Review

Role of probiotics and bacterial replacement therapy in periodontal disease management

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ABSTRACT

The application of health-promoting bacteria for therapeutic purposes is one of the strongest emerging fields. The effect of probiotics on systemic health is well documented. So far probiotics & bacterial replacement therapy have been evaluated primarily in the management of dental caries, but their effect in treatment of periodontal diseases is still obscure. This article reviews possible role of probiotics & bacterial replacement therapy in periodontal disease management.

KEY WORDS: Periodontal diseases, Bacterial replacement therapy, Probiotics

INTRODUCTION

Periodontitis is essentially a microbial disease and dental plaque is considered as primary etiologic agent. Prevention and Treatment of periodontitis mainly focuses on the reduction of the bacterial load.

Conventional treatment modalities include surgical and non-surgical management, which emphasizes mainly on mechanical debridement, often accompanied by antibiotics. These treatment modalities are aimed at eliminating the entire microflora irrespective of their pathogenicity.

Due to the emergence of antibiotic resistance and frequent recolonization of treated sites with pathogenic bacteria, there was a need for a new treatment paradigm to be introduced to treat periodontal diseases. This need was fulfilled by the introduction of Probiotics and Bacterial Replacement therapy in the field of periodontics. This article endeavors to introduce the concept of Probiotics and bacterial replacement therapy in periodontics as well as to clarify the subtle yet significant differences between the two treatment modalities. Studies done using probiotics and bacterial replacement therapy to treat various periodontal conditions have also been highlighted.

Probiotics and bacterial replacement therapy are based on the concept of "BACTERIAL INTERFERENCE"[1], whereby one microorganism can prevent and or delay the growth and colonization of another member of the same or a different ecosystem.

BACTERIAL REPLACEMENT THERAPY[1]

The possibility of usage of antagonistic organisms to control pathogens and prevent disease has been termed as "Replacement Therapy". This approach has the potential advantage that, it provides life-long protection with minimal cost or compliance on behalf of the recipient, once colonization by the "effector"strain has been achieved[2].

There are two main approaches by which replacement therapy is being considered as a means of enhancing colonization resistance in plaque to prevent periodontal diseases.

1. Pre-emptive colonization &
2. Competitive displacement

PRE-EMPTIVE COLONIZATION

In this approach, ecological niches within plaque are filled by a harmless or potentially beneficial organism before the undesirable strain has had an opportunity to colonize or become established.[1]

COMPETITIVE DISPLACEMENT

In this approach, a competitive strain would displace a pre-existing organism from plaque. It is not dependent on treatment with the "effector" strain at or before colonization by the undesired organism.

PROBIOTICS

The term Probiotics was introduced in1965 by Lilly & Stillwell. Probiotics has been defined by WHO/FAO as "Live microorganisms which when administered in adequate amounts confer a health benefit on the host."[4]

Although both replacement therapy and probiotics use live bacteria for the prevention or treatment of infectious disease[5], there are some differences between replacement therapy and probiotic therapy which are enumerated in Table1

TABLE NO.1
DIFFERENCES BETWEEN REPLACEMENT THERAPY AND PROBIOTIC THERAPY

REPLACEMENT THERAPY	PROBIOTIC THERAPY
Effector strain is not ingested and is applied directly on the site of infection by clinician	Probiotics are generally used as dietary supplements Can be used by individual
Colonization of the site by the effector strain is essential	Probiotics are able to exert a beneficial effect without permanently colonizing the site
Involves dramatic and long-term change in the indigenous microbiota	Involves transient microbiological change
Directed at displacing or preventing colonization of a pathogen	
Has a minimal immunological impact	Exerts beneficial effects by influencing the immune system

PROBIOTICS IN PERIODONTAL THERAPY

Various probiotic organisms used in periodontal therapy are Lactobacillus species, Bifidobacterium species & Streptococcus species[6].

These organisms can be delivered as food products (cheese, milk, yogurt) or supplements as chewing gum, lozenges, capsules, tablets, mouth rinses, sprays, etc.
Probiotics can be used in treatment of various periodontal conditions like,

1. Gingivitis,
2. Periodontitis, and
3. Halitosis

The mechanisms of probiotics in management of periodontal diseases[7] are illustrated in Table.2

TABLE NO.2
MECHANISMS OF PROBIOTICS IN MANAGEMENT OF PERIODONTAL DISEASES[7]

INHIBITION OF SPECIFIC PATHOGENS	EFFECTS ON HOST RESPONSE
1.Inhibition of pathogen adhesion, Colonization & Biofilm Formation 2.Inhibition of pathogen growth by various substances	1. Inhibition of collagenases & reduction of inflammation associated molecules 2. Induction of expression of cyto protective proteins on host cell surfaces 3. Modulation of pro inflammatory pathways induced by pathogens 4. Prevention of cytokine induced apoptosis 5. Modulation of host immune response

