Probiotic Bacteria in the Prevention and the Treatment of Inflammatory Bowel Disease

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KEYWORDS

• Inflammatory bowel disease • Crohn disease • Ulcerative colitis • Pouchitis
• Probiotics • Prebiotics • Synbiotics

KEY POINTS

- The gastrointestinal microbiota is highly diverse. Alterations in this microbiota have been show to both cause and abrogate systemic inflammatory disorders.
- Probiotics are defined as microbiotia that have a beneficial effect on human health.
- Recently, probiotics and probiotic preparations have been studied as therapeutic agents to modify the gastrointestinal microbiota and thereby treat inflammatory bowel diseases (IBDs).
- Randomized clinical trials have shown that select probiotics are efficacious for the induction and maintenance of remission in ulcerative colitis and for the maintenance of remission in pouchitis.
- Not all probiotics are the same or have similar efficacy. Adequately powered, randomized controlled clinical trials are required for each probiotic to confirm its efficacy in IBD.

INTRODUCTION

The traditional classification of IBD into Crohn disease and ulcerative colitis offers health care providers a logical and evidenced-based approach in developing a meaningful therapeutic approach for the prevention and treatment of these diseases. Current therapies may leave many patients and physicians frustrated, because persistent symptomatology and endoscopic or histopathologic evidence of active disease usually persist despite optimum medical and surgical management. As comprehension of these diseases has progressed, advanced pharmacologic biologic therapies have been developed, such as anti–tumor necrosis factor α (anti–TNF-α) agents,

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which have resulted in improved symptom and disease control in many patients. Currently, however, a definitive curative strategy for these diseases, using medical therapy alone, remains elusive. Furthermore, these medications are not without significant cost nor are they without risk of potential, and often substantial, side effects. For these reasons, there is a prevalent interest in patients with IBD in pursuing nonconventional avenues of therapy for both symptoms and disease control.[1]

Given these considerations, there has been an increasing appreciation of the importance in understanding the complexities of the interactions between the human host immune system and its resident gastrointestinal luminal microbial population. Current models for the pathogenesis of IBD have demonstrated evidence for a disturbance in this equilibrium, resulting from either an aberrant host immune response to usual luminal microbiota,[2] an exaggerated physiologic immune phenomenon to an abnormal population of microbes in the gastrointestinal tract,[3] or a combination of both.

Probiotic organisms, which are defined as "live microorganisms which when administered in adequate amounts confer a health benefit on the host,"[4] have been used in attempts to take advantage of this relationship to treat various gastrointestinal diseases, including acute traveler's diarrhea,[5] infectious diarrhea,[6] and irritable bowel syndrome[7]; in the prevention of infantile necrotizing enterocolitis in neonates[8]; and to alter gut microflora in patients with minimal hepatic encephalopathy to prevent the growth of ammonia-producing bacteria in patients with hepatic cirrhosis.[9]

Although the spectrum of diseases of the intestines is broad, this article focuses on the actual and potential roles of the probiotic organism in patients with Crohn disease and ulcerative colitis. To begin with, the basic aspects of the enteric microorganism are reviewed, as they pertain to the development of IBD, and they are compared and contrasted with the host-specific responses to probiotic administration, in both the IBD and non-IBD host. Then the available clinical literature is reviewed, focusing on the use of probiotics in Crohn disease and ulcerative colitis, examining the roles of the probiotic organism in induction of remission as maintenance therapy and in the surgical patient with IBD. Finally, future roles of probiotic therapy in the realm of IBD are proposed.

GASTROINTESTINAL MICROBES AND IBD

The human gastrointestinal tract provides a suitable environment to a diverse microbial population, with more than 400 to 500 different species of bacteria currently identified.[10] The primary introduction of this array to the host most likely occurs in close relationship to labor and delivery of the neonate, with *Lactobacillus* and *Prevotella* spp predominating within the vaginal canal at the time of delivery.[11,12] Once established, this microbial population maybe susceptible to changes in diet,[13] age of the host,[14] disease states, and lifestyle. Nevertheless, the specific changes that are effected in the microbial population by each of these variables, however, remain to be fully elucidated.

The importance of the microbe in IBD is demonstrated by clinical and histologic improvement in fecal diversion in patients with Crohn disease[15]; recurrence of symptoms and inflammation with re-exposure of the terminal ileum to luminal contents is the rule. Several studies have magnified the importance of enteral microorganisms in the development and maintenance of IBD. Analysis of mucosal-associated and fecal bacteria reveals diminished commensal microbial diversity (decreased numbers of *Faecalibacterium prausnitzii* and *Lactobacillus*),[16–21] an increased number of mucosal-associated microorganisms,[22,23] and an orientation toward phylogenetic groups of proinflammatory microbes, such as *Escherichia coli,* in patients with active inflammation in Crohn disease and ulcerative colitis.[24,25] It remains to be seen whether