

Probiotics in Allergy Management

Jon A. Vanderhoof

Vice President, Global Medical Affairs, Mead Johnson Nutritionals, Evansville, IN, USA

ABSTRACT

The gut contains a diverse bacterial flora that is acquired at birth and has a number of physiological functions. Administration of prebiotics or probiotics may favourably alter this gut microflora. Prebiotics are poorly digested oligosaccharides that promote the growth of desirable bacteria and may have other beneficial gastrointestinal and systemic effects. Probiotics are “helpful” human bacteria that provide a variety of health benefits when administered exogenously. Probiotics produce beneficial effects in the prevention and treatment of traveller’s diarrhoea, viral diarrhoea, and diarrhoea in day care centres. Moreover, probiotics have been shown to reduce relapses associated with *Clostridium difficile*, and *Lactobacilli* are effective in the prevention of antibiotic-associated diarrhoea. Probiotics may also be efficacious in the treatment of gastroenteritis. Clinical studies of probiotics in inflammatory bowel disease have proved

disappointing, but beneficial effects in adults with irritable bowel syndrome have been reported with *Bifidobacterium infantis* 35624. *Lactobacilli* GG reduces the incidence of gastrointestinal symptoms and gut permeability in patients with atopic dermatitis, and administration of probiotics reduces the frequency and severity of atopic eczema when administered to pregnant women and then to newborn infants. In conclusion, probiotics are effective in the treatment and/or prevention of a number of conditions, including diarrhoea, irritable bowel syndrome and atopic dermatitis, and the product used should be selected based on the particular indication. *JPGN* 47:S38–S40, 2008. © 2008 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

IMPORTANCE OF GUT MICROFLORA

Normal microbial flora of the gut comprises more than 400 species, most of which are acquired perinatally via the maternal vagina and faecal flora. The microbial composition of the gut in infants born by caesarean section may differ. In all infants, some environmental acquisition may occur early in life. The microbiota of the gut is important for a variety of reasons including immune regulation, gut barrier function, and nutrient metabolism in absorption, and it is a potential source of infection.

MODIFICATION OF GUT FLORA

Gut microbiota can be modified via the use of probiotics or prebiotics (Table 1). Probiotics are human derived and are usually exogenous strains of bacteria that may be supplied via the diet or supplements to provide a specific health benefit. Conversely, prebiotics are poorly digested oligosaccharides that promote the growth of desirable strains of commensal bacteria.

The most common probiotics are several strains of bacteria (*Lactobacillus* or *Bifidobacterium*), yeast (*Saccharomyces boulardii*), or killed organisms and subfractions. The benefits of probiotics are strain specific, and the benefits of some strains have been proven in robust clinical trials. It is important to note that not all strains with proven efficacy are suitable for use in all indications.

PROBIOTICS IN ACUTE DIARRHOEA

In individuals with acute diarrhoea, probiotics (eg, *L reuteri*, LGG) have been shown to reduce the severity and duration of viral diarrhoea, the risk of traveller’s diarrhoea, and the incidence of diarrhoea in day care centres. In addition, probiotics also reduce the incidence of relapsing diarrhoea due to *Clostridium difficile*, and the incidence of antibiotic-related diarrhoea.

A number of mechanisms of action have been proposed for probiotics in the protection from diarrhoeal disease, including competitive exclusion, stimulation of intestinal mucin secretion, and stimulation of the immune response. A meta-analysis of 9 randomized, double-blind, placebo-controlled trials in adults and children demonstrated that probiotics were effective in the prevention of antibiotic-associated diarrhoea. The odds ratio

The author is an employee of Mead Johnson Nutritionals and is a shareholder in Bristol-Myers Squibb.

TABLE 1. *Modification of the gut microbiota: prebiotics versus probiotics*

Prebiotics	Probiotics
Increase the number of "helpful" bacteria	Redirect the immune system toward fighting infections and may be helpful in allergy
Produce short-chain fatty acids in the bowel, which strengthen the lining and protect against invasion	Potentially block access of pathogens to receptors
Lower the intestinal pH, which may enhance calcium absorption	Stimulate other parts of the intestinal defence system (eg, mucin)
Normally present in breast milk, and enhance strains that are already present	Essentially, these are foreign bacteria that are not recognised by the immune system and elicit an immune response
May play a role in immunomodulation (yet to be proven)	

in favour of active treatment was 0.39 ($P < 0.001$) for yeast and 0.34 ($P < 0.01$) for *Lactobacilli* (1).

A modest but clinically significant benefit has been demonstrated in the treatment of acute gastroenteritis, especially with LGG. Further research is needed to establish the efficacy of other strains and firm conclusions cannot be made regarding prevention because of heterogeneity of studies.

