TLUS or symptoms of enteric illness in the diet intervention groups were compared by the Mann-Whitney U test. Only those individuals with a symptom of enteric illness at baseline were included in the analysis at 24 and 48 h after initiation of antimicrobial therapy. The analysis of symptoms compared the numbers of subjects who had no, mild, moderate, or severe symptoms at 24 and 48 h with the numbers at baseline, but, for simplicity of presentation, the data are recorded in the table as mean indices, such that a report of no symptoms received a score of 0, mild received a score of 1, moderate received a score of 2, and severe received a score of 3. Frequency counts of the antimicrobials used by subjects in and between diet intervention groups were calculated by the Pearson χ² test. Data was interpreted in a 2-tailed fashion to estimate P values. A P value <.05 was considered to be significant. The data were processed using MS Excel (Microsoft) and SAS (SAS Institute).

RESULTS

In the intent-to-treat analysis, 48 subjects were randomized to the restricted diet intervention, and 57 subjects were randomized to the unrestricted diet intervention. Subjects in the 2 dietary groups were similar with respect to mean age, sex, ethnicity and weight. Similar numbers in each dietary group received one of the various antibiotics under study.

Review of the daily logs determined that adherence to the diet in each group was excellent and that those assigned to the unrestricted diet ate a wide variety of foods during the observation period. Only 5 subjects did not adhere to their assigned diet intervention. Three students assigned to the unrestricted diet practiced a restricted diet, and 2 students assigned to the restricted diet practiced an unrestricted diet. In an efficacy analysis, 47 subjects practiced a restricted diet, and 58 subjects practiced an unrestricted diet. As in the intent-to-treat analysis,
demographic characteristics and antibiotics used were similar between the 2 dietary groups.

No statistical differences were noted in or between diet intervention groups in the use of antimicrobials in the intent-to-treat ($P = 0.79$) or efficacy analyses ($P = 0.63$). In the intent-to-treat analysis, the mean TLUS was 37 h (range, 0–99 h) for those subjects who practiced a restricted diet and 33 h (range, 0–120 h) for those subjects who practiced an unrestricted diet ($P = 0.59$). In the efficacy analysis, the mean TLUS was 35 h (range, 0–99 h) for those subjects who practiced a restricted diet and 33 h (range, 0–120 h) for those subjects who practiced an unrestricted diet ($P = 0.77$).

Table 1 summarizes the clinical symptoms at baseline and at 24 and 48 h after initiation of antimicrobial therapy, according to the diet intervention to which subjects were assigned (intent-to-treat analysis). No differences in clinical symptoms were noted between subjects in the restricted and unrestricted diet groups at baseline or at 24 or 48 h after initiation of antimicrobial therapy in either the intent-to-treat or the efficacy analysis (data not shown). In the restricted diet group, 4 of 6 clinical symptoms (abdominal pain, gas, fever, and tenesmus) were reported somewhat less often at 24 h, and 3 of 6 clinical symptoms (gas, tenesmus, and fever) were reported somewhat less often at 48 h; however, none of these differences were statistically significant.

**DISCUSSION**

We believe that this is the first study examining diet as an intervention in the treatment of acute travelers’ diarrhea in adults. Our pilot study found no clinically important differences between the diet intervention groups in the duration of diarrhea or in clinical symptoms of acute diarrhea during the 48 h of observation in either the intent-to-treat or the efficacy analysis. These results suggest that there are no differences in the duration of diarrhea or in clinical symptoms according to the diet assigned or practiced among antibiotic-treated patients. However, a much larger study would be necessary to prove that the dietary interventions had equivalent or possibly different clinical effects.

The subjects in this study were part of 2 studies that examined the role of antibiotic treatment for travelers’ diarrhea [4, 5]. Both clinical trials were randomized, double-blind clinical trials. In both of these clinical trials, the time between initiation of therapy and passage of the last unformed stool and the number of unformed stools passed during the 4-day follow-up period were found to be similar [4, 5]. In our study, the percentages of subjects receiving either antibiotic regimen were similar between the 2 diet intervention groups. Thus, we do not believe that the results of this study are influenced by the antibiotics received by the subjects.

Few dietary recommendations, aside from oral rehydration solutions [10], exist in the treatment of acute diarrhea. The only consensus about diet is the primary need for fluid intake and consumption of at least a limited number of calories [11–15]. Study of major dietary changes on the course of travelers’ diarrhea in otherwise healthy adult travelers is lacking.

In our study, the restricted diet initially focused on clear fluids and simple carbohydrates and did not include dairy products, fatty foods, spicy foods, and complex carbohydrates. Recommendations have been made for patients to avoid dairy products for the first 2 days of illness, owing to small bowel mucosal inflammation and resultant transient lactase deficiency that can perpetuate diarrhea-associated symptoms when dairy products are consumed [6]. Fatty foods may stimulate secretion of bile. In diarrheal illness, bile salts, which are normally absorbed in the terminal ileum, may be washed past the terminal ileum into the colon, where they stimulate secretion of water.

<table>
<thead>
<tr>
<th>Table 1. An intent-to-treat comparison of clinical symptoms of acute diarrhea at baseline (hour 0), and 24 and 48 h after students were treated with an antimicrobial agent and assigned to a restricted or an unrestricted diet.</th>
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</thead>
<tbody>
<tr>
<td><strong>Symptom, hours after treatment</strong></td>
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<tr>
<td><strong>Mean symptom index</strong></td>
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<tr>
<td>Abdominal pain</td>
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<td>0</td>
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<td>48</td>
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<tr>
<td>Gas</td>
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<td>0</td>
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<td>48</td>
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<td>Nausea</td>
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<td>Tenesmus</td>
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<td>48</td>
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**NOTE.** Only subjects experiencing a symptom were included in the baseline, 24-h, and 48-h calculations. For illustrative purposes, the mean index scores were calculated by scoring no symptom as 0, mild as 1, moderate as 2, and severe as 3.
and sodium. Unabsorbed hydroxy fatty acids can cause physiologi-cal states that are similar to those of fatty foods in patients with diarrheal illness [7]. Complex carbohydrates may resist digestion in the small bowel during diarrheal illness and may serve as substrates for colonic bacteria, leading to an osmotic load, and then as cathartics.

In conclusion, our study showed no obvious benefit of a restricted diet in the treatment of acute travelers’ diarrhea among those receiving an antimicrobial agent. We believe that patients who develop acute travelers’ diarrhea should be encouraged to eat if they are hungry. Food intake during diarrheal illness is important to allow for enterocyte repair, regeneration, and intestinal recovery from the inflammatory process [8, 16]. Early feeding has not been shown to prolong diarrhea [6]. Although temporary fasting and restricted diet seems logical when diarrhea is associated with excessive nausea and vomiting, adequate oral fluid intake is necessary to prevent dehydration. Data from one study, however, underscores how use of ad lib fluid intake, as opposed to oral rehydration solution, is sufficient in the treatment of acute travelers’ diarrhea for adults who are also receiving the antisecretory and antimotility drug loperamide [17]. Data from other studies suggest that supplementation with zinc [18] and dietary nucleotides [19] may be of benefit in diarrheal illness. In the future, studies might examine specific foods (e.g., complex carbohydrates [20]) in the nonspecific treatment of acute travelers’ diarrhea to determine whether the incidence of persistent diarrhea owing to poor enterocyte repair can be decreased by dietary means.

Acknowledgments

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References