PROBIOTICS, PREBIOTICS AND SYNBIO蒂ICS IN PEDIATRICS

Shortly after birth, the intestine of the human neonate becomes rapidly colonized with microorganisms that interact with a large, highly active mucosal surface. The mammalian intestinal tract contains a complex and diverse population of both pathogenic and nonpathogenic bacteria.

Mechanisms of Action of Probiotics

- The concept of a microbiological balance existing in the intestine, involves competition between probiotic and pathogenic bacteria for specific binding sites on intestinal epithelial cells. However, recent research has turned toward understanding the role of probiotic bacteria and their secretion products in enhancing and modulating innate and adaptive immune responses in the host by other mechanisms. With the demonstration that immune and epithelial cells can discriminate between different microbial species through activation of receptors, the idea that probiotics may exert some of their protective functions through modulation of immune activity and epithelial function in both the large and small intestine has arisen.

- Probiotic bacteria can enhance barrier function through distinctly different mechanisms. Either by inhibiting the adhesion and invasion of bacteria into human intestinal cell lines, by enhancing phosphorylation in the tight junction region or by maintaining barrier function with the ability of preventing cytokine-induced apoptosis in intestinal epithelial cell through the inhibition of a tumor necrosis factor (TNF).

- It has been well documented that probiotic bacteria can interact with epithelial and immune cells and alter metabolic response in the presence or absence of pathogenic bacteria and cytokines. Epithelial cells respond to whole bacteria and bacterial components with epithelial and immune cells and alter metabolic response in the presence or absence of pathogenic bacteria and cytokines. Epithelial cells respond to whole bacteria and bacterial components with epithelial and immune cells and alter metabolic response in the presence or absence of pathogenic bacteria and cytokines.

- The term “Synbiotic” refers to the combination of probiotics and prebiotics. This possibility of matching prebiotics with probiotics strains to induce physiological benefit has been described as well as the combination of different prebiotics (inulin and oligofructose) that may also elicit synergetic effects.

- Probiotics, prebiotics, and synbiotics are assuming a real place in the mainstream of medical therapy. This trend has been facilitated by our ever-increasing understanding of the mechanism of action of these agents and by the development of molecular methods for analyzing and identifying complex bacterial communities within the mammalian intestine. This increased knowledge will have important implications for studies on the efficacy of probiotic oligosaccharides and on the development of novel forms with specific functional enhancements.

Potential Clinical Therapeutic uses of Probiotics

The role for probiotics in the treatment and prevention of bacterial infection is described to be associated with both probiotic-induced inhibition of bacterial growth and adhesion to epithelial cells and an effect on the host immune system.

- Several studies have been published addressing the efficacy of probiotics on the treatment of acute infectious diarrhea, especially in children, aiming at the shortening of the duration or preventing recurrence of diarrhoeal episodes. Evaluating well-
of probiotics in reducing urinary tract infections, bacterial sepsis, and necrotizing enterocolitis were not conclusive. Nevertheless, it is well accepted that probiotics appear to be efficacious in both *C. difficile* diarrhea and antibiotic-associated diarrhea.

- In relation to *pancreatitis*, it is well accepted that colonization of the lower gastrointestinal tract and oropharynx with Gram-negative organisms often precedes contamination of the pancreas. It is also known that pancreatic necrosis and associated pancreatic infection are determinants of poor outcome in patients with severe acute pancreatitis. Well-conducted studies in patients with acute pancreatitis receiving probiotics showed a major reduction in the occurrence of infected abscesses as well as a trend toward a shorter mean length of hospital stay.

- Several clinical trials have focused on the impact of probiotics in the treatment of *irritable bowel syndrome* (IBS). The results were not conclusive. There was no significant difference in mean gastrointestinal transit measurements, bowel function scores, or satisfactory global symptom relief between the two treatment groups. The mechanism of action of probiotics in IBS is poorly understood and has been thought to be attributable to alterations in the composition of indigenous colonic microflora or to changes in fermentation products. Once again, these discordant results support the concept of specific probiotic strains being more effective than others across varied disease states.

- The interest of probiotics in inflammatory bowel disease (IBD) is based on the assumption that disturbance in the gastrointestinal microflora, or the host response to this flora, has been demonstrated to play a critical role in the pathogenesis of this condition. Some clinical trials have demonstrated the efficacy of probiotics in the maintenance or remission of pouchitis, prevention of pouchitis after surgical formation of the ileal-anal reservoir, maintenance or remission of, and treatment of active *ulcerative colitis*. Despite promising data on ulcerative colitis, the contradictory findings in *Crohn’s disease* strongly suggest that more studies need to be done before a conclusive opinion is taken.

- Although there are no published human studies on the effects of probiotics on *colon cancer*, there are some animal models studies demonstrating that probiotics, in combination with probiotics, are potentially useful in reducing the risk of colon cancer. This protection seems to be associated with metabolic activities of intestinal microflora, alteration of physicochemical conditions in the colon, binding and degradation of potential carcinogens. Quantitative and/or qualitative alterations in the intestinal microflora incriminated in the production of carcinogens, production of anti-tumorigenic or anti-mutagenic compounds, enhancing the host’s immune response, and effects on the physiology of the host have been also associated with probiotics administration.

- Adverse effects associated with probiotic therapy are extremely rare and are estimated to occur at a rate of approximately 0.05% to 0.4% of all cases of infective endocarditis and bacteremia. Nevertheless, case reports have identified fungemia in two immunosuppressed patients and exacerbation of diarrhea in two patients with ulcerative colitis who had consumed *S. boulardi*.

**Conclusions**

- Several high-quality randomized clinical trials have demonstrated the potential therapeutic uses for probiotics. The demonstration of specificity between immune and epithelial cells and different microbial species has extended the known mechanisms of action of probiotics beyond simple barrier and antimicrobial effects. It has also confirmed that probiotic bacteria modulate mucosal and systemic immune activity and epithelial function.

- The accumulated knowledge of these mechanisms of action has led to new justification for the use of probiotics and prebiotics in clinical medicine. Clear evidence now exists in support of the therapeutic use of probiotics in recurrent *C. difficile*-induced infections, and postoperative pouchitis. There is a substantial potential use of probiotics in other gastro-intestinal infections, however, it is advisable that better designed clinical trials should be conducted taking into consideration the accumulated information in the literature as well as controlling the confounding variables previously observed. In relation to diarrheal diseases, better emphasis should be given to prolonged episodes of acute diarrhea and prevention of persistent diarrhea in children, in the prevention of postoperative bacterial translocation, in IBS, and in both ulcerative colitis and *Crohn’s disease*.

- Nevertheless, the present literature is based on a mixture of studies with different probiotic strains showing that not all probiotic bacteria have similar therapeutic effects. Future clinical trials will need to incorporate this fact into trial planning and design. The use of symbiotics, seems to be more promising than the use of a single compound. With the accumulated information on the mechanisms of action, well-designed randomized, controlled trials will soon provide the necessary evidence to support the present and other important therapeutic uses for probiotics, prebiotics, and symbiotics.

**Recommended literature:**


