Gastrointestinal Prophylaxis in Sports Medicine

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Context: Because sports participation at all levels often requires international travel, coaches, athletic trainers, and team physicians must effectively protect athletes from gastrointestinal infections. Traveler's diarrhea is the most common travel-related illness and can significantly interfere with training and performance.

Evidence Acquisition: A review of relevant publications was completed using PubMed and Google Scholar.

Study Design: Clinical review.

Level of Evidence: Level 5

Results: Enterotoxigenic and enteroaggregative *Escherichia coli* are the most common bacterial causes of traveler's diarrhea. Traveler's diarrhea generally occurs within 4 days of arrival, and symptoms tend to resolve within 5 days of onset. There are several prophylactic agents that physicians can recommend to athletes, including antibiotics, bismuth subsalicylate, and probiotics; however, each has its own unique limitations. Decision-making should be based on the athlete's destination, length of stay, and intent of travel.

Conclusion: Prophylaxis with antibiotics is highly effective; however, physicians should be hesitant to prescribe medication due to the side effects and risks for creating antibiotic-resistant bacterial strains. Antibiotics may be indicated for high-risk groups, such as those with a baseline disease or travelers who have little flexible time. Since most cases of traveler's diarrhea are caused by food and/or water contamination, all athletes should be educated on the appropriate food and water consumption safety measures prior to travel.

Keywords: traveler's diarrhea; athlete health; sports; gastrointestinal illness; prophylaxis

Sports participation at all levels often requires frequent international travel for training and competition. Athletes of every age must travel across multiple time zones and continents, encountering a variety of obstacles, including jet lag, climate and altitude changes, and dietary challenges, that may negatively affect athletic performance.[23] Coaches and medical staff have a responsibility to ensure that the appropriate precautions are taken to prevent illness and optimize athletic performance during international travel.[18]

Acute diarrhea is the most common travel-related illness, affecting more than half of those who travel from developed countries to developing countries.[3,14] Traveler's diarrhea (TD) is defined as having 3 or more unformed stools within a 24-hour period, paired with at least 1 enteric symptom such as vomiting, abdominal pain, nausea, or fever.[9,21,33] TD is particularly distressing for athletes because it can affect their ability to train and their performance during competition. Steffen et al[33] found that the onset of TD occurs early during a stay abroad, typically within 4 days of arrival.[3] The duration of TD is usually short, and symptoms tend to resolve fully within 3 to 5 days of onset.[29] However, TD may result in multiple episodes of vomiting and diarrhea per day, leading to severe dehydration and significantly limiting physical activity.[12] Athletes may experience total incapacitation for up to 1 to 2 days, causing significant loss of training time and poor performance while competing abroad.

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The authors report no potential conflicts of interest in the development and publication of this article.

DOI: 10.1177/1941738117732733

INCIDENCE

The incidence of TD varies with destination. The Centers for Disease Control and Prevention (CDC) categorize world regions by risk of contracting TD.[5] Low-risk countries include developed countries, such as the United States, Canada, Australia, New Zealand, Japan, and countries in Northern and Western Europe. Intermediate-risk countries include those in Eastern Europe, South Africa, and some of the Caribbean islands. High-risk countries include most of Asia, the Middle East, Africa, and Central and South America.[5]

Steffen et al[32] found that the incidence of TD doubled during travel to India and Kenya compared with intermediate-risk destinations such as Jamaica and Brazil. Incidence of TD is also high in individuals traveling from other developed areas. In a 1991 study of 296 Canadian travelers, more than 50% of individuals reported some form of diarrhea after traveling to a high-risk country.[4] Similarly, a 1980 study by Guerrant et al[13] of North American students traveling to Latin America found that 71% of the students contracted diarrhea. The incidence of TD may be lower among competitive athletes. A 2009 study of elite British athletes traveling to the 2008 Youth Commonwealth Games in India found that 20% (24/122) of team members contracted TD.[37]

ETIOLOGY

The origin of TD varies with geographic region; however, the most common causes are bacterial and viral due to the ingestion of food and beverages that are contaminated with fecal matter.[9,12,24] Global etiological studies have found enterotoxigenic *Escherichia coli* and enteroaggregative *E coli* to be the most common bacterial pathogens associated with TD.[27] In a study of 21 individuals traveling to Mexico from the United States, Canada, and Europe who contracted diarrhea, 81% of stool samples contained a toxic form of *E coli* and no other pathogenic bacteria.[21] *Campylobacter* is also a common bacterial cause of TD, with reported cases caused by travel to countries such as Thailand, Spain, Turkey, Morocco, and India.[7]

