Yeasts in Endodontics : Role in Apical Periodontitis and its Management

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Fungi in Primary Endodontic Infection

Fungi have not been reported to be the common members of the microbiota associated with primary endodontic infections. Even so their occurrence has been reported by some researchers using culturing, molecular genetic methods and in situ electron microscopy.[1]

Baumgartner et al [2] detected C. Albicans in 5 of 24 root canal samples by means of PCR. In contrast, Siqueira et al, who also used PCR, detected fungi in only 1 of the 50 infected root canals. Siqueira et al[3] investigated the patterns of microbial colonization in primary root canal infections through scanning electron microscopy and found yeastlike cells in 1 of 15 examined teeth. They were forming a large colony with some cells in the process of budding. In addition, the presence of yeasts cells was shown in the resorption lacunae of periapical root surfaces and also in periradicular granuloma.

Fungi in Persistent or Secondary Endodontic Infections

Fungi have occasionally been found in primary root canal infections, but they seem to be more common in the root canals of obturated teeth in which the treatment has failed. Waltimo et al[4] reported the occurrence of fungi in 47 of 692 cases of persistent endodontic infection either in pure culture or along with other bacteria. Sundqvist et al[5] isolated C. Albicans from 2 0f 24 canals of teeth in which endodontic treatment has failed. Taken together from other studies, we can come to assertion that fungi can gain access to the root canals through contamination during endodontic therapy and can be involved in the etiology of recalcitrant periradicular lesions.

Accompanying Bacteria in Yeast Infections

Recent studies have shown that yeasts can survive as a monoinfection of the root canal. However, they are usually found in mixed cultures with bacteria. Yeasts may often be isolated together with facultative gram-positive bacteria such as alpha and non-hemolytic streptococcus species, whereas gram-negative isolates are rare. The dominance of the facultative gram-positive accompanying bacteria may be due to the ecological conditions of the root canal during prolonged treatment, which would favor yeasts and streptococci. There may be synergism between these organisms. It has been reported that C.albicans may prolong the viability of â-hemolytic streptococci. Furthermore, C. Albicans co-aggregates with a variety of streptococci such as S. Gordonii, S. Mutans and S. Sanguis. This may promote their colonization and thus explain the concomitant occurrence of these microbial species.[6]

Treatment Strategies

Mechanical preparation does not suffice to free a tooth with apical periodontitis from all bacteria in the root canal. Furthermore, soft tissue remnants may be left behind after mechanical root canal preparation. Collagen and other soft tissue components provide a source of nutrition for microorganisms that survived root canal therapy, allowing them to remultiply[7]. Thus, a so-called 'chemo-mechanical' treatment strategy is advocated with the aid of antimicrobial and tissue-dissolving irrigants to minimize the amount of infected dentine, pulpal remnants, and the number of microorganisms in the root canal system. However, complete disinfection of the root canal system cannot be predictably completed by chemomechanical preparation alone.[8]

Persistent microorganisms, such as E. faecalis or C. Albicans, are often present in root canal infections resistant to conventional therapy. Therefore, attention should be paid to adequate treatment strategies.

Susceptibility to Antimicrobial Endodontic Medication

Endodontists have been long aware of the need to use proper antimicrobial strategies that include fungi elimination from the infected root canals. This can be attested to by the statement of Grossman[9]: "one of the problems in endodontic treatment is the presence of Candida organisms in infected root canals; it is necessary to eliminate these organisms to maintain the periapical tissue in a normal state or to restore it to the state of health". He proposed the use of antifungal agents as intracanal medication.

From the 1950s to the 1970s, the antibiotic pastes contained an antifungal agent, mainly Nystatin or Sodium caprylate. However with the development of resistant microorganisms and host sensitization, the use of substances with antifungal effects in endodontic therapy was paid little attention.

Because fungi is involved mainly in failed cases the spectrum of endodontic medicaments and irrigants should have antifungal effectiveness which may assists in successful management of persistent or secondary endodontic infection caused by fungi.

Smith and Wayman[10] in their study concluded that citric acid was not as effective as NaOcl and C. Albicans was more resistant than E.faecalis. Sen et al[11] investigated the antifungal properties of 0.12% chlorhexidine, 1% NaOCl and 5% NaOCl and found C. Albicans to be more resistant in the presence of smear layer than in the absence of smear layer. When smear layer was absent, NaOCl started to display antifungal activity after 30 minutes. In another study Sen et al[12] evaluated the antifungal effect of EDTA on C.albicans and revealed that EDTA had the most effective antifungal activity. Nystatin, ketaconazole and 1.5% chlorhexidine gluconate solution exhibited the next most effective activity. They have suggested that EDTA demonstrated its antifungal activity in 2 particular ways: anticolonization (reducing adhesive properties) and antigrowth (i.e., decreasing the metabolic activity and pathogenicity of C.albicans by extracting calcium ions both from the cell wall and the medium). Therefore, EDTA may be strongly recommended during the endodontic treatment of patients with a particularly high incidence of oral candidosis.

