Probiotics in Dentistry

Karthavya .S

1. Introduction

Probiotics can be defined as living microbes, or as food ingredients containing living microbes, that beneficially influence the health of the host when used in adequate numbers. As adopted by the International Scientific Association for probiotics and prebiotics, "Live microorganisms, which when administered in adequate amounts, confer beneficial effect on the health of the host.[1] An International Life Science Institute Europe consensus document proposed a simple and widely accepted definition of probiotics as "Viable microbial food supplements which beneficially influence the health of human." These bacteria should belong to the natural flora in order to resist gastric secretion and survive during intestinal transit. They should also adhere to the intestinal mucosa and finally should have the ability to inhibit gut pathogens [2,3,4]. Prebiotics are non digestible food ingredients such as fructooligosaccharides (FOS), Lactulose and inulin that beneficially affect the host by selectively stimulating growth and / or increase activity of a limited number of probiotic like bacteria in a colon.

2. History

The idea of probiotics dates back to the first decade of 1900s when the Ukranian bacteriologist and Nobel Laureate Metchnikof (1908) studying the flora of the human intestine developed a theory that senility in humans is caused by poisoning of body by the products of some of these bacteria. To prevent the multiplication of these organisms he proposed a diet containing milk fermented by lactobacilli, which produce large amounts of lactic acid that could increase the life span of humans. The concept of probiotics was thus born and a new field of bacteriology was opened [5]. Lilley and Stillwell (1965) introduced the term probiotics. Mann and Spooering in 1974 discovered that the fermented yogurt reduced blood serum cholesterol. In 1984 Hull identified the first probiotic species, the lactobacillus acidophilus. Later in 1991, Holcombh identified *bifidobacterium bifidum*. WHO in 1994 described the probiotics as next most important in immune defense system following antibiotic resistance. These incidences paved way for a new concept of probiotics in medicine and dentistry [6,7,8].

3. Probiotic Bacteria for Oral Health

The most commonly used strains belong to the genera Lactobacillus and Bifidobacterium, genera that are commonly found in the oral cavity, including caries lesions (9). These were the first probiotic species to be introduced into research (Lactobacillus acidophilus by Hull et al. 1984 and Bifidibacterium bifdum by Holcombh et al., 1991) (10). Lactobacillus rhamnosus GG, ATCC 53103 produces a growth inhibitory substance against Streptococcus sobrinus and it has been proposed to reduce the risk for caries (9). Lacto bacilus rhamnosus strain GG, ATCC 53103 was originally isolated from the human intestinal flora in 1985 and named after the discoverers, Sherwood Gorbach and Barry Goldin (8). Also, Streptococccus 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 (10). Other strains considered as probiotics in the oral cavity include: L. acidophilus, L. casei, L. casei Shirota, L. paracasei, L. reuteri, L .johnsonii, propionibacterium, W. cibaria (11). A successful effector strain for replacement therapy of a bacterial disease must have the following basic properties. It must not cause disease itself or otherwise predispose the host to other disease states by disrupting the ecosystem in which it resides (12). To be able to have probiotic effects in the mouth, a bacterium must adhere to oral surfaces and become part of the biofilm (13). Finally, an effector strain should possess a high degree of genetic stability (12). Current evidence indicates that probiotic effects are strain-specific; therefore, a beneficial effect attributed to one strain cannot be assumed to be provided by another strain, even when it belongs to the same species (14). A combination of strains can enhance adherence in a synergistic manner (8).

4. Properties of Probiotics

- Should be non toxic and non pathogenic preparation
- Produce beneficial effect
- Should withstand gastrointestinal juice
- Should have good shelf life
- Should replace and reinstate the intestinal microflora

5. Mechanism of Probiotic Action on Oral Health

The general mechanisms of action of probiotics can be divided into three categories
Modulation of immune response

- Normalization of intestinal microbiota
- Metabolic effects.
- Modulation of immune response
- Normalization of intestinal microbiota
- Metabolic efforts

