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Using Probiotics Instead of Pharmaceuticals to Treat Gastrointestinal Disorders

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Abstract

Gastrointestinal disorders affect the majority of the population. While many people can go to the store and buy an antacid to alleviate their symptoms, millions of people each month seek out treatment from a physician and are prescribed H2 blockers and proton pump inhibitors (PPIs) to treat their digestive discomfort. Antacids used for a short period of time do not typically exhibit any negative side effects. If used properly, H2 blockers present very few side effects or negative health outcomes. PPIs on the other hand, are being linked to a myriad of serious side effects and permanent long-term health complications. Now that H2 blockers and PPIs are available for purchase without a prescription, it is virtually impossible to track the symptoms or disorders that are being treated with these medications. Probiotics are natural, healthy bacteria that offer the consumer health benefits from consumption. Probiotics are being studied for their role in positive health outcomes as well as treatment options for a variety of disease states including gastrointestinal disorders. Many strains of probiotics have been shown to alleviate symptoms of digestive tract discomfort as well as enhancing the microbiome. Given the severity of long-term use of antacids, H2 blockers, and PPIs, more research needs to be put into using probiotics to treat gastrointestinal disorders. Physicians and patients need to explore the possibility of using probiotics to treat gastrointestinal disorders in place of using pharmaceuticals that can have very serious, and potentially deadly, side effects.

Keywords: *H. pylori*; Peptic ulcer; Antibiotics; Probiotics; Proton pump inhibitor

Introduction

Gastrointestinal disorders such as indigestion, heartburn, GERD, peptic ulcers, irritable bowel syndrome, ulcerative colitis, and inflammatory bowel disease, have become very common, presenting at least once yearly in 60% of the general population [1]. Upon commercialization of antibiotics, they quickly became the primary treatment option for infection [2]. When *Helicobacter pylorus* was discovered as a possible cause for peptic ulcers in 1982, the justification for using antibiotics to eradicate this bacterium was made. Over the last several decades, the use of antacids, histamine (H2) blockers, and proton pump inhibitors (PPIs) has increased dramatically, producing a multi-billion-dollar industry.

The ideal pH of the stomach is approximately 1.0-2.0 for optimal gastric digestion. The stomach is lined with a mucus layer to protect it from the acidic environment and if that lining becomes irritated or disrupted, the stomach can be damaged by the acid [3]. An antacid is an alkaline substance that reduces acidity in the stomach. H2 blockers reduce acid through a different mechanism. Histamine is a biological compound that has receptors in the stomach and when the histamine binds to these receptors, it stimulates the stomach lining to produce hydrochloric acid (HCl). An H2 blocker competitively binds to the histamine receptors, decreasing the production of HCl, which decreases the acidity in the stomach. Proton pump inhibitors (PPIs) work by blocking the proton pumps in the stomach. The proton pump releases protons into the stomach, resulting in an acidic environment which is needed for digestion and to kill pathogenic bacteria. PPIs are indicated for use by individuals who have acid erosion in their digestive tract.

Literature Review

Acid-related gastrointestinal problems have been increasing in prevalence over the last several decades, with up to 60% of the population experiencing GERD symptoms at least once a year and 20% to 30% weekly [1]. Complaints of heartburn, indigestion, and nausea continue to rise across every population as physicians strive to find safe long-term treatments that reduce gastric acidity [4]. Antacids that are currently available offer immediate short-term relief of heartburn and other acid-related diagnoses but are meant to be taken for short periods of time. Taking an antacid for a long period of time can lead to health problems such as electrolyte imbalance and kidney disease [5]. It is important to note that antacids are only indicated for treatment of heartburn. More serious digestive tract issues should be treated with a more appropriate medication. Both recurrent heartburn and other digestive symptoms should be treated by a physician as the

progression of digestive tract symptoms can lead to very serious and sometimes irreversible disease states.

As the occurrence of digestive symptoms has shifted from primarily heartburn to more serious diagnoses such as GERD, gastritis, peptic ulcers, Barrett's esophagus, functional gastrointestinal disorders (FGIDs), and esophageal cancer, the focus of treatment has turned from antacids to H2 blockers and proton pump inhibitors. If GERD is not treated, a person can develop very serious illnesses such as asthma, esophagitis, and Barrett's esophagus which can all increase the likelihood of developing esophageal cancer [4]. H2 blockers were the preferred treatment for peptic ulcers in the 1980s. Although H2 blockers reduce acidity in the stomach, the introduction of PPIs as products that will reduce acid as well as promote healing of the digestive tract have led to PPIs becoming the preferred treatment option for recurrent acid-related digestive symptoms. From April 2014 to March 2015, Nexium, the top-selling PPI, was prescribed over 15 million times per month and the sales during that period were $5.3 billion [6]. Despite their explosion on the pharmaceutical market available both as prescriptions and over-the-counter products, PPIs have been linked to numerous negative side effects and serious health problems. "Since the introduction of proton pump inhibitors (PPI), clinical management of GORD has markedly changed, shifting the therapeutic challenge from mucosal healing to reduction of PPI-resistant symptoms" [7].

