Probiotics and Periodontal Disease - A Review

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ABSTRACT:

Probiotics are live micro-organisms that when administered in adequate amounts confer health benefits upon the host. A few conventional foods containing probiotics are yogurt, fermented and unfermented milk, soy beverages etc. Most often, they come from two groups of bacteria, Lactobacillus or Bifi dobacterium. Evidence now suggests that probiotics may function not only by direct inhibition of pathogenic micro-organisms, but also by more subtle mechanisms including modulation of the mucosal immune system. Little attention has been paid to the identification of beneficialoral bacterial species. Probiotic technology represents a breakthrough approach to maintaining oral health by using natural beneficial bacteria to provide a natural defense against the pathogenic bacteria species. This review endeavours to introduce the concepts of probiotics in periodontics.

Key words: Bifi dobacterium, lactobacillus, probiotics

INTRODUCTION

Bacteria have always been associated with disease and have caused the human race much grief. Hence the concept of harnessing bacteria for health benefits has a poetic ring to it. The concept of beneficial for health micro-organisms dates back to the ideas of Ukrainian Nobel laureate Ilya Metchnikov, working at the Pasteur Institute in Paris, during the early years of 20th century.[1] The term 'probiotic' is a relatively new word and is currently used to name bacteria with beneficial effects for humans and animals.

The term "probiotics", the antonym of the term "antibiotics", was introduced in 1965 by Lilly and Stillwell as substances produced by microorganisms which promote the growth of other microorganisms.[2] The term "probiotics" is derived from the Greek word, meaning "for life." [3] The use of microorganism to promote health is very ancient and can even be traced back to the classical Roman literature where

food fermented with microorganisms was used as a therapeutic agent.[4] There is a long tradition, particularly in parts of Europe and Asia, of ingesting microbes or food products that affect the intestinal microbiota in ways that are believed to provide beneficial health effects, i.e. intake of probiotics and prebiotics.[5]

Probiotics, most commonly belong to the genera - Lactobacillus and Bifidobacterium. Lactobacillus species from which probiotic strains have been isolated include L. acidophilus, L. johnsonii, L. casei, L. rhamnosus, L. gasseri, and L. reuteri. Bifidobacterium strains include B. bifidum, B.longum, and B. Infantis.[6] Lactobacilli found in raw milk and fermented dairy products such as cheese, yoghurt and fermented milk are ubiquitous in the diet and are found in the gastrointestinal tract soon after birth.[7] Furthermore, certain strains of Aspergillus, Propionibacterium, Saccharomyces, Streptococcus, Enterococcus and non-pathogenic strain of E.coli, Clostridium butyricum, are among others which have demonstrated probiotics properties.[8, 9]

Probiotics can help prevent and treat disease through several mechanisms.

1. Direct interaction: Probiotics interact directly with the disease-causing microbes, making it harder for them to cause the disease.
2. Competitive exclusion: Beneficial microbes directly compete with the disease, developing microbes for nutrition or enterocyte adhesion sites.
3. Modulation of host immune response: Probiotics interact with and strengthen the immune system and help prevent disease.[10]

Given the widespread emergence of bacterial resistance to antibiotics, the concept of probiotic therapy has been considered for application in oral health. Oral probiotics have been evaluated primarily in the management of dental caries.[11] However there seems to be no reason why probiotic therapy might not also be applicable for controlling the periodontal disease. Taking into account the two major treatment strategies for periodontal disease viz, elimination of specific pathogens and suppression of destructive host response, the probiotic approach may add some value in achieving these treatment goals.

COMPOSITION OF PROBIOTICS

Probiotics which are regulated as dietary supplements and foods, consist of yeast or bacteria. They are available as capsules, gels, pastes, tablets, packets, liquids, or powders, and are contained in various fermented foods, most commonly yogurt or dairy drinks. Probiotic products may contain a single microorganism or a mixture of several species. Probiotics can be bacteria, moulds, yeast. But most probiotics are bacteria. Among bacteria, lactic acid bacteria are more popular.[12]

MICROORGANISMS USED AS PROBIOTICS [13, 14]

Lactic acid producing bacteria	Non-lactic acid producing bacteria	Bifido-bacterium species
L. acidophilus	Bacillus cereus	B. adolescentis
L. bulgaricus	Propionibacterium	B. animalis
L. casei	Enterococcus faecalisa	B. bifidum
L. crispatus	Enterococcus faeciuma	B. breve
L. crispatus	Escherichia coli Nissle	B. infantis
L. reuteri	Escherichia coli Nissle	B. lactis