PROBIOTICS IN MANAGEMENT OF GINGIVITIS:

1.**Krasse and colleagues** assessed the beneficial effect of Lactobacilli reuteri against gingivitis. Although the exact mechanisms of action of L. reuteri remain to be elucidated, previous studies have suggested at least 3 plausible possibilities[8]:

A. L. reuteri is known for its secretion of two bacteriocins, reuterin and reutericyclin, that inhibit the growth of a wide variety of pathogens
B. L. reuteri has a strong capacity to adhere to host tissues, thereby competing with pathogenic bacteria and
C. The recognized anti-inflammatory effects of L. reuteri on the intestinal mucosa, leading to inhibition of secretion of proinflammatory cytokines, could be the foundation for a direct or indirect beneficial effect of this bacterium on people with periodontal disease.

However, additional studies with larger patient cohorts are needed to confirm the long-term potential of L. reuteri in preventing and/or treating gingivitis.

2. **Staab B , Eick S, et al,** observed the reduction of MMP-3, Elastase activity on 50 students with plaque induced gingivitis after having probiotic milk drink for 8 weeks which contained Lactobacillus casei species[9].

PROBIOTICS & PERIODONTITIS

1. Among healthy individuals, the prevalence of lactobacilli (particularly Lactobacillus gasseri, L.salivarius and L. fermentum) & Bifidobacterium species were greater than in

patients with chronic periodontitis. Various studies have reported the capacity of lactobacilli to inhibit the growth of periodontopathogens, including P. gingivalis, Prevotella intermedia and A. actinomycetemcomitans. Together, these observations suggest that lactobacilli residing in the oral cavity could play a role in oral ecological balance[8].

2. **Riccia and colleagues** in 2007 studied the anti-inflammatory effects of Lactobacillus brevis in a group of patients with chronic periodontitis. Anti-inflammatory effects of L. brevis could be attributed to its capacity to prevent the production of nitric oxide and, consequently, the release of PGE2 and the activation of MMPs induced by nitric oxide.[10]

3. 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 the bone resorption associated with periodontitis[11].

4. Chewing Gum "PERIO BALANCE" is the first probiotic specifically formulated to fight periodontal disease. It contains combination of two strains of L. reuteri specially selected for their synergetic properties in fighting cariogenic bacteria and periodontopathogens. Each dose of lozenge contains at least 2×10^8 living cells of L. reuteri prodentis. Users are advised to use a lozenge every day, either after a meal or in the evening after brushing their teeth, to allow the probiotics to spread throughout the oral cavity and attach to the various dental surfaces. Additional studies are required to evaluate the long-term effects of using these products[12].

PROBIOTICS AND HALITOSIS

Breath malodor is a considerable social problem and majority of the pathology (85%) causing halitosis are present in the oropharynx (Tongue coating, Gingivitis, Periodontitis, Tonsillitis)

The common organisms implicated in halitosis are Fusobacterium nucleatum, P.gingivalis, P. intermedia and Treponema denticola. These organisms degrade salivary and food proteins & generate amino acids, which are in turn transformed into volatile sulphur compounds (VSCs).

Current treatments for halitosis focus on the use of chemical or physical antibacterial regimens to reduce the numbers of these bacteria. However, most of these treatments exhibit only a transient effect. This can be explained by the recolonization of halitosis-causing bacteria after treatment is stopped.

To prevent the regrowth of odor-causing organisms, pre-emptive colonization of the oral cavity with probiotics might have a potential application as adjuncts for both the treatment and prevention of halitosis.

1. **Kang and colleagues** reported that various strains of Weissella cibaria have the capacity to coaggregate with Fusobacterium nucleatum and to adhere to epithelial cells & also 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.[13]

These authors also found that gargling with a solution containing W. cibaria was associated with a net reduction in the production of hydrogen sulphide and methanethiol and consequently a reduction in bad breath[13].

2. Another species, Streptococcus salivarius, was detected most frequently among people without halitosis and is therefore considered a commensal bacteria of the oral cavity. S. salivarius is known to produce bacteriocins, which could contribute in reducing the number of bacteria that produce volatile sulphur compounds.

The use of gum or lozenges containing S. salivarius K12 reduced levels of volatile sulphur compounds among patients diagnosed with halitosis[14].

However, additional studies with larger patient cohorts are needed to confirm the long-term potential of probiotics in preventing and/or treating halitosis.

