Penny Hodge

Mouthwashes: Do They Work and Should We Use Them? Part 1: Antiplaque Efficacy of Mouthwashes

Abstract: This article will focus on the antiplaque efficacy of mouthwashes. An antiplaque agent inhibits the formation of plaque and also reduces gingivitis. There is good evidence that chlorhexidine digluconate, used in the correct concentrations, is the gold standard agent against which all others should be measured. It does, however, have some unwanted side-effects. One of the major problems for antiplaque mouthwashes is that they have a much reduced effect on established plaque within the oral environment. Although they can flow into the biofilm channels and kill bacteria in the superficial layers of dental plaque, they cannot penetrate the biomass and inhibit the pathogenic bacteria adjacent to the tooth surface and gingival margin. There is no evidence that they prevent the progression of periodontitis.

CPD/Clinical Relevance: The evidence supporting the use of 'over the counter' antiplaque mouthwashes is evaluated. This provides guidance for dentists and dental care professionals of when it is appropriate to recommend mouthwash use to their patients.

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There are various reasons why a patient may wish to use a mouthwash. These include:

- Having fresh breath;
- Finding flossing difficult;
- To kill bacteria;
- Because of bleeding gums; or
- To prevent decay.

A member of the dental profession might consider recommending the use of a mouthwash as an antiplaque agent, to deliver topical fluoride, to combat oral malodour or for a patient with a dry mouth. For members of the public the array of mouthwashes available and the claims made by manufacturers can be confusing. A newspaper article raised the question '*Mouthwash or hogwash: experts argue that not only is a mouthwash useless, it can also be harmful to your health*' (Times newspaper 15 September 2008). The aim of this series of papers is to review the available evidence for the efficacy of 'over the counter' mouthwashes and to give guidance for dentists and dental care professionals of when it is appropriate to recommend mouthwash use to their patients.

Evidence regarding mouthwashes may be divided into:

- Antiplaque efficacy;
- Caries prevention;
- Antihalitosis efficacy;
- Dry mouth relief;
- Safety.

This narrative review will be split into three parts. The first part will focus on antiplaque efficacy of mouthwashes. The second part will address caries prevention, antihalitosis efficacy and dry mouth relief. The third part will cover safety of mouthwashes.

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Antiplaque efficacy

Background

Experimental gingivitis studies conducted in the 1960s showed that the accumulation of dental plaque leads to the development of chronic gingivitis[1,2] (Figure 1). The consensus is that, without treatment, chronic gingivitis will, ultimately, proceed to chronic periodontitis in a majority of the population[3] (Figure 2). The severity of periodontitis is determined by other factors including those listed in Table 1.[4] It is estimated that between 5 and 15% of the population worldwide are affected by severe periodontitis.[5-7] It has been shown that improvement in plaque control can

Figure 1. Plaque infected dentition with signs of chronic gingivitis.

Figure 2. Signs of chronic gingivitis and chronic periodontitis.

reduce the prevalence of gingivitis (Figure 3) and periodontitis[6] and that thorough supragingival scaling and root surface debridement, together with good oral hygiene, may arrest periodontitis[8] (Figure 4).

Rationale for the use of mouthwashes

Although supragingival dental plaque can be effectively removed using either manual or electric toothbrushes and interdental cleaning aids, the most recent data available from the Adult Dental Health Survey showed that the oral hygiene of the UK population was poor.[9] Of dentate adults, 66% and, on average, 23% of all teeth, had visible plaque present and 68% of adults had calculus deposits visible in at least one sextant. Of those subjects, 64% who said that they cleaned twice a day, and 61% of those who attended regularly for a check-up had visible plaque present.[9] When subjects who cleaned their teeth were asked if they used additional methods to supplement oral hygiene, 31% indicated that they used a mouthwash. Mouthwash use decreased with advancing age and there was no difference between the sexes or between different socio-economic groups. The percentage of subjects using a mouthwash had increased over the years (1988: 10%; 1998: 23%; 2009: 31%). Interestingly the percentage flossing had decreased since 1998 (1988: 21%; 1998: 28%; 2009: 22%).[9] This may reflect the public's perception, encouraged by the manufacturers, that mouthwash use can replace the need to floss or the use of interdental brushes. The most recent survey excluded data from Scotland.

Factors affecting the severity of periodontitis

- Cigarette smoking
- Diabetes mellitus
- Genes
- Socioeconomic status
- Osteoporosis
- Stress
- Alcohol
- Diet
- Obesity
- Exercise

Table 1. Factors affecting the severity of periodontitis.

Antiseptics present in mouthwashes are effective *in vitro* against the bacteria found within dental plaque, when they are in a planktonic form, and can show both *bacteriostatic* and *bacteriocidal* activity. Mouthwashes have a number of advantages:

- They are available without prescription;
- They have a good safety record;
- No significant bacterial resistance has been reported; and
- They require little skill and motivation on behalf of the patient.

Antiplaque agents

An antiplaque agent reduces the amount of dental plaque to such an extent that it inhibits the development of gingivitis. Most of the research into the clinical efficacy of antiplaque agents has focused on their effect on levels of plaque and gingival inflammation. One of the most important characteristics of an antiplaque agent is its persistence of action or *substantivity*. This depends on its ability to adsorb to oral surfaces and remain active for a prolonged period. Available antiplaque agents are listed in Table 2.

Chlorhexidine digluconate

The use of chlorhexidine digluconate-containing mouthwashes in preventing plaque formation is supported by a huge body of scientific evidence over decades.[10,11] Chlorhexidine is active against Gram +ve and Gram –ve bacteria, fungi, yeast and viruses. It has 12 hours substantivity and shows both bacteriostatic and bacteriocidal activity, depending on concentration. It has been demonstrated in experimental gingivitis studies that rinsing with chlorhexidine mouthwash for one minute twice daily can completely inhibit plaque formation and gingivitis[10] (Table 3). Prescribed in the following formulations and doses it is the gold standard antiplaque agent against which all others are compared:[12]

- 10 ml of 0.2% equivalent to 20 mg twice per day;
- 15 ml of 0.12% equivalent to 18 mg twice per day.

Evidence supporting the clinical antiplaque effectiveness of lower concentrations is weak.[13] However, it has been shown that an alcohol-free 0.12% chlorhexidine-containing mouthwash was as effective as the same mouthwash also containing 11% alcohol, compared with a placebo.[14]

Side-effects

Chlorhexidine is considered to be safe because of its dicationic nature which inhibits absorption through the skin, mucous membranes and the gut. Therefore, no systemic toxicity has been reported. There are no publications recording bacterial resistance or superinfection following its use. However, there are some side-effects which contra-indicate prolonged use (Table 4).

Staining occurs as a result of dietary chromogens binding to chlorhexidine which is bound to the oral surfaces (Figure 5). Staining occurs with all correctly formulated products.[11] Long-term use of chlorhexidine has been reported to result in more calculus formation than a placebo mouthrinse.[15,16] It has been suggested that this could arise because chlorhexidine increases pellicle thickness by precipitating salivary proteins. It may also precipitate phosphate and then calcium onto the pellicle.[17] If a burning sensation or mucosal erosion arises, the patient can be advised to double dilute to reduce the

a

b

Figure 3. Chronic gingivitis **(a)** before and **(b)** after non-surgical treatment. (Reproduced by kind permission of Dr Bill Jenkins.)

a

b

Figure 4. Generalized chronic gingivitis and aggressive periodontitis **(a)** before and **(b)** after non-surgical treatment (with acknowledgment to Dr Frank van Schaik and Mr Dimitri van Hezik, dental technician, for the new crowns). In Figure 4b gingival recession around LR4, LR2 and LL1 has been caused by overbrushing.

concentration of chlorhexidine, ensuring that the dose remains the same.[18]

In rare cases, parotid swelling has been observed. If this occurs the patient should be advised to discontinue use of the mouthwash. One report has indicated that this problem is not specific to chlorhexidine mouthwash and may be caused by the method of rinsing, but this needs to be confirmed in larger studies.[19] It has also been reported that, in rare cases, chlorhexidine may give rise to significant immediate hypersensitivity which very rarely may lead to a severe anaphylactic reaction.[20]

Sodium lauryl sulphate, an anionic detergent found in most toothpastes, inhibits the action of chlorhexidine by binding to the molecule.[21] For this reason, patients should be advised to leave an interval of an hour between using the mouthwash and toothbrushing.

The clinical applications and misuse of chlorhexidine mouthwash are listed in Table 5.

Antiplaque agents
- Bis-biguanides, eg chlorhexidine digluconate
- Essential oils
- Quaternary ammonium compounds, eg cetyl pyridium chloride
- Amine alcohols, eg delmopinol hydrochloride

Table 2. Antiplaque agents.

Characteristics of chlorhexidine
- Substantivity of 12 hours
- Active against Gm +ve and Gm –ve bacteria, fungi, yeast and viruses
- Bacteriostatic and bacteriocidal
- Shown to completely inhibit plaque formation and gingivitis when used in the correct formulation

Table 3. Characteristics of chlorhexidine.

Essential oils

Listerine® (Johnson and Johnson) is a widely used hydro-alcohol based mouthwash containing essential oils in the following concentrations: thymol (0.064%); eucalyptol (0.092%); menthol (0.042%); and methyl salicylate (0.060%). In most of the products, alcohol is used to solubilize the essential oils and alcohol content varies between 21% and 27%, depending on the formulation. In 2009, the manufacturers launched an alcohol-free version of Listerine® which contains propylene glycol as the solubilizing agent. The antiplaque effect of Listerine® is not as great as chlorhexidine.[22] Gunsolley conducted a systematic review and meta-analysis of studies of a minimum of six months' duration.[23] He found that in studies comparing the two agents, chlorhexidine mouthwash was significantly more effective at reducing plaque than Listerine®. When the placebo effect was removed, chlorhexidine reduced plaque by 40% and essential oils by 27%. Although chlorhexidine mouthwash was also more effective at reducing gingivitis (28% compared with 18% for essential oils), the difference between the two agents was not significant. These findings were confirmed in another systematic review and a series of meta-analyses, which investigated differences in plaque index, gingival index and gingival bleeding between the two mouthwashes used daily for less than four weeks and more than or equal to four weeks.[24] The authors also investigated differences in calculus index and staining index and found chlorhexidine showed higher scores than the essential oil mouthwash for both these indices. However, a meta-analysis of studies including calculus indices could not be performed because none of the studies met the required criteria.[24] A clinical trial investigated the antiplaque effect of alcohol-free compared with alcohol-containing essential oil mouthwash. The authors found that the alcohol-free mouthwash was less effective at reducing plaque formation over a three-day period than the alcohol containing one.[25]

It has been claimed that an essential oil mouthwash could be used as an alternative to flossing because it shows at least equivalent benefit to flossing in plaque reduction and bleeding on probing in six-month clinical trials.[26,27] Both these studies were funded by the manufacturer which may introduce bias. The purpose of both flossing and toothbrushing is to disrupt early plaque formation when the biofilm is thin. If an antiplaque-containing mouthwash can substitute for brushing in preventing plaque formation, we would expect it also to be able to substitute for flossing. However, penetration of the mouthwash into interdental niches may be inhibited by the presence of impacted food.[28] It is therefore

Side-effects of chlorhexidine
- Extrinsic staining of oral surfaces
- Taste disturbance
- Burning sensation
- Mucosal erosion
- Parotid swelling
- Immediate hypersensitivity reaction

Table 4. Side-effects of chlorhexidine.

Figure 5. Staining due to long-term use of chlorhexidine.

Clinical applications of chlorhexidine
- Short term use for specific problems
- Post oral or periodontal surgery
- For use by physically or mentally disabled patients; although use of a chlorhexidine spray may be more effective because of an inability to rinse effectively

Misuse
- Use in patients with plaque-infected dentitions (Zanatta *et al* 2007[34])
- Using once per day when pharmacological considerations require twice daily use
- Using two or three times a week

Table 5. Clinical applications and misuse of chlorhexidine.

difficult to understand how an antiplaque mouthwash used for 30 to 60 seconds could reduce plaque burden interdentally to the same extent as mechanical removal of plaque by flossing.

Side-effects

Initial use often induces a burning sensation and it has a bitter taste. It does not cause staining and does not appear to induce resistant strains of pathogenic bacteria in longer-term studies.[29]

Cetyl pyridinium chloride

Cetyl pyridinium chloride is a quaternary ammonium compound commonly found in many branded mouthwashes. It is monocationic in nature and shows similar antimicrobial activity to chlorhexidine *in vitro*. However, despite initially appearing to be adsorbed to oral surfaces better than chlorhexidine, cetyl pyridinium chloride has much reduced substantivity.[30]

Two systematic reviews have been conducted investigating the efficacy of mouthwashes containing cetyl pyridinium chloride.[23,31] The first restricted studies to a minimum of six months' duration. Four studies showed a statistically significant plaque-inhibitory effect and three did not. Overall, little evidence of an antiplaque or antigingivitis effect was demonstrated. The test for heterogeneity between the studies was positive. In particular, different concentrations of cetyl pyridinium chloride were used in different studies ranging from 0.01–0.1%.[23] The second systematic review restricted studies to a minimum of four weeks' duration. Eight studies were included. The authors concluded that mouthwashes containing cetyl pyridinium chloride, used as adjuncts to either supervised or unsupervised oral hygiene, had a small but significant effect in reducing plaque and gingivitis compared with toothbrushing alone or in combination with a placebo rinse.[31] It is difficult to understand how they reached this conclusion based on the data presented in the paper and the discussion. They discuss the heterogeneity between studies in both the concentration of the cetyl pyridinium chloride products evaluated and in the results obtained. In addition, six of the studies included in the review had authors from industry or were industry-funded, leading to conflicts of interest which may have caused bias.[31]

Side-effects

Cetyl pyridinium chloride has shown no long-term disruption to the normal oral flora. It does produce staining because of its cationic nature but not to the same degree as chlorhexidine. It is also inactivated by sodium lauryl sulphate in the same way as chlorhexidine.

