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REVIEW ARTICLE

CONCEPT OF PROBIOTICS IN ENDODONTICS.

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Abstract

The main goal of endodontics is the prevention of apical periodontitis. This condition is the result of persistent pathogenic microorganismsremaining in the root canal systems of teeth, and the ability of these organisms to directly cause acute and chronic inflammation in the periapical tissues. Probiotics have been introduced in dentistry and oral medicine after years of successful use in gastro-intestinal disorders. Probiotics are dietary supplements which contain potentially beneficial bacteria or yeasts. They help in stimulating health promoting flora and also suppressing pathogens which cause and spread diseases.

The concept of the use of probiotics has not yet been evaluated in addressing endodontic disease, but probiotics approach has shown promising results in the oral health with respect to control of chronic disease such as dental caries, periodontitis, and recurring problems like candidal infections and halitosis. This review explores the possibility of shifting the established paradigm of endodontic treatment, which has focused on eliminating all bacteria from the canal system, to elimination of specificbacteria thus altering bacterial ecology by using probiotics.

Probiotics are still in "infancy" in terms of endodontic health benefits but surely have opened possibilities of treating disease on a nano – molecular mode. The aim of this review is to understand the mechanism of action of probiotic bacteria in the root canals and summarize observed effects of probiotics as well as their potential applications in the field of endodontics.

Introduction:-

The endodontic triad to achieve success in clinical endodontics, are these three basic principles (a) thorough debridement of the root canal system, (b) disinfection, and finally (c) complete obturation of the root canal system. A key question in endodontics which continues to remain unanswered is, "Can pathogenic microorganisms actually be eliminated from an infected root canal"?

Apical periodontitis is defined as inflammation and destruction of periradicular tissues caused by the presence of etiological agents of endodontic origin (Nair, 2004). These agents have been recognized as being either microorganisms or their metabolic products (Kakehashi et al., 1965; Fabricius et al., 1982; Gomes et al., 2004). According to multiple studies, (Sundqvist, 1994; Nair, 2004; Fabricius et al., 2006; Fujii et al., 2009 and Chavez 2004) bacteria that normally inhabit the oral cavity have the ability to invade root canal systems during and after pulp necrosis. Conditions exist in root canal systems that permit growth of anaerobic bacteria because they are capable of fermenting amino acids and peptides for metabolic needs. During the course of infection, interrelationships develop between microbial species, and microbial population shifts are produced as a result of

these interactions (Sundqvist, 1994; Nair, 2004; Fujii et al., 2009). These microbial interactions play a significant role in the ecological regulation and eventual development of an endodontic habitat adapted polymicrobial flora.

It has been proposed that it is impossible to obtain complete disinfection within any given root canal system. Multiple accessory and lateral canals can never be either completely debrided of tissue or micro-organisms (Seltzer & Bender, 2003). It is recognized and acknowledged that all that can be achieved is a reduction in the number of microorganisms in the main canal, or in other words, a reduction in the so called "bioload". Any perceived clinical success obtained from treatment of teeth with known positive root canal cultures can probably be ascribed to a reduction in the number of microorganisms, removal of most inflamed or necrotic tissue, and a favourable systemic background (Nair, 2004 and Seltzer & Bender, 2003). Thus findings from multiple studies lead to speculation that there is a missing link or some unknown etiological factor in endodontic theory and practice.

This "missing link" could be an ongoing misunderstanding and even possibly incorrect concept of endodontic infection, with that thinking being restricted to the belief that all microorganisms must be removed from the root canal system, regardless of their pathogenicity or other characteristics. Rather, and in light of current and emerging findings in microbiology, it now seems reasonable that a better approach to addressing and dealing with microbial infection should be to maintain a state of equilibrium within the "Human Microbiome". The "Human Microbiome" is defined as "the recognized, normal microbial component of all humans and animals which is needed for health" (Gueimonde & Collado, 2012; Dominguez & Blaser, 2008). The human microbiome is a necessary component for the health of the host, and alterations in its ecological equilibrium can lead to disease; therefore, logic suggests that it is necessary to maintain a continuous state of equilibrium between these diverse microbial communities in order to maintain health (Gueimonde & Collado, 2012; Dominguez & Blaser, 2008). Accepting that the dentition is a part of the Oral Human Microbiome, it is proposed that there should be healthy organisms (probiotics) associated with the teeth in order to establish endodontic health, since complete sterility is impossible anywhere within the oral cavity. Therefore, to maintain or restore the equilibrium of the endodontic infrastructure, the host could be provided with microbiota which would then produce beneficial effects, shifting any deficiencies to a more favorable ecological system.

