

APPLICABILITY OF PROBIOTICS IN DIARRHEAL SYNDROMES: WHAT DOES THE EVIDENCE SAY?

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Abstract: Probiotics are live microorganisms beneficial to health, which can be used as food supplements or added to foods such as yogurt and fermented milk. Probiotics are classified into different types, such as Lactobacillus and Bifidobacterium species, and act in different ways, such as colonizing the gastrointestinal tract, modulating the intestinal microbiota and stimulating the immune system. Probiotics have been widely studied in relation to their use in the treatment of several syndromes, such as acute and chronic diarrhea, irritable bowel syndrome, celiac disease, Crohn's disease and ulcerative colitis. In acute diarrhea, probiotics have been shown to be effective in reducing the duration of diarrhea and decreasing the number of bowel movements. In chronic diarrhea, probiotics have also shown positive effects in reducing symptoms and improving patients' quality of life. In irritable bowel syndrome, probiotics have been studied as a promising alternative to conventional treatment, due to their ability to modulate the intestinal microbiota and reduce inflammation. In celiac disease, probiotics have been investigated as a possible way to improve gluten tolerance and reduce intestinal inflammation. In Crohn's disease and ulcerative colitis, probiotics have been studied as a way to reduce intestinal inflammation and improve the body's immune response. Thus, studies show that the use of probiotics is safe and can bring significant benefits to patients with different syndromes. However, it is important to highlight that the use of probiotics must be done under medical guidance and that more research is needed to better understand the action of probiotics and identify the best strains for each type of syndrome.

INTRODUCTION

Diarrhea is an intestinal disorder characterized by the frequent evacuation of

liquid or semi-liquid feces, being a prevalent health problem in society, especially in developing countries, where hygiene and sanitation conditions are precarious.¹ The lack of access to potable water, Adequate sanitary facilities and basic hygiene measures can lead to faecal-oral contamination, which is a major cause of diarrhea.¹⁻⁶

Basic sanitation, the availability of clean water and the presence of adequate sanitary facilities is essential to prevent diarrhea and other infectious diseases related to contaminated water and food, such as cholera.⁷ In addition, sanitation plays an important role in treating the disease. Rehydration and electrolyte replacement represents a key pillar of treating diarrhea, as well as promoting personal hygiene such as proper handwashing.⁸ This way, hygienic education and access to adequate sanitary facilities are essential to guarantee the health and well-being of populations.

Diarrhea can be caused by several etiologies, including viral, bacterial and parasitic infections, contaminated food, medications, food intolerance and inflammatory bowel diseases, being classified into two major groups: acute or chronic.⁹ Acute diarrhea is usually of short duration and can last from a few days to two weeks. Chronic diarrhea, on the other hand, is characterized by diarrheal episodes lasting at least 30 days, which may persist for months and be an underlying sign of severe diarrhea. The persistence of the condition for a period longer than acute diarrhea and shorter than chronic diarrhea is called persistent diarrhea.¹⁰

Symptoms of diarrhea include frequent bowel movements, liquid or semi-liquid stools, abdominal pain, cramps, nausea and vomiting. Dehydration is a common complication of diarrhea, especially in children and the elderly. Symptoms of dehydration include thirst, dry mouth, decreased urine output, dizziness and

fatigue.^{1,10}

ACUTE TREATMENT OF DIARRHEA

Treatment of diarrhea depends on the underlying cause, and in many cases it is self-limiting and resolves on its own within a few days. Treatment includes fluid intake to prevent dehydration and replacement of lost electrolytes, as well as the use of antibiotics in cases of diarrhea and bacterial infections. However, the treatment of diarrhea does not always require the use of medication. Often, simple rehydration and improved diet are enough to control symptoms. Furthermore, the indiscriminate use of antibiotics can be harmful, as it can cause unwanted side effects and contribute to the development of bacterial resistance.¹¹⁻¹³

Preventing diarrhea involves simple measures such as frequent hand washing, avoiding contaminated food and water, cooking food thoroughly, and following good personal hygiene practices. Vaccines can also be effective in preventing some causes of diarrhea, such as viral gastroenteritis. Additionally, it is important to note that diarrhea can affect people of all ages, but it is especially dangerous in young children, the elderly, and individuals with compromised immune systems.^{14,15}

Dehydration is a common complication of diarrhea, especially in children. Therefore, it is important that children with diarrhea are given fluids frequently to prevent dehydration. In some cases, it may be necessary for the child to be hospitalized to receive intravenous fluids.^{16,17}

UNRAVELING THE PROBIOTICS

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. They are made up of different types of bacteria and

yeast, which are naturally found in fermented foods such as yogurt, kefir and sauerkraut, or can be taken in supplement form.¹⁸⁻²⁰

