

Antimicrobial mouthrinse use as an adjunct method in peri-implant biofilm control*

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Abstract: Great possibilities for oral rehabilitation emerged as a result of scientific consolidation, as well as a large number of dental implant applications. Along with implants appeared diseases such as mucositis and peri-implantitis, requiring management through several strategies applied at different stages. Biofilm accumulation is associated with clinical signs manifest by both tooth and implant inflammation. With this in mind, regular and complete biofilm elimination becomes essential for disease prevention and host protection. Chemical control of biofilms, as an adjuvant to mechanical oral hygiene, is fully justified by its simplicity and efficacy proven by studies based on clinical evidence. The purpose of this review was to present a consensus regarding the importance of antimicrobial mouthrinse use as an auxiliary method in chemical peri-implant biofilm control. The active ingredients of the several available mouthrinses include bis-biguanide, essential oils, phenols, quaternary ammonium compounds, oxygenating compounds, chlorine derivatives, plant extracts, fluorides, antibiotics and antimicrobial agent combinations. It was concluded that there is strong clinical evidence that at least two mouthrinses have scientifically proven efficacy against different oral biofilms, i.e., chlorhexidine digluconate and essential oils; however, 0.12% chlorhexidine digluconate presents a number of unwanted side effects and should be prescribed with caution. Chemical agents seem beneficial in controlling peri-implant inflammation, although they require further investigation. We recommend a scientifically proven antiseptic, with significant short and long term efficacy and with no unwanted side effects, for the prevention and/or treatment of peri-implant disease.

Keywords: Mouthwashes; Biofilms; Peri-Implantitis; Mucositis; Dental Implants.

Introduction

Aiming at controlling dental caries and periodontal disease (two of the most prevalent diseases in the world population) and also maintaining fresh and enjoyable breath, dental clinical routine should include several steps, such as detailed anamnesis, clinical examination, image analysis, moldings, treatment plan, and oral hygiene instructions. With the scientific consolidation of implant dentistry and the widespread use of dental implant applications, new and great possibilities for oral rehabilitation are emerging. However, the advent of implants has also brought

new diseases, such as peri-implant mucositis and peri-implantitis,¹ whose management also requires several strategies applied at different stages.

The indication for using mouthrinses has become customary in the last decades, usually following mechanical means for biofilm control. Chemical control of different biofilms present in the oral environment is fully justified by its simplicity and efficacy, proven by evidence from clinical studies.

Therefore, the purpose of this paper was to present a consensus regarding the importance of antimicrobial mouthrinses as an adjuvant method for the chemical control of peri-implant biofilm.

Dental and peri-implant biofilm

Biofilm is a bacteria-structured aggregate that forms on hard surfaces, in the presence of fluids.² In the oral cavity, biofilm formation occurs on both teeth and implant surfaces.³ This aggregate is composed of bacterial microcolonies, which are considered independent communities that communicate dynamically via water channels that allow the passage of nutrients and other chemicals.⁴ The presence of biofilm on both tooth and implant surfaces initiates an immune-inflammatory response in local tissue and may lead to an inflammatory process in gums (gingivitis) or peri-implant mucosa (peri-implant mucositis). Failure to control biofilm over time may promote inflammatory process progression, with consequent destruction of supporting structures around the teeth (periodontitis) or destruction of bone around implants (peri-implantitis).³

Regarding microbiological aspects, there are some similarities and differences between teeth and implant biofilms. Botero *et al.*⁵ compared the subgingival microbiota around implants and teeth and reported a positive correlation for gram-negative species between periodontal and peri-implant sites. Using qualitative techniques for periodontal pathogen detection, Cortelli *et al.*⁶ compared bacterial frequencies between equivalent periodontal and peri-implant conditions, namely, periodontal or peri-implant health, peri-implant mucositis or gingivitis, and periodontitis or peri-implantitis. Results showed that bacterial frequency increased from a healthy condition to an irreversible diseased condi-

tion in both teeth and implants. *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* frequencies were similar between periodontitis and peri-implantitis. Despite differences related to periodontal pathogen occurrence, there are also differences between periodontitis biofilm and that related to peri-implantitis. Peri-implantitis biofilm consists of a more complex microbiota than that observed in periodontitis.⁷ In peri-implant biofilm, bacterial communities were identified belonging to the genera *Butyrivibrio*, *Campylobacter*, *Eubacterium*, *Prevotella*, *Selenomonas*, *Streptococcus*, *Actinomyces*, *Leptotrichia*, *Propionibacterium*, *Peptococcus*, *Campylobacter* and *Treponema*,⁸ whereas some of these were not observed on dental biofilm.

