The Importance of Antimicrobial Agents in Oral Hygiene

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Introduction

Adequate oral hygiene is one fundamental step in a successful periodontal therapy or implant maintenance plan. When dental plaque is not frequently removed, the development of oral diseases may occur.[1] The gold standard of oral hygiene is tooth brushing and flossing. Nevertheless, the prevalence of gingival inflammation is still high, despite the efforts of mechanical plaque control.[2] In an effort to reduce oral biofilm formation and especially pathogenic bacteria, chemical substances have been utilized in several types of oral application without causing systemic influences.[2,3] When supragingival biofilm is the main target, most chemical agents are available as mouthwashes, but can also come as a gel, spray, or toothpaste. Their main objectives are to reduce microorganisms and, consequently, gingival inflammation.

Ideally, a mouthwash should have a broad spectrum in order to be efficient against microorganisms responsible for gingival inflammation.[4] Another important characteristic is substantivity, which is the capacity of a mouthwash to be maintained in the oral cavity even after its use; this helps guarantee efficacy, since the agent needs contact time to act on bacteria and inhibit biofilm formation.[5] Moreover, a mouthwash should be stable and secure of possible local and systemic side effects.[6]

This report reviews the supporting role of some of the most commonly used chemical agents in oral hygiene – chlorhexidine (CHX), cetylpyridinium chloride (CPC), hydrogen peroxide (H_2O_2), and triclosan.

Chlorhexidine

Chlorhexidine was developed in the 1950s and first commercialized as a topical antiseptic. Previously it was used in surgical procedures; its first use in dentistry was in pre-surgical disinfection and endodontics.[7]

This cationic bisbiguanide antiseptic is able to inhibit biofilm formation and interfere with the metabolism of bacterial enzymes, with a substantivity of approximately 12 hours.[8] With a broad spectrum, CHX acts on fungus, yeasts, viruses, and Gram-positive and negative bacteria. It can be bactericidal or bacteriostatic, depending on the concentration that may pass through bacterial membranes.[9] It is also stable, non-toxic to oral tissues, and has a minimum absorbance through the mucosa, which ensures no systemic side effects.[10]

The more widely used form of CHX is in mouthwashes, which are considered the gold standard of chemical antiplaque and antigingivitis agents.[11] Clinical studies with CHX-containing mouthwashes, ranging in duration from three months to two years, have demonstrated significant reductions in plaque and gingivitis.[12] CHX mouthwashes are less effective in the presence of biofilm, which means that a mechanical biofilm removal should be completed first.[13]

CHX-containing mouthwashes are usually sold in concentrations of 0.2% or 0.12%. One of the pioneer studies on CHX-containing mouthwashes demonstrated inhibition of plaque formation and development of gingivitis when a 0.2% CHX mouthwash was used for 60 seconds twice daily, even in the absence of mechanical plaque removal.[7]

Studies have shown that 0.2% chlorhexidine has a slight superiority on inhibition of biofilm formation when compared with 0.12% concentration, but this likely has no clinical relevance.[14] A systematic review has demonstrated that use of 0.12% CHX resulted in a mean reduction of 28% in gingival inflammation and 40% in plaque formation.[2]

Long-term clinical studies have also confirmed the excellent safety profile of CHX formulations.[15] Additionally, CHX has not been related to bacterial resistance,[16-18] but some local side effects have been reported, such as tooth staining (and also staining of tongue, gingiva, and resin restorations); taste disturbance (reduction of bitter and salty taste sensations); and promotion of calculus formation.[1] Those side effects do not permit the widespread long-term use of CHX as a daily adjunct to normal oral hygiene procedures; it is, therefore, rather restricted to short- to moderate-term use and in special clinical situations. Two rare side effects that can be disturbing to the patient are parotid swelling and hypersensitivity to the agent, which could vary from a local harsh sensitivity to an even more rare effect, which is anaphylactic reaction with glottis edema.[19]

Two recent systematic reviews have shown that CHX can be successfully formulated into a dentifrice/gel and will inhibit plaque growth to some degree, but not to the same extent as CHX incorporated into a mouthwash.[20,21] When CHX comes in a 1% concentration gel, its distribution throughout the oral cavity is more deficient. Nevertheless, for individuals with a mental disability, a tray with CHX-containing gel has been useful.[22,23] Sprays containing CHX have been shown to inhibit plaque formation similar to 0.2% CHX mouthwashes, and are also useful for individuals with mental and physical disabilities.[24]

Chemicals in toothpaste, especially anionic compounds such as sodium lauryl sulfate (SLS), may reduce or inhibit the activity of CHX, because of its cationic nature. A systematic review has concluded that there are adequate reasons to believe CHX and SLS dentifrices are not compatible.[25]

Taking all these considerations into account, mouthwashes are the main vehicles for CHX, but its long- and mid-term local side effects restrict its use to some special situations:

- Complementary to oral hygiene for a period of time when mechanical oral hygiene is compromised for some reason;
- Before surgical and non-surgical procedures, in order to reduce bacterial load in the oral cavity, minimizing bacterial dissemination throughout aerosols in dental procedures; and
- After surgical procedures, in order to inhibit plaque formation in the oral cavity.

