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308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
Mob: +92 300 3008585, Fax: +92 41 8815544
E-mail: editorpjn@gmail.com

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The Importance of Probiotics in Pediatrics

Nayil Dinkçi, *Gülfem Ünal, Sibel Akalin and Siddik Gönç
Department of Dairy Technology, Faculty of Agriculture, Ege University, 35100, Bornova, Izmir, Turkey

Abstract: Probiotics have been defined as living microorganisms, which upon ingestion in certain numbers have beneficial effects on human health beyond inherent general nutrition. These effects are attributed to the restoration of increased intestinal permeability and unbalanced gut microflora, improvement of the intestine's immunological barrier functions and alleviation of the intestinal inflammatory response. The application of probiotics in pediatric practice currently lies in enhancing these barrier functions in the gut and reducing the risk of diseases associated with their dysfunction. It has been widely accepted that human milk is the best food for infants. Although human milk is the first choice for the newborn infant, milk substitutes play an indispensable role in infant nutrition when breast-feeding is not possible, desirable and sufficient. Infant milk formulas have been designed to provide infants with the required nutrients for optimal growth and development. In this concept probiotic bacteria (such as lactobacilli and bifidobacteria) have been successfully used in infant formulas. Several studies have been carried out using probiotic bacteria in the treatment or prevention of infectious diarrhea and allergic diseases. It has been also demonstrated that supplementing with *Bifidobacterium animalis BB-12* or *Lactobacillus* GG modifies the allergic inflammation in infants with atopic eczema. Furthermore a number of fermented dairy products have already been developed by using specially selected strains of lactobacillus and bifidobacteria for infant feeding. Although most of these products have been used safely for years, results of scientific researches should be evaluated carefully before routinely recommending these products, especially for children.

Key words: Probiotics, nutrition, infant formula

Introduction

It has been widely accepted that breast-feeding is the best food for infants. Mother's milk provides all the nutritive elements for normal growth and for infants' digestive conditions. Breast milk also contains a number of protective and immunoregulatory components that may have a beneficial effect on the development of the infant's immune system. Breastfed infants suffer fewer gastrointestinal and respiratory infections, which is especially highlighted in the lower socioeconomic groups of developing countries.

Although human milk is the first choice for the newborn infant, milk substitutes play an indispensable role in infant nutrition when breast-feeding is not possible, desirable or sufficient. Infant milk formulas have been designed to provide infants with the required nutrients for optimal growth and development. Therefore probiotics have been used successfully in infant formula production (Alles *et al*., 2004).

Probiotics are live microbial food ingredients which are beneficial to health. This probiotic action includes survival in and adhesion to specific areas of the gastrointestinal tract and competitive exclusion of pathogens or harmful antigens. Currently, most probiotics have been selected from members of the normal healthy adult microbiota. The strains with beneficial properties, which are potential sources of probiotics most frequently belong to the genera *Bifidobacterium* and *Lactobacillus* (Isolauri, 2004).

In recent years, besides classical bacterial cultures specific starter cultures have been used in the production of fermented dairy products and they have taken place in the market. Fermented dairy products prepared using specially selected strains of lactobacillus and bifidobacteria play an important role in infant nutrition. Acidophilus milk, bifidus milk, yoghurt, kefir and related products intended for infant feeding have already been developed and found suitable for feeding both normal and sick infants. Inadequacy in breast milk and modified infant formulas have led to the suggestion for the development of fermented dairy products for infant feeding (Sarkar, 2003).

The basic foundation of nutrition lies in a healthy, balanced diet to meet the needs for growth and development in children. In a disease state, specific requirements for energy and nutrients may change and a deficiency of these may contribute to a deterioration of nutritional status and growth failure in children. Beyond this function in the prevention of direct diet-related deficiencies, the role of diet has changed as the science of nutrition is currently directed towards improvement of the defined physiologic functions, including the potential to reduce the risk of disease (Isolauri, 2004).

The aim of this review is to evaluate the use of probiotics in infant nutrition by discussing their effects on certain diseases that are common among infants and children.

Health effects of probiotics in pediatrics: In probiotic foods, cultures of beneficial live microorganisms characteristic of the healthy human gut microbiota are administered in order to provide a safe microbial stimulus. The probiotic effects are attributable to the restoration to the normal of increased intestinal permeability and an unbalanced gut micro ecology. They improve the intestine's immunological barrier functions, alleviate the intestinal inflammatory response, and reduce generation of pro-inflammatory cytokines characteristic of local and systemic allergic inflammation (Isolauri, 2004).

