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The Use of Probiotics in Diverticular Disease

By

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Capstone Project

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Introduction

Probiotics are becoming an important source of preventative treatment, due to their possible mechanism of action in modulating the immune system in the gut. Probiotics are also cost effective and have easy accessibility, which can play a role in treatment for gut related diseases. One disease that affects many people in society is diverticular disease, which has been shown to have inflamed and altered gut microbiota. Not only does this disease reduce the quality of life for patients, but also has an increased mortality rate.¹ This increase in mortality is mainly due to complications of the disease process.¹ Obesity has also become a social burden and is a difficult disease to treat from a medical standpoint. Obesity is an important modifiable risk factor in diverticular disease. Both of these diseases are impacted by altered gut microbiome, which is a significant part of the probiotic treatment. With this addition, probiotics can enhance the quality of life and reduce complications in diseases such as diverticular disease.

The Variety of Probiotic Supplements

Probiotic supplements have become a widespread development in medical therapeutics with a variety of different diseases. Recently, there has been a tremendous shift in how medicine views the gut microbiome and diseases that are affected by altered gut microbiome. One of these conditions that plagues individuals is diverticular disease. In diverticular disease, how do probiotic supplements compared to no treatment affect patient outcome within treatment protocol? With little to no side effects, probiotic supplements can become an ideal preventative treatment that individuals can take.

Diverticular Disease in Medicine Today

Diverticular disease is a spectrum of disorders that mainly affect industrial nations. This particular disease increases with age and has a variety of different symptoms. One part of the spectrum is diverticulosis, a condition in which diverticula are present in the colon. Not to be confused with diverticulitis, which is actual inflammation or infection of the diverticula.² Even though this disease has been around since the early 1900's, the pathophysiology is still unknown. There are many theories regarding the pathogenesis of diverticular disease. However, only two will be discussed in this review. The first theory circles around the actual structure of the colonic wall, and the second theory deals with the colonic motility. Both are seen to cause defects that contribute to the outpouching of diverticula.

In regard to the first theory, studies have shown thinning of the muscular layers in the colon. These areas in the colonic wall are weakened specifically in the circular muscle layer. Over time, these weakened areas will atrophy and can cause penetration to the mucosa.² Scientists have also looked at the tissue strength in the submucosa. It has been shown that patients with diverticulosis have a loss of compliance in this tissue, which in turn makes the submucosa stiffer and unable to stretch.² Such abnormalities in the colonic wall could lead to diverticulosis and worsening of disease.

Colonic motility also plays a role in diverticular disease. The greatest generated pressure of the bowel happens in the sigmoid colon, which is the narrowest part of the lumen.² The colon is designed to function as a united tube. However, if the colon functions as individual compartments, this will create extra pressure and produce an obstruction.² A study analyzing the pressure in the sigmoid colon showed that patients without diverticular disease had an amplitude

of 10 mm Hg pressure, while patients with diverticular disease had an amplitude of 90 mm Hg.² In reviewing these theories it is evident that probiotic treatment will help restore the normal flora microbiota, preventing breakdown of the mucosal layer and enhancing colonic motility.

It has been shown that in diverticular disease there is depletion in the microbiota that causes mucosal immune activation, which in return causes inflammation in the microbiota.³ The gut microbiome is an important part of the treatment in diverticular disease. The disease itself has a variety of stages that include asymptomatic, uncomplicated, symptomatic, and acute diverticular disease.⁴ In this regard, treatment has been focused on the gut microbiota with medication such as fiber, probiotics, as well as others. In a literature review of 764 patients, it was shown that probiotics consumption reduced abdominal symptoms in symptomatic uncomplicated diverticular disease.⁴

Gut Microbiome

The gut microbiome is a complex organ that has become an important focus in today's healthcare. The microbiome is composed of many parts that include viruses, bacteria, and more.⁵ This major organ also has countless functions in our health like immune, metabolic, as well as the normal basic functions of the gastrointestinal system.⁵ Medicine has begun to study the gut and understand the functions of a normal healthy gut microbiome. However, in many cases of disease there is a known alteration and inflammation in the gut microbiome. This alteration leads to the treatment in restoring the normal balance.

Probiotic use in Diverticular Disease

There are many symptoms that occur during uncomplicated symptomatic diverticular disease. Symptoms include constipation, diarrhea, mucorrhea, back pain, and abdominal pain.

One of the main symptoms that has been proven to diminish with probiotic use is constipation. Research studies have shown that in diverticular disease there is an increase in certain bacteria, such as clostridia, that cause inflammation and changes to the gut. In a 2009 study by Lamik, patients were given lactobacilli and bifidobacterial probiotic in a six-month trial and these particular probiotics prevented recurrent symptoms.⁶ Studies have also shown that there was no adverse side effects or diverticulitis during the use of probiotics.⁶

In one randomized clinical trial, 210 patients were broken into four different groups that contained either Lactobacillus, mesalamine, a combination, or a placebo.⁷ The goal of this double-blind study was to prevent remission of symptomatic uncomplicated diverticular disease. Lactobacillus in conjunction with mesalamine was shown to prevent remission of uncomplicated diverticular disease in this 12-month trial.⁷

In addition, a double-blind placebo trial of 120 patients showed significant improvement of symptoms in the treatment group compared to the placebo group.⁸ The focus of this particular trial was to see if probiotics could be used as a treatment for symptomatic uncomplicated diverticular disease, rather than a preventive treatment.⁸ These patients were asked to record the frequency of symptoms during the 3-month trial and were instructed to take 1mL/kg liquid probiotics or a placebo on an empty stomach every day. Symptoms such as constipation, diarrhea, mucorrhea and back pain were greatly improved with the use of different Lactobacillus strains as well as Enterococcus faecium.⁸ Probiotics are becoming more of a popular treatment choice due to their mechanism of action, and being able to modulate the gut immune microbiome.

There are many strains of probiotics, but one probiotic in particular has been tested in many clinical trials. Lactobacillus has been proven to keep symptoms in remission for 12 months.⁹ The key to using probiotics in diverticular disease is to maintain the normal healthy gut bacteria that prevent symptoms and inflammatory disease from occurring. Lactobacillus as well as other strains of beneficial bacteria can be used to stabilize the gut microbiome in the GI tract.⁹ Maintaining the balance of beneficial bacteria versus the pathogenic bacteria will help with symptoms in patients with diverticular disease.

Obesity and Risk Factor

One particular disorder that has become prevalent in today's current practice is obesity. Increased body weight is a controllable risk factor in diverticular disease. A study with 7,500 males found that men with a BMI >30 were four times more likely than men with normal BMI (20-22.5) to have complicated diverticular disease.¹⁰ Another study with 47,000 men found that the risk of diverticulitis was 78% higher in men with a BMI >30 compared to men with normal BMI (<21).¹⁰ There have also been studies showing the increased risk of obesity and diverticular disease in women. Women with a BMI > or equal to 30 had a 33% higher risk of diverticular disease, as well as a 2-time greater risk of abscess or perforation.¹⁰ Probiotic use in obesity has become a particular interest to many in the medical community. Studies have shown that the gut microbiome is altered in obesity and other metabolic disorders.¹¹ Very few human trials have been composed that evaluate the degree of use of probiotics in obesity. However, the idea that the gut microbiome is altered in obese patients shows that probiotics may be of use.

Probiotics are not only being used for diverticular disease and obesity, but other diseases as well. A literature review has shown that probiotics are used in conditions such as hypertension, dyslipidemia, liver disease, and allergic diseases in children.¹²

Conclusion

There is a current lack of conclusive evidence to support the use of probiotics in diverticular disease. It is important to note that the American Gastroenterological Association guidelines do recommend against the use of probiotics after acute uncomplicated diverticulitis.¹³ This recommendation was based on very little data that showed little to no efficacy when using probiotic supplements in acute uncomplicated disease. This recommendation is pending further research.¹³

Current studies that have been done are limited in patient size as well as actual trials. There are many limitations to understanding where the future of probiotic use is meant to be. The term probiotic supplements in itself is a broad term. The main strands that have been studied such as Lactobacillus, have not yet been regulated on the specific amount of culture forming units needed to show efficacy. There are many other numerous strands of different probiotics that have not been investigated.

The gut microbiome is a new area of interest in medicine and has been linked to other diseases of the human body. Even in a normal healthy person who has no chronic illness, there can be a potential benefit from using a daily probiotic supplement. There are constant physiological stressors that have an effect on our gut microbiome. A lot of diseases feed off of that altered and inflamed gut microbiome. Research can help identify treatment to maintain a healthy and stable gut microbiome. Probiotic supplements can restore beneficial bacteria, which

will reduce inflammation and improve immune function for the prevention of diverticular disease.

In diverticular disease, how do probiotic supplements compared to no treatment affect patient outcome within treatment protocol? In theory, probiotics can help reduce inflammation and restore the normal bacteria, leaving the gut microbiome in a healthier state, compared to no treatment. Probiotics also have a low side effect profile and easy accessibility, which can help with a great spectrum of patients. This new area of medicine has gained a lot of focus, and with continued research and investigation of more specific treatment will be available for patients. With further clinical trials, the use of probiotic supplements can change the focus of preventative medicine and improve the overall quality of life for patients.

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