The majority of Americans experience occasional heartburn and the number of diagnoses of peptic ulcers, GERD, and other gastrointestinal disorders continues to increase. A number of factors are implicated in the rise of gastrointestinal disorders such as stress, smoking, obesity, poor diet, socioeconomic status, and microbiome dysbiosis. The human microbiome is a complex network of bacteria, yeast, and fungi that work with the human body to keep it healthy and functioning properly. When a person thinks they are suffering from heartburn or other digestive abnormalities, the problem could actually be caused by insufficient acid in the stomach. The digestive tract needs sufficient acid to digest proteins, absorb vitamins and minerals, and fight off pathogenic bacteria. If a person takes antacids too often or for unwarranted reasons, this could cause complications such as vitamin deficiency, bone fractures, heart arrhythmia, muscle cramping, anemia, and food poisoning [8,9]. It is important for a person who experiences digestive problems to seek out medical attention for proper diagnosis.

After the discovery of *H. pylori*, antibiotics were considered an effective and safe treatment for gastrointestinal problems. In 1994, the NIH authorized eradication of *H. pylori* when associated with peptic ulcer [10]. The problem with eradicating *H. pylori* from the digestive tract is that *H. pylori,* like *E. coli*, can be present in a healthy gut, but dysbiosis can cause pathogenesis. When *H. pylorus* was initially discovered in patients with gastric ulcers, the conclusion was made that the *H. pylori*, being a Gram-negative opportunistic bacterium, was the cause of peptic ulcers. Antibiotics were prescribed to eradicate the *H. pylori* and eliminate the root cause of the ulcer. The problem with using an antibiotic to treat any gastrointestinal disorder is that the antibiotic kills bacteria nonspecifically, causing an even stronger disruption in the microbiome. A single round of antibiotics can permanently alter a person's microbiome [11]. Antibiotics need to be prescribed cautiously when a disorder of the gastrointestinal tract is being treated to avoid further disruption to the microbiome whenever possible. A maximal density and variety of healthy bacteria is needed for a healthy digestive tract. Once an antibiotic has been introduced into a person, the density and variety of the gut bacteria are sharply decreased and studies have shown that while the density eventually rebounds, the variety of strains does not. Families of healthy bacteria compensate for the loss of density but cannot repopulate strains that have been completely eradicated. This leads to an overall loss in microbiome diversity which can be amplified over time with repeated or multiple rounds of antibiotic therapy.

Discussion

Studies have shown that exposure to antibiotics and emulsifiers greatly reduce the efficacy of the microbiome to protect the digestive tract from pathogenic infection [12,13]. It is possible that throughout life, exposure to antibiotics, emulsifiers, and other substances cause disruption in the microbiome. When too much glucose is ingested and the gut digestion results in excess sulfate and hydrogen, the oxidation process is not in balance and this can result in bacterial infection [14]. The microbiome is a very delicately balanced composite of living organisms that, when in balance, enhance the overall health of the individual in which they reside. When out of balance, the microbiome wreaks havoc on its host. The interaction of the organisms within the microbiome is a complex network of reactions based on the bacteria being fed essential nutrients such as complex sugars, fiber, and protein, which are digested into products needed for bacterial metabolism further down the digestive tract. The end result of microbial metabolism is nutrients needed for proper human health [15].

Ensuring that the gut bacteria have a sufficient supply of nutrients is important. Gut bacteria ferment protein and carbohydrates, producing short-chain fatty acids and gases [16]. A person needs to consume a well-balanced diet that includes raw foods such as vegetables and fruits to supply the gut bacteria with a source of food. When the gut bacteria break down the protein and sugars, they produce byproducts that help protect the intestinal lining as well as make vitamins and minerals more bioavailable for absorption in the intestines, and at the same time produce energy and food sources for other organisms in the microbiome [14,16]. The gut bacteria serve many important purposes in the intestine – they line the intestine to protect it from pathogenic bacteria, they produce cytotoxins that help eradicate pathogens, and they aid in digestion [16]. Maintaining a healthy microbiome is important and can attribute to better overall health for a person [12,13,17,18]. Unfortunately, taking medications such as antacids, H2 blockers and PPIs, causes additional imbalance

in the digestive tract which may result in more significant microbiome dysbiosis [9].

Probiotics have been shown to restore the microbiome to a more healthful and natural balance in an individual. The probiotic strains *L. plantarum* 299v and *L. reteuri* have been shown to reduce gastrointestinal symptoms such as diarrhea, inflammation, overgrowth of pathogenic bacteria and decreased intestinal barrier function which can lead to leaky gut syndrome [19,20]. According to Orel, "several *Lactobacillus reuteri* strains exhibit various characteristics such as secretion of antimicrobial reuterin, production of short-chain fatty acids, down-regulation of inflammatory immune response, and direct influence on enteric nervous system among the others, which render them good candidates for prevention and treatment of various FGIDs" [20]. *L. rhamnosus* GG has been shown to be effective in treating several gastrointestinal disorders such as IBS and is reported to be tolerated well and with no reports of adverse reactions [21].

Negative side effects related to long-term use of proton pump inhibitors (PPIs) show that these medications, while effective, are not ideal for long-term treatment of reducing stomach acid [22]. PPIs have been associated with negative side effects such as hypomagnesemia, hypocalcemia, hypoparathyroidism, chronic kidney disease, end-stage renal disease, hip fracture, community-acquired pneumonia, *Clostridium difficile* infection, and increased risk of SIBO (small intestinal bacterial overgrowth) [9,22-25]. Millions of prescriptions are written and filled each year for antacids, H2 blockers, and PPIs [6]. "It has been estimated that 25% to 70% of PPI prescriptions have no appropriate indication" and these prescriptions are often taken longer than necessary [24]. To further complicate this problem, varying strengths of each of these medications are also available for purchase without a prescription. Many of these pharmaceuticals, especially PPIs, have serious drug interactions [8,24]. People who experience gastrointestinal distress can purchase a medication which may not be appropriate for their symptoms and which can disrupt their microbiome, causing long-term health problems if they continue to take these medications without medical supervision. PPIs have been shown to be more damaging to the microbiome than antibiotics [8,26]. H2 blockers and PPIs are now being prescribed to infants and children [27]. This may result in modifying an individual's microbiome from an early age, leading to a lifetime of complications arising from microbiome dysbiosis.

Given the prevalence of gastrointestinal disorders and the negative side effects of current medications that include antacids, H2 blockers, and PPIs, probiotics need to be further examined for their efficacy in treating gastrointestinal disorders [28,29]. If the probiotics are shown to be effective as they have been in initial studies [21], they should be used in place of the current medications when possible. Probiotics are healthy bacteria that are a part of the human digestive tract; using them to treat gastrointestinal disorders and help return the gut to a state of homeostasis is preferable to introducing medications that will further eradicate the healthy gut bacteria and increase the risk of more serious gastrointestinal distress [30-32]. As Horveth discusses, individual strains need to be tested first and then probiotic combination therapies to develop effective probiotics to treat gastrointestinal disorders [21].

H2 blockers have not been found to produce the same negative side effects as PPIs, especially renal complications [24]. If medication is required to treat gastrointestinal symptoms, instead of prescribing a PPI, an H2 blocker can be prescribed for the same indications as a PPI [24]. Patients using PPIs have a 50% increased rate of renal disease [8] and 51% increased risk of death [24]. If a PPI is needed for treatment, H2 blockers should be introduced as an alternative treatment once symptoms have subsided. H2 blockers exhibit less serious long-term side effects and if a person requires long-term acid reduction in the stomach, an H2 blocker is a preferable long-term treatment option. Ideally, using probiotics to return the digestive tract to a homeostatic state will help eliminate the need for acid-reducing medicines. For the patients who must remain on medications for long periods of time, close monitoring of any potential side effects is crucial as well as probiotic therapy to maintain a healthy microbiome.

Conclusion

There is a growing trend in the interest of natural medical treatments. Probiotics are strains of bacteria normally found in a healthy gut. Using probiotics to treat gastrointestinal symptoms will increase both the diversity and density of the gut bacteria, help restore the digestive tract to a healthy state, and eliminate the need for medications which may cause additional harm to the digestive system. Before the introduction of antibiotics, and later H2 blockers and PPIs, the treatment for digestive disorders most commonly prescribed by physicians was probiotics. In Europe, probiotics are still commonly prescribed for digestive problems, and the incidence of digestive disorders overall is less common than in the United States where the preferred treatment has become commercial medications. Bacteriotherapy, or the administration of probiotics, should be considered as a complementary and when possible, replacement, therapy for pharmaceutical treatment of gastrointestinal disorders.

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