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Probiotics and its role in Diarrhoea – A Review Article

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ABSTRACT *The increasing cost of health care, the steady increase in life expectancy and the desire of the elderly for improved quality of their lives are driving factors for research and development in the area of functional foods. Although the concept of functional foods was introduced long ago with Hippocrates and his motto "Let food be your medicine", fairly recently the body of evidence started to support the hypothesis that diet may play an important role in modulation of important physiological functions in the body. Among a number of functional compounds recognized so far, bioactive components from fermented foods and probiotics certainly take the center stage due to their long tradition of safe use, and established and postulated beneficial effects. Probiotics have made their way into healthcare and are more likely to be our friend than our enemy. Despite our rapidly increasing knowledge of pathogen–host interactions, the role of beneficial bacteria in preventing the emergence of pathogenic species health remains obscure. There is a great need to elucidate the role of the beneficial microbiota, to identify beneficial bacteria and to conduct proper large-scale studies on the usefulness of probiotics to maintain or improve health.*

Introduction

The concept behind probiotics was introduced in the early 20th century, when Nobel laureate Elie Metchnikoff, known as the "father of probiotics," proposed in The Prolongation of Life: Optimistic Studies that ingesting microorganisms could have substantial health benefits for humans. Microorganisms are invisible to the naked eye and exist virtually everywhere. Scientists continued to investigate the concept, and the term "probiotics"—meaning "for life"—eventually came into use.[1]

As today's consumers become increasingly aware of the processes that may be necessary for maintenance of their environment, health, and nutrition, scientific research has focused on the roles that diet, stress, and modern medical practices (e,g.: the use of antibiotics and radiotherapy) play in threatening human health. In particular, the shifting of population dynamics toward older societies is increasing the incidence of illnesses that may be caused by deficient or compromised microflora, such as gastrointestinal tract infections, constipation, irritable bowel syndrome, inflammatory bowel disease (Crohn's disease and ulcerative colitis), food allergies, antibiotic-induced diarrhea, cardiovascular disease, and certain cancers (e.g.: colorectal cancer) [2]

Probiotics have been defined as "a live microbial food supplement which beneficially affects the host by improving the intestinal microbial balance" and, more broadly, as "living micro-organisms, which upon ingestion in certain numbers, exert health affects beyond inherent basic nutrition" .[2]

Probiotics are available in foods and dietary supplements (for example, capsules, tablets, and powders) and in some other forms as well. Examples of foods containing probiotics are yogurt, fermented and unfermented milk, ice creams, juices and soy beverages. In probiotic foods and supplements, the bacteria may have been present originally or added during preparation. [3]

In 1994, 0the World Health Organization deemed probiotics to be the next-most important immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. The use of probiotics in antibiotic resistance is termed microbial interference therapy. With increasing understanding that beneficial microbes are required for health, probiotics may become a common therapeutic tool used by health care practitioners in the not-too-distant future.[4]

History

Initially established in the middle and Far East of Asia, the tradition of fermenting milk was spread throughout the east Europe and Russia by the Tartars, Huns and Mongols during their conquests. As a consequence, a wide range of fermented dairy products still exists in these regions and some popular products such as yoghurt and kefir are claimed to originate from the Balkans and Eastern Europe.[1]

Lactic acid bacteria were first discovered by Pasteur in 1857. Their isolation from rancid milk was reported in 1878 by Lister, and later they were also isolated from the intestinal tract.[6] Escherich in 1885 was the first to recognize the importance of examining bacteria appearing in normal faeces and the intestinal tract, and consequently understanding the physiology of digestion and the pathology and therapy of intestinal diseases of microbial origin.[1] In 1889, Tissier discovered Bifidobacterium spp., and in 1900 Moro discovered *Lactobacillus acidophilus*. According to G. Reid probiotics were first promoted for therapeutic relief of intestinal disorders in 1906 by Tissier in a thesis present at the University of Paris.[5]

German professor Alfred Nissle, in 1917, isolated a strain of *Escherichia coli* from the faeces of a World War I soldier who did not develop enterocolitis during a severe outbreak of shigellosis. In those days, antibiotics were not yet discovered, and Nissle used the strain with considerable success in acute cases of infectious intestinal diseases (salmonellosis and shigellosis). *Escherichia coli Nissle* 1917 is still in use and is one of the few examples of a non-LAB probiotic.

After Metchnikoff's death in 1916, the centre of activi-

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ty moved to the US. It was reasoned that bacteria originating from the gut were more likely to produce the desired effect in the gut, and in 1935 certain strains of *Lactobacillus acidophilus* were found to be very active when implanted in the human digestive tract. Trials were carried out using this organism, and encouraging results were obtained especially in the relief of chronic constipation.

The term "probiotics" was first introduced in 1953 by Kollath. Contrasting antibiotics, probiotics were defined as microbially derived factors that stimulate the growth of other microorganisms. In 1989 Roy Fuller suggested a definition of probiotics which has been widely used: "A live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance". Fuller's definition emphasizes the requirement of viability for probiotics and introduces the aspect of a beneficial effect on the host.