Delmopinol hydrochloride

Delmopinol hydrochloride (0.2%) mouthwash is a third generation antiplaque agent which has been available on the continent for some years. It has almost no bacteriostatic or bacteriocidal activity *in vitro* or *in vivo*. Delmopinol's mechanism of action is to interfere with plaque matrix formation and prevent attachment and adherence of bacteria to the acquired pellicle.

During the 1990s, the manufacturers of this product commissioned eight clinical trials of the adjunctive effect of 0.2% delmopinol mouthwash on usual oral hygiene. Meta-analyses of these trials were conducted in 2007.[32] Seven independent research groups conducted the studies but only three of the studies have been published in the scientific literature. The authors of the meta-analyses of the supervised and unsupervised studies concluded that the mouthwash had an adjunctive effect in reducing plaque and gingivitis. The differences in reduction in plaque, bleeding and gingival inflammation between the delmopinol and the placebo mouthwashes were highly statistically significant. The reduction in plaque index overall was around 35% compared with the placebo. However, the reduction in bleeding, and in the gingival index were very small across all of the studies and of doubtful clinical significance. Two of the published studies compared 0.2% delmopinol with 0.2% chlorhexidine, as well as the placebo rinse. The authors found that delmopinol reduced the plaque index and percentage bleeding on probing by around half as much as chlorhexidine.[16,33]

Side-effects

One of the most commonly reported adverse events when using delmopinol is transient anaesthesia of the tongue which showed similar incidence to chlorhexidine.[32] Taste disturbance was also an unwanted side-effect and was

reported at similar levels to chlorhexidine use.[16] Tooth and tongue staining have been reported but were at least 50% less than with chlorhexidine.[16]

Other relevant issues

One of the major problems for antiplaque mouthwashes is that they have a much reduced effect on established plaque.[34] An *in vitro* study has investigated the antimicrobial effects of mouthwashes on saliva-derived plaque biofilms in both static and flow through systems.[35] In the static system, it was shown that Listerine® was more effective than chlorhexidine and cetyl pyridium chloride at killing bacteria within 16–18 hour biofilms.[35] For 65 hour biofilms twice daily, 30-second treatments resulted in antibacterial effects of 21.3% (±3.1%) for Listerine® and 23.1 (±5.5%) for chlorhexidine, which were significantly different from the control ($p<0.001$ for both agents). In the flow through system, Listerine® and chlorhexidine showed equivalent effects, which were significantly greater than cetyl pyridium chloride and chlorhexidine combined, and water.[35] In a series of elegant studies, Robinson used the 'Leeds *in situ* device' for undisturbed plaque biofilm collection, which may better represent plaque located in inaccessible interdental areas.[36] They showed that antiplaque agents can only penetrate around a third to half of the way from the surface into the plaque biofilm after 30 seconds' and two minutes' immersion. The agents flowed into the biofilm channels and were able to kill bacteria in the superficial layers of dental plaque, but only fluoride was able to penetrate deep into the biomass after 30 minutes' exposure. Because of this inability to penetrate deep into the plaque biomass, mouthwashes may have little effect on the pathogenic bacteria adjacent to the tooth surface and gingival margin, which may explain the following:

- There is sparse evidence that using mouthwashes on a regular basis instead of subgingival debridement has any effect on preventing the progression of periodontitis;
- There is no evidence that sporadic use of antiplaque mouthwashes has any clinical benefit to patients.[37]

Conclusions

The systematic reviews and meta-analyses which have been conducted into mouthwash efficacy have highlighted the heterogeneity between studies, which makes conclusions regarding the comparison of different agents less reliable.[23,24] Standardization of methodology in clinical trials would increase the number of studies eligible to be included in meta-analyses and provide better estimates of the effect of chlorhexidine compared with other agents.[38] Good plaque control is essential for periodontal health. Although mouthwashes have been shown to have varying degrees of antiplaque efficacy, because of the possible side-effects, it is sensible to restrict their use for the treatment of specific problems on a short-term basis. The best method of personal plaque control remains mechanical removal using toothbrushes and other aids for interdental cleaning, including floss and interproximal brushes.[38]

An enhanced oral hygiene behaviour change strategy (Oral Hygiene TIPPS) was described in the recent guidance document on *The Prevention and Treatment of Periodontal Diseases in Primary Care* published by The Scottish Dental Clinical Effectiveness Programme (SDCEP). The guidance document can be downloaded free of charge from the SDCEP website (**www.sdcep.org.uk**).

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