Koyanagi *et al.*⁹ also reported higher microbial diversity in peri-implantitis. Additionally, the *Staphylococcus aureus* species has been identified as relevant in early peri-implantitis, unlike periodontitis.¹⁰

In addition to the differences between teeth and implant surface biofilm, there may also exist differences in the composition of the biofilm present on different implant surfaces.^{11,12}

Peri-implant mucositis and peri-implantitis

Peri-implant mucositis experimental studies have shown that biofilm accumulation on the peri-implant surface may induce an inflammatory response in the mucosa around the implant.^{1,13} Although clinical parameters did not differ between experimental gingivitis and experimental peri-implant mucositis in the Pontoriero *et al.*¹ study, a more recent comparative study of peri-implant mucositis and gingivitis in humans reported that an immune-inflammatory response was more intense around implants than in teeth.¹³ The authors observed a greater increase in matrix metalloproteinase 8 (MMP-8) and interleukin-1 β (IL-1 β) in the crevicular fluid from implants, as compared with that from teeth, throughout a 6 week experimental period.¹³

When considering peri-implant mucositis progression, *in vivo* study design limitations leave some questions unanswered. A study in dogs evaluated the progression of induced periodontal and peri-implant diseases, and its authors observed more pronounced

bone loss around implants than around teeth.¹⁴

According to a literature review, peri-implantitis affects about 10% of implants and 20% of patients about 5 to 10 years after implant placement. Factors such as smoking are associated with higher disease rates.¹⁵ Additionally, previous periodontal disease history negatively influences peri-implant disease occurrence,¹⁶ suggesting that preventive measures should be implemented before implant placement. According to Costa *et al.*,¹⁷ preventive measures could also influence the peri-implant condition over time. Among these measures, proper intra-oral biofilm control is paramount, since under similar levels of supragingival biofilm build-up, Abreu *et al.*¹⁸ reported greater annual bone loss for implants than for teeth.

Mechanical methods of controlling biofilm on the implant surface

Mechanical biofilm control

Supra/subgingival biofilm elimination is considered the main way of reducing most oral pathologies, especially dental caries and periodontal diseases.^{19,20} Similarly, peri-implant mucositis and peri-implantitis treatments should consider mechanical and chemical peri-implant biofilm control and calculus removal on the implant surface, often achievable only by surgical means.^{21,22,23} Preventive office visits to record clinical parameters and conduct radiographic follow-up allow early peri-implantitis diagnosis, thus promoting higher implant longevity.^{3,24,25,9} However, it should be noted that non-surgical treatment can be effective for peri-implant mucositis treatment, although this has not been observed for peri-implantitis. Several surgical treatments have shown promising results for peri-implantitis; however, most published studies on peri-implant diseases are case reports or case series with an undeniable bias in data interpreting. Many studies address several therapeutic and complex procedures, making them difficult to interpret. We have also observed few comparative studies or randomized clinical trials showing the best treatment options for peri-implant diseases, thus providing little evidence to establish a definitive treatment protocol.

In addition to professional biofilm control, home oral care hygiene measures are widely known to be essential to maintaining oral health. Despite the central role of proper toothbrush use,²⁶ tooth brushing has not proved effective enough to maintain good hygiene especially in difficult-to-reach areas, such as interproximal areas.²⁷

There are several devices available on the market today, which can serve as additional oral hygiene implements, among which we can highlight interproximal cleaning brushes and tongue cleaners. However, patient adherence to this routine seems to be the most difficult task. Studies show that only 10% of the population use dental floss/tape and interdental brushes regularly.²⁸

Furthermore, studies show that proper oral care hygiene measures at home are key to maintaining dental implant stability and to preventing tissue inflammation and possible complications.^{29,30}

Bacterial accumulation is associated with clinical signs of both tooth and implant inflammation.³¹ Accordingly, regular and complete biofilm elimination becomes essential for disease prevention and host protection.