Commonly used probiotics

The most commonly used strains belong to the genera **Lactobacillus** and **Bifidobacterium** genera that are commonly found in the oral cavity, including carious lesions. Probiotic Lactobacillus and Bifidobacterium strains have been reported to exert potentially beneficial effects for the mouth: *L. rhamnosus* GG (ATCC 53103) produces a growth inhibitory substance against *S.sobrinus* and it has been proposed to reduce the risk for caries.[6] Also *S. salivarius* strains appear to be excellent candidates for an oral probiotic, since they are early colonizers of oral surfaces and are amongst the most numerically predominant members of the tongue microbiota of healthy individuals. *Streptococcus salivarius* has not been implicated either in caries or in other infectious diseases of humans and is most closely related to *S. thermophilus,* a bacterium widely used in the dairy food industry.[7] Recent progress is particularly evident in the application of avirulent *S. mutans* to control dental caries, alpha hemolytic streptococci to reduce otitis media recurrences, and *S. salivarius* to prevent streptococcal pharyngitis.[8]

EFFICACY OF PROBIOTICS FOR DIARRHOEAL DISEASE

Infectious diarrhoea

Infectious diarrhoea is the most widely investigated area for probiotic use in children, with several meta-analyses published. Most of the randomised controlled trials included in these meta-analyses involved children in developed countries in a health care setting. All meta-analyses were challenged by a lack of heterogeneity between studies. However, despite the variability between probiotics tested, dose and duration of treatment, participant groups, and definitions of diarrhoea and outcome, all reviews concluded that probiotics, co-administered with standard rehydration therapy, decrease the duration of acute diarrhoea.

A Cochrane review comprised 23 studies with a total of 1917 participants (1449 children). Pooled results showed that probiotics reduced the risk of diarrhoea at 3 days (relative risk [RR], 0.66; 95% CI, 0.55–0.77; random effects model, 15 studies) and the mean duration of diarrhoea by 30.5 hours (95% CI, 18.5–42.5 hours; random effects model, 12 studies). None of the studies reported adverse effects.[9]

L. rhamnosus GG (LGG) is the most investigated probiotic strain for this condition. A meta-analysis of paediatric studies contained a subgroup analysis restricted to LGG therapy, which comprised 10 study arms. The pooled estimate showed that LGG reduced the duration of diarrhoea by 1.2 days (95% CI, −1.6 to −0.8 days; P <0.001). The Cochrane review suggested that LGG may be particularly effective for rota-viral diarrhoea. Rotavirus is the most common cause of severe diarrhoea in children worldwide.

From these meta-analyses, it appears that probiotics are more effective if given early in the course of illness and at daily doses of at least 10 billion colony-forming units (CFU). Thus, there is good evidence to support the use of probiotics in infectious diarrhoea of viral aetiology, when given early in the illness. There is no evidence to support the efficacy of probiotics in diarrhoeal illnesses of bacterial origin.

Antibiotic-associated diarrhoea

Antibiotic-associated diarrhoea is defined as otherwise unexplained diarrhoea that occurs in association with antibiotic administration. It is a common problem, occurring in upto 25% of patients receiving antibiotics, with rates varying depending on the population studied and the antibiotic used. While *C. difficile* is the most common infectious agent isolated, in most cases of antibiotic-associated diarrhoea a causative organism is not found. Antibiotic-associated diarrhoea can begin after a single antibiotic dose or occur up to 6 weeks after the commencement of treatment. Oral antibiotic agents, such as cephalosporins, clindamycin and broad-spectrum penicillins, are more likely to cause antibiotic-associated diarrhoea than parenteral antibiotics. The rationale for using probiotics in antibiotic-associated diarrhoea rests on the assumption that antibiotics alter the normal intestinal flora. Several probiotics have been evaluated in treating or preventing antibiotic-associated diarrhoea, including *L. acidophilus*, *L.casei*, LGG, and S. *boulardii*[10]

Clostridium difficile diarrhoea

There is little evidence to support the routine use of probiotics to prevent or treat *C. difficile* diarrhoea, according to two systematic reviews. [12]

In the study by Surawicz et al. a subgroup analysis of subjects receiving high-dose vancomycin, who were more likely to have severe *C. difficile* associated diarrhoea, demonstrated a beneficial effect of the probiotic (risk difference 33, 95% CI –0.3 to 62.0). However, the CI's in the subgroup analyses from both studies were very wide, which made it difficult to ascertain the magnitude of the effect.

In the 4 studies in which prevention of antibiotic-associated diarrhea was the primary outcome, probiotic therapy had no significant effect on the prevention of CDAD.[13]

Traveller's diarrhoea

The results from trials studying the role of probiotics in preventing traveller's diarrhoea are inconsistent, possibly reflecting the variation in probiotic strains used. However, meta-analysis of 12 studies showed that probiotics decreased the risk of traveller's diarrhoea (RR, 0.85; 95% CI, 0.79–0.91; p<0.001). One placebo-controlled trial showed a beneficial prophylactic effect of LGG26, while another failed to demonstrate any benefit.[14]

Conclusion

Probiotics have made their way into healthcare and are more likely to be our friend than our enemy. Despite our rapidly increasing knowledge of pathogen–host interactions, the role of beneficial bacteria in preventing the emergence of pathogenic species health remains obscure. There is a great need to elucidate the role of the benefi-

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