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Probiotics in Endodontics - A Literature review

Dental Science

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ABSTRACT

AIM: This paper aims to provide a review of the therapeutic effect of probiotics in the treatment of endodontic disease in humans. The administration of probiotic strains might play a role in caries lesion prevention and in the control of caries-related risk factors as well as therapeutic effect in endodontic disease.

BACKGROUND: Probiotics are live bacteria that confer a health benefit to the host. The organisms which have been used in the past as probiotics have been certain strains of *Lactobacillus* and *Bifidobacteria*. Probiotics have been shown to promote health in the intestines and the oral cavity through the consumption of certain yogurts and lozenges. Some of the mechanisms of action of these probiotics include the productions of bacteriocin-like inhibitory substances and the altering of the local pH, competing for nutrients, forming physical barriers and stimulating the immune response. The World Health Organization recognizes probiotics as a significant avenue of health preservation in the event that current antibiotics become useless due to the development of bacterial resistance. As far as is known, there are limited studies on probiotics in terms of their therapeutic effect in the treatment of endodontic disease.

KEYWORDS:

INTRODUCTION:

Probiotics are defined as living microorganisms, primarily bacteria, which provide beneficial health effects beyond basic nutrition when digested in sufficient quantities [5]. Prebiotics are non-digestible oligosaccharides that affect the proliferation of normal flora that could then provide probiotic effects. Many times probiotics and prebiotics are used together to improve the balance of health-promoting bacteria. [4,36]

The dietary use of living microorganisms has a long history, well before their existence of was even recognized by modern science. "Sacred milks" and cultured dairy products have been used throughout history as therapeutic elements. [36] The term "Probiotic" was initially coined to oppose the term "Antibiotic" by Lilley and Stillwell in 1965. The first probiotic species, *Lactobacillus acidophilus,* was introduced through research by Hull in 1984. In 1994, the World Health Organization deemed probiotics to be the next, most important immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. This concept has fueled research for using probiotics in medicine and dentistry.

The mechanisms of action for the effectiveness of probiotics have been proposed as including: the inhibition of pathogen biofilm formation, induction of cytoprotective proteins, reduction of inflammation, stimulation of the host immune system, killing of pathogens through the production of bacteriocins and acids/peroxides along with altering the local environments pH. [36]

Probiotic safety

Since probiotics are live microorganisms, one possible concern is that they may result in an infection in the host. Several studies have reported that the risk of infection with *Lactobacilli* or *Bifidobacterium* is similar to infections with commensal strains. The risk of infection with these strains is negligible even to those consumers who are immunocompromised (Ouwehand, 2003). However, many cases of sepsis have been recorded secondary to *Lactobacillus rhamnosus* or *Lactobacillus casei* (Simhon, 1982). Therefore, guidelines from the World Health Organization have been developed. These guidelines include: Phase I, II, and III clinical trials to prove health benefits, adequate manufacturing practice, studies examining mechanism of action in-vivo, precise information labeling, and the expansion of proven strains to benefit the oral cavity, nasopharynx, respiratory tract , etc. (WHO 2002 guidelines).

Probiotic benefits in the human gastrointestinal tract

Probiotics have been shown to be effective in treating infantile diarrhea, necrotizing enterocolitis, antibiotic associated diarrhea, Rota virus diarrhea, *Heliobacter pylori* infections as well as traveler's diarrhea (Reid, 2003).

A human trial study administered 2.5 x 10^8 live *Lactobacillus acidophilus* and 2.5 x 10^8 live *Bifidobacterium infantis* to 1237 newborns in Colombia. It resulted in a 60% reduction in the incidence of necrotizing enterocolitis. This study supported the health value of early colonization by probiotics (Walker, 2000). In terms of antibiotic associated diarrhea, a meta-analysis to evaluate the efficacy of probiotic prevention treatment showed an odds ratio of .39 in favor of active treatment with *Saccharomyces boulardii* over a placebo (D'Souza, 2002). This supports the odds that the outcome of preventing diarrhea will occur when a patient is exposed to the probiotic as opposed to the placebo. Meta-analysis examining the use of probiotics in the treatment of traveler's diarrhea also favored the use of probiotics, including *Saccharomyces boulardii* and *Lactobacillus acidophilus* (Mcfarland 2007). Many randomized, double-blind and placebo-controlled studies have shown beneficial effects for the prevention and treatment of diarrhea caused by the rotavirus in children (Szajewska, 2001). *Heliobacteria pylori* is a major cause of chronic gastritis and peptic ulcers. In vitro studies have shown that probiotics can reduce *Heliobacteria pylori* associated with gastrointestinal inflammation in an animal model (Lesbros, 2007).

Probiotic use in dentistry

Probiotic use has been studied for the treatment of oral health problems. Specifically, the use of probiotics has been explored to aid in the treatment of periodontal problems, halitosis and caries prevention. [14]

In terms of periodontal health, it has been observed that the

prevalence of normally occurring *Lactobacillus* is higher in healthy oral cavities as opposed to the oral cavities of patients with chronic periodontitis. [13] In a clinical study where patients with moderate to severe gingivitis were given either a *Lactobacillus reuteri* formulation or a placebo, the *Lactobacillus reuteri* group had reduced plaque and gingivitis scores compared to the placebo group. [14]

Lactobacillus brevis was studied for its anti-inflammatory effects in a group of patients with chronic periodontitis. Reduction in salivary levels of prostaglandin E2 was observed. The authors of this study claimed the possibility that the probiotics were able to prevent the production of nitric oxide and therefore prevented the release of prostaglandin E2 (Riccia, 2007).

It has been reported that *Lactobacillus gasseri* has been shown to inhibit the growth of *Actinomyces actinomycetemocomitans*, *Porphyromonas gingivalis,* and *Porphyromonas intermedia*, all known periodontal pathogens. [13] In addition, it has been found that during the fermentation process, *Lactobacillus helveticus* produces short peptides that stimulate oseteoblasts to increase bone production. This could contribute to reducing bone resorption associated with periodontitis (Narva, 2004). In recent times, a company based in Switzerland by the name of Sunstar began marketing the first probiotic formulated to fight periodontal disease. "Gum Perio Balance" contains a patented combination of two strains of *Lactobacillus reuteri* selected for their synergistic properties. Each lozenge single dose contains at least $2x10^8$ living cells of *Lactobacillus reuteri.* Although many forms of halitosis have causes related to certain types of food consumption, most cases arise from an imbalance of the commensal microflora of the oral cavity. [21] Peroxide production by the probiotic *Weissella cibaria,* which is commonly present in fermented foods, has been shown to inhibit the production of volatile sulphur compounds that contribute to oral malodor by *Fusobacterium nucleatum in vitro* and in exhalations following mouth rinsing by adults (Kang, 2006).

Probiotics have also been investigated for use in preventing dental caries. A randomized controlled trial using milk supplemented with *Lactobacillus rhamnosus*, with caries as an endpoint, was published in 2001 by Nase. Probiotic bacteria were given to 594 children aged 1-6 years. The study showed a significant reduction in caries increment in the probiotic milk group after 7 months compared to the control group for the 3-4 year olds. The authors claimed that a 5-day-a-week intake of probiotic milk significantly reduced the risk of caries.

It should be noted that there are several studies that have been completed using probiotics in oral health that have found non-significant clinical results. A randomized clinical trial was conducted using orally administered tablets of *Lactobacillus reuteri*. The effects upon the subgingival and salivary microbiota in 40 patients with gingivitis was noted during a course of 8 weeks. A parallel placebo group was also used. It was pointedly noted that the levels of *Prevotella intermedia* and *Porphyromonas gingivalis* were decreased in the test group. However, there were no significant changes between the test and placebo groups in terms of clinical variables such as plaque formation and gingival bleeding (Iniesta, 2012).

Endodontic therapy

As far as we know, probiotic use has not yet been evaluated for use in endodontic therapy. Endodontics is the branch of dentistry that is concerned with the morphology, physiology, and pathology of the human dental pulp and periradicular tissues. It has been established that the primary etiology of endodontic infections is bacteria. [24] In healthy conditions, the dental pulpodentin complex is sterile and the overlaying enamel and cementum helps to keep the complex isolated from microorganisms in the oral cavity. If these natural shields are compromised as a result of caries, microfractures and cracks, trauma from blunt injury or even dental procedures, the pulp is at risk of infection. Primary infections of the necrotic pulp tissue are generally composed of a mixed bacterial community. [18] This community still is dominated by anaerobic bacteria that are Gram negative. Persistent infections, those infections which are present after root canal therapy has been completed, tend to be dominated by a more specific community of bacteria. These bacteria tend to be anaerobic and Gram positive. [28]

The goal of treating infected root canal systems is to remove the primary etiology through chemomechanical means. The root canal system is physically enlarged with various instruments to provide cleansing and shaping. Irrigants such as sodium hypochlorite and chlorhexidine are used to decrease even further the bacterial presence. Inter-appointment medicaments, such as calcium hydroxide, are used for similar reasons. Obturating the prepared canals is performed for many reasons, one of which is to deny space for bacteria to recolonize. A coronal seal through adequate and timely restoration is required to further seal the pulp chamber from bacterial re-contamination from the oral cavity. The main focus of endodontic therapy is to eliminate or control bacteria within the root canal system.

Prevalence of *Enterococcus faecalis* in failing root canal treatments

When teeth are treated by root canal therapy under proper conditions and standard of care, the success rate is generally high. [19] Many cases of failure can be due to technical problems during treatment, and some fail even when treated without difficulties. Reasons for failure have been attributed to extraradicular infections, foreign body reactions, and true cysts (Nair, 1990). Yet, the most common reason that endodontic treatments fail is due to the presence of persisting microorganisms in the apical parts of the roots of obturated teeth (Nair, 1990). The bacteria involved with failed root canal treatments appear to be limited. [24] (Table 1)

TABLE 1 MICROBIAL SPECIES COMMONLY FOUND IN FAILED ROOT CANAL TREATMENTS

Enterococcus faecalis
Streptococcus anginosus
Streptococcus constellatus
Streptococcus intermedius
Streptococcus mitis
Streptococcus parasanguis
Peptostreptococcus micros
Actinomyces israelii
Pseudoramibacter alactolyticus
Eubacterium timidum
Lactobacillus catenaforme
Propionibacterium acnes
Propionibacterium propionicum
Fusobacterium nucleatum
Bacteroides gracilis
Candida albicans

The main aim of endodontic therapy is the prevention of apical periodontitis. This condition is the result of persistent pathogenic microorganisms such as *Enterococcus faecalis (E. f)* and *Candida albicans (C. a)* remaining in the root canal systems of teeth, and the ability of those organisms to directly cause acute and chronic inflammation in the periapical tissues. The concept of the use of probiotics has been evaluated in addressing endodontic disease only in few studies, but probiotics have proven successful in treating periodontal disease. A study by Hammad (2013) showed that there is no inhibitory effect of lactobacillus on E. faecalis whereas another study by Seifelnasr (2014) suggested that probiotics were effective against endodontic pathogens.Limitations of sufficient studies on use of probiotics in endodontics suggest further evaluations for their possible use in treating endodontic infection. [36,37]

CONCLUSION:

There are other probiotics that could be explored, perhaps even a combination of probiotics.

Success with any such future studies could then lead to experimental designs using extracted tooth models and then perhaps animal studies and progress onward.

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