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Plaque inhibition of two commercially available chlorhexidine mouthrinses

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Abstract

Background: Chlorhexidine (CHX) 0.2% solution is still ''the leading oral antiseptic'' for controlling gingivitis. Side effects, however, limit the acceptability to users and the long-term employment of a 0.2% CHX antiseptic in preventive dentistry. This stimulated the development of new formulations. The aim of the present study was to assess the effect on plaque inhibition and taste perception of two commercially available mouthrinses (0.12% CHX non-alcohol base with 0.05% cetyl pyridinium chloride (Cpc) *versus* 0.2% CHX alcohol base).

Methods: The study was designed as a single-blind, randomized two group parallel experiment, to compare two different commercially available mouthrinses, during a 3-day plaque accumulation model. Forty healthy volunteers were enrolled in the study and received a thorough dental prophylaxis at the beginning of the test period. Over a 72-h experimental non-brushing period, during which subjects abstained from all forms of mechanical oral hygiene, one group (test) used a 15 ml alcohol free 0.12% CHX (= 18 mg) mouthrinse on a Cpc base (Perioaid®, CHX ⊕ Cpc), twice daily for 30 s. The other group (control) used a 10 ml 0.2% CHX (= 20 mg) mouthrinse on an 11.8% ethanol alcohol base (Corsodyl®, CHX ⊕ Alc), twice daily for 60 s. After 72 h of plaque formation, the amount of plaque was evaluated. By the use of visual analogue scale, the subjects were asked for their appreciation of the taste of the mouthrinse they had used.

Results: The mean plaque index for the CHX ⊕ Cpc group was 0.97 and for the CHX ⊕ Alc group 0.78. After 72 h of non-brushing, there was no significant difference in plaque accumulation between the two groups. The answers to the questions (taste perception and after-taste) showed a statistically significant difference between the two groups. The mean visual analogue scale (VAS) scores for taste appreciation on a scale from very bad to very good taste (0–10) were 5.92 for the CHX ⊕ Cpc group and 4.10 for the CHX ⊕ Alc group ($p = 0.02$). The mean visual analogue scale (VAS) scores for the after-taste on a scale from very short to very long (0–10) were 7.24 for the CHX ⊕ Cpc group and 5.38 for the CHX ⊕ Alc group.

Conclusions: Within the limitations of the present study design, it can be concluded that rinsing with a 0.12% CHX mouthrinse on a non-alcohol base with 0.05% Cpc (Perio-Aid®) is not significantly different from rinsing with a 0.2% CHX mouthrinse on an alcohol base (Corsodyl®). It appears that the subjects appreciated the taste of the non-alcohol CHX solution better but the after-taste of the rinse remained longer in the mouth.

Key words: chlorhexidine; plaque

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A long-term plaque-free dentition seems to be an unrealistic goal. To overcome deficiencies in mechanical tooth cleaning as practiced by many individuals (Bouwsma 1996) and some minority groups (Shaw et al. 1984, Ferritti et al. 1987, Francis et al. 1987), the use of an effective antiseptic agent, could have clear benefits.

Chlorhexidine (CHX), a bisguanide, appears to be the most effective chemical agent in plaque control. CHX is free from systemic toxicity in oral use.

Microbial resistance and supra-infection do not occur. CHX as a 0.2% concentration has been readily available as ''the leading oral antiseptic'' for the last 2 decades. Rinsing for 60 s twice daily with 10 ml of a 0.2% (= 20 mg dose) CHX-digluconate solution in the absence of normal tooth cleaning, inhibits plaque re-growth and helps to prevent inflammation of the gums and tooth decay (Löe & Schiøtt 1970).

Nonetheless, most practitioners do not recommend long-term daily use of CHX as a mouthrinse, mainly because of the cosmetic problem of tooth staining and the perturbation of the taste. These two side effects limit the acceptability to users and the long-term employment of a 0.2% CHX antiseptic in preventive dentistry. Although long-term field studies on compliance in the use of mouthrinses are still lacking, those unpleasant factors may have the consequence that patients do not follow the rinsing instructions conscientiously. Manufacturers have tried to modify the taste of their mouthrinses, but the bitter taste of CHX is evidently difficult to mask. Plaque inhibition by CHX is dose-dependent, and similar plaque inhibitions can be achieved with larger volumes of lower concentration solutions (Bonesvoll & Germo 1978). In order to improve the taste, some brands have lowered the concentration of CHX in mouthrinses. Also the alcohol, which serves as a delivering vehicle, has been removed. The use of alcohol as a base for mouthrinses was already a common practice in Roman times. Nowadays, ''in vitro'' data (Poggi et al. 2003) suggest that deleterious effects of the alcohol may occur ''in vivo''. These authors have therefore proposed that clinicians should be alerted to the potentially adverse effect of alcohol containing mouthrinses to promote oral health. In this perspective it would be of common interest to omit alcohol in routinely used commercial mouthrinses.

These concerns led to the search for new formulations. CHX mouthrinse products with a concentration of 0.1% and 0.12% are already available. Recently, a new 0.12% CHX formulation (Perio-Aid®) has been marketed in Europe using an alcohol free base with 0.05% Cpc. To date little is known about the efficacy of CHX when used in an alcohol free base. Rinsing with this new formulation might cause fewer side effects, but on the other hand may be less efficient.

The aim of the present study was therefore to assess the effect on plaque inhibition of two commercially available CHX mouthrinses (0.12% CHX Perio-aid® non-alcohol Cpc base *versus* 0.2% CHX Corsodyl® alcohol base). In addition, the study evaluated the individual taste perception.

Material and Methods

Subjects

Forty healthy participants of both genders were recruited from dental students of the University. They were selected on good general health without a medical history or medication that might interfere with the conduct of the study. Other selection criteria were a dentition with at least 24 teeth (minimum of five teeth per quadrant), pockets <5 mm and no orthodontic or removable dental appliances.

They were not allowed to participate if they reported to be allergic to CHX and/or if they had used antibiotics in the previous 3 months. All eligible subjects were given oral and written information about the products and the purpose of the study. After screening for suitability, they were all requested to give their written informed consent.

Procedure

This study was designed as a single-blind, randomized, two group parallel experiment.

Over a 72-h experimental non-brushing period, during which subjects abstained from all forms of mechanical oral hygiene, one group (test) used an alcohol free 0.12% CHX mouthrinse on a 0.05% Cpc base (Perioaid®, CHX $\oplus$ Cpc), twice daily for 30 s. The other group (positive control) used a 0.2% CHX mouthrinse in an 11.8% ethanol alcohol base (Corsodyl®, CHX $\oplus$ Alc), twice daily for 60 s.

At baseline, all participants were stained for plaque and received a thorough supragingival dental prophylaxis to remove all stain, calculus and plaque. This was performed using hand instruments and rotating brushes with polishing paste. Any remaining plaque was stained for a second time using erythrosine disclosing solution and cotton swabs to make sure all visible plaque was removed.

Subjects were randomly assigned to the test or the control group. The subjects in the test group received a bottle of mouthrinse containing 300 ml 0.12% CHX (Perioaid®, CHX $\oplus$ Cpc). The subjects in the control group received a bottle of mouthrinse containing 200 ml 0.2% CHX (Corsodyl®, CHX $\oplus$ Alc).

All subjects were instructed to rinse twice daily (in the morning and in the evening), which is the standard therapy with CHX mouthrinses (Wennström et al. 1996). The test group (CHX $\oplus$ Cpc) rinsed with 15 ml for 30 s and then expectorated, while the control group (CHX $\oplus$ Alc) rinsed with 10 ml for 60 s and then expectorated. Both regimens are suggested by the manufacturers in the instructions. Rinsing with water for the subsequent 30 min. after this procedure was not allowed. Written instructions were provided explaining how to use the mouthrinses. To check for compliance, subjects were asked to note down the times at which they rinsed on a rinsing calendar. All participants were instructed to refrain from using any other form of oral hygiene during the experimental period.

After 72 h all subjects were disclosed with a 1% erythrosine solution and the plaque in both groups was recorded at six sites per tooth on a 5-point scale using the Quigley & Hein (1962) plaque index as modified by Turesky et al. (1970) and further modified by Lobene et al. (1982). All measurements were carried out under the same conditions by the same blinded examiner who was unaware of the mouthrinse used by the participants. Finally, all subjects received a questionnaire using a visual analogue scale designed to evaluate their attitudes to the mouthrinse, which they had used. They were questioned about their appreciation of the taste of the mouthwash. Subjects marked a point on a 10 cm long uncalibrated line with the negative extreme response (0) on the left and the positive extreme (10) at the right end.

- Corsodyl® GlaxoSmithkline, Zeist, The Netherlands
- Perioaid®, Dentaid Benelux, Houten, The Netherlands

Statistical analysis

The plaque scores were used as the main response variable. Mann–Whitney tests were used to compare data between groups. Data considering the VAS-scores of the questionnaire were analysed using Mann–Whitney tests. p-values $\leqslant 0.05$ were considered as statistically significant.

Results

Of the 40 subjects, which were entered into the study, 39 completed the 72-h rinse period. One subject was lost because of an illness unrelated to the study product. The results of this study are presented in Table 1. The mean plaque index (on a 5-point scale) for the CHX ⊕ Cpc test group was 0.97 and for the CHX ⊕ Alc control group 0.78 after 72 h of non-brushing. Statistical analysis showed that there was no significant difference in plaque index between the two groups.

The questionnaire was completed by the subjects after the plaque was scored. Table 1 shows the VAS scores of the subject's appreciation of the mouthrinses. The answers on the questions (taste perception and after-taste) showed a statistically significant difference between the two groups.

The mean VAS scores on a scale from very bad to very good taste (0–10) were 5.92 for the CHX ⊕ Cpc group and 4.10 for the CHX ⊕ Alc group. It appears that the subjects appreciated the taste of CHX ⊕ Cpc better than the taste of CHX ⊕ Alc ($p = 0.02$). The subjects were also asked how they experienced the length of the after- taste of the two mouthrinses. On a scale from very short to very long (0–10), the CHX ⊕ Cpc group had a VAS score 7.24 whereas the CHX ⊕ Alc group had a mean VAS score of 5.38. It appeared that the taste of the CHX ⊕ Cpc rinse remained longer in the mouth ($p = 0.04$).

Discussion

The long-term efficacy and safety of a CHX mouthrinse has been proven in several ''in vitro'' and ''in vivo'' studies (Löe & Schiøtt 1970, Löe et al. 1976, Mackenzie et al. 1976, Brecx et al. 1990). A 0.2% CHX mouthrinse, accepted as the gold standard, shows a persistent bacteriostatic action lasting in excess of 12 h (Schiøtt et al. 1970). In order to reduce disturbing local side effects, which are mainly cosmetic problems, consideration has been given to CHX mouthrinses with lower concentrations. With reduced CHX concentration, decreased side effects have been reported (Flötra et al. 1971, Cumming & Löe, 1973, Agerbaek et al. 1975). Longer-term clinical studies have shown no differences in plaque-inhibition between 0.1%, 0.12% and 0.2% CHX rinses (Flötra et al. 1972, Lang et al. 1982, Segreto et al. 1986). More than the concentration, the dose of CHX appears of considerable relevance to the efficacy of mouthrinse formulations (Bonesvoll & Germo 1978, Jenkins et al. 1994, Keijser et al. 2003). The optimum dose of CHX is generally considered to be in the region of 20 mg twice daily (Cummings & Löe 1973, Agerbaek et al. 1975, Jenkins et al. 1994) which balances efficacy against local side effects and user acceptability (Flötra et al 1971). Concentrations of 0.12% CHX appear as effective as 0.2% if the volume of the rinse was increased from 10 to 15 ml, giving an 18 mg dose on each occasion (Keijser et al. 2003). The present study confirms these previous findings and showed no significant advantage with regard to plaque inhibition for the 0.2% CHX ⊕ Alc over the 0.12% CHX ⊕ Cpc. The 0.2% CHX ⊕ Alc was used for 60 s, whereas the 0.12% CHX ⊕ Cpc was used for 30 s. Both procedures were according to the manufacturer's instructions. This design is comparable with an earlier study (Keijser et al. 2003) which evaluated two mouthrinses with concentrations of CHX per delivered volume and rinsing times, similar to the two groups in the present study. However, in the study of Keijser et al. (2003) the 0.12% CHX was of a different brand which did have an alcoholic base. Also in their study no difference was observed between the two groups.

CHX has been included in mouthwashes not only at different concentrations, but also in different formulations. Alcohol, especially ethanol, is commonly used as a chemical agent in mouthwash solutions. Although ethanol showed only a slight antibacterial efficacy against oral bacteria (Gjermo et al. 1970, Myklebust 1985, Sissons et al. 1996), about 90% of mouthwash preparations in Germany contained alcohol. (Friedmann 1991, Netuschil 1997). The purpose of the addition of alcohol is fourfold: (1) as a vehicle to dissolve other ingredients, (2) as an antiseptic agent, (3) to stabilize certain active ingredients and (4) to improve the shelf-life of the product (Otomo-Corgel 1992, Penugonda et al. 1994). The American Dental Association and Food and Drug Adminstration accepted CHX mouthrinse formulation includes 11.6% of alcohol (Mandel 1994). Although there is no scientific evidence, some concern has been raised about the association of alcohol containing mouthrinses with oral cancer (Elmore & Horwitz 1995). Most commercial mouthrinses contain ethanol that could increