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PROBIOTICS: A PARADIGM SHIFT IN PERIODONTICS

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Abstract: Periodontitis is one of the most common chronic inflammatory diseases. The etiology is clearly bacterial, and a number of alleged bacterial pathogens have been associated with it. Treatment of periodontal disease in has moved toward an antibiotic/antimicrobial model of disease management. With increase in the incidence of resistance to antibiotics, probiotics may be a promising area of research in periodontal therapy. This paper reviews the evidences for the use of probiotics or prebiotics for the prevention of dental caries or periodontal diseases, and addresses the risk associated with their prolonged use. Many questions have been raised pertaining to the benefits of probiotic administration, as the role of probiotics in periodontics is still in infancy, and a complete understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics is essential to assess their long-term consequences for oral health and disease.

Index Terms **- probiotics, lactobacillus, Periodontitis**

I. INTRODUCTION:

"The preservation of health is easier than the cure for disease!!"

Periodontitis is a multifactorial disease that encompasses the hard and soft tissue, microbial colonization (with or without invasion), inflammatory responses and adaptive immune responses [1]. Conventional treatment modalities of periodontal disease include non-surgical and surgical management, which emphasizes mainly on mechanical debridement, often accompanied by antibiotics. Due to the emergence of antibiotic resistance and frequent recolonization of treated sites with pathogenic bacteria, there was need for a new treatment paradigm to be introduced to periodontal disease. This need was fulfilled by introduction of "Probiotics" in the field of Periodontics.

II. DEFINITIONS:

Probiotics:

Probiotics are defined as living microorganisms, principally bacteria, that are safe for human consumption and, when ingested in sufficient quantities, have beneficial effects on human health, beyond basic nutrition [2].

Prebiotics:

Prebiotics (i.e., inulin-type fructans, maltodextrin, fructooligosaccharides and galactooligosaccharides) have been defined as non-digestible oligosaccharides that affect the proliferation of resident commensal bacteria that may then exert probiotic effects [3].

Symbiotic:

Symbiotic is defined as "mixtures of probiotics and prebiotics that beneficially affect the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract of the host [4]."

III.HISTORY:

Metchnikoff was the first to state that probiotics could provide a health benefit, and proposed that Bulgarian people had a longer longevity due to fermented milk containing viable bacteria. "Probiotic" term, was initially proposed by **Lilley and Stillwell** in 1965. First probiotic species to be introduced in research was *Lactobacillus acidophilus* by **Hull et al**. in 1984; followed by *Bifidobacterium bifidum* by **Holcombh et al.** in 1991 [5].

In 1994, the **World Health Organization** deemed probiotics to be the next-most important immune defence system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. These incidences paved way for a new concept of probiotics in medicine and dentistry [6,7].

IV. PROBIOTICS OF INTEREST:

The most common probiotic strains 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*. Similarly, the *bifidobacterium* strains include *B. bifidum, B. longum*, and *B. infantis*. *Streptococcus oralis* and *Streptococcus uberis* have been shown to inhibit the growth of pathogens both in the laboratory and animal models [8].

V. IDEAL CHARACTERISTICS:

- Should be non- pathogenic
- Should be of human origin
- Should be able to send signals and interact with immune cells
- Have High cell viability and resistance to low pH
- Adhesion to cancel the flushing effect
- Have capacity to influence local metabolic activity [9].

VI. MECHANISMS OF ACTION:

PROBIOTICS:

There are common themes emerging in studies of the modes of action of probiotics and numerous mechanisms have been proposed including:

- Inhibition of pathogen adhesion, colonization and biofilm formation
- Induction of expression of cytoprotective proteins on host cell surfaces
- Inhibition of collagenases and reduction of inflammation associated molecules
- Stimulation and modulation of the host immune system
- Modulation of cell proliferation and apoptosis
- Killing or inhibition of growth of pathogens through production of bacteriocins or other products, such as acid or peroxide, which are antagonistic towards pathogenic bacteria.
- Probiotics can also modify the surrounding environment by modulating the pH and/or the oxidation–reduction potential, which may compromise the ability of pathogens to become established [10,11].

PREBIOTICS:

The major mechanism of action of prebiotics is assumed to be indirect, i.e. facilitating the proliferation of beneficial components of the resident microflora. 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 stabilization of the gut mucosal barrier [13].