PROBIOTICS IN ORAL CAVITY

More than 700 species of oral microbiota have been detected in the human mouth and the resident microbiota of one individual may consist of 30-100 species.[9] An essential requirement for a microorganism to be an oral probiotic is its ability to adhere to and colonize surfaces in the oral cavity. Studies suggest that lactobacilli as members of resident oral microflora could play an important role in the micro-ecological balance in the oral cavity. The studies further demonstrated that lactobacilli strains with probiotic properties may indeed be found in the oral cavity. Yet there is no evidence whether these lactobacilli strains were detected due to the frequent consumption of dairy products leading to temporary colonization only, or if the oral environment is their permanent habitat.[7, 9]

Criteria for Probiotics

To be considered for use as probiotic following criteria needs to be fulfilled.[7, 15, 16]

1. It should capable of exerting a beneficial effect on the host animal, e.g. increased growth or resistance to disease.
2. It should be of human origin.
3. It should have high cell viability.
4. It should be non-pathogenic and non-toxic.
5. It should be able to interact or to send signals to immune cells.
6. It should have capacity to influence local metabolic activity
7. It should be capable of surviving and metabolising in the gut environment e.g. resistance to low pH and organic acids.
8. It should be stable and capable of remaining viable for periods under storage and field conditions.

PROBIOTICS IN PERIODONTAL DISEASE

Periodontal disease is characterized by the presence of gingival inflammation, periodontal pocket formation, and loss of connective tissue attachment and alveolar bone around the affected teeth.[17] The current concept concerning the etiology of periodontitis considers 3 groups of factors that determine whether active periodontitis will occur in a subject: a susceptible host, the presence of pathogenic species and the absence of so called "beneficial bacteria".[18] Taking into account the two major treatment strategies for periodontal disease viz, elimination of specific pathogens and suppression of destructive host response, the probiotic approach may add some value in achieving these treatment goals.

MECHANISMS OF ACTION OF PROBIOTICS

Probiotics can help prevent and treat disease through several mechanisms including direct interaction, competitive exclusion and modulation of host immune response. The treatment strategies conferred by probiotics against periodontal diseases are mainly anticipated to be either by inhibition of specific pathogens or by altering the host immune response through the following multiple factors,[7, 15, 16]

Inhibition of specific organisms

- Inhibition of pathogen adhesion, colonization and biofilm formation
- Inhibition of pathogen growth by various substances such as organic acids, hydrogen peroxide and bacteriocins against oral pathogens.

Effects on host response

- Inhibition of collagenases and reduction of inflammation associated molecules
- Induction of expression of cytoprotective proteins on host cell surfaces
- Modulation of pro-inflammatory pathways induced by pathogens
- Prevention of cytokine-induced apoptosis
- Modulation of host immune response

As stated above, a probiotic candidate bacterium should be able to adhere to and successfully establish itself in the oral biofilm to exert health effects. The ability of probiotics to adhere to saliva coated surfaces varies among species and it has been reported that L. rhamnosus and L. paracasei strains possesses strong binding activity.[19] Recently Haukioja et al have shown that probiotic Lactobacilli (L. rhamnosus GG, Lactobacillus casei) may affect the oral ecology by specifically preventing the adherence of other bacteria and by modifying the protein composition of the salivary pellicle. Eventually when a species binds well to structures of the oral biofilm, it could be anticipated that this might affect the pathogenic potential of the species based on antimicrobial activity, which infact is another evaluation criterion for probiotics.[20] W. cibaria secretes a significant quantity of hydrogen peroxide as well as bacteriocin that acts against gram positive bacteria. This bacterial species has the capacity to coaggregate with Fusobacterium nucleatum and to adhere to epithelial cells.[21, 22]

Probiotics in Periodontal Disease - An Evidence Based Approach

Probiotics for periodontal therapy have not been extensively studied. Studies on probiotics and periodontal disease are particularly sparse and at present few clinical studies have evaluated the efficacy of probiotic species from a periodontal disease perspective. Streptococcus oralis and Streptococcus uberis have reported to inhibit the growth of pathogens both in the laboratory and animal models. They are indicators of healthy periodontium. When these bacteria are absent from sites in the periodontal tissues, those sites become more prone to periodontal disease.[23] Lactobacillus reuteri and Lactobacillus brevi are among the species able to affect gingivitis and plaque composition positively as well as being specific markers for periodontal disease.[24]

The oral administration of a tablet containing L. salivarius WB21 was able to decrease the plaque index significantly, and the pocket probing depth markedly, in subjects who were smokers. Another finding in this clinical trial was the ability of L. salivarius WB21 to successfully reduce the prevalence of periodontal pathogens.[25] According to Narva et al, during the fermentation process in milk, Lactobacillus helveticus produces short peptides that act on osteoblasts and increase their activity in bone formation. These bioactive peptides could thereby contribute in reducing bone resorption associated with periodontitis.[26] Koll-Klais et al reported that resident lactobacilli flora inhibits the growth of P. gingivalis and Prevotella intermedia in 82% and 65%, respectively.[27] Ishikawa et al. observed in vitro inhibition of P. gingivalis, P. intermedia, and P. nigrescens by daily ingestion of L. salivarius in tablet form.[28]

