

Probiotics in inflammatory bowel disease

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Probiotics are live micro-organisms that alter the enteric microflora and have a beneficial effect on health. Bacteria associated with probiotic activity have frequently been lactobacilli or bifidobacteria, but *Escherichia coli* and enterococcal strains have been used, as have non-bacterial organisms such as *Saccharomyces boulardii*.

The rationale for using probiotics in inflammatory bowel disease (IBD) is based on persuasive evidence implicating intestinal bacteria in the pathogenesis of IBD.^{1,2} The most compelling evidence is derived from animal models; despite great diversity in genetic defects and immunopathology, a consistent feature is dependency on the presence of normal enteric flora for full expression of disease. It appears that the pathogenesis of IBD, particularly Crohn's disease, involves genetically influenced dysregulation of the mucosal immune response to antigens present in the normal bacterial flora. In susceptible individuals, tissue damage results from immunological misperception of danger within the indigenous flora or failure of normal regulatory constraints on mucosal immune responsiveness to enteric bacteria.³

Conventional drug therapy for IBD addresses only one aspect of the pathogenesis by targeting the mucosal immunoinflammatory response. Optimal disease management may require the environmental contribution to be addressed. However, manipulating the enteric microenvironment is a significant challenge. Intestinal bacteria outnumber cells in the human body 10-fold, account for 400–500 species, many of which can still not be cultured, and have the collective metabolic activity of a virtual organ—the “neglected organ”. Bacterial species vary in capacity to drive intestinal inflammation; various *Lactobacillus* and *Bifidobacterium* species have no proinflammatory capacity, hence their choice as probiotics. Potential mechanisms of probiotic action include competitive interactions, production of antimicrobial metabolites, dialogue with the epithelium, and immune modulation.¹

Probiotic therapeutic efficacy in experimental murine models, including IL-10^{-/-} mice and lymphocyte transfer models, has been encouraging.^{4–6} It is noteworthy that organisms vary in their probiotic performance depending on the experimental model. This might predict that strain specific indications will be required for subset specific forms of human IBD. Probiotics also appear to diminish the rate of progression from inflammation through dysplasia to coloncancer in experimental animals,⁶ and the use of probiotics in colon cancer

prevention has been linked with several putative mechanisms of action.⁷ Controlled data in human IBD are limited. A non-pathogenic strain of *E coli* has been found in two studies to exhibit efficacy similar to that of mesalazine in patients with ulcerative colitis.^{8,9} Results using a probiotic cocktail in patients with pouchitis have been impressive.¹⁰ More ambitious controlled trials in humans are about to get underway and will assess comparative probiotic performance.

In conclusion, probiotics may offer a simple adjunct to conventional therapy and empower patients with a sense of control by shifting the emphasis of diet from one of nutritional replenishment alone to a more functional role. Enthusiasm for probiotics in IBD is strong on rationale and preclinical data but still weak on rigorous evidence for clinical efficacy. There are also worrisome gaps in knowledge of the normal flora. In addition, the notion that a single probiotic will be equally suited to all patients is simplistic, given the apparent heterogeneity of IBD.

Key points

- The pathogenesis of IBD involves an internet of genes, bacteria, and immunity.
- Most conventional drug therapies suppress host immunity but modification of the microflora has a sound rationale and may represent a safe therapeutic adjunct.
- Mechanisms of probiotic action are multiple and include bacterial competition, mucosal conditioning, and immune modulation.
- Preliminary results with probiotics in animal models and humans with IBD are encouraging but more rigorous scientific pursuit is necessary.
- Fulfilment of the therapeutic potential of probiotics is likely to require more complete understanding of the normal intestinal microflora.

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