"Probiotics", as defined by the World Health Organization, are, live microorganisms which, when administered in adequate amounts, confer a health benefit on the host". Probiotics have been successfully used to control gastrointestinal diseases and appear to act through colonization resistance and/or immune modulation (Gueimonde & Collado, 2012; Dominguez & Blaser, 2008). Recently, probiotics have been introduced to dentistry for the treatment or prevention of disease. Experimental studies and clinical trials have demonstrated that certain gastrointestinal bacteria may control the growth of some oral microorganisms, including cariogenic species associated with dental decay. Probiotics thus potentially provide a means of preventing dental caries (Al-Dajani & Limeback, 2012; Allaker & Douglas, 2009; Grover & Luthra, 2012; Meurman 2005; Reddy et al., 2011). The oral administration of probiotics has also been explored in the control of periodontal disease by reducing plaque levels and gingival inflammation (Allaker & Douglas, 2009 and Krasse et al., 2006). The purpose of this article is to contemplate the possible role of probiotics in endodontic therapy.

How do probiotics work?

As per Elavarasu (2012); Prathap & Prathap (2011) and Awadhesh, K.S. (2012) the mechanisms of action for the effectiveness of probiotics have been proposed as including:

1. Prevention ofadhesionof pathogens to host tissues.
2. Stimulation and modulation of the mucosal immune system.
3. Modulation of cell proliferation and apoptosis
4. Improvement of intestinal barrier integrity and upregulation of mucin production.
5. Killing or inhibition of growth of pathogens through production of bacteriocins or other products.
6. Beneficial microbes directly compete with the disease developing microbes for nutrition or enterocyte adhesion sites.
7. Inhibition of pathogen biofilm formation,
8. Induction of cytoprotective proteins,
9. Reduction of inflammation,
10. Stimulation of the host immune system,
11. Killing of pathogens through the production of bacteriocins and acids/peroxides along with altering the local environments pH (Geier, 2007)

Probiotic bacteria for oral health:-

The most commonly used strains belong to the Lactobacillus and Bifidobacterium genera that are commonly found in the oral cavity, including caries lesions (Haukioja et al., 2006).These were the first probiotic species to be introduced into research, Lactobacillus acidophilus by Hull et al., 1984 and Bifidibacterium bifidum by Holcombh et al., 1991 (Caglar, et al., 2005). Lactobacillus rhamnosus GG, ATCC 53103 has been proposed to reduce the risk for caries by producing a growth inhibitory substance against Streptococcus sobrinus (Haukioja et al., 2006). It was originally isolated in 1985 from the human intestinal flora and named after the discoverers, Sherwood Gorbach and Barry Goldin (Meurman, 2005). Streptococccus salivarius strains appear to be excellent candidates for an oral probiotic, since they are amongst the most numerically predominant members of the tongue micro biota of healthy individuals and are early colonizers of oral surfaces. Other strains of probiotics in the oral cavity include: L. acidophilus, L. casei Shirota, L. paracasei, L. casei, L .johnsonii, L. reuteri, propionibacterium, Weisella cibaria (Meurman and Stamatova, 2007).

A successful effector strain for replacement therapy of a bacterial disease must have some basic properties like it must not cause disease itself or otherwise predispose the host to other disease states by disrupting its residing ecosystem (Hillman et al., 2000). To be able to have probiotic effects in the mouth, a bacterium must adhere to oral surfaces and become part of the biofilm (Knuuttila, 2006). Finally, an effector strain should have a high degree of genetic stability (Hillman et al., 2000). Current evidence indicates that probiotic effects are strain specific; so, a beneficial effect attributed to one strain cannot be provided by another strain, even if it belongs to the same species (Senok, 2005).