Waltimo et al[13] studied the susceptibility of common oral candida species to saturated aqueous calcium hydroxide solution. They observed that all Candida species showed either equally high or higher resistance to aqueous calcium hydroxide than did E. Faecalis. Because C. Albicans can survive in a wide range of pH values, the alkalinity of saturated calcium hydroxide solution may not have any effect on C. Albicans. In addition, calcium hydroxide solution may readily display the ca^{++} ions necessary for the growth and morphogenesis of Candida. These mechanisms may explain why calcium hydroxide has been found to be ineffective against C. Albicans.

Due to resistant to contemporary calcium hydroxide formulation renewed interest has been generated regarding the association of calcium hydroxide with other antimicrobial substances, such as camphorated mono-chlorophenol (CPMC), chlorhexidine, iodine or potassium iodide, or even the use of alternative intracanal medications.[14] Siqueira et al[15] investigated the antifungal ability of several medicaments: the paste of calcium hydroxide in CPMC or glycerin showed the most pronounced antifungal effects. Calcium hydroxide in glycerin or chlorhexidine or chlorhexidine in detergent also showed antifungal activity that was much lower than the paste of calcium hydroxide in CPMC/ glycerin.

Ferguson et al[16] in his study revealed that NaOCl, hydrogen peroxide and

chlorhexidine digluconate were effective against C.albicans even when significantly diluted. Aqueous calcium hydroxide had no activity.

IPI, used as an intravisit dressing for 10 min, has also shown some promise as an endodontic disinfectant. However, iodine preparations may not offer any additional value against yeasts when used in combination with sodium hypochlorite, because they have a similar mode of action. In addition, IPI may stain teeth and is potentially allergenic[17].

On the basis of these reports, it seems that some medicaments, such as chlorhexidine digluconate, calcium hydroxide combinations (with CPMC or chlorhexidine) and EDTA have the potential to be used as effective intracanal medicaments for patients in whom fungal infection is suspected.

Factors Inhibiting Disinfectants

Recent studies, in vitro, have demonstrated that there are several factors that interfere with the clinical efficacy of disinfectants. These factors include dentin, smear layer, and fungal biofilms which consists of a mono- or multilayer of microorganisms embedded in an extracellular matrix. The protein and mineral component of dentin can bind and inhibit activity of disinfectants and smear layers and biofilms may serve as barriers which prevent the exposure of microorganisms to effective concentration of the disinfectants.[11]

Microorganisms living in the surface layers of root canal biofilm are directly affected by the disinfectant or irrigating solution. However, the extracellular matrix may protect the microorganisms in the deeper layers from the full-strength activity of the endodontic disinfectants. Hence, the strains may become more resistant and the infection may therefore persist in the root canal. This finding demonstrates the importance of local inhibitory factors and it emphasizes the need for effective mechanical preparation during root canal therapy. Endodontic instrumentation "disorganizes" and exposes biofilm cells to endodontic disinfectants/ irrigating solutions.

Susceptibility of C. Albicans to Antifungal Agents

Systemic or local antifungal agents may be considered in some acute or persistent cases after a microbiological diagnosis of a root canal yeasts infection. The medicaments commonly used are Amphotericin B, 5-fluorocytocine, and 3 azole-group agents (fluconazole, miconazole and clotrimazole), ketoconazole, nystatin etc. Although Amphotericin B has been extensively used for more than 30 years, the emergence of resistant strains is rare. In some study, strains resistant to 5-fluorocytocine are frequently isolated. The Candida species are increasingly resistant to azole group of antifungal agents as determined by some studies.[18] Ketaconazole and nystatin are effective against C. Albicans. However with the treatment strategies based on disinfectants, the use of antifungal agents should be limited to acute cases and, particularly, to medically compromised patients.

Conclusion

C. Albicans is by far the most common yeast in endodontic infections. Yeasts can be found in low numbers both from primary infections as well as from post-treatment infections. The ability of C. Albicans to interact with dentine may be important for its ability to survive in the ecologically demanding environment of the necrotic or treated root canal. C. Albicans is more sensitive to sodium hypochlorite than E. Faecalis and it is also rapidly killed by low concentrations of chlorhexidine. In the future, combinations of present and new disinfecting agents and substances that may act in a synergistic manner with dentine may take us closer to the goal of complete dentine disinfection.

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Table 1

Virulence Factors of C. Albicans & their Possible Contributions to Apical Periodontitis

Virulence Factor	Possible Contribution to Apical Periodontitis
Adherence	Colonization of dental hard tissues
Hyphal Formation	Penetration into dentinal tubules
Thigmotropism	Penetration into dentinal tubules
Protease Secretion	Survival in conditions with limited nutrient supply
Phenotypic Alteration	Adaptation in ecologically harsh conditions

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