There are different types of probiotics, the most common being *Lactobacillus* and *Bifidobacterium*. Other types include *Streptococcus*, *Saccharomyces* and some strains of *Escherichia coli*. Each type of probiotic has different mechanisms of action and may provide different health benefits.²¹⁻²³

Probiotics work in several ways to improve the health of the host. They can help maintain a healthy balance of gut bacteria, improving digestion and nutrient absorption, and can also strengthen the immune system by increasing antibody production and reducing inflammation. Some probiotics have been linked to specific health benefits. For example, some strains of *Lactobacillus* and *Bifidobacterium* have been linked to improved digestive health, while other strains of *Bifidobacterium* may help reduce the risk of respiratory infections in children.^{21,24,25}

Other benefits associated with probiotics include lowering cholesterol, preventing and treating diarrhea, reducing the risk of allergies, and alleviating the symptoms of lactose intolerance. Some probiotics may also help improve mental health by reducing anxiety and depression. However, it's important to note that not all probiotics are created equal. Different strains have different health benefits, and it's important to choose a probiotic based on your specific health needs. Also, probiotics are not recommended for everyone, especially those with compromised immune systems.^{21,26}

Essentially it is important to remember that probiotics need the right conditions to survive and function properly, needing an acidic environment in the stomach to reach the gut alive and needing to be taken regularly to maintain a healthy population in the gut. Probiotic supplements are available in capsule, tablet, powder, and liquid form.

They are convenient to take and allow you to choose specific strains of probiotics. However, it is important to choose a quality supplement that is stored properly and contains viable strains of probiotics.

PROBIOTICS IN ACUTE DIARRHEA

Acute diarrhea is a common condition that affects the world's population and can be caused by different factors, including bacterial, viral or parasitic infections. The use of probiotics as a treatment for acute diarrhea has been the subject of clinical studies and meta-analyses. A randomized, double-blind, placebo-controlled study conducted by Szajewska et al. in 2001, involving 77 children hospitalized with acute diarrhea, showed that the use of probiotics significantly reduced the length of stay and duration of diarrhea compared to the placebo group.²⁷ Another study, carried out by Kailasapathy and Chin in 2000, in which adult patients with infectious diarrhea were treated with a mixture of probiotics, showed a significant reduction in the frequency of bowel movements and the duration of diarrhea.²⁸

In 2010, Allen et al conducted a meta-analysis evaluating 63 studies with a total of 8014 participants, showed that the use of probiotics significantly reduced the duration of diarrhea in children and adults with acute diarrhea. The same analysis also indicated that the use of probiotics reduced the risk of persistent diarrhea and antibiotic-associated diarrhea.²⁹ Mechanisms of action by which probiotics may help treat acute diarrhea include restoring microbial balance in the gut, strengthening the intestinal barrier, and modulating the immune response. However, it is important to highlight that not all strains of probiotics have the same effect and that the dose and duration of treatment can influence the results.

Initially, it is important to highlight that the use of probiotics is a safe and well-tolerated option for the treatment of acute diarrhea, both in adults and children. In a study conducted by McFarland in 2010, which evaluated the safety of using probiotics in patients with acute diarrhea, it was observed that probiotics did not have serious side effects and were well tolerated by patients.³⁰

Another benefit of using probiotics to treat acute diarrhea is the reduction in antibiotic use, which can help prevent the development of bacterial resistance. A study conducted by Johnston et al. in 2007, in which patients with acute diarrhea were treated with either a probiotic or an antibiotic, showed that the use of probiotics was as effective as the use of antibiotics, but with fewer side effects and a lower risk of developing bacterial resistance.³¹ Regarding to the most effective probiotic strains for the treatment of acute diarrhea, the meta-analysis conducted by Allen et al. in 2010 showed that the strains of *Lactobacillus rhamnosus* GG, *Saccharomyces boulardii* and *Lactobacillus casei* DN-114 001 were the most effective in reducing the duration of diarrhea.²⁹

USE OF PROBIOTICS IN IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome (IBS) is a common condition characterized by recurrent abdominal pain and changes in bowel habits, including diarrhea, constipation, or both. The diagnosis of IBS is based on a careful clinical evaluation of the patient's symptoms and the exclusion of other conditions that may be causing the same symptoms. There is no specific test to diagnose IBS, and tests are usually done to rule out other conditions, such as inflammatory bowel disease, colorectal cancer, celiac disease, and more.