Probiotic products:-

Probiotics are provided in products in four basic ways:

1. As a culture concentrate added to a beverage or food (such as fruit juice).
2. Inoculated into prebiotic fibers.
3. Inoculants in a milk-based food (dairy products such as milk, milk drink, yogurt).
4. As dietary supplements in concentrated and dried cells packaged (non-dairy products).

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, 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).

Role of probiotic in dentistry:-

Probiotics are seen to be effective in dentistry for the following (Malathi et al., 2014):

1. Prevention of caries
2. Prevention of periodontal diseases
3. Halitosis
4. Management of Aphthous ulcer
5. Effects on candidal infections

Potential in endodontics:-

In refractory cases of apical periodotnitis where bacteria like Enterococcus faecalis & Candida albicans are implicated and sometimes difficult to treat, probiotics may play a role against those bacteria. Lactobacilli can produce different antimicrobial components including organic acids, hydrogen peroxide, low-molecular weight antimicrobial substances, bacteriocins, and adhesion inhibitors, and have gained prominence as probiotics. Probiotics are a new potential emerging technology to treat infectious diseases in dentistry and still there are no clear researches about its application in the field of endodontics. The use of Probiotics may help in eliminating the pathogenic bacteria.Intra-canal medications are known to have very limited effect, if any, in killing bacteria in the intra-radicular spaces. The use of Probiotics between visits may enhance this process of elimination. It may play a role in the success of Apexogenesis & apexification.

Review of the studies involving probiotics in endodontics:-

The literature shows that there is a need for an innovative method of handling endodontic infections other than the currently used methods. A promising approach would be to manage endodontic treatment as part of the human microbiome and utilize probiotics in the same manner that they are used for other oral conditions to re-establish equilibrium of healthy flora.

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.

Despite great promises, probiotics works are limited to gut and periodontium. Endodontic works are sparse and need validation by in – vitro, in – vivo research and large randomized trials.

Need of probiotic research in endodontics:-

Microorganisms have been well known to play a role in pulpal and periapical diseases. The bacteria associated with primary endodontic infections are mixed, but are predominantly gram-negative anaerobic rods, whereas the bacteria associated with secondary infection comprise only one or a few bacterial species – most important of which is Enterococcus faecalis. Because of the complex nature of the root canal system and the presence of many inaccessible areas, a combination of mechanical instrumentation and irrigation is necessary to decrease the amount of micro-organisms in the root canal system. However chemo- mechanical preparation is often not enough and many bacteria may remain in the root canal system.

Intracanal medicaments in endodontics have been used for a number of reasons including the elimination or reduction of microorganisms, rendering canal contents inert, prevention of post-treatment pain, and to enhance anaesthesia (Yadula & Sharma, 2014). It has been unequivocally shown to contribute to favourable outcomes when treating endodontic infections. The need for intracanal medication is greater in those cases where bacteria are resistant to routine treatment, and where the therapy cannot be successfully completed due to the presence of pain or continuing exudate.

Many hand and rotary instrumentation techniques tend to produce round preparations (especially in oval canals) leaving some areas uninstrumented and hence possibly containing infected debris. The remaining necrotic tissue remnants may provide a source of nutrition for any surviving bacteria. In addition, bacteria are likely to remain in dentinal tubules after instrumentation. If this occurs, calcium hydroxide and other disinfectants that require direct physical contact with pathogens may be ineffective. The longstanding popular notion of entombment and perishing of intraradicular microbes following treatment lacks scientific validity. The presence of micro- organisms inside a root canal may not necessarily lead to the failure of treatment, but their absence will certainly favour healing.

There is a need for an innovative or novel approach to the current treatment modalities which can possibly result in a higher, long term success in endodontic therapy. Despite the universal and widely spread advancement of technology throughout all facets of dentistry, the same basic approach, in conjunction with the same materials, has been employed over the past several decades in providing endodontic treatment. Various intracanal medicaments like calcium hydroxide, antibiotics, steroids, etc have been tried and calcium hydroxide based intracanal medicaments are the gold standard. Studies done to test the antibacterial efficacy of calcium hydroxide show that calcium hydroxide is ineffective against E. Faecalis. It resists calcium hydroxide for about 10 days. Calcium hydroxide shows limited action against facultative anaerobes and Candida species but is effective against obligate anaerobes. Calcium hydroxide is the most commonly used intracanal medicament, however its efficacy towards Enterococcus faecalis is questionable (Mohammadi, Z. and Dummer, P.M.H. 2011). The most common corticosteroid preparation used as intracanal medicament is ledermix paste. Corticosteroid based antibiotic containing pastes have been developed. All these pastes contain the same underlying vehicle of polyethylene glycol. Various excipients and fillers are added, which do not exert antimicrobial activities. These antibacterial agents are not very effective against microorganisms in the root canal. Chlorhexidine gluconate gel is widely used in dentistry as an intracanal medicament (Yadula & Sharma, 2014). Studies show that Chlorhexidine is more effective in elimination of E. faecalis inside dentinal tubules. The disadvantage is that it does not act as a physical barrier against microbial recolonization and does not have any detoxifying ability against endotoxins. Triple antibiotic paste is a combination of three antibiotics namely minocycline, ciprofloxacin and metronidazole. Triple antibiotic powder, either mixed with normal saline or 2% chlorhexidine, produced the largest zone of inhibition against E. faecalis. The

minocycline component is most effective against E. faecalis. However, Triple antibiotic paste is shown to be most cytotoxic to human periodontal ligament fibroblasts. It causes exacerbated inflammatory reaction in subcutaneous connective tissue. The minocycline component causes discolouration of teeth (Murvindran & Raj, 2014).

Use of plant products in medicine is known as phytomedicine or phytotherapy. Natural and herbal intracanal medicaments such as articum lappa, propolis, casearia sylvetris, curcuma longa, liquorice etc have been researched in dentistry. The in-vitro studies conducted so far have shown that herbs can have a promising role as intracanal medicaments. However, further clinical trials and investigations are required to be considered as effective alternatives to the synthetic intracanal medicaments (Jain & Rajan, 2014).

Intracanal medicaments are mandatory in cases like non vital tooth, periapical pathology, periapical or radicular abscess and traumatised teeth. Adequate disinfection assisted by the intracanal medicament reduces the bacterial population and favours the prognosis. Literature has appraised various intracanal medicaments used in root canal therapy. As future scope, further studies are required to improvise the characteristics and properties of intracanal medicaments. The concept of the "Human Microbiome" has been neglected in the development of new and better strategies used in endodontic therapy including newer intracanal medicaments, even though it is now known to be an integral and undeniable part of human health. The novel concept in endodontics that the intentional establishment of a microbial equilibrium inside the root canal system by utilizing probiotics, a procedure which might result in improved overall success rates in the reduction of apical periodontitis, needs to be carefully examined and explored. As previously mentioned, the use of probiotics has gained universal acceptance by the gastroenterology community and some probiotics have been shown to be successful in treating certain gastrointestinal diseases. The concept of using probiotics has been utilized for the prevention of both dental caries and periodontal disease. Periodontal disease is known to have a number of pathogenic microorganisms in common with those found in endodontic infections, and therefore utilizing probiotics within the root canal system may also be found to be beneficial in endodontics. Thus it is important to evaluate if probiotics would have any inhibitory effect against known endodontic pathogens.

Conclusion:-

Probiotics play an important role in combating issues with overuse of antibiotics and antimicrobial resistance. It is right time to change the way bacteria are treated in today's new technological era. Significant research is required to understand the ability of probiotic bacteria to survive, grow, and have a therapeutic effect when used for endodontic treatment. Further in vitro and in vivo studies are needed to determine the full potential of "Bacteriotherapy" and its application in endodontics suggesting the best probiotic strains and means of their delivery in root canals. With fast evolving technology and integration of biophysics with molecular biology, designer probiotics pose huge opportunity to treat diseases in a natural and non-invasive way.

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