Enteric viruses, such as norovirus and rotavirus, account for approximately 5% to 10% of TD cases.[38] A study of 124 students who traveled from the United States to Guadalajara and acquired diarrhea during the trip showed that 69% of students were infected with norovirus.[19] In addition, infection by parasites such as *Cryptosporidium* may be the cause of approximately 10% of TD cases.[22,28]

PROPHYLAXIS

Antibiotics

Although highly effective in the prevention of TD, antibiotic prophylaxis should be used with caution due to the risk of creating drug-resistant organisms and long-term complications.[3] The 1985 Consensus Conference at the National Institute of Health concluded that despite the excellent protection rates of antibiotics against TD, routine administration of antibiotics should not be recommended to healthy travelers who wish to avoid TD.[24] Previous studies examining the cost effectiveness of antibiotic chemoprophylaxis for TD support the conclusions of the 1985 Consensus Conference and recommend against prophylaxis; however, an exception may be considered for high-risk groups such as travelers with severe baseline disease, politicians, athletes, or performers who have little flexible time.[1,12,25,36]

Prophylaxis with doxycycline (100 mg/d) demonstrated initial effectiveness due to the broad-spectrum coverage of tetracyclines against TD pathogens. Its effectiveness, however, became limited after the evolution of doxycycline-resistant strains of bacteria. Similarly, the effectiveness of other antimicrobials such as trimethoprim-sulfamethoxazole became limited after the evolution of drug-resistant strains and narrowed their application to certain geographic areas and seasons, such as inland Mexico in the summer.[24]

Antibiotic agents, such as fluoroquinolones (norfloxacin, ciprofloxacin, fleroxacin, ofloxacin, and levofloxacin; 200-500 mg daily), remain the drugs of choice when indicated and have been shown to provide up to 90% protection against TD in adults.[1,12,24] Fluoroquinolones are effective because of their excellent safety profile and broad-spectrum coverage against enteropathogenic bacteria.[15,24,26] Heck et al[15] found that taking ciprofloxacin (500 mg daily) for 5 to 14 days during travel to Central and South America provided 85% protective efficacy against TD in a group of American travelers. Similarly, Scott et al[26] found that a 7-day regimen of norfloxacin (400 mg daily) during travel to Egypt provided up to 93% protection against TD in military personnel originating from low-risk countries. Side effects that have been observed with fluoroquinolones include skin rash, vaginal candidiasis, reactions of the central nervous system, phototoxicity, gastrointestinal complaints, and anaphylaxis.[24] Additional concerns for fluoroquinolone prophylaxis and treatment in the athlete population are the risks of disabling and potentially permanent side effects to the tendons, muscles, joints, nerves, and central nervous system that can occur together in the same patient.[2,11] Moreover, fluoroquinolones are not approved to be used for prophylaxis in children and women who are pregnant.[24]

The evolution of fluoroquinolone-resistant bacterial strains has resulted in the development of novel antimicrobial agents. Rifaximin, a broad-spectrum oral antibiotic, is available in Europe, Asia, and Latin America for the treatment of acute bacterial diarrhea and was recently approved in the United States as a therapy for uncomplicated TD.[6] Rifaximin is poorly absorbed in the gut, which increases its intestinal presence, results in high concentrations of the drug directly to the site of enteric infection, and minimizes risk for systemic adverse effects, toxicity, and drug interactions.[35] Side effects of rifaximin that have been previously observed are mild and include dizziness, weakness, and increased gas.[6]

A 2013 randomized controlled trial by Zanger et al[39] found rifaximin (200 mg daily) to have moderate efficacy against TD when traveling to South and Southeast Asia, with 48% protection from departure to 7 days after the trip compared

with placebo. Similarly, a 2012 meta-analysis by Hu et al[16] found that prophylaxis with rifaximin significantly reduced incidence of TD caused by noninvasive enteric pathogens, like enterotoxigenic *E coli*. A 2012 meta-analysis by Alajbegovic et al[1] noted that the effectiveness of fluoroquinolone antibiotics was greater than the efficacy of rifaximin against TD, likely due to its broader spectrum of coverage and the systemic distribution of the drug class. Estimates of fluoroquinolone efficacy against TD were found to be 88%, compared with 77% for rifaximin.[1,6] The moderate effectiveness and minimal side effects of rifaximin may make it an ideal prophylactic agent for athletes when indicated; however, further research is still needed to assess its clinical utility in the prevention of TD, especially in children.[31]