PROBIOTICS IN BOWEL DISEASE

Inflammatory Bowel Disease

VSL#3, a combination of 8 different strains of bacteria, prevents recurrence of pouchitis and may be useful in ulcerative colitis, but to date no conclusive benefits have been demonstrated in Crohn disease. The *Escherichia coli* strain Nissle may be effective, but studies with LGG have yielded disappointing results. In a study of 75 children 5 to 21 years old with Crohn disease in remission, no apparent benefit of probiotics was evident. Children had a slightly but not significantly shorter time to relapse following treatment with LGG (9.8 months vs 11 months for placebo) (2). Overall, 31% of patients receiving LGG relapsed compared with 17% of patients receiving placebo.

Irritable Bowel Syndrome

In adults with irritable bowel syndrome ($n = 77$), *B. infantis* 35624 was more effective than *L. salivarius* in reducing pain, bloating, and difficulty with defecation and increased the peripheral blood mononuclear cell interleukin (IL)-10/IL-12 ratio (3). As yet, there are no positive studies in paediatric patients with irritable bowel syndrome.

PROBIOTICS IN ALLERGY

LGG has demonstrated beneficial effects in atopic dermatitis in allergic infants (4). It is likely that a few other strains will be effective; however, more data are

necessary. These benefits are likely to be limited to infants and small children and do not yet include asthma.

Probiotic therapy has also been shown to prevent atopic disease in 1 of 2 similarly designed studies (4,5). In a randomized, double-blind, placebo-controlled trial conducted in Finland, LGG was administered to pregnant women with a first-degree relative with atopic eczema. The newborn infants then continued to receive LGG and were evaluated at the age of 2 years (4). The frequency and severity of atopic eczema was reduced in infants receiving LGG (Figure 1). The second study in a German population of infants at high risk found no such advantage (5). The investigators suggested that the difference in results could be attributed to the baseline or demographic differences between the patient populations, such as gene-pool-profile differences [eg, Finnish (4) vs German (5)] or differences in risk for atopic dermatitis (5). The researchers concluded that additional studies could clarify whether particular patient subgroups are more likely to benefit from supplementation with probiotics.

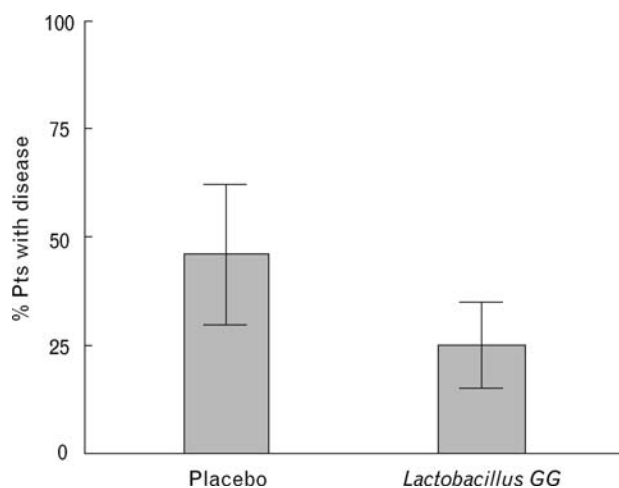


FIG. 1. Efficacy of LGG in 2-year-old children with atopic eczema; adapted from Kalliomaki et al (4).

SUMMARY

Probiotics are useful in a variety of diarrhoeal diseases and they may also have some utility in the treatment of inflammatory and allergic disorders. The effects of probiotics have been proven to be strain specific, and clinical studies are required to determine the efficacy of each strain in specific diseases. Probiotics appear to be safe, even for infants, unless they have central lines. To date, the most positive data are for *Lactobacillus* strains (LGG and *L reuteri*). There is considerable enthusiasm for the routine use of probiotics in neonates, despite a lack of knowledge about the long-term effects. Previous studies suggest that inactivated probiotic bacteria, their DNA, and/or soluble products are likely to provide the beneficial properties of live bacteria, but may be safer alternatives because the dose of these agents can be readily controlled and they are less likely to establish lifelong niches. Probiotics should be considered in much the same way as antibiotics. The most effective and the

appropriate probiotic should be selected for a particular indication. There are no data to suggest value in treating everyone with probiotics.

REFERENCES

1. D'Souza AL, Rajkumar C, Cooke J, et al. Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis. *BMJ* 2002;324:1361.
2. Bousvaros AS, Guandalini S, Baldassano RN, et al. A randomized, double-blind trial of lactobacillus GG versus placebo in addition to standard maintenance therapy for children with Crohn's disease. *Inflamm Bowel Dis* 2005;11:833–9.
3. O'Mahony L, McCarthy J, Kelly P, et al. Lactobacillus and bifidobacterium in irritable bowel syndrome: symptom responses and relationship to cytokine profiles. *Gastroenterology* 2005;128:541–51.
4. Kalliomaki M, Salminen S, Arvilommi H, et al. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. *Lancet* 2001;357:1076–9.
5. Kopp MV, Hennemuth I, Heinzmann A, et al. Randomized, double-blind, placebo-controlled trial of probiotics for primary prevention: no clinical effects of Lactobacillus GG supplementation. *Pediatrics* 2008;121:e850–6.