Cetylpyridinium Chloride

Cetylpyridinium chloride (CPC) is a cationic quaternary ammonium compound that has demonstrated effectiveness and safety as a plaque inhibitory agent in a range of concentrations between 0.045 and 0.1%.[26] CPC is capable of killing Gram-positive pathogens and yeasts through its interaction with the bacterial membrane function, leakage of cytoplasm material, and the ultimate collapse of the intracellular equilibrium.[27]

Several studies have shown the efficacy of CPC against plaque formation and gingivitis,[28-32] but results have been heterogeneous. This could be due to different formulations and also to its use right after tooth brushing, since CPC is also a cationic antiseptic that is inhibited by anionic formulations of toothpastes.[26] The use of CPC mouthwash twice a day for a month was shown to be effective in reducing plaque when associated with basic oral hygiene in patients

undergoing orthodontic treatment with fixed appliances, and also improved the periodontal health of these patients.[33] A systematic review[2] has shown CPC mouthwash reduces gingivitis by a mean of 13.4% and plaque index by 15.4%. The most recent systematic review[34] demonstrated a significant mean reduction in plaque index score of -0.39 and a significant mean reduction in gingivitis of -0.33 when compared to a control group.

One of CPC's main deficiencies is its low substantivity, since it is eliminated from the oral cavity much faster than CHX. Its therapeutic effects do not last more than 90 minutes, while CHX lasts for 12 hours.[29] On the other hand, CPC has not been related to bacterial resistance and it shows fewer side effects as compared with CHX.[35] CPC has been related to staining, ulcerations, and burning sensations, but these side effects seem to be fewer marked compared with CHX.[26,32]

Those characteristics bring CPC to the category of over-the-counter products and received a Category I (safe and effective) label from the United States Food and Drug Administration (FDA) Advisory Panel in 2004.

Hydrogen Peroxide

Oxidative agents, such as hydrogen peroxide, were recommended as plaque control and pyorrhea control agents in 1913 in order to lower costs and complexity of treatments available at that time.[36] Today, these agents are recommended to lower symptoms and to help treat pericoronitis and acute necrotizing ulcerative gingivitis.[37]

Hydrogen peroxide has antimicrobial effects on Gram-positive and negative bacteria through the liberation of oxygen in the environment.[38] Since oxygen is toxic to anaerobic bacteria, their survival is compromised. Further, H_2O_2 efficacy has been attributed to a physical removal of bacterial plaque throughout the bubbling resultant of the liberation of oxygen.

Although some improvement has been demonstrated in plaque index and gingival index,[39] there is little evidence that validates hydrogen peroxide as an antiplaque agent.[11] The use of H_2O_2 does not prevent biofilm formation,[37] although there is some evidence that it may reduce gingival redness when used for longer periods combined with mechanical oral hygiene.[40]

The concentration of H_2O_2 in mouthwashes may vary from 0.013% to 3%, and although there is no consensus as to which would be the best therapeutic concentration, it appears that concentrations ≤ 1% do not yield any clinical benefits.[41-43]

There have been some reports of side effects related to H_2O_2 at 3%,[44] such as oral ulcerations and burning sensation.[45] No important side effects have been related to the use of H_2O_2 at low concentrations (≤ 1.5%).[38]

The use of H_2O_2 should be recommended only in specific cases, such as necrotizing ulcerative gingivitis, and its daily use should not be part of the clinical practice.

Triclosan

Triclosan is a nonionic, phenolic agent with low toxicity, and it has a broad spectrum of activity. It has antibacterial and antifungal properties, breaking cytoplasmic bacterial membranes through the interruption of fatty acid biosynthesis. It works against Gram-positive and negative bacteria, being bacteriostatic in small concentrations and bactericidal in higher concentrations.[46]

Although its activity is less than CHX, it has the advantage of being compatible with toothpaste ingredients. Triclosan was created in the 1960s, and it has been added to dentifrices[26] associated with copolymers, enhancing its substantivity and allowing its effects to last for 12 hours.[46]

Studies have shown that the use of triclosan is related to a significant reduction of gingivitis.[47-50] A systematic review demonstrated that triclosan-containing dentifrices are able to reduce plaque formation and gingivitis.[51]

Triclosan has also demonstrated an anti-inflammatory effect, since *in vitro* studies have shown that it is able to inhibit cytokine release through human fibroblasts.[46,52]

There are no reports in the literature regarding the lack of safety or side effects in hard or soft tissues with the use of triclosan,[53] although there has been some warning with regard to bacterial resistance if it is used for long periods. Although this has been shown in laboratory studies, no clinical study could prove bacterial resistance.[46] A clinical study using a triclosan-containing dentifrice demonstrated no bacterial resistance or microorganism growth,[54] therefore triclosan-containing toothpastes offer value for improving oral care.

Conclusions

The use of chemical agents as an adjunct to mechanical oral care has proven to be important in reducing plaque and gingivitis. Chlorhexidine is the gold standard among antigingivitis and antiplaque agents, though its mid- and long-term side effects do not permit its everyday use. CPC mouthwashes are more adequate for daily use, since their safety and minimal side effects have been reported. Oxidative agents have a lower effect on plaque reduction, but are important tools against some acute diseases, such as pericoronitis and necrotizing ulcerative gingivitis. Triclosan-containing toothpastes are also important tools in oral care, and their safety allows their use on a daily basis.

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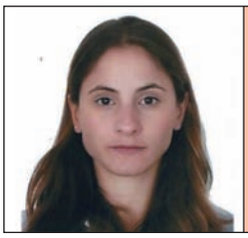

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