The mechanisms of probiotic action in the oral cavity could be analogous to those described for the intestine. Thus far oral colonization by probiotic bacteria has often been considered essential for them to exert oral effects; however, the possibility of systemic effects cannot be excluded, although the total IgA levels in saliva seem unaffected by probiotic use.[15,16]Normalization of intestinal/oral microbiota is supported by the ecological plaque hypothesis which suggests that the selective pressure present in environmental conditions can alter the balance between disease and oral health.[17] As bacteria can influence their environment, and both antagonistic and synergistic interactions are suggested for bacteria in dental plaque, the environmental pressure described in the ecological plaque hypothesis could be introduced partly by bacteria. As there are bacterial species associated with oral diseases, there are some species that seem to be associated with oral health; however, it is still questionable that bacteria administered in food could be used as probiotics to normalize oral micro biota. There are many possible mechanisms for how pathogen exclusion may take place. First, several probiotics alter the ability of pathogens to adhere to or invade colonic epithelial cells in vitro. Second, probiotics could sequester essential nutrients from invading pathogens and impair their colonization ability. Third, probiotics may inhibit the expression of virulence functions by altering the gene expression program of pathogens. Lastly, probiotics may create an unfavourable environment for pathogen colonization by altering the mucus layer, pH and other factors in the local surroundings.

6. Probiotics and Dental Caries

A number of researchers are developing “probiotic” methods to treat the caries causing infection. “Probiotic”, as used here, means that mechanisms are employed to selectively remove only the (odonto) pathogen while leaving the remainder of the oral ecosystem intact (18). One of the replacement therapy options entails the application of a genetically engineered “effector strain” of S. mutans that will replace the cariogenic or “wild strain” to prevent or arrest caries and to promote optimal remineralisation of tooth surfaces that have been demineralised but that have not become cavitated. S. mutans strain BCS3-L1 is a genetically modified effectors strain designed for use in replacement therapy to prevent dental caries. Recombinant DNA technology was used to delete the gene encoding lactate dehydrogenise in BCS3-L1 making it unable to produce lactic acid.

This effector strain was also designed to produce elevated amounts of a novel peptide antibiotic called mutacin 1140 that gives it a strong selective advantage over most other strains of S. mutans (19). A clinical trial began early in 2005 to test the effectiveness of replacement therapy. Thus, it is too early to determine the potential of this treatment method to prevent new caries lesions and to arrest existing lesions without any significant side effects. Another approach is based on a genetic modification of two plaque streptococci to create organisms that produce ammonia from urea and arginine. These organisms will reside in dental plaque, and the ammonia produced from salivary and dietary substrates will prevent the colonization of cariogenic bacteria and ensure internal pH homeostasis. If the effector strain is better adapted than the pathogen, colonization or outgrowth of the pathogen will be prevented by blocking the attachment sites, by competing for essential nutrients, or via other mechanisms. As long as the effector strain persists as a resident of the indigenous flora, the host is protected potentially for an unlimited period of time (19). A different way of accomplishing the removal of the pathogens is to develop “targeted antimicrobials”. The basic idea is to develop an inexpensive targeting molecule that will reliably attach to only the organism of interest, in this case S. mutans, S. sobrinus, or other chosen pathogen. Once the targeting molecule is perfected, then a “killer” molecule is optimized and chained to the targeting molecule. The combined unit then selectively eliminates the infection of interest. In the case of the oral cavity and dental caries, this system is attractive from the perspective of eliminating all the pathogens thereby precluding the re growth of the original infection. There is also compelling evidence from clinical trials and laboratory efforts demonstrating that once the bacterial ecosystem is free of S. mutans, it is difficult to reintroduce the organisms (another competitive inhibition situation) (18).

7. Role of Probiotics in Periodontitis

Riccia and colleagues in 2007 studied the anti inflammatory effects of *Lactobaillus brevis* in a group of patients with chronic periodontitis. Anti-inflammmatory effects of *L.brevis* could be attributed to its capacity to prevent the production of nitric oxide and consequently the release of PGE2 and activation of MMPs induced by nitric oxide [20].

