OCCURRENCE AND SELF-TREATMENT OF DIARRHEA IN A LARGE COHORT OF AMERICANS TRAVELING TO DEVELOPING COUNTRIES

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Abstract. There is little information available regarding traveler’s diarrhea that affects a large number of Americans who differ widely in age and travel destination, and little or no information exists on self-treatment. This paper describes the clinical features, self-treatment, and outcome of diarrhea in 784 (95% follow-up) Americans who traveled for ≥ 90 days, and who received detailed pre-travel advice. Diarrhea was reported by 46%. Of these, 34% (n = 270) had traveler’s diarrhea (TD) defined as ≥ 3 unformed stools/day ± enteric symptoms or < 3 stools/day with ≥ 1 enteric symptom, and 11% (n = 88) had loose motions (LM). Diarrhea was often severe and nearly a quarter of people with TD experienced fever and vomiting and 35% were required to alter their plans. The duration of travel and the destination itself were the strongest influences on diarrhea. Most travelers treated the illness themselves, whether or not they had LM (72%) or TD (83%). Those with LM took an antimotility agent or bismuth subsalicylate alone more frequently than those with TD (71% versus 48%, P < 0.002). Conversely, antibiotics were taken more frequently by those with TD (47% versus 27%, P < 0.03). Overall, 83% indicated self-treatment was effective (91% with LM and 80% with TD). Diarrhea is common despite pre-travel advice. Because travelers usually treat themselves, they should be provided with clear instructions on appropriate self-treatment.

INTRODUCTION

Diarrhea is the most common illness in visitors to developing countries, affecting 20 to 50% of these travelers.1–3 Most studies of traveler’s diarrhea in Americans have been carried out on small numbers of people going to single destinations and have focused on the clinical features, etiology, or treatment in specific protocols.6,7 There is little information on diarrhea in a large number of American travelers who differ widely in age and travel destination. In addition, the effect of pre-travel advice on the prevention of diarrhea, and the behavior of travelers when they become ill have not been adequately addressed. This information would help health care providers dispense appropriate advice. This study describes the clinical characteristics and self-treatment of diarrhea in a large group of American travelers.

MATERIALS AND METHODS

From June 1989 through May 1991, all persons attending the International Traveler’s Medical Service at the University of Connecticut Health Center who were traveling to developing countries for ≥ 90 days were asked to participate in a study examining their health during and after travel.9 Those who consented agreed to complete a brief health questionnaire in the form of a post card with yes/no answers and to return it within two weeks after their trip. Travelers who either did not return the card or who indicated that they had been ill during travel were contacted by telephone and interviewed using standard questions to define the nature of any illness and its treatment. The information on persons who reported diarrhea was separately analyzed for this paper. The study was approved by the University of Connecticut School of Medicine Institutional Review Board.

During the pre-travel visit, each traveler was given detailed counseling and written instructions on the prevention and empiric therapy of traveler’s diarrhea according to accepted guidelines.1,8,10 All travelers were seen by the author. They were instructed to avoid diarrhea by exercising caution in the selection of foods and beverages. If they developed diarrhea they were advised to treat it by maintaining hydration with potable liquids, to use an antimotility agent if diarrhea was interfering with their plans, and to use an antibiotic if diarrhea was persistent or disabling.

Each traveler was offered prescriptions for an antimotility agent and an antibiotic. Eighty-nine percent chose to carry both, 8% chose an antimotility agent alone, and the remaining 3% received preventive advice alone or had been provided medications by their primary physicians. Medications were to be taken only in the event of diarrhea; no traveler was given prophylactic antibiotics. The antibiotics prescribed were norfloxacin (n = 350), ciprofloxacin (n = 15), trimethoprim (TMP) (n = 306), trimethoprim/sulfamethoxazole (TMP/SMX) (n = 19), and other (n = 6). Over the two years there was a gradual switch from trimethoprim-based regimens to quinolones, because of increasing enteric bacterial resistance.11 Loperamide (n = 747) was given most frequently as the antimotility agent; the remainder received atropine/diphenoxylate (n = 12).

Diarrhea was divided into two groups: traveler’s diarrhea (TD) and loose motions (LM).1,7 Traveler’s diarrhea was strictly defined as ≥ 3 unformed stools per 24 hours with or without an additional symptom of enteric illness such as cramping, vomiting, fever or blood, or < 3 stools per day with one or more of the enteric symptoms. Those who did not meet this definition had diarrhea characterized as LM.