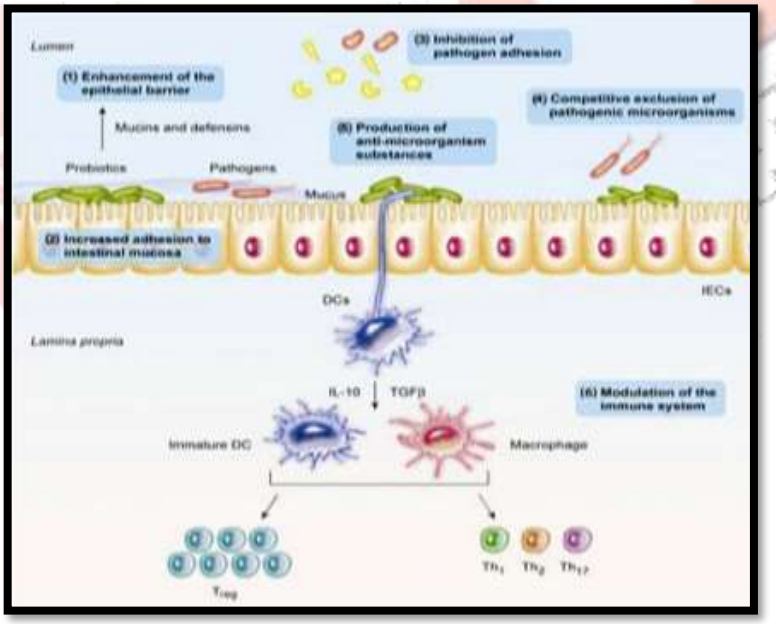

Figure 1: Mechanism of Action of Probiotics

VII. PROBIOTICS AND GENERAL HEALTH:

Traditionally, probiotics have been used in gastroenterology. Evidence-based reviews indicate that certain strains of probiotics contribute to the microbial balance of the gastrointestinal tract – supporting the immune system and reducing inflammation (**Ciorba, 2012**) [14]. Clinical trials have assessed the effects of probiotics in antibiotic-associated diarrhoea, gastroenteritis, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, obesity, rheumatoid arthritis and allergies (**Meurman, 2005; Vaghef-Mehrabany et al., 2014**) [15,16].

VIII. PROBIOTICS AND ORAL HEALTH:

Probiotics have been evaluated in caries control and have demonstrated the capacity to reduce *Streptococcus mutans* levels in saliva (**Näse et al., 2001**) [17]. A recent meta-analysis indicated that probiotics could have a positive effect in caries prevention (**Laleman et al., 2014**) [18]. There are also probiotic evaluations in oral conditions, e.g., *candidiasis*, chemotherapy- induced mucositis or halitosis (**Stamatova and Meurman, 2009; Laleman and Teughels, 2015**) [19,20].

IX. PROBIOTICS AND PERIODONTAL HEALTH:

Krasse et al evaluated *L. reuteri* in a recurrent gingivitis case. A parallel, double blind, randomized, placebo-controlled study with 59 patients having moderate to severe gingivitis were selected. *L. reuteri* strains were administered via chewing gums twice a day for 2 weeks at a concentration of 1×108 CFU along with scaling and root planing. After 2 weeks, the clinical parameters were improved in the group consuming probiotic chewing gums [21].

Kang et al in a cross over, open label placebo-controlled study including 72 subjects evaluated the efficacy of a probiotic *W. cibaria* CMS1 rinse. Subjects were instructed to rinse in the morning, afternoon and evening with a 15 ml rinse after brushing. There was a significant reduction in plaque scores in the probiotic rinse group [22].

Hillman et al carried out a parallel open label placebo- controlled study on 24 gnotobiotic rats including a single baseline application and showed significant decreased levels of *A. actinomycetemcomitans* when compared with placebo group [23].

Teughels et al conducted a split mouth study on beagle dogs with artificially created pockets. Bacterial pellets of *S. sanguis KTH-4*, *S. salivarius TOVE* and *S. mitis BMS* were applied locally in pockets at 1,2 and 4 weeks. They showed decreased counts of anaerobic bacteria and *C. rectus* with decreased pocket recolonization and bleeding on probing when compared with controls [24].

Mayanagi et al studied the effect of *L. salivarius WB21* tablets on periodontopathic bacteria in a double blind, placebo controlled, randomized clinical trial on 66 healthy subjects. The results showed significant reduction in the sum total of five periodontopathic bacteria: *A. actinomycetemcomitans, P. intermedia, P. gingivalis, T. denticola* and *T. forsythia* in the probiotic group compared to the placebo group [25].

