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Role of Probiotics In Periodontics
Review Article

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Abstract

The concept of microbial ecological change as a mechanism for preventing dental disease is an important one while altered microbial ecology may lead to a dental disease. New methods such as probiotic approaches (i.e. whole bacteria replacement therapy) to eliminate pathogenic members of the microbiota can be investigated. Bacteriotherapy is an alternative and promising way to combat infections by using harmless bacteria to displace pathogenic microorganisms. Probiotics are one of the new agents which are widely used for their therapeutic action.Periodontitis is a multifactorial disease that encompasses the hard and soft tissue, microbial colonization (with or without invasion), inflammatory responses and adaptive immune responses. Treatment of periodontal diseases in recent years has moved towards an antibiotic/antimicrobial model of disease management. Probiotics might be a promising area of research in the treatment of periodontitis with limited scientific research. So extensive studies are needed to know about the interaction of probiotic species and periodontal pathogens and also about their effect on periodontium.

Key words : Probiotics; Prebiotics; Bacteriotherpy; Bifidobacterium; Lactobaciilus

1. Introduction

There has been a paradigm shift towards an ecological and microbial community-based approach to understanding oral diseases. This has significant implications for approaches to therapy and has raised the possibility of developing novel strategies through manipulation of the resident oral microbiota and modulation of host immune responses.[1]

A complete understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics will be essential to assess their long term consequences for oral health and periodontal disease. [2]

Probiotics utilize naturally occurring bacteria to confer a health benefit when administered in adequate amounts. A few conventional foods containing probiotics are yoghurt, fermented and unfermented milk, soy beverages etc. Most often, they come from two groups of bacteria, Lactobacillus or Bifidobacterium.[3]

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Extensive research to create a probiotic product intended to maintain dental and periodontal health is needed.

There are only very few experimental studies exploring probiotic use in periodontal diseases, partly reflecting a poorer understanding of the precise aetiology of the disease and of the conditions that promote health.[4] Results of studiesindicated that Probiotic mouth rinse containing nisin had the potential of inhibiting plaque accumulation and was effective in reducing gingivitis.[5]

This article reviews about the data on the use of probiotics with their scientific understanding and their potential for preventing and treating periodontal disease.

1.1 Probiotics

A 'probiotic, by the generally accepted definition, is a 'live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance'.[6] The organisms that have been used as probiotics are primarily certain species of lactobacilli and bifidobacterium and Saccharomyces spp. But some streptococci, enterococci and commensal *Escherichia coli* have also been claimed to have beneficial effects in certain situations.[1]

1.2 Probiotics and general health

A number of potential benefits arising from the use of probiotics have been proposed, including:-

• Increased resistance to infectious diseases

• Alleviate lactose tolerance

• Prevention from gut , diarrhoea, gastritis, vaginal and urogenital infections

• Reduction in blood pressure and regulation of hypertension , serum cholesterol concentration

• Reduction in allergy , respiratory infections

• Resistance to cancer chemotherapy and decreasing risk of colon cancer

1.2.1 Mechanism of action

• *Probiotics:* There are common themes emerging in studies of the modes of action of probiotics and numerous mechanisms have been proposed [7,8] including:-

• Prevention of adhesion of pathogens to host tissues.

• Stimulation and modulation of the mucosal immune system, e.g. by reducing production of pro-inflammatory cytokines through actions on NFαB pathways, increasing production of anti-inflammatory cytokines such as IL-10 and host defence peptides such as β-defensin 2, enhancing IgA defences and influencing dendritic cell maturation.

• Modulation of cell proliferation and apoptosis through cell responses to, for example, microbially produced short chain fatty acids.

1.3 Prebiotic

The bacterial population of the human gastrointestinal tract constitutes an enormously complex ecosystem. Most of these organisms are beneficial (e.g. Bifidobacterium and lactobacillus) but some are harmful (e.g. Salmonella species, Helicobacter pyroli, Clostridium perfringens). Some dietary substances, the so- called 'prebiotics' can favour the growth of these beneficial bacteria over that of harmful ones.

