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Review Article

Prophylaxis, diagnosis, and treatment of Traveler's diarrhea

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ABSTRACT

Evidence still indicates that traveler's diarrhea might have unpleasant consequences over the affected patients' time and health, and can increase the frequency of hospitalization and other health-related parameters. As a result of the newly developing serious issues about the resistance of bacteria to the different antibiotics, the management guidelines of traveler's diarrhea are frequently changing based on this new data to ensure that proper management is delivered to the affected patients and enhance the healthcare practices. In the present literature review, we have discussed the diagnosis, treatment, and prophylaxis against traveler's diarrhea based on evidence from the current investigations in the literature. The diagnosis of the condition is mainly based on the presence of symptoms suggestive of gastroenteritis, and having a travel history to an endemic country. Besides, cultures might be needed in certain situations to indicate the diagnosis, especially among resistant cases. The best prophylactic approach is to enhance the eating and drinking practices when travelling to endemic countries, in addition to the frequent washing of ingested food by clean water that is obtained from a safe source. The administration of antibiotics is not always recommended, and only moderate and severe cases should be indicated to receive antibiotics based on their clinical evaluation. The administered antibiotics should be based on the resistance and safety profiles among each country to enhance the efficacy of these antibiotics and obtain favorable outcomes.

Keywords: Traveler's diarrhea, Prophylaxis, Treatment, Management, Diagnosis, Evaluation

INTRODUCTION

Reports from global settings indicate that traveler's diarrhea is a serious condition in the past and present that is associated with bad and non-satisfying outcomes over the affected patients.[1] A substantial impact of the condition has been reported among the different affected patients and estimates show that the impact is recently decreasing due to the significant improvements in the

management guidelines and practices among the different clinical settings, in addition to the enhanced hygiene measures among travellers.[2] However, despite the significant improvements, evidence still indicates that traveler's diarrhea might have unpleasant consequences over the affected patients' time and health, and can increase the frequency of hospitalization and other health-related parameters.[1] Therefore, the management of the condition should be critically addressed to enhance the outcomes related to the patient's health.

As a result of the newly developing serious issues about the resistance of bacteria to the different antibiotics, the management guidelines of traveler's diarrhea are frequently changing based on this new data to ensure that proper management is delivered to the affected patients and enhance the healthcare practices.[3,4] In the present study, we aim to discuss the diagnosis, treatment, and prophylaxis against traveler's diarrhea based on data from investigations in the literature.

LITERATURE REVIEW

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 16th September 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, accprding to the database. To avoid missing poetential studies, a further manual search for papers was done through Google scholar while the reference lists of the initially included papers. Papers discussing traveler's diarrhea were screened for useful information. No limitations were posed on date, language, age of participants, or publication type.

DISCUSSION

Diagnosis

Before initiating the treatment plan, an adequate diagnosis of traveler's diarrhea should be established to determine the most appropriate treatment modalities. It has been demonstrated that patients with traveler's diarrhea usually present with symptoms within 1-2 weeks after arrival at their destination, however, estimates also show that this period is not specific. Furthermore, many patients have reported developing similar symptoms shortly after their arrival. A simple definition of traveler's diarrhea to help patients identify these symptoms was introduced to the literature by many investigations. It has been reported as a two-fold increase in the baseline habits of the bowel or the passage of at least 3 loose stools/day.[5] Moreover, it should also be noted that diarrhea is also usually accompanied and precipitated by other symptoms, including fever, abdominal cramps, nausea, and vomiting. Physicians should also ask their patients about other symptoms as the presence of fever, or blood in the stool, and any other associated manifestations. Besides, a thorough travelling history should also be obtained from the affected patients, including the specific timeline of travelling, the amount of consumption of food and fluids and the types that were consumed, any potential sexual exposure, and whether the patient experienced similar manifestations in previous travels.[6,7]

Furthermore, some cases with traveler' diarrhea might also present with diffuse abdominal tenderness on physical examination. Capillary refill and skin turgor should also be approached by physicians to test for the presence of dehydration. High fever, severe abdominal pain, and signs of hypovolemia might also be present in patients suffering from a severe condition. Most cases do not require performing any specific laboratory investigations. However, in some cases that might present with unusual manifestations as hematochezia, high fever, or tenesmus, performing a stool analysis might be indicated in such situations. Fecal leukocytes assessment, stool culture, and lactoferrin are the main related tests for stool examination in these situations. Looking for a parasitic infection should also be established by stool analysis in patients suffering from prolonged manifestations. Besides, evidence also indicates the validity of performing polymerase chain reactions for potentially detecting the presence of certain organisms.[8] However, such approaches are not widely available and are expensive, and therefore, should not always be considered to achieve an adequate diagnosis. In some situations, imaging studies might also be indicated. For instance, X-rays to the ureters, kidney, and bladder can be approached to evidence the potential presence of perforation in severe cases. For further assessment of an intra-abdominal pathology, computed tomography can also be furtherly used for adequate validation.[9]