Well controlled clinical studies have shown that lactobacillus and bifidobacteria can safely be applied for the nutritional management of patients with gastrointestinal infection and inflammatory diseases. In these studies probiotics have been found as beneficial in the treatment of diarrhea, inflammatory bowel diseases and allergic diseases.

Diarrhea: Diarrhea is a common complication of antibiotic therapy, especially in children using broad-spectrum agents. Moreover it contributes substantially to pediatric morbidity and mortality worldwide and occur among 16.5 million children in the United States annually (Vanderhoof and Young, 2002; Van Niel *et al.,* 2002). One of the primary areas of probiotic research in children has been in the treatment and prevention of diarrhea. Well-demonstrated positive effects in pediatric antibiotic-associated diarrhea, as well as *Clostridium difficile*-associated diarrhea, which can occur after antibiotic therapy, have been identified with *Lactobacillus* GG (Young and Huffman, 2003; Vanderhoof and Young, 1998). *Lactobacillus* GG is the most widely studied in clinical trials, but others include *Streptococcus thermophilus*, *Lactobacillus bulgaricus*, *Bifidobacterium bifidus* and *longum*, *Lactobacillus acidophilus*, *Enterococcus faecium*, *Lactobacillus reuteri*, *Lactobacillus casei Shirota* and the yeast *Saccharomyces boulardii* (Davisson and Butler, 2000; Isolauri, 2003; Isolauri, 2004). The consistent effect of probiotic therapy in infectious diarrhea has been explained by a reduction in the duration of rotavirus shedding normalization of gut permeability after rotavirus infection, and by an increase in the expression of mucin and IgA-secreting cells working against rotavirus (Isolauri, 2004; Tuohy *et al.*, 2003).

Lactobacillus GG has been found to reduce the incidence of antibiotic-associated diarrhea in children treated with oral antibiotics for common childhood infections (Vanderhoof *et al.*, 1999). A similar result has been obtained from *Lactobacillus* GG in prevention of nosocomial diarrhea in infants (Szajewska *et al.*, 2001). Lactobacillus has also been found to be safe and effective as a treatment for children with acute infectious diarrhea (Van Niel *et al.*, 2002).

Lactobacillus GG has been shown to prevent traveler's diarrhea in the United States tourists visiting developing countries with a protective rate of 47 % (Davisson and Butler, 2000).

Saccharomyces boulardii, a non-pathogenic yeast, has been shown to be effective in the prevention and treatment of antibiotic-associated diarrhea and in reducing relapse of *Clostridium difficile*-associated diarrhea after therapy (Davisson and Butler, 2000). While both *Saccharomyces boulardii* and *Lactobacillus* GG have demonstrated efficacy in the prevention of relapsing *Clostridium difficile* diarrhea, the data is much stronger for *Saccharomyces boulardii* (Vanderhoof and Young, 2002).

The use of probiotics in the treatment of acute diarrheas, particularly viral diarrhea, has been extensively studied by several groups in placebo-controlled studies in both Europe and the United States. In these studies, *Lactobacillus* GG, *Lactobacillus reuteri*, *Lactobacillus acidophilus*, *Saccharomyces boulardii* and a combination product of *Streptococcus thermophilus*, *Lactobacillus acidophilus* and *Lactobacillus bulgaricus* led to decreased severity and duration of diarrhea when administered alone or as part of oral rehydration therapy (Young and Huffman, 2003). *Lactobacillus plantarum* has been also shown to have some benefit by decreasing the diarrhea symptoms associated with irritable bowel syndrome (Young and Huffman, 2003).

Inflammatory bowel diseases: Probiotic use in the treatment of inflammatory bowel diseases has importance in both infants and children (Vanderhoof and Young, 2002; Reid, 2002; Young and Huffman, 2003). Related reports indicate that there are beneficial effects attained by probiotic intervention in reversing some immunological disturbances, in modification of disease activity and in normalization of increased intestinal permeability in children with Crohn's disease. The strains assessed include *Lactobacillus* GG, a non-pathogenic *E.coli*, a preparation containing 4 strains of lactobacilli (*L.casei*, *L.plantarum*, *L.acidophilus* and *L.bulgaricus*) and 3 bifidobacteria strains (*B.longum*, *B.breve* and *B.infantis*) together with *Streptococcus thermophilus* (Isolauri, 2004).