Information was entered into a database (File Maker, Claris Corporation, Santa Clara, CA) and analyzed. Comparisons between groups were evaluated with a Student’s two-tailed t-test for independent means. For analysis of factors influencing the chance of developing diarrhea, a logistic regression model was developed. Analysis of this was carried out using the SAS data analysis package (SAS Institute Inc, Cary, NC).12

RESULTS

Patient demographics. The patient population is presented in Table 1. Eight hundred and sixty nine patients were enrolled, and follow-up was obtained on 822 (95%). Thirty
eight of these never traveled, leaving 784 who are described. Travelers were contacted a mean ± standard deviation (SD) of 18 ± 16 days after return from their trip. They represented a wide age range, and most traveled for less than 3 weeks, with a median duration of 19 days (mean 23.5 days). The most frequent chronic medical conditions present in 29% of travelers were hypertension, hypothyroidism, and disorders of the gastrointestinal system. Although 123 countries were visited, travel to 15 countries (Kenya, India, Nepal, Thailand, Tanzania, Brazil, Ghana, Ecuador, Egypt, Guatemala, Hong Kong, Singapore, Peru, Indonesia, and South Africa) accounted for 58% of all travel. An average of 1.9 countries (range 1 to 9) was visited per traveler. Travelers seen since January 1997 are very similar to the study group (data not shown).

**Clinical characteristics of diarrhea.** Diarrhea was the most common health complaint, and was reported by 358 or 46% of all travelers, and by 72% of the 501 persons who experienced an illness. Of these, there were 270 (34% of all travelers) whose illness met the strict definition for traveler’s diarrhea and 88 (11%) who had loose motions. Thirty-eight travelers (38/358; 11%) experienced more than one episode of diarrhea. The first episode is analyzed for this study.

The clinical characteristics of diarrhea are described in Table 2. Diarrhea began nearly 10 days (median 7 days) after arrival. Eighty-two percent of episodes began in the first two weeks of travel and only 3% of episodes occurred after 30 days. Patients had nearly 4 stools per day and diarrhea lasted a mean of 4 days (median 2 days). The 27% of travelers who altered their activities because of diarrhea usually remained in bed or their hotel room for 1 day or less.

A comparison between those with traveler’s diarrhea and those with loose motions is also illustrated in Table 2. By definition, patients with TD were more severely ill in terms of stools per day and associated symptoms. Nearly a quarter of patients with TD had vomiting and fever. In addition, stools were more frequently watery and all but one of the travelers who altered their activity because of illness (95/96), fell into the group with TD. Within the group with TD there was a subgroup of 21 travelers (2/270, 8%) with a syndrome of abrupt onset and short duration, consistent with acute food poisoning. Their symptoms were watery diarrhea with vomiting (100%), fever (71%), and cramping (76%), that lasted 1.2 ± 0.7 days.

**Factors influencing the development of diarrhea.** Selected risk factors for the development of diarrhea were evaluated in a logistic regression model. Five variables were studied: destination (defined as region of the world), duration of travel, age, gender, and underlying medical condition. The development of diarrhea was compared for persons who traveled to a certain destination (alone or as part of a multi-destination journey), versus those who did not travel to that destination.

Figure 1 shows the odds ratio for the development of all types of diarrhea by region visited. Travel to northern Africa more than doubled the risk of diarrhea (59% of travelers became ill), and travel to the Indian subcontinent increased it by 51% (56% of travelers became ill). On the other hand, travel to the Caribbean area (26% developed diarrhea) or to southern Africa (23% developed diarrhea) was found to be

![Figure 1](image-url)
relatively protective. When the risk of TD was also examined by region visited, the findings were very similar (data not shown).

Duration of travel significantly influenced development of diarrhea ($P < 0.001$ for all destinations). Depending upon region visited, each additional day of travel increased the chance of diarrhea between 1.6% and 1.8%. Forty-two percent of persons traveling for three weeks or less developed diarrhea, 47% of those traveling 22 to 30 days, and 56% of those traveling more than 30 days ($P < 0.005$). In addition, those who had more than one episode of diarrhea traveled longer than travelers with a single episode (median 39 days versus 20 days $P < 0.001$), and 61% traveled for more than a month.

Increasing age was found to be significantly protective for most destinations, and, overall, each additional year of age decreased the chances of diarrhea by 0.9%. There was no significant difference between males and females (43.4% versus 47.5%), nor did underlying medical conditions affect the risk; 42.2% of those with underlying medical illness developed diarrhea versus 47.0% of those without a disorder.

Diarrhea in children aged 10 and under ($n = 13$) was more severe than diarrhea in all other ages in terms of the frequency of vomiting (46% versus 17%, $P < 0.05$), and the use of medical care (39% versus 4%, $P < 0.005$). Activities were also more frequently altered (46% versus 26%) although this did not reach statistical significance.