Prophylaxis

Although antibiotics can be effectively used to intervene against the development of these conditions, misuse of antibiotics is a serious problem that has been associated with resistance of different organisms, leading to serious health problems. Therefore, antibiotics should not be administered by travelers as a prophylactic approach against developing traveler's diarrhea. However, it should be noted that prophylaxis with antibiotics can be administered in high-risk patients that suffer from serious enteric diseases, which might be altered by traveler's diarrhea, and in patients that might suffer from significant morbidity and complications.[10] Antibiotics can also be indicated as a prophylactic approach for patients that might not be able to afford sickness from traveler's diarrhea. However, it should be noted that all individuals should not administer antibiotics until medical advice is obtained regarding the type of the administered antibiotics and the duration of administration to reduce the prevalence and severity of resistance. Using bismuth subsalicylate can also be used as a prophylactic approach that can substitute the administration of antibiotics for traveler's diarrhea. Evidence indicates that the administration of the modality can be associated with a useful effect that might be up to 60% in intervening

against the development of traveler's diarrhea.[11,12] Tinnitus is a rarely reported adverse event to this drug, and little evidence shows that black tongue and stool might be noticed in some cases.[11] Other disadvantages of the modality also include the potential poor compliance due to the frequent dosage system and that the drug is contraindicated in pregnant, children, with aspirin administration, and in patients that are allergic to aspirin.

It should be noted that in cases when antibiotics were indicated, the administration of rifaximin has been recommended.[10] This is because the drug has no systemic effects, and a low resistance profile among most related organisms, in addition to not having remarkable adverse events. The drug has been validated by many previous investigations, and evidence regarding the dosing system has been previously discussed. Furthermore, it should be noted that trials investigating the safety of the drug only assessed the short-term outcome of the disease. Therefore, recommendations indicate that it should not be administered for a longer duration until further evidence has been obtained regarding the validity of safety on a long-term basis. The administration of fluoroquinolones has also be practiced for a long period, however, this is no longer recommended because of the significant adverse events that might be associated with the administration of these antibiotics, in addition to the high risk of the emerging resistance that has been reported with the enteric pathogens. The administration of azithromycin for prophylaxis against traveler's diarrhea is no longer recommended as well since 2017.[10] Other non-pharmacological practices should be implied by traveler's and pharmacists should encourage them to adopt these practices.

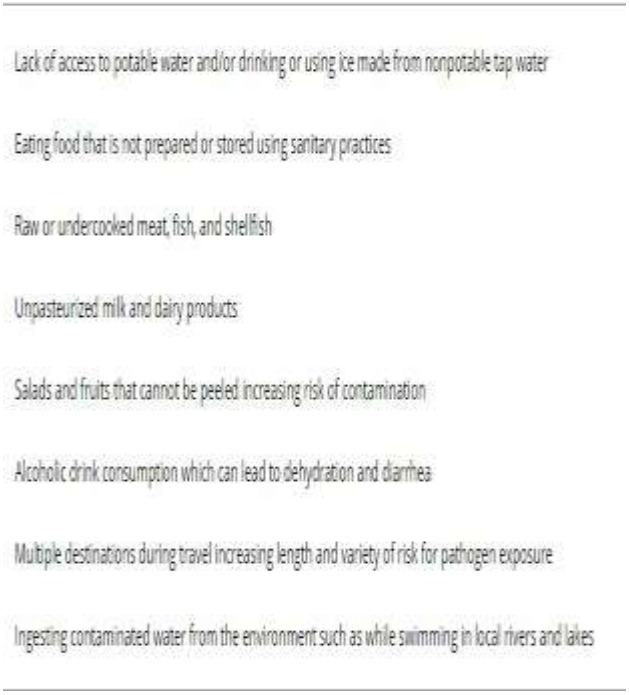

Figure 1: Different risk factors for catching an infection that might cause traveler's diarrhea.[9]

For instance, reduced exposure to the different risk factors of catching an infection (Figure 1), and frequently washing hands, especially before eating, and consumption of healthy food and water are the most important measures that can enhance prophylaxis. Washing hands should be done with warm water and soup and with frequent use of alcohol. Food should also be properly cooked, and unknown sources of food and fluids should be avoided. For instance, buying sealed commercial water bottles should be a safe approach for travelers to drink and use water for other food-related activities rather than local water.[13,14] Other preventive measures are presented in Figure 2.