L. acidophilus contained in a tablet named Acilact was first clinically tested by pozharitskaia et al in 1994 and they found improved clinical parameters in periodontitis patients and shifts in local microflora towards gram positive cocci and lactobacilli. Later in the year 2002 Grudianov et al also carried out a clinical study where they obtained a probiotic mix in the tablet forms, viz Acilact and Bifidumbacterin and found normalization of micro flora and reduction of signs of gingivitis and periodontitis.[29, 30] A study done by Vivekananda MR using Prodentis lozenges showed plaque inhibition, anti-inflammatory, and antimicrobial effects of Prodentis. The study proposed that probiotics could serve as a useful adjunct or alternative to periodontal treatment when SRP might be contraindicated.[31]

Shimazaki and colleagues, in an epidemiological study found that individuals, particularly nonsmokers, who regularly consumed yoghurt or beverages containing lactic acid exhibited lower probing depths and less loss of clinical attachment than individuals who consumed few of these dairy products. A similar effect was however not observed with milk or cheese.[32] Twetman et al used L. reuteri-containing chewing gum in 42 healthy patients and assessed its effects on crevicular fluid volume, cytokine (interleukin-1β, interleukin-6, interleukin-10, and TNF-α) levels, and bleeding on probing. Crevicular fluid volume, as well as TNF-α and interleukin-8 levels, and bleeding were significantly reduced.[33]

A particular concern when evaluating probiotic effects on periodontal disease relates to the means of administration of these bacteria. Generally probiotics are delivered in dairy products (mainly fermented milks), as food supplements in tablet forms or in soft drinks. However these routes of administration cannot provide prolonged contact with oral tissues, facilitating probiotic adhesion to saliva coated surfaces. A lozenge form or chewing gum tablet or gum might better serve the needs for periodontal health prophylaxis. Longitudinal studies are required however to clarify the observed relationship between regular consumption of products containing probiotics and periodontal health.

Guided Pocket Recolonization (GPR)

Recently, Teughels et al reported that the subgingival application of a bacterial mixture including Streptococcus sanguinis, Streptococcus salivarius (S. salivarius), and Streptococcus mitis after scaling and root planing significantly

suppressed the re-colonization of Porphyromonas gulae (canine P. gingivalis) and P.intermedia in a beagle dog model. Animal study performed to test the concept of bacterial replacement therapy in the treatment of plaque related periodontal disease, this study assessed quantitative changes in the subgingival microbiota after root planing when beneficial bacteria were applied adjunctively. Although application of beneficial bacteria did not exclude pathogen recolonization, it did delay the recolonization process significantly.[34]

In another animal study evaluated radiologically the impact of replacement therapy by monitoring bone density changes and alveolar bone level in periodontal pockets in a dog model. The bone density within periodontal pockets treated with beneficial bacteria improved significantly after 12 weeks, there was a significant increase in the bone level at the end of the study for the pockets receiving beneficial bacteria, and no significant changes were noted in the control pockets.[35] This novel approach of Guided Pocket Recolonization may provide a valuable addition or alternative to the armamentarium of treatment options for periodontitis.

Safety Aspects of Probiotics

Increased probiotic supplementation of different food products during the recent years has raised safety concerns. When probiotics are applied orally, at least a part of them will be ingested and can interact with a patients systemic health. When ingested orally, probiotics are generally considered safe and well tolerated with bloating and flatulence occurring frequently.[8] The increased probiotic consumption inevitably leads to increased concentrations of these species in the host organism. Although rare, cases of probiotics-related bacteraemia, lactobacillus endocarditis and liver abscess secondary to L. rhamnosus have been reported in the literature and such cases have responded well to appropriate antibiotic therapy. Recently, major and minor risk factors for probiotics-associated sepsis have been identified. Major risk factors include immunosuppression (including a debilitated state or malignancy) and prematurity in infants.[9] Although administration of probiotics generally can be considered safe, each strain of probiotics has specific properties that should be considered before its use in any patient.

CONCLUSION

Probiotics represent a new area of research in periodontal therapy. Probiotics play an important role in combating issues with overuse of antibiotics and antimicrobial resistance. Today.s new technological era would be the right time to change the way bacteria are treated. Clinical trials should be directed to assess the method of probiotic administration in oral cavity and dosages for different therapeutic uses. Studies have been largely conducted in animals, and human studies have not been of sufficient duration to assess the impact on periodontal disease. Much more scientific developments are needed to have a better understanding of these tiny forms of lives in order to broaden their potential applications.

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