Chemical methods recommended for peri-implant biofilm control

As in the precautions required for natural dentition, the prevention of biofilm formation and its elimination from the implant surface is the first step to treating peri-implant disease. Peri-implant mucositis therapy is based on non-surgical therapy with supra- and submucosal scaling, whether associated to antimicrobial agents or not, including chlorhexidine and essential oils.^{32,33,34} However, not all antimicrobials can offer additional clinical benefits. Studies evaluating antimicrobial activities on peri-implant biofilms are important because the biofilm formed on dental surfaces has different characteristics from that formed on a titanium surface.^{11,12}

Gosau *et al.*³⁵ evaluated biofilm reduction on titanium specimens affixed to removable dental appliances and found that antimicrobial substances, such as sodium hypochlorite, 3% hydrogen peroxide, 0.2% chlorhexidine digluconate and essential oils, were able to reduce bacteria viability on the biofilm

that developed on a titanium surface, as compared with saline solution. Likewise, 0.5% cetylpyridinium chloride and 40% citric acid were not effective in reducing biofilm.

Antimicrobial action on peri-implant biofilm was also demonstrated by Baffone *et al.*³⁶ According to these authors, 0.2% chlorhexidine, essential oils, stannous fluoride and hexetidine associated with methylparaben and propylparaben were effective in reducing peri-implant biofilm *in vitro*. Among the antimicrobials evaluated, chlorhexidine and essential oils proved most effective in reducing biofilm under experimental conditions.

In a peri-implant induced disease model, Trejo *et al.*³⁴ evaluated the adjuvant action of antimicrobials associated to mechanical treatments, and the results demonstrated effects similar to those of an unassociated mechanical treatment for 3 to 4 mm deep peri-implant mucositis pockets. In humans, chlorhexidine used in the form of an irrigation solution,³⁷ gel³⁸ or chemical agent in a full-mouth disinfection approach²² also did not offer any additional clinical and/or microbiological benefits over the mechanical treatment alone.

Felo *et al.*³³ reported that when diluted 0.06% chlorhexidine is used in a powered irrigator, as compared to rinsing with 0.12% chlorhexidine gluconate once daily, it may be a valuable adjunct for oral health in patients with implants, in reducing plaque and gingivitis 3 months after initial prophylaxis; however, there was no mechanical treatment group in this study. The superior results of chlorhexidine irrigation, compared with chlorhexidine mouthrinse, in reducing plaque and marginal bleeding were also identified in a systematic review published by Grusovin *et al.*³⁹

On the other hand Ciancio *et al.*³² demonstrated that essential oil mouthrinses used twice a day were effective in reducing plaque and marginal bleeding, as compared with placebo in dental implant patients on maintenance therapy. Mouthrinses containing essential oils were also statistically superior to placebo in reducing plaque and marginal bleeding, according to Grusovin *et al.*³⁹ Ramberg *et al.*⁴⁰ confirmed that brushing with a toothpaste containing triclosan reduced gingival bleeding and pocket depth,

compared with placebo dentifrice. These findings corroborate the conclusions by Renvert *et al.*,²¹ i.e., that mechanical non-surgical therapy is not effective for peri-implant mucositis treatment, and its effects are boosted by particular chemical agents. Furthermore, according to these authors, mechanical treatment for peri-implantitis is limited, and chlorhexidine offers few additional benefits.

In addition to the active ingredients found in mouthrinses, there are those found in toothpastes. For example, toothpaste containing triclosan also showed clinical benefits when used to control peri-implant biofilm. Moreover, 0.3% triclosan with a 2% copolymer formulation associated to sodium fluoride was more effective in controlling peri-implant mucosal biofilms and inflammation than toothpaste containing sodium fluoride alone.^{41,42}

Figure 1 illustrates in what peri-implantitis clinical conditions antimicrobial agents can be incorporated in association with supra- and submucosal scaling.

Active ingredients used for chemical biofilm control

The most common therapeutic agents found in commercial mouthrinse brands include a combination of four essential oils (thymol, eucalyptol, menthol and methyl salicylate),⁴³ hexetidine, chlorhexidine gluconate,⁴⁴ benzalkonium chloride, cetylpyridinium chloride, hydrogen peroxide, and sometimes domiphen bromide, fluoride⁴⁵ and xylitol.⁴⁶ These rinses have often been tested as adjuvants for daily oral hygiene procedures, and at least two agents, particularly 0.12% chlorhexidine digluconate and essential oils, have demonstrated clinical efficacy in both inhibiting and reducing dental biofilm formation, as a way of diminishing periodontal and peri-implant disease severity.^{47,48}