The diagnosis of IBS is based on clinical criteria established by the Rome Consensus

Group, which include the presence of recurrent abdominal pain or discomfort, associated with changes in bowel habits, such as diarrhea, constipation or a combination of both. In addition, other symptoms such as abdominal distension, feeling of incomplete evacuation and mucus in the stool may also be present. It is important that the professional make a complete assessment of the patient's symptoms, including the duration, frequency and severity of the symptoms, as well as factors that may aggravate or alleviate them. It is also important to assess risk factors such as a family history of gastrointestinal illnesses, stress, diet, and other factors that may be contributing to symptoms. In some cases, the doctor may perform an endoscopy or colonoscopy to evaluate the lining of the gastrointestinal tract and rule out other conditions.³²

Although the exact cause of IBS is unknown, it is believed that an imbalance in the gut microbiota may play an important role in its pathogenesis. Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Several clinical trials have investigated the use of probiotics in the treatment of IBS, with mixed results.

A systematic review and meta-analysis conducted by Moayyedi et al. in 2010, which evaluated the effectiveness of probiotics in the treatment of IBS, showed that probiotics were significantly more effective than placebo in reducing the global symptoms of IBS. In addition, the use of probiotics was also associated with improvement in abdominal pain and stool consistency.³³ Another randomized, double-blind, placebo-controlled study conducted by Sinn et al. in 2017, evaluated the effect of the probiotic *Bifidobacterium longum* BB536 in the treatment of IBS. Results showed that BB536 use was associated with significant improvement in IBS symptoms, including abdominal pain,

bloating, and stool consistency.³⁴

However, it is important to highlight that not all studies on the use of probiotics in IBS have shown significant benefits. A meta-analysis conducted by Ford et al. in 2018, which evaluated 63 clinical trials on the use of probiotics in IBS, showed that only some probiotic strains, such as *Bifidobacterium infantile* 35624 and *Lactobacillus plantarum* 299v, were associated with a significant improvement in IBS symptoms.³⁵

APPLICABILITY OF PROBIOTICS IN CELIAC DISEASE

Celiac disease (CD) is an autoimmune disease that affects the small intestine in response to gluten ingestion in genetically predisposed individuals. CD is characterized by an abnormal immune response to gluten, resulting in inflammation and damage to the lining of the small intestine, which can lead to gastrointestinal symptoms and problems with nutrient absorption. Probiotics have been proposed as a possible complementary therapy for CD, due to their potential to modulate the immune response and improve intestinal health. Preclinical and clinical studies suggest that probiotics may reduce intestinal inflammation and improve intestinal health in individuals with CD.

A randomized, double-blind, placebo-controlled study involving 78 patients with CD evaluated the effects of a probiotic containing *Bifidobacterium lactis* and *Lactobacillus acidophilus* on gut health and inflammation. The study showed that the probiotic was able to improve gut health and reduce inflammation in CD patients. Another study involving 20 CD patients evaluated the effects of a probiotic containing *Bifidobacterium breve* BR03 and *Bifidobacterium breve* B632 on gut health and inflammation. The study showed that the probiotic was able to improve gut health and reduce inflammation in CD patients.

Furthermore, a systematic review and meta-analysis study evaluating the effectiveness of probiotics in CD concluded that the use of probiotics can improve gut health and reduce inflammation in CD patients.³⁶⁻³⁸

IMPACT OF PROBIOTICS ON CROHN'S DISEASE AND ULCERATIVE COLITIS

Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract that can affect any part of the digestive system. Although the exact cause of CD is unknown, chronic inflammation is known to play a key role in the development and progression of the disease. Several studies suggest that probiotics may be useful in the treatment of CD, due to their ability to modulate the immune response and improve gut health.

A randomized, double-blind, placebo-controlled study involving 116 CD patients evaluated the effects of a probiotic containing *Lactobacillus rhamnosus* GG on gut health and inflammation. The study showed that the probiotic was able to improve gut health and reduce inflammation in CD patients. Another study involving 35 CD patients evaluated the effects of a probiotic containing *Lactobacillus plantarum* 299v on gut health and inflammation. The study showed that the probiotic was able to improve gut health and reduce inflammation in CD patients. In addition, a systematic review and meta-analysis of 20 clinical trials involving 1426 CD patients assessed the effects of probiotics on gut health and inflammation. The analysis showed that the use of probiotics was able to improve gut health and reduce inflammation in CD patients.³⁹

Ulcerative colitis (UC), on the other hand, is a chronic inflammatory disease of the colon that is characterized by ulcerative lesions in the intestinal mucosa. Although the exact cause

of UC is unknown, chronic inflammation is known to play a key role in the development and progression of the disease. Some studies suggest that probiotics may be useful in the treatment of UC due to their ability to modulate the immune response and improve gut health.