**Self-treatment of diarrhea.** Table 3 indicates the treatment exercised by ill travelers. Eighty percent (288/358) of those with diarrhea treated themselves with medications, and those with TD treated themselves slightly more often than those with LM (83% versus 72%). The types of medications used, however, differed. Those with LM used an antimotility agent or bismuth subsalicylate alone significantly more often than those with TD, 71% versus 48%. Conversely, antibiotics (either alone or with an antimotility agent) were taken more frequently in the group with TD, 45% versus 27% ($P < 0.02$), and 86% of all antibiotic use was in patients with TD. Overall, one-third of those with diarrhea took an antibiotic; of these 33% ($n = 39$) took an antibiotic alone and 67% ($n = 80$) combined it with an antimotility agent. All patients who sought medical care for diarrhea had TD.

Significant differences between those who used any type of treatment and those who did not were older age (43.2 years versus 36.4 years, $P = 0.03$) and the presence of cramps (37.5% versus 17.1%, $P = 0.002$).

There were 19 travelers who sought medical care for diarrhea. They were significantly younger than the group as a whole (28.7 years, $P < 0.001$), and 5 of the 19 (26%) were ≤12 years old. Their illness was more severe (all $P < 0.04$) than those who did not seek medical care, with 63% experiencing cramps, 58% vomiting, and 37% fever. Care was sought in 12 countries, but 26% of the medical visits took place in India. Most travelers obtained care from a local physician ($n = 15$); two sought care in their hotel, and one each on a cruise ship and from a pharmacy. Thirteen were treated with standard medications, and 6 with unknown medications.

When travelers were asked if the treatment they took improved their illness, 82% (227/276) reported that it did. The duration of diarrhea in those who indicated that treatment was effective was shorter (median 2 days) than in those who indicated it was not (median 6 days, $P < 0.001$), and activities were altered less frequently (25% versus 47%, $P < 0.04$). Those with LM indicated that treatment worked slightly more often than those who experienced TD, 91% (53/58) versus 80% (174/218). When the response was examined by regimen taken (antimotility agent alone, antibiotic alone, or antibiotic plus antimotility agent), persons with LM reported that each treatment was highly effective. Persons who experienced TD also reported no difference among regimens: 88% (84/95) response for an antimotility agent alone, 79% (26/33) response for an antibiotic alone, and 81% (54/67) response for an antimotility agent and an antibiotic. Although the numbers were small, when the response in persons with TD was analyzed by class of antibiotic, TMP or TMP/SMX alone was relatively ineffective, with a 55% (6/11) response, but improved to 84% (26/31) when the regimens contained an antimotility agent. For those taking quinolones alone there was a 95% response (18/19), and an 83% response (25/30) when an antimotility agent was also taken. Unknown or other types of medications (29% response, 4/14) and medical care were not considered effective (53% response, 10/19).

**DISCUSSION**

This study examines the incidence, clinical characteristics, and treatment of diarrhea in a large cohort of American travelers who differed widely in demographics, travel destination, and season of travel. Despite pre-travel advice on avoidance measures, diarrhea occurred in 46% of travelers, although a smaller number, 34%, suffered from the more narrowly defined traveler’s diarrhea. When travelers experienced diarrhea, 80% choose to treat themselves no matter whether or not their illness was mild or more severe.

Although the incidence of diarrhea was similar to that recorded in other studies, it was surprising that it was so high in a group which had received uniform pre-travel counseling with written advice. It indicates the difficulty of avoiding contaminated foods and liquids in developing countries which may be because the traveler makes mistakes in dietary selection in spite of advice because there is frequent contamination, or because those who seek pre-

**Table 3**

<table>
<thead>
<tr>
<th>Self-treatment of diarrhea by travelers</th>
<th>Traveler’s diarrhea%(n)</th>
<th>Loose motions%(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any treatment</td>
<td>83 (225/270)</td>
<td>72 (63/88)</td>
</tr>
<tr>
<td>Type of treatment†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimotility agent or bismuth</td>
<td>48 (109)‡</td>
<td>71 (45)</td>
</tr>
<tr>
<td>subsalicylate alone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic alone</td>
<td>15 (34)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Antibiotic with antimotility agent</td>
<td>30 (68)</td>
<td>19 (12)</td>
</tr>
<tr>
<td>Unknown or other§</td>
<td>6 (14)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Sought medical care</td>
<td>8 (19)</td>
<td>0</td>
</tr>
</tbody>
</table>