Chlorhexidine has been reported to reduce biofilm buildup in approximately 60% and gingivitis severity in 50% to 80% of cases, as shown by way of improvements in clinical parameters.⁴⁹ It has been demonstrated that the use of a mouthrinse containing 0.12% chlorhexidine digluconate results in a significant decrease in total anaerobes, total aerobes, *Streptococci* and *Actinomyces*, after

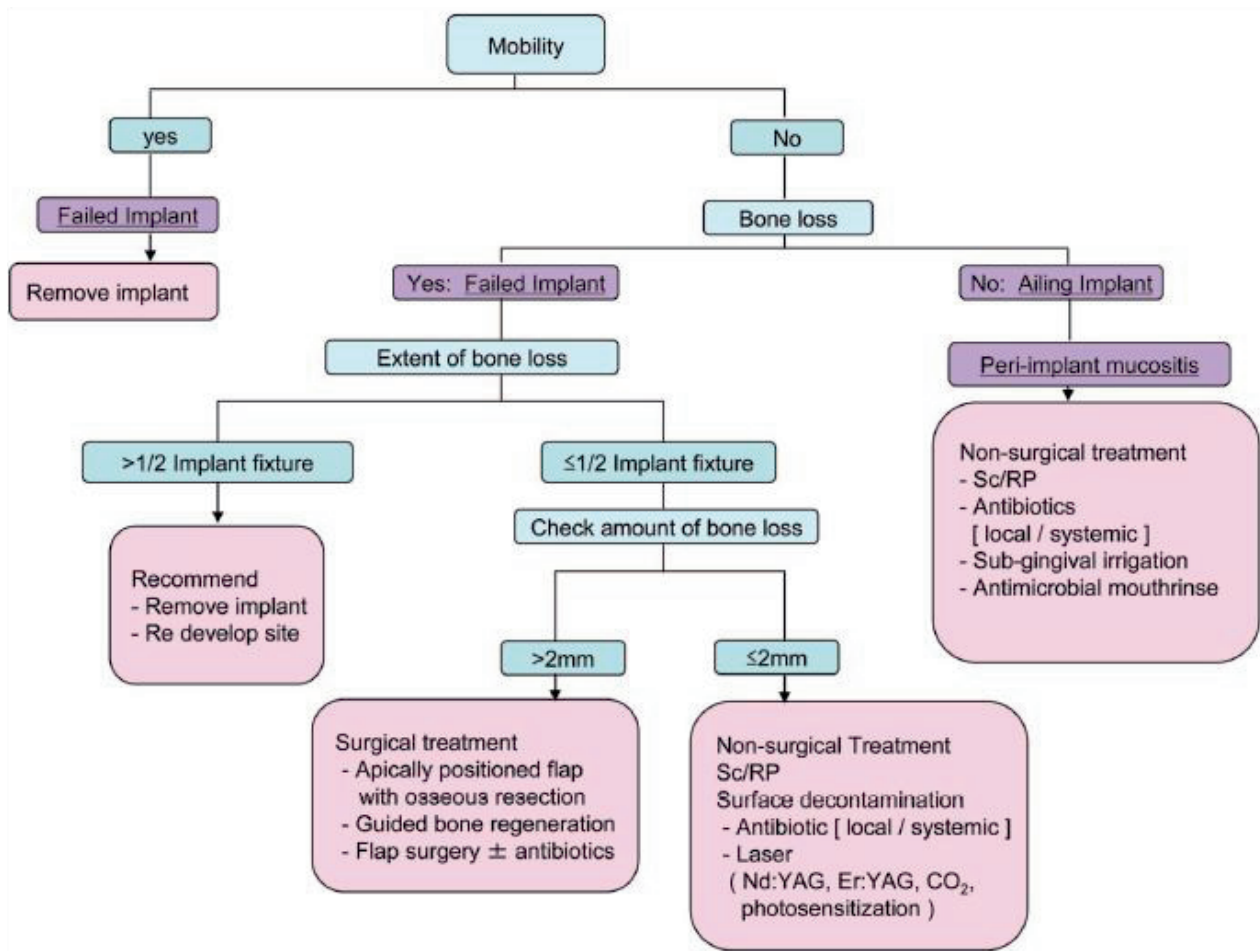


Figure 1 - Decision tree for the management of peri-implant diseases [Figure published in: Okayasu K, Wang LH. Decision tree for the management of peri-implant diseases. *Implant Dent.* 2012 Jun, 21 (3):253].