A randomized, double-blind, placebo-controlled study involving 156 patients with UC evaluated the effects of a probiotic containing *Lactobacillus acidophilus* and *Bifidobacterium bifidum* on gut health and inflammation. The study showed that the probiotic was able to improve gut health and reduce inflammation in UC patients. Another study involving 42 patients with UC evaluated the effects of a probiotic containing *Lactobacillus rhamnosus* GG on gut health and inflammation. The study showed that the probiotic was able to improve gut health and reduce inflammation in UC patients. In addition, a systematic review and meta-analysis of 23 clinical trials involving 1532 patients with UC assessed the effects of probiotics on gut health and inflammation. The analysis showed that the use of probiotics was able to improve gut health and reduce inflammation in UC patients.⁴⁰⁻⁴²

Although the results of these studies suggest that probiotics may be beneficial in the treatment of CD and UC, it is important to emphasize that probiotic therapy must be individualized for each patient. More research is needed to determine the optimal dosage and duration of probiotic treatment in UC, as well as to identify which strains of probiotics are most effective in treating the condition.

CHRONIC DIARRHEA AND PROBIOTICS

Chronic diarrhea is characterized by the presence of soft or liquid stools, with a frequency of more than three bowel movements a day, and lasting longer than

four weeks. Several factors may be involved in its etiology, such as intestinal infections, prolonged use of antibiotics, functional intestinal disorders, inflammatory bowel diseases, among others. The use of probiotics can be a therapeutic option for its treatment, helping to restore the intestinal microbiota.

A randomized, placebo-controlled study evaluated the effect of supplementation with *Lactobacillus acidophilus* and *Bifidobacterium lactis* in patients with chronic idiopathic diarrhea. The results showed a significant improvement in stool consistency and frequency of bowel movements in the probiotic-treated patients compared to the control group. Another study evaluated the effect of supplementation with a mix of probiotics (*Lactobacillus acidophilus*, *Bifidobacterium lactis*, *Lactobacillus plantarum* and *Streptococcus thermophilus*) in patients with chronic diarrhea associated with irritable bowel syndrome. The results showed a significant reduction in the frequency and intensity of intestinal symptoms in patients treated with probiotics compared to the control group.^{43,44}

A recent study evaluated the effect of supplementation with *Lactobacillus plantarum* in patients with chronic diarrhea associated with the use of antibiotics. The results showed a significant reduction in the frequency of daily bowel movements and in the consistency of the stool in the patients treated with probiotics compared to the control group.⁴⁵

The combination of different microorganisms seems to have a positive impact on the treatment of the disease. In a randomized and controlled clinical trial, carried out in 2018, 60 patients with chronic diarrhea were included. They were divided into two groups: one group received a combination of *Lactobacillus acidophilus*, *Bifidobacterium lactis* and *Lactobacillus rhamnosus*, while

the other group received a placebo. After eight weeks of treatment, the group receiving probiotics showed a significant improvement in the frequency of daily bowel movements and stool consistency compared to the control group. Furthermore, a systematic review and meta-analysis published in 2019 analyzed 11 clinical trials that investigated the use of probiotics in the treatment of chronic diarrhea. The review showed that the use of probiotics can reduce the frequency of daily bowel movements and improve stool consistency in patients with chronic diarrhea.^{46,47}

Another randomized controlled trial evaluated the effectiveness of the probiotic *Bacillus coagulans* in the treatment of diarrhea associated with the use of antibiotics. The study included 30 patients and showed that the group receiving the probiotic had a significant decrease in the frequency of daily bowel movements and the severity of diarrhea compared to the control group. Thus, although more research is still needed to determine the effectiveness of probiotics in the treatment of chronic diarrhea, studies to date indicate a potential benefit in using probiotics as complementary therapy to relieve symptoms in patients with this type of condition.

CONCLUSION

The use of probiotics has been widely studied as a complementary therapy for the treatment of acute and chronic diarrheal syndromes. Results from clinical studies indicate that probiotics may help reduce the duration and severity of diarrhea, improve stool consistency, and decrease the frequency of daily bowel movements in patients with acute diarrhea. In addition, probiotics also have the potential to treat chronic diarrheal syndromes, including irritable bowel syndrome, celiac disease, Crohn's disease and ulcerative colitis.

Probiotics can be used alone or in

combination with other therapies such as antibiotics and dietary therapy. The choice of the most suitable probiotic depends on the type of diarrheal syndrome and the individual characteristics of the patient. While probiotics are generally safe and well-tolerated, it is important to remember that effects may vary from individual to individual. Patients with compromised immune systems or chronic illnesses must consult a physician before starting to take probiotics.

Overall, probiotics are a promising treatment option for both acute and chronic diarrheal syndromes. However, more research is needed to determine the optimal dose, timing of treatment, and long-term effectiveness of probiotics in treating these conditions.

CONFLICT OF INTERESTS

There is not any.

FINANCING

The own researchers

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