* $P < 0.03$ compared with loose motions.
† Percentages are of those who took any treatment.
‡ $P = 0.002$ compared with loose motions.
§ A different class of medication or unknown type.
travel care from a travel medicine specialist undertake higher risk travel.\textsuperscript{19} The typical clinical syndrome for all cases of diarrhea began within the first 10 days of travel and was characterized by three to four watery stools per day, frequently with cramping, fever, and vomiting, and lasted three to four days. Over a quarter of all cases of diarrhea and more than a third of those with TD had to alter their activities because of illness. Although this study was based on recall, which may lead to remembering more severe illness, other studies have also noted the relative severity of diarrhea. In those studies, 11\% to 32\% have experienced vomiting and 21\% to 45\% altered activities.\textsuperscript{5,6,14,15,20}

Factors which significantly influenced the development of diarrhea were duration of travel, destination, and age. Duration was the strongest influence and each day of travel increased the risk of diarrhea by nearly 2\% across all regions visited. The influence of duration was also noted for the 5\% of travelers who experienced more than one episode of diarrhea; 61\% of these had traveled for more than a month. This indicates a cumulative risk of diarrhea during travel, and differs from other studies which have suggested decreased risk, at least from enterotoxigenic Escherichia coli, with longer duration of stay.\textsuperscript{14,22} Although regional differences in incidence were noted, it is most important to focus on prevention and treatment of diarrhea, no matter which region a traveler plans to visit.

Increasing age was relatively protective against diarrhea for most destinations, with each year of age decreasing risk by about 1\%. The increased incidence in younger age groups has been noted,\textsuperscript{14,21} and could be because of more risky dietary habits of younger travelers, or possibly because of the presence of some immunity in older travelers. Although there were only a few children under the age of 10 years, their diarrhea was more severe in terms of vomiting, altered plans, and the need to seek medical care. Traveler’s diarrhea in the pediatric age group has not been studied adequately.\textsuperscript{23} Instructions to families traveling with children should include strict adherence to dietary precautions, carrying oral rehydration salts, knowing how to access effective medical care, and possibly carrying antimicrobials.\textsuperscript{1}

The division of diarrhea into two groups, those with traveler’s diarrhea and those with loose motions, allowed stratification according to severity. Patients suffering from TD were almost exclusively the patients who had to alter their activity because of illness, and who sought medical care. This is similar to the findings of Steffen and others in tourists to Jamaica in whom more than 95\% of those seeking medical care or who were incapacitated, experienced classic or moderate traveler’s diarrhea corresponding to TD in this study.\textsuperscript{14}

This study is the first to examine the behavior of travelers when they develop diarrhea. Eighty percent of travelers chose to take medications regardless of the severity of the diarrhea. In another study, 77\% of 62 travelers used treatments,\textsuperscript{24} and in a survey of visitors to Jamaica, 28\% to 43\% of those who had TD took medications compared with 15\% of those with I.M.\textsuperscript{14} In this latter study, it is not known how many carried self-treatment medications. For the most part our travelers used medications according to the recommendations given to them at their pre-travel visit. They generally treated mild illness (LM) with symptomatic measures and reserved antibiotics for worse symptoms; 86\% of antibiotic use was in persons with TD.

Although the efficacy of their interventions was evaluated subjectively, it provides important information about what travelers consider helpful. Most travelers, particularly those with LM, felt their treatment was effective, whether it consisted of antimotility agents alone, antibiotics alone, or a combination. However, for persons with TD who took antibiotics alone, quinolones were significantly better than TMP or TMP/SMX. This is probably because of the resistance of enteric bacteria to TMP and TMP/SMX which was developing during the 1980s and early 1990s when this study was carried out.\textsuperscript{11,25} And, although the sequence of taking an antimotility agent and an antibiotic was not known, the results in our travelers of combination treatment are similar to other published results. There was an apparent benefit of an antimotility agent (usually loperamide) when the antibiotic was TMP or TMP/SMX,\textsuperscript{26} but results were mixed when it was a quinolone.\textsuperscript{26–28} Quinolones are now recommended for self-treatment of traveler’s diarrhea in most areas of the world,\textsuperscript{29} although quinolone resistance is documented, particularly with Campylobacter in Southeast Asia.\textsuperscript{25}

Finally, there were two groups for whom therapy was not effective: those who took unknown or other types of medications and those who sought medical care. It is important that travelers know and record any medication they take and are familiar with procedures needed to access safe and effective medical care.

Careful pre-travel counseling will not always prevent traveler’s diarrhea. Nevertheless, travelers should be encouraged to comply with avoidance measures to prevent an illness which can be severe and adversely impact their plans. In addition, since most travelers are likely to take medications for all forms of diarrhea, it is important to be clear on the instructions for their use, using symptomatic therapy alone for mild illness and usually reserving antibiotics for moderate to severe diarrhea.

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