both three- and six-month periods.⁵⁰ Nevertheless, essential oils delay biofilm development in 45% to 56% of cases and reduce the existing biofilm in 39% to 48% of cases, whereas a reduction of up to 59% in gingivitis is also observed after their continuous use. Studies have shown that essential oils have an effect on microbial total mass and promote an overall decrease in both biofilm activity and biomass.^{49,51,52,53,54} Essential oils also have some interesting and desirable features, such as reducing bacterial endotoxins and pathogenicity.^{55,56} They also promote deep biofilm penetration, which destroys more pathogenic resistant forms (lysis),^{51,52} have great clinical efficacy and deliver action that alters microorganism cell surface integrity.⁵⁷ Other important features are their residual effect, derived

from antibacterial activity that continues even after rinsing,^{58,59,60} and their ability to maintain oral microbiota balance by not allowing the emergence of opportunistic species.⁶¹

According to good clinical practices and systematic reviews,^{62,63} only two active ingredients, 0.12% chlorhexidine digluconate⁶⁴ and essential oils,^{65,66} should be considered the most effective, since they have been thoroughly tested and proven as effective for decades, and are also the only ones carrying the ADA seal of approval.^{67,68} Moreover, 0.05% cetylpyridinium chloride and 0.03% triclosan active principles have been mentioned extensively in the literature, indicating their use in reducing plaque (24% to 28.2% and 24% to 29.1%) and gingivitis (24% to 29.1% and 16.9% to 23%, respectively);⁴⁹ however,

they have less significant results in comparison with chlorhexidine and essential oils.

Unwanted side effects on dental implant surfaces

Although not directly related to dental implants, mouthrinses with different active ingredients can lead to some unwanted effects. Long-term use of mouthrinses containing chlorhexidine has led to some undesirable effects, such as staining of dental restorations and soft tissues, changes in the sense of taste, an increase in supragingival dental calculus formation,^{69,70} mucosal erosions and some cases of parotid gland swelling,^{71,72,73} but it is important to mention that these effects disappear after cessation of use. Despite these local adverse effects, no systemic change has been observed in association with long-term chlorhexidine use.^{69,73} Unfortunately, this is not the case of triclosan, whether associated to Gantrez or not. In an *in vivo* investigation, Cherednichenko *et al.*⁷⁴ suggested that triclosan weakens cardiac and skeletal muscle contractility in a manner that may negatively impact muscle health, especially in susceptible populations.

In regard to cetylpyridinium chloride, a quaternary ammonium compound, the following side effects have been reported in association with its use:

- burning sensation of oral mucosa,⁷⁵
- tongue dorsum and dental staining similar to that of chlorhexidine,⁷⁵ and
- recurrent ulceration similar to aphthae.⁷⁶

Among other active ingredients associated with adverse effects, fluoride can corrode titanium dental implants and prosthetic components,⁷⁷ and mouthrinses containing antibiotics are not cost-effective and have several side effects, such as causing chang-

es in the sense of taste, tooth and soft tissue staining, irritation, peri-implant mucositis, and bacterial resistance or opportunistic infection.⁷⁸

Conclusions

It is known that gaps between a pillar and a dental implant are still inevitable. Gaps can facilitate bacterial microleakage, causing problems such as bad breath and peri-implantitis.⁷⁹ The prevalence of peri-implant diseases is growing; therefore, effective prevention methods seem to be as important for implant recommendation as the improvement of professional training. Some conclusions may have been presented, but more scientific evidence is required to elucidate the most effective method for treating peri-implant diseases. Further research should include an analysis of the real impact of different adjuvant therapies, with their benefits and risks, the additional costs involved, the time required and the increase in the number of individuals with dental implants.

Based on this review, it can be concluded that:

- There is strong clinical evidence that at least two mouthrinses have proven efficacy against different oral biofilms, namely, chlorhexidine digluconate and essential oils.
- 0.12% chlorhexidine digluconate presents a number of unwanted side effects and should be prescribed with caution.
- Chemical agents seem to be beneficial in controlling peri-implant inflammation, but require further investigation.
- We recommend an antiseptic with scientifically proven efficacy, with a significant short- and long-term effect, and with no unwanted side effects, for the prevention and/or treatment of peri-implant disease.

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