BACTERIAL REPLACEMENT THERAPY (GUIDED PERIODONTAL POCKET RECOLONIZATION) IN PERIODONTICS:

The concept of Bacterial replacement therapy in periodontics was first introduced by W.Teughels, M.G.Newman et al (2007). They had induced periodontitis experimentally in beagle dogs. Scaling and root planing was done followed by administration of a mixture of probiotic microorganisms comprising of S.sanguinis, S. salivarius and S.mitis into the periodontal pockets. Reductions in probing pocket depth, bleeding on probing and gain in clinical attachment level was observed.[15]

Nackaerts O, Jacobs R, Quirynen, et al (2008), used Replacement therapy for regeneration of periodontal osseous defects in beagle dogs by local application of Streptococcus sanguinis, Streptococcus salivarius and Streptococcus mitis. They noticed a significant increase in the bone levels .[16]

SUMMARY

Recent data seems to reinforce that putative periodontal pathogens are a constant presence not only in patients with periodontitis but are also present consistently in those who are healthy and resistant to periodontal disease.[17]

Disease sets in when these organisms are present in sufficiently large numbers to promote the release of inflammatory cytokines that would result in periodontal breakdown. It seems therefore significant that the modulation of the dental plaque to ensure that it is colonized by bacteria that are associated with health, could accrue more benefits to individuals at risk to periodontal disease.

Guided Periodontal Pocket Recolonization (Bacterial Replacement Therapy) seems to afford greater long term benefits than the systematic and continual removal of plaque by patients who have been sent ' to life' on supportive periodontal care.

While many more clinical trials that are randomized and longitudinal would be required before a final word is said on the benefits of Bacterial Replacement Therapy, it seems to offer a promising and paradigm shift in the management of periodontal disease.

REFERENCES:

1. P.Marsh,Microbial ecology of dental plaque and its significance in health and disease, Adv Dent Res 8(2):263-271, July, 1994
2. Hillman JD, Socransky SS (1989). The theory and application of bacterial interference to oral diseases. In: Myers HM, editor. New biotechnology in oral research. Basel: Karger,1-17.
3. Donoghue HD (1990). Can the colonisation resistance of the oral microflora be enhanced? Microb Ecol Hlth Dis 3:i-iv. October 2009, Vol. 75, No. 8
4. Food and Health Agricultural Organization of the United Nations and World Health Organization. Guidelines for the evaluation of probiotics in food. Joint FAO/WHO Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food. 2002. Available: ftp://ftp.fao.org/es/esn/ food/wgreport2.pdf (accessed 2009 Aug 31).
5. Wim Teughels, Mark Van Essche, Isabelle Sliepen & Marc Quirynen, Probiotics and oral healthcare, Periodontology 2000, Vol. 48, 2008, 111–147
6. Laetitia Bonifait, DEA; Fatiha Chandad, PhD; Daniel Grenier, PhD, Probiotics for Oral Health: Myth or Reality? JCDA ,
7. Iva Stamatova, Jukka H.Meruman, Probiotics and periodontal disease, Periodontology 2000, Vol. 51, 2009, 141–151
8. Talarico TL, Casas IA, Chung TC, Dobrogosz WJ. Production and isolation of reuterin, a growth inhibitor produced by Lactobacillus reuteri. Antimicrob Agents Chemother. 1988;32(12):1854-8.
9. Staab B ,Eick S,etal,The influence of a probiotic milk drink on the development of gingivitis:a pilot study,journal of clinical Periodontology 2009,36,850-856.
10. Riccia DN, Bizzini F, Perilli MG, Polimeni A, Trinchieri V, Amicosante G, et al. Anti-inflammatory effects of Lactobacillus brevis (CD2) on periodontal disease. Oral Dis. 2007;13(4): 376-85.
11. Narva M, Halleen J, Väänänen K, Korpela R. Effects of Lactobacillus helveticus fermented milk on bone cells in vitro. Life Sci. 2004;75(14):1727-34.
12. Wilson M. Manipulation of the indigenous microbiota. In:Wilson M, editors. Microbial inhabitants of humans. New York: Cambridge University Press, 2005: 395–416.
13. Kang MS, Kim BG, Chung J, Lee HC, Oh JS. Inhibitory effect of Weissella cibaria isolates on the production of volatile sulphur compounds. J Clin Periodontol. 2006;33(3):226-32.
14. Burton JP, Chilcott CN, Moore CJ, Speiser G, Tagg JR. A preliminary study of the effect of probiotic Streptococcus salivarius K12 on oral malodour parameters.J Appl Microbiol. 2006;100(4):754-64.
15. W.Teughels, M.G.Newman, et. al. Guiding periodontal pocket recolonization: A proof of concept, Journal of dental research 2007,vol. 86,(11),1078-1082.
16. Nackaerts O, Jacobs R, Quirynen M, Rober M, Sun Y, Teughels W. Replacement therapy for periodontitis: pilot radiographic evaluation in a dog model. Journal Clinical Periodontology 2008; 35: 1048–1052.
17. Birgit Riep, Lilian Edesi-Neuß, Friderike Claessen, Horst Skarabis, Benjamin Ehmke, Thomas F. Flemmig, Jean-Pierre Bernimoulin, Ulf B. Gobel, and Annette Moter. Are Putative Periodontal Pathogens Reliable Diagnostic Markers? Journal of clinical microbiology, June 2009, p. 1705–1711.