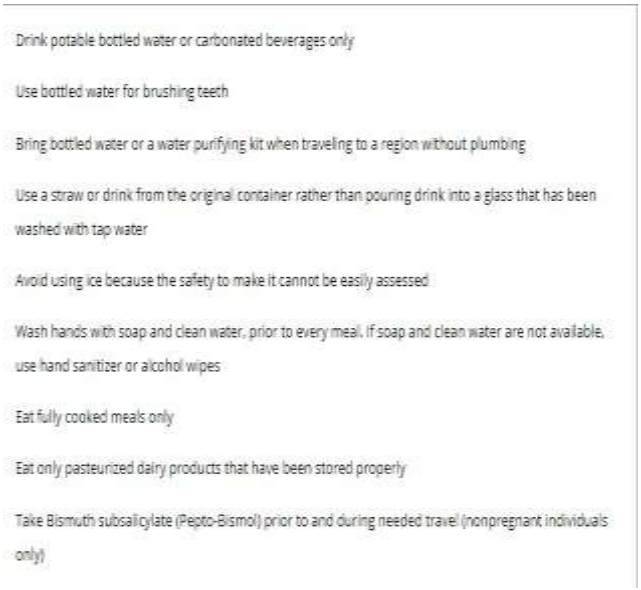

Figure 2: Prevention measures to reduce the risk of developing traveler's diarrhea.[9]

Treatment

Among the studies in the literature, the treatment of traveler's diarrhea has been divided into different plans for mild, moderate, and severe cases. For mild cases, recommendations suggested that the administration of antibiotics should be avoided. Instead, supportive management should be adequately applied. For instance, rehydration and antimotility medications can be administered. Previous studies have demonstrated that loperamide can be effectively used to reduce the duration of diarrhea.[15,16] Although weak evidence previously contraindicated the administration of this drug because it might intervene against the passing of pathogens from the gut, many studies have demonstrated its efficacy and safety.[17,18] The use of bismuth subsalicylate and loperamide has been adequately validated, and evidence supports that the latter is superior to the former.[15] Besides, other modalities like activated charcoal are not recommended over loperamide. However, it should be noted that antibiotics should be administered in cases when symptoms are not relieved and are progressively becoming more apparent. In moderate cases, antibiotics

can be prescribed, regardless of loperamide therapy, and other supportive management modalities were prescribed to the affected patients. It has been demonstrated that the administration of antibiotics in these situations can effectively reduce the duration of illness up to 36 hours, and further evidence also shows that the duration can be reduced to 12 hours only in cases when loperamide was combined in the management modality.[19-21] However, it should be noted that the administration of antibiotics should be done based on the specific guidelines that regulate the administration of these modalities based on a case-by-case analysis to reduce the potential complications, which might even worsen the prognosis of the condition, and also to reduce the risk of resistance. Evidence indicates that fluoroquinolones can still be effectively used for moderate cases, irrespective of the increasing evidence that supports the resistance against these modalities.[22] However, these antibiotics should not be used in certain areas, including South Asia, where the modalities are not clinically beneficial due to the high resistance rates.[1] Accordingly, azithromycin has been demonstrated as an effective alternative to fluoroquinolones, with a reported similar efficacy between both of these modalities in managing moderate cases of traveler's diarrhea.[19] It should also be noted that the administration of azithromycin can be used as the first line of treatment in severe cases. In addition to its reported efficacy, azithromycin also has a low resistance profile globally in most countries , and it is safer than fluoroquinolones despite some complications as prolonged QT interval might be associated.[23] Rifaximin was also described in the literature as a safe and efficacious modality that can be used as an alternative drug to fluoroquinolones in cases with moderate traveler's diarrhea. However, it should be noted that the drug is not widely available in many countries and is not very effective against some invasive pathogens.[24] Among the different cases suffering from severe traveler's diarrhea, it has been demonstrated that the administration of azithromycin is recommended in these situations because of the reduced resistance and high safety profiles among the different worldwide reports.[25,26] The administration of the modality should be based on a single-dose administration, and studies indicate that it should be continued for at least three days when symptoms persist. Therefore, clinicians and pharmacists should urge their patients to administer the complete course of the antibiotic based on the recent guidelines. It has been furtherly demonstrated that the administration of fluoroquinolones can also be done in some severe cases that are non-dysenteric and are not detected in South Asia.[27] Rifaximin was also reported to have some efficacy against relevant pathogens causing non-dysenteric severe traveler's diarrhea. However, it should be administered in certain countries that do not have a high resistance rate against this antibiotic. However, it should be noted that the modality is not widely available among the different clinical settings, and therefore, alternatives should be used. Furthermore, evidence also indicates that the administration of antibiotics alone does not significantly enhance the outcomes as compared with the administration of combination therapy of antibiotics with loperamide. It should be noted that using this combination is not favorable in cases when dysentery is associated.[10]

CONCLUSION

The diagnosis of the condition is mainly based on the presence of symptoms suggestive of gastroenteritis, and having a travel history to an endemic country. Besides, cultures might be needed in certain situations to indicate the diagnosis, especially among resistant cases. The best prophylactic approach is to enhance the eating and drinking practices when travelling to endemic countries, in addition to the frequent washing of ingested food by clean water that is obtained from a safe source. The administration of antibiotics is not always recommended, and only moderate and severe cases should be indicated to receive antibiotics based on their clinical evaluation. The administered antibiotics should be based on the resistance and safety profiles among each country to enhance the efficacy of these antibiotics and obtain favorable outcomes.

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