The use of probiotic chewing gum containing *L. reuteri* ATCC55730 and ATCCPTA5289 also decreased levels of pro-inflammatory cytokines in GCF [21] and the use of *L.brevis* decreased MMP(collagenase) activity and other inflammatory markers in saliva [23]. The common organisms involved in halitosis are *Fusobacterium nucleatum, P. gingivalis, P.intermedia* and *Treponema denticola*.These organisms degrade aminoacids, which are in turn transformed into volatile sulphur compounds which cause halitosis. Kang and colleagues reported that various strains of *Weissella cibaria* have the capacity to co aggregate with *fusobacterium nucleatum* and to adhere to epithelial cells and these bacteria produce hydrogen peroxide as well as a bacteriocin which inhibited the proliferation of *F. nucleatum*. These properties could enable *W. cibaria* to effectively colonize the oral Cavity and limit the proliferation of *F. Nucleatum* [22] and thus can prevent halitosis. Another species, *Streptococcus salivarius* is detected most frequently among people without halitosis and is therefore considered a commensal bacterium of the oral cavity. *S.salivarius* is known to produce bacteriocins, which contribute in reducing the number of bacteria that produce Volatile sulphur compounds (VSC). The use of gum or lozenges containing *S. salivarius* K12 reduce levels of VSC among diagnosed with halitosis [23].

8. Role of Probiotics in Orthodontic Treatment

Fixed orthodontic appliances are considered to jeopardize dental health due to accumulation of microorganisms that may cause enamel demineralization, clinically visible as white spot lesions [24] Furthermore, the complex design of orthodontic bands and brackets may create an ecological environment that facilitates the establishment and growth of cariogenic mutans streptococci strains [25].

White spot lesion formation can be seen as an imbalance as an imbalance between mineral loss and mineral gain and recent systematic reviews have examined methods to prevent this side effect of orthodontic treatment [26]. Cildir et al. [27] in 2009 conducted a clinical study with probiotics and found out that daily consumption of fruit yogurt with *Bifidobacterium animalis* subsp. Lactis DN -173010 could reduce the salivary levels of mutans streptococci in orthodontic patients with fixed appliances. Further studies are needed to clarify if this approach is an alternative strategy for prevention of demineralization and white spot formation during orthodontic treatment [28].

9. Role of Probiotics in Infection and Oral Disease

Recently it has been postulated that the probiotic bacteria may slow down AIDS progression. Lin Tay and his colleagues screened hundreds of bacteria taken form saliva of volunteers. The results showed that some Lactobacillus strains had produced proteins capable of binding a particular type of sugar found on HIV envelope, called mannose. The binding of the sugar enables the bacteria to stick to the mucosal lining of the mouth and digestive tract, forming colonization. One strain secreted abundant mannose binding protein particles into its surroundings, neutralizing HIV by binding to its sugar coating. They also described that immune cells trapped by lactobacilli formed a clump. This configuration would immobilize any immune cells harbouring HIV and prevent them from infecting other cells [29].

10. Delivery Mechanism of Probiotics

Advances in biomedical engineering will prove to be equally important to molecular biology in terms of the developing systems that deliver bacteria and / or nutritional factors to the host. These will include encapsulating probiotics, such that they rehydrate at specific sites, and encasing prebiotics in nano-aggregates that protect against stomach acid and deliver their payload when the pH reaches 7.4. Potentially, such nano encapsulation will also allow delivery in foods such as biscuits, whereas targeted, water protected macrocapsules containing probiotic organisms may prove useful in animal food pellets and perhaps in liquids, which currently cannot be used because of problems with shelf stability. At the macromolecular level, it will soon be possible to coat capsules with biosensors that detect the optimal conditions for the release of probiotic contents [29]. In summary, molecular, nano, biochemical, microbiological and engineering sciences hold the key to future advances in the clinical applications of probiotic and prebiotic products.

The oral cavity with a well maintained balance of the species and species interactions may be a potential source for health-promoting probiotic bacteria. On the other hand, daily intake of probiotic supplements may control common oral and dental infections. The research regarding the benefits of probiotics in oral health and disease has been undertaken in the recent years. Further double-blind, randomized, placebo-controlled trails with specifically selected and defined strains are the need of the hour before clinical recommendations for possible use can be made [30]

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