X. COMMERCIALLY AVAILABLE PROBIOTICS WITH PERIODONTAL EFFECTS:

Acilact a biopreperation of live lympholised acidophilic lactobacillus has shown to reduce gingivitis and periodontitis. **Gum – perio balance**, the first probiotic specifically designed to fight periodontal disease is a lozenge containing at least 2x 10^8 *Lactobacillus reuteri* belonging to two strains having synergistic properties in fighting cariogenic and periodontopathogenic bacteria. **Periobiotic** is a fluoride free tooth paste containing *Lactobacillus paracasei* ADP-1 strain. **ProBiora3** is a mouthwash containing specific strains of naturally occurring oral bacteria – *Streptococcus oralis* strain KJ3sm, *Streptococcus uberis* strain KJ2sm, and the spontaneous **lactiProdentis** a *Lactobacillus reuteri* preparation showed to inhibit plaque formation, exert anti-inflammatory activity and antimicrobial activity [26].

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

The concept of bacterial replacement therapy in periodontics was first introduced by **Teughels et al** in 2007. They reported that the subgingival application of a bacterial mixture including *Streptococcus sanguis, S. salivarius*, and *Streptococcus mitis* after scaling and root planing significantly suppressed the recolonization of *Porphyromonas gulae* (*canine P. gingivalis*) and *P. intermedia* in a beagle dog model [27].

Nackaerts et al observed that the subgingival application of beneficial oral bacteria (i.e. *Streptococcus sanguinis*, *Streptococcus salivarius* and *S. mitis*) delays recolonization by periodontal pathogens, reduce inflammation, and improve bone density and bone levels in a beagle dog model [28].

XII. PROBIOTICS IN HALITOSIS MANAGEMENT:

Kang et al reported that *W. cibaria* has the capacity to coaggregate with *F. nucleatum*, adhere to epithelial cells and produce hydrogen peroxide as well as bacteriocin which inhibits the proliferation of *F. nucleatum*. Gargling with a solution containing *W. cibaria* was associated with a net reduction in hydrogen sulphide production and consequently reduction in bad breath [29].

Tomoyuki et al did a randomized controlled trial to evaluate the efficacy of *L. salivarius* WB21 tablets in halitosis management and showed that oral malodor parameters significantly reduced at the end of 2 weeks of administration of the probiotic tablet compared to placebo tablets [30].

Burton et al conducted a randomized placebo- controlled trial on 23 subjects to assess the efficacy of *S. salivarius* K12 lozenge for oral malodor correction. The results showed significantly reduced VSC levels in the S. salivarius lozenge group at 1 week compared to placebo [31].

XIII. POTENTIAL RISKS OF PROBIOTIC THERAPY:

Bacteremia and fungaemia has been reported following use of probiotics in immunocompromised individuals, infants, patients with chronic disease, short gut syndrome and individuals with prior history of prolonged hospitalization and surgical intervention. Lactobacillus endocarditis was reported following dental treatment in a patient with mitral regurgitation who was taking a probiotic preparation containing *Lactobacillus rhamnosus*.

Land et al reported development of LGG endocarditis 3 weeks after being on a probiotic therapy of LGG 1010 CFU/day for antibiotic related diarrhoea after cardiac surgery [32]. **Richard et al** reported bacteraemia that developed following use of an oral preparation containing *Bacillus subtilis* spores which was used for treatment of tube feeding related diarrhoea [33]. None of the cases with serious side effects were reported in healthy individuals.

XIV. CONCLUSION AND FUTURE PROSPECTS:

"Are Probiotics a 'Step Ahead' in Periodontics….??"

Periodontitis has been established as a risk factor for various systemic diseases like diabetes, atherosclerosis, hyperlipidaemia, chronic kidney diseases, and spontaneous preterm birth. Thus, a need to establish good periodontal health for attaining good systemic health is of utmost importance and probiotics are promising and safe options, which are required to be explored in depth for periodontal application. Extensive work is needed to fully optimize and quantify the extent of this benefit. Hence probiotics, though in its juvenile stage of research in terms of periodontal health benefits is a promising modality for treating periodontal diseases.

XV. CONFLICT OF INTEREST:
The authors declare that there is no conflict of interest.

XVI. FINANCIAL SUPPORT:
None declared

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