Evidence-based control of plaque and gingivitis


Abstract

Most adults brush and floss inadequately, and constant education and/or reinforcement is often required. Bacteria are usually left behind with mechanical oral health routines, and chemotherapeutic agents may have a key role as adjuncts to daily home-care. To date, two antiseptic mouthwashes have received the ADA Seal of Acceptance: Peridex® (Zila Pharmaceuticals, Phoenix, AZ, USA; CHX, chlorhexidine) and Listerine® (Pfizer Consumer Healthcare, Morris Plains, NJ, USA; essential oil (EO) mouthwash). CHX has a strong affinity for tooth and tissue surfaces, but can cause brown staining on the teeth and tongue. Patients must also wait until all traces of toothpaste are removed before rinsing with CHX. Long-term use of an EO mouthwash is microbiologically safe, with no changes observed in the bacterial composition of supragingival plaque, and no evidence of antimicrobial resistance. A number of trials have demonstrated the long-term plaque- and gingivitis-reducing properties of both CHX and EO mouthwashes. These studies clearly demonstrate that these agents have lasting efficacy, and can access hard-to-reach areas.

Keywords: oral health; plaque; gingivitis; chlorhexidine mouthwash; essential oil mouthwash

The limitations of home oral-care practices suggest that other strategies are urgently required. As noted by DePaola et al. (1989), mechanical methods of plaque removal require time, motivation and manual dexterity. This makes it difficult to effectively educate, train and encourage some patients to reduce plaque solely by mechanical means. Perhaps even a greater issue is that discussed in Section One (Ciancio 2003), i.e. that even when patients are adequately trained, without constant education and reinforcement, compliance appears to diminish significantly (Axelsson & Lindhe 1987).

Mechanical home-care methods have long been regarded as the best way for patients to remove plaque, yet bacteria are often left behind. This is partly because of inadequacies in brushing and flossing techniques. Even well-trained patients may miss hard-to-reach areas around posterior teeth or marginal gingivae. Additionally, elderly patients, those with physical or mental limitations, and those with malposed teeth, bridge-work or orthodontic appliances may find brushing and interdental cleaning especially difficult (Baker 1993, Ciancio 1988).

Flossing is widely regarded as tedious, time consuming and difficult, and motivation and compliance often wanes over time, although this may partially be compensated by the use of alternative interdental cleansing devices (e.g. toothpicks). For these reasons, chemotherapeutic agents may have a key role as adjuncts to mechanical methods for preventing and treating periodontal disease (Wolff 1985, Bouwmsa 1996). However, long-term field studies on patients’ compliance in the use of mouthwashes are also still lacking.

Ideal properties of mouthwashes should be (Baker 1993):

- quick and safe;
- able to kill plaque bacteria in hard-to-reach areas;
- palatable;
- low in cost;
- easy to use and able to reach the location of disease initiation (supragingival for gingivitis; subgingival for periodontitis).

Antiseptic mouthwashes have the potential to meet most of these criteria relative to gingivitis. To date, two antiseptic mouthwashes have received the American Dental Association Council on Scientific Affairs Seal of Acceptance based on clinical studies: Peridex® (Zila Pharmaceuticals, Phoenix, AZ, USA; chlorhexidine, CHX) and Listerine® (Pfizer Consumer Healthcare, Morris Plains, NJ, USA; essential oil, EO) (Council on Dental Therapeutics 1988a, 1988b). Although some generic EO mouthwashes have also obtained the ADA Seal of Acceptance, these are solely based on in vitro studies of each of their ingredients, and not on clinical studies of efficacy against plaque and gingivitis. Listerine® and Peridex® are therefore the two mouthwashes that are discussed in this article.
Peridex® is a 0.12% solution of CHX, a bisbiguanide antiseptic (Peridex 2001), while the active ingredients in Listerine® are four EOs: thymol 0.064%, eucalyptol 0.092%, methyl salicylate 0.060% and menthol 0.042% (Listerine 2002).