Prebiotics are non-digestable food ingredients. Thus, these include insulin, fructo-oligosaccharides (FOS), galactooligosaccharide and lactulose.[9] FOS are naturally occurring carbohydrates that cannot be digested or absorbed by humans. They support the growth of bifidobacteria. As a result of this effect, it was recommended that patients taking bifidobacteria also supplement with FOS.[10]

1.3.1 Prebiotics : Mechanism of action

• The ability of certain oligosaccharides to enhance the growth of resident commensal gut bacteria, particularly bifidobacteria and lactobacilli, is well documented.[11]

• The major mechanism of action of prebiotics is assumed to be indirect, i.e. facilitating the proliferation of beneficial components of the resident microflora, with probiotic effects resulting from the actions of these bacteria.

• There is evidence that some prebiotics also exert direct effects on the host, independent of their effects on resident bacterial populations.[12] These include stimulation of expression of IL-10 and interferon γ, enhancement of IgA secretion, modulation of inflammatory responses to pathogens and stabilisation of the gut mucosal barrier.[13]

2. Current Application of Probiotics & Prebiotics

Although some of the experimental evidence and data clinical trials is conflicting, there is growing evidence for their efficacy in protecting against acute diarrhoeal disease, gastroenteritis and antibiotic associated diarrhoea, inflammatory bowel diseases and pouchitis.[14]

There is also evidence to support further investigation of the use of probiotic and prebiotics in the treatment of illness affecting sites other than intestinal tract e.g. urinary tract infection, vaginal infections, arthritis, atopic eczema, pharyngitis and otitis media.[15]

2.1 Possible effects of probiotics on oral health

Lactobacilli are the most common probiotic bacteria associated with the human gastrointestinal tract, therefore it mayalso play an important role in the eco physiology of oral microbiota.[16]

Development of the new ways to block the pathogenesis of oral infections can reduce tissue destruction associated with oral infection and chronic inflammation. There is a concept where these 'beneficial' microorganisms can inhabit a bio-film and actually protect oral tissue from disease.[17]

2.2 Probiotics and Periodontal health

There are fewer experimental studies exploring probiotic use in periodontal diseases, partly reflecting a poorer understanding of the precise aetiology of the disease and the conditions that promote health.

Some oral strains of lactobacilli and streptococci[18] and bifidobacteria [19] have been reported to have *in vitro* inhibitory activity against periodontal pathogens, while others are more active against *S.mutans*. The subgingival application of beneficial oral bacteria (e.g. *Streptococcus sanguinis, Streptococcus salivarius and S.mitis*) (replacement therapy) has been shown to delay recolonisation by periodontal pathogens, reduce inflammation and improve bone density and bone levels in a beagle dog model.[20]

Koll-Klais *et al* [21] observed that *Lactobacillus gasseri* strains isolated from periodontally healthy subjects were more efficient at inhibiting the growth of *A.actinomycetemcomitans* than strains from periodontally diseased subjects and also the growth of *P.gingivalis and P. intermedia;* this correlated with an inverse relationship between carriage of homofermentative lactobacilli and subgingival colonisation by *A.actinomycetemcomitans*, *P.gingivalis* and *P.intermedia.*

Probiotics lower the pH so that plque bacteria cannot form dental plaque and calculus that causes the periodontal disease. They make an excellent maintenance product because they produce antioxidants. Antioxidants prevent

plaque formation by neutralizing the free electrons that are needed for the mineral formation. Probiotics are able to breakdown putrescence odours by fixating on the toxic gases (volatile sulphur compounds) and changing them to gases needed for metabolism.

Probiotic therapy may be an alternative approach, but regularly and safety issues for human periodontal vaccine trials must be considered.

2.3 "Probiotics" in the treatment of periodontal disease

Probiotics can help prevent and treat disease through several mechanisms:

a. Direct interaction: Probiotics interact directly with the disease causing microbes, making it harder for them to cause the disease.

b. Competitive exclusion: Beneficial microbes directly compete with the disease, developing microbes for nutrition or enterocyte adhesion sites.

c. Modulation of host immune response: Probiotics interact with and strengthen the immune system and help prevent disease.

The most common probiotic strains belong to genera Lactobacillus and Bifidobacterium.

3. The Effect of Probiotic Mouthrinse on Plaque and Gingival Inflammation

The long term success of periodontal treatment is dependant on satisfactory oral hygiene practices by individuals to maintain plaque levels compatible with gingival health.[22]Periodontal treatment is also directed towards eliminating subgingival plaque which itself is derived from supragingival plaque.