Animal studies in inflammatory bowel disease have demonstrated the ability of probiotics to reduce the level of microscopic inflammation, as well as decrease inflammatory cytokines (Young and Huffman, 2003).

Both intestinal flora and the immune system are known to play a role in the development of cancer. Theoretically, the use of probiotics may be of benefit, particularly in preventing tumors. Animal studies have demonstrated the ability of probiotics to decrease fecal concentrations of enzymes and mutagens thought to be involved in colon carcinogenesis (Young and Huffman, 2003). A research which had been done to evaluate the potential

role of probiotic therapy in pediatric urology concluded that it has positive effects on preventing and managing inflammatory and some carcinogenic diseases (Reid, 2002).

Allergic diseases: There are data to suggest that the prevalence of atopic diseases (i.e. atopic eczema, allergic rhino conjunctivitis and asthma) has increased ever recent decades throughout the industrialized world. In general, the 'hygiene hypothesis' of allergy implies that recent advances such as improved sanitation and lifestyle changes, including the declining family size, in Western societies have reduced the extent of microbial exposure. Infectious disease in early childhood may in fact prevent allergic disease. Exposure should occur very early, because the first expression of the atopic immune responder type frequently occurs within the first few months of life. The establishment of the gut microbiota in providing an initial and massive source of microbial stimuli may be a good candidate 'infection'. Delayed compositional development of the normal intestinal microbiota has indeed been shown to hinder the maturation of host defense mechanisms in the gut in early infancy, when exposure to novel allergenic challenges in diet and environment continues, thereby carrying a potential risk for atopic disease (Isolauri *et al.*, 2002).

The idea underlying probiotic use in allergic disease is to provide a microbial stimulus for the host immune system by means of cultures of beneficial live microorganisms that are characteristics of the healthy infant gut microbiota (Isolauri *et al.*, 2002). Recent studies from Finland have demonstrated a reduced incidence of milk allergy in infants given *Lactobacillus* GG during early infancy. Likewise, treatment of milk allergic infants with *Lactobacillus* GG seems to ameliorate both the extent and the severity of allergic eczema (Vanderhoof and Young, 2002).

Lactobacillus GG has been shown to improve the clinical course of dermatitis in children fed a probiotic-supplemented extensively hydrolyzed whey formula compared to the formula alone. This was attributed to the ability of these organisms to alter intestinal permeability or by a direct effect on the intestinal immune response (Davisson and Butler, 2000).

Rosenfeldt *et al.* (2003) have investigated the clinical and anti-inflammatory effect of probiotic supplementation in children with atopic dermatitis. In the study, 2 probiotic Lactobacillus strains (lyophilized *Lactobacillus rhamnosus* 19070-2 and *Lactobacillus reuteri* DSM 122460) were given in combination for 6 weeks to 1- to 13-year old children with atopic dermatitis. A combination of *Lactobacillus rhamnosus* 19070-2 and *Lactobacillus reuteri* DSM 122460 has been found to be beneficial in the management of atopic dermatitis and also IgE levels had increased.

Conclusion: Probiotics contain species of beneficial bacteria that are commonly found in the intestinal tract. Studies suggest that consumption of certain probiotic strains, primarily *Lactobacillus* GG, may temporarily alter the intestinal microflora to produce a beneficial effect. Most commercially available strains of lactobacilli and bifidobacteria species are generally considered safe and may be especially helpful in treatment of pediatric diarrheal illnesses. However, clinical benefit of probiotic therapy is dependent on numerous factors such as type of bacteria, dosing regimen, delivery method, and other underlying host factors.

For example, a few strains of certain species of lactobacillus may be capable of shortening the duration of rotavirus diarrhea, whereas most others are not. The genetic variability among various strains of lactobacilli is considerable. Probiotic benefits are most often dependent on the ability of the organism to colonize the bowel. This usually requires the presence of receptors on the bacterial cell wall that permit attachment to the gastrointestinal epithelium. Most strains do not have such receptors. Certain strains are more bile- and acid-resistant than others and some strains produce bacteriocins, which kill adjacent organisms.

As a result analysis of these statements are necessary while recommending a specific probiotic. Although the risk of adverse effects is thought to be very low, use of probiotic agents in premature infants and children with altered immune function, and the use of newer strains of nontraditional probiotics without a long history of safe use should be carefully considered and studied further.

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