Bismuth Subsalicylate

Athletes may also consider prophylaxis with bismuth subsalicylate, which has a 65% protective efficacy against TD when the substance is administered as 2 tablets 4 times daily (2.1 g/d) for a maximum of 3 weeks while traveling.[12,31] Bismuth subsalicylate is readily available over the counter in both tablet and liquid form and is a relatively inexpensive medication.[29] A randomized double-blind study by Steffen et al[30] compared stool samples of Swiss adults traveling to tropical countries and found a greater prevalence of various bacteria, including enterotoxigenic *E coli*, in subjects taking placebo medication compared with those taking bismuth subsalicylate.

Some travelers may experience mild side effects after taking bismuth subsalicylate, including blackened tongues and stools, nausea, constipation, and tinnitus. Bismuth subsalicylate should be utilized with caution by athletes traveling to countries where malaria is prevalent. Bismuth subsalicylate can deplete the absorption of doxycycline and reduce its circulating levels, which may impact the antibiotic's effectiveness in malaria prophylaxis.[8] Although effective in preventing and treating TD, prophylaxis with bismuth subsalicylate may not be an attractive option for competitive athletes with limited time and/or schedule flexibility because of the large quantity of tablets and high frequency of consumption, which may reduce protocol compliance.[24,29]

Other Prophylaxis

Water and Food Safety

Since most cases of TD are caused by ingesting contaminated food and/or water, athletes can take several hygiene measures to reduce their risk of contracting illness during international travel.[3,12] Consuming iced beverages and water from unknown sources are known risk factors for the development of diarrhea.[17,29] Iced beverages may pose a significant risk to traveling athletes because freezing may preserve pathogens that may be present in the water. Also, avoiding soda from a soda fountain/machine is important as the water used is usually from the tap; soda directly from a sealed can or bottle is the better choice. Proper hygiene measures for water consumption include drinking carbonated bottled water, boiling tap water vigorously, and ensuring purchased bottles and cans are unopened.[29]

Food is a major source of many enteropathogens, including enterotoxigenic *E coli*.[10] Athletes should avoid high-risk foods such as fresh fruit and vegetable juices, fresh salads, unpasteurized dairy products, open buffets, undercooked meats, condiments, and food from street vendors. Low-risk foods that may be safe to consume include thoroughly cooked hot meals, dry food products, and self-peeled fruits and vegetables.[29]

There is little evidence that food and water precautions decrease the incidence of TD. It is more probable that factors outside of the athlete's control, such as poor restaurant hygiene, contribute to the risk of illness.[28] Despite this, traveling athletes should be aware of the appropriate hygiene measures.

Probiotics

The use of probiotic substances may be an attractive prophylactic alternative for athletes because of their lack of toxicity and drug interactions; however, no probiotic medication has been found to provide clinically relevant worldwide protection against TD.[24] A 2005 meta-analysis of 12 studies examining the use of probiotics for TD prevention concluded that several probiotics, including *Saccharomyces boulardii* and a mixture of *Lactobacillus acidophilus* and *Bifidobacterium bifidum*, had minimal, but significant, protective efficacies.[20] In contrast, a meta-analysis of 5 randomized controlled trials showed that probiotics had no effect in preventing TD.[34] Before definitive recommendations about the prophylactic use of probiotics can be made to athletes, additional high-quality trials are needed to assess their effectiveness.[12,34]

CONCLUSION AND RECOMMENDATIONS

Traveler's diarrhea affects more than half of people who travel from developed to developing countries and is characterized by having 3 or more loose stools over a 24-hour period accompanied by enteric symptoms. TD generally occurs within 4 days of arrival and resolves within 3 to 5 days of onset. The incidence of TD varies by destination, and the CDC has developed a classification system categorizing regions of the world by risk or contracting the illness. Prophylaxis with antibiotics is highly effective; however, physicians should be hesitant to prescribe medications because of their side effects and the risk of creating antibiotic-resistant bacterial strains. Antibiotics may be indicated for high-risk groups, such as those with a baseline disease or travelers who have little flexible time; however, careful evaluation of antibiotic choice is essential in athletes especially because of the tendon risk profile of fluoroquinolones—the most effective TD prophylaxis. Since most cases of TD are caused by food and/or water contamination, all athletes should be educated on the appropriate food and water consumption safety measures prior to travel.

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