Therefore, chemical agents have increasingly been used as adjuncts to mechanical plaque control. It is now recognised that chemical anti- plaque agents may be of value at inhibiting or reducing plaque formation and thus gingival inflammation .[23]

The most tested and effective anti- microbial agent known today is chlorhexidine which has been used for more than two decades. In oral use as a mouthrinse, chlorhexidine has been reported to have a number of local side effects. These side effects are brown discoloration of the teeth and tongue, oral mucosal erosion and taste perturbation.[24]

A Probiotic mouthrinse contains nisin, bacteriocins of short chain polypeptides produced by *Lactococcus* lactis cultured in a fermentor. These peptides are separated and purified from all other components including the lactic acid bacterial cells and then incorporated into the mouthrinse.

Bacteriocins are one of a number of antimicrobial substances produced by lactic acid bacteria (LAB), including organic acids, hydrogen peroxide, diacetyl and inhibitory enzymes.[25] Bacteriocins are loosely defined as biologically active protein moieties with a bacteriocidal mode of action. Bacteriocins are ribosomally synthesized peptides or proteins and usually act against closely related species.

Nisin is bactericidal agent against a wide range of Gram-positive bacteria.[26] Nisin has been shown to kill a wide range of organisms including Actinomyces, Bacillus, Clostridium, Corynebacterium , Enterococcus, Gardnerella, Lactococcus, Listeria, Micrococcus, Mycobacterium, Propionibacterium, Streptococcus and Staphylococcus.[27]

It was also shown by earlier researcher that nisin; the active ingredient in Probiotic mouthrinse had bactericidal action against a wide range of Gram – positive bacteria.

The Probiotic mouthrinse may achieve its anti

plaque activity by inhibiting the growth and proliferation of these microorganisms on the tooth surface and also by modifying plaque biochemistry to reduce the formation of cytotoxic product and modifying plaque ecology to a less pathogenic flora.

Here the Nisin has shown high aqueous solubility in its aqueous delivery vehicle which can facilitate its release to the oral cavity during application as an antiplaque agent.

3.1 Clinical evidence of probiotic effectiveness in periodontal disease

Studies on probiotics and periodontal disease are particularly sparse and at present only a few clinical studies have evaluated the efficacy of probiotic species in this indication.

Lactobacilli reuteri and *Lactobacillus brevis* are among the species able to affect gingivitis and plaque composition positively as well as being specific markers for periodontal disease.[28] A significant decrease to gingival bleeding and reduction in gingivitis were observed after a two-week intake of probiotic species. The observed improvement in clinical status may be attributed to the effective colonization of the probiotic bacteria within the oral cavity.

The intake of lactobacilli showed gingival crevicular fluid values of lactoferrin that corresponded to values in the healthy state, suggesting that a probiotic intervention could be a useful tool for the treatment of inflammation and the clinical symptoms of periodontitis.[29]

A more in depth study of the molecular mechanisms, whereby probiotics may affect periodontal disease, has revealed that those species could effectively reduce the levels of inflammation-associated molecules, such as prostaglandin E2 and interferon ã and weaken matrix metalloproteinase activities in saliva.[30]

By Russian study it was found that Probiotic (L.casi 37) cell suspension, when added to a collagenous periodontal dressing, resulted in a decrease in the no of aggressive microbial species from periodontal pockets, thus extending remission periods up to 10-12 months.[31]

3.2 Limitation of probiotics use in periodontics

There is note of caution concerning the use of probiotics for the purpose of preventing oral disease. The species that most commonly exhibit probiotic benefits are lactobacilli and other lactic acid bacteria, and the production of acid is often thought to be an important component of their protection against pathogenic colonisation. However, *Lactobacillus spp.* and acid production by acidogenic plaque populations play a significant part in the development of caries, and a probiotic strain of *L.salivarius* has been shown to be cariogenic in a rat model.[32]

So one of the biggest problems to overcome may be that the probiotic activities and micro-organisms that protect against oral disease could increase the risk of development of dental caries. Therefore, a prebiotic type approach to enhance endogenous beneficial commensals may be more attractive.

4. Conclusion

Based on the current research data the effects of probiotics on periodontal health and its maintenance are not clear. Hence, systemic studies and randomized controlled trials are needed to find out best probiotic strains and means of their administration in different oral health conditions and the potential of prebiotics to maintain and enhance the benefits provided by the resident oral micro biota will be investigated.

Better scientific understanding and extended research of these tiny forms of life and their effect on humans in the treatment of periodontal diseases might further broaden the field of potential applications.

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