CHX has a strong affinity for tooth and tissue surfaces, and these serve as a reservoir even after rinsing or irrigation with the agent is completed (Turesky et al. 1977).

CHX mouthwash does, however, have several disadvantages. It can cause brown stains on the teeth and tongue (Ciancio 2000), and restorations. Such staining requires professional removal. CHX may also alter taste perceptions for up to 4 h after rinsing and, in some cases, its use has been associated with supragingival calculus build-up (Ciancio 2000). These unwanted effects arising from regular use are not commonly seen with EO mouthwashes, although there have been some complaints about their taste (DePaola et al. 1989, Charles et al. 2001, Lamster et al. 1983, Overholser 1988, Overholser et al. 1990).

In general, mouthwashes should be recommended after the patient has brushed and cleaned interdentally. However, with CHX, as many dentifrice ingredients can reduce its antibacterial efficacy, the manufacturer recommends that the patient should be instructed to completely rinse all traces of toothpaste from the mouth or wait 0.5 h between the tooth cleaning and rinsing (Peridex 2001). Patients using the EO mouthwash do not need to take these precautions.

In microbiological terms, long-term use of EO mouthwashes has been shown to be safe. After 6 months of daily, continued use, EO mouthwashes cause no change in the bacterial composition of supragingival plaque (although they do produce a decrease in total microbial flora). Specifically, there is no evidence of increased putative and/or opportunistic oral pathogens (Minah et al. 1989, Walker et al. 1989). Similar observations were made for CHX mouthwash (Emilson & Fornell 1976, Schiott et al. 1976, Briner et al. 1986).

Furthermore, the oral microflora show no change in antiseptic susceptibility over time, suggesting that EO and CHX mouthwashes do not promote the emergence of antimicrobial resistance (Minah et al. 1989).

As data on the single therapeutic efficacy of mouthwashes on periodontitis are scarce, they have not been reviewed in this supplement. Given that the parameters are more common, the supplement has instead concentrated on placebo-controlled EO or CHX efficacy studies, which investigate the effects of EO and CHX on plaque control and gingivitis over a period of at least 6 months. These studies are summarized in Table 1.

CHX has been studied in a number of controlled trials for periods of 6 months or longer. In these studies, plaque reduction has ranged from 16 to 45% and gingivitis reduction has ranged from 27 to 80%. It is noteworthy that the duration of one study was as long as 24 months and bacterial resistance to CHX was not detected.

The demonstration of safety and efficacy of 0.12% CHX (Peridex®) provided the evidence for the product to be awarded the ADA Seal of Acceptance as a chemotherapeutic product for the control of gingivitis. For ADA acceptance at 6 months, one study showed a mean plaque score and gingivitis score among the 380 patients completing the study to be significantly lower in the CHX group than in the placebo group. A 61% reduction in plaque was noted, while a 39% reduction in gingivitis was demonstrated when compared with the vehicle control ($P < 0.05$) (Grossman et al. 1989). Slightly smaller but still significant results ($P < 0.05$) were seen in another Grossman study (Grossman et al. 1986).

Also, a 1-year study in 10 patients who had been treated non-surgically for periodontal disease showed that CHX can be used as an adjunct to inadequate mechanical oral hygiene over a period of 1 year. Although minor changes in plaque scores were noted, bleeding was significantly reduced by up to 80%. In this study the subjects were instructed to use CHX (0.2%) twice daily as a rinse but were not given any other formal oral hygiene instructions (Christie et al. 1998).

Similarly designed studies for Listerine showed plaque reductions ranging from 22 to 36% and gingivitis reductions ranging from 23 to 36%, with the longest study being 9 months.

Three double-blind, parallel-group, placebo-controlled clinical studies conforming to ADA Acceptance Program Guidelines were the supporting studies for acceptance as a chemotherapeutic product for the control of gingivitis. A total of 337 healthy adults patients aged 18–60 years were evaluated. All subjects had plaque and mild-to-moderate gingivitis on study entry (DePaola et al. 1989, Lamster et al. 1983, Gordon et al. 1985). The placebo used in all cases was a hydro-alcohol solution, which mimicked the colour, taste and aroma of Listerine®. Also, before being examined, the patients used the products at home and not at the study centre. Both these factors helped maintain the double-blind design of these studies.

Two of the studies also incorporated a negative control arm, using

### Table 1. Summary of placebo-controlled efficacy studies, which investigate the effects of EO mouthwash (Listerine) or CHX on plaque control and gingivitis over a period of at least 6 months

<table>
<thead>
<tr>
<th>Trial author</th>
<th>Trial length (months)</th>
<th>No. of patients</th>
<th>Agent used</th>
<th>Plaque reduction (%)</th>
<th>Gingivitis reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grossman et al. (1989)</td>
<td>6</td>
<td>481</td>
<td>CHX 0.12%</td>
<td>49</td>
<td>31</td>
</tr>
<tr>
<td>Grossman et al. (1986)</td>
<td>6</td>
<td>380</td>
<td>CHX 0.12%</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>Loe et al. (1976)</td>
<td>24</td>
<td>120</td>
<td>CHX 0.2%</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td>Lang et al. (1982)</td>
<td>6</td>
<td>158</td>
<td>CHX 0.1%</td>
<td>16</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CHX 0.2%</td>
<td>19</td>
<td>80</td>
</tr>
<tr>
<td>Gordon et al. (1985)</td>
<td>6</td>
<td>85</td>
<td>Listerine (EO)</td>
<td>19.5</td>
<td>23.9</td>
</tr>
<tr>
<td>Lamster et al. (1983)</td>
<td>6</td>
<td>145</td>
<td>Listerine</td>
<td>22.2</td>
<td>28.2</td>
</tr>
<tr>
<td>Overholser et al. (1990)</td>
<td>6</td>
<td>124</td>
<td>Listerine</td>
<td>36.1</td>
<td>35.9</td>
</tr>
<tr>
<td>Charles et al. (2001)</td>
<td>6</td>
<td>316</td>
<td>Listerine</td>
<td>56.1</td>
<td>22.9</td>
</tr>
<tr>
<td>DePaola et al. (1989)</td>
<td>6</td>
<td>107</td>
<td>Listerine</td>
<td>34</td>
<td>34</td>
</tr>
</tbody>
</table>

CHX = chlorhexidine; EO = essential oil.
sterile, coloured water (Lamster et al. 1983, Gordon et al. 1985). In two studies, the subjects received a complete dental prophylaxis at baseline to measure EO mouthwash efficacy in inhibiting redevelopment of plaque and gingivitis (DePaola et al. 1989, Lamster et al. 1983). In the third study, no baseline prophylaxis was administered to compare EO mouthwash ability in reducing existing plaque and gingivitis from baseline (Gordon et al. 1985).

In all studies, the subjects rinsed twice daily as an adjunct to their usual oral hygiene routine and were monitored for 6–9 months (DePaola et al. 1989, Lamster et al. 1983, Gordon et al. 1985).

During the 6–9-month follow-up period, the EO mouthwash solution was found to be significantly superior to the hydroalcohol placebo rinse. Compared with placebo, plaque redevelopment was reduced by an additional 19–34% (P < 0.01 and P < 0.001, respectively) (DePaola et al. 1989, Gordon et al. 1985).

Similarly, the EO mouthwash-driven reduction in the redevelopment of gingivitis was between 22% and 34% higher than placebo (P < 0.05 and P < 0.02, respectively) (DePaola et al. 1989, Gordon et al. 1985).

At 6 and 9 months, the EO mouthwash solution was also significantly better than the sterile-water control, significantly increasing inhibition of plaque redevelopment (P < 0.01), and significantly increasing inhibition of gingivitis compared with control (P < 0.05) (DePaola et al. 1989, Gordon et al. 1985). In this study Listerine demonstrated similar reductions for both plaque (20.8%, 22.2%) and gingivitis (27.7%, 28.2%) compared with a hydroalcohol vehicle (26.9% ethanol) and a separate water control treatment group, respectively. In other words, both controls exhibited the same effect. The results of this long-term study clearly indicate that alcohol provides no incremental effect over and above the essential oils. The lack of an effect of alcohol in the formulations was also demonstrated in the 6-month study by Lamster et al. 1983). Therefore, ethanol (denatured alcohol) serves as a vehicle in essential oil mouthrinses to solubilize the active ingredients but provides no individual contribution to plaque and gingivitis reduction.

Other controlled studies have shown similar results on plaque and gingivitis reduction. In a 6-month randomized, double-blind study of 124 healthy adults with pre-existing plaque and gingivitis, an EO and CHX mouthwash were compared. After a dental prophylaxis, the subjects were randomized into three groups: EO mouthwash (Listerine®), CHX mouthwash (Peridex®), or a placebo rinse (hydroalcohol solution). Subjects used their assigned rinse twice daily as an adjunct to their usual oral care practices, including a fluoridated toothpaste (Overholser et al. 1990).

After 6 months, both the EO and CHX mouthwashes inhibited supragingival plaque and gingivitis significantly better than the placebo rinse. Compared with the preprophylaxis baseline, the EO mouthwash inhibited the accumulation of plaque by 36.1% vs. placebo (P < 0.001), while CHX inhibited the accumulation of plaque by 50.3% vs. placebo (P < 0.001). Similarly, the EO mouthwash inhibited the development of gingivitis by 35.9% vs. placebo (P < 0.001), while CHX inhibited it by 30.5% vs. placebo (P < 0.001) (Overholser et al. 1990).

The authors concluded that although the CHX mouthwash was better than the EO mouthwash in terms of its effects on plaque, the two rinses had equal efficacy in terms of their effects on gingivitis. Further, the subjects who rinsed with the EO mouthwash showed no signs of tooth staining or supragingival calculus formation, whereas the subjects rinsing with the CHX mouthwash had a significant increase in tooth surface.

The study concluded that both mouthwashes were effective agents in a regimen for the control of plaque and gingivitis (Overholser et al. 1990).

Mouthwashes have the advantage that their antimicrobial activity can access hard-to-reach areas. Confirming this, a randomized, observer-blind, crossover study was conducted to assess the in vivo antimicrobial activity of an EO mouthwash on interproximal plaque bacteria (Charles et al. 2000). Recoverable bacterial counts from proximal tooth surfaces were 43.8% lower with the mouthwash compared with control (P < 0.001), demonstrating that EO mouthwashes penetrate and exert antimicrobial activity interproximally (Charles et al. 2000). These clinical studies also clearly demonstrate that EO mouthwashes have excellent safety and tolerability profiles. They showed no evidence of extrinsic tooth stain compared with controls, and intraoral soft-tissue examinations showed no aberrations of any kind (DePaola et al. 1989, Charles et al. 2001, Lamster et al. 1983, Overholser et al. 1990, Gordon et al. 1985). In addition, the users reported no changes in taste perception and showed no increase in calculus formation (Charles et al. 2001, Overholser et al. 1990).

Additionally strict postmarketing surveillance performed for the EO mouthwash, as it is for all products subject to US FDA and other regulatory agency monitoring, strongly supports the safety of the product. It should also be noted that an EO mouthwash has been widely available world-wide for more than 100 years with minimal reports of adverse effects.

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References


Address:
Antonio Santos
Department of Periodontology
Universitat de Catalunya
c/ Gomera s/n Sant Cugat del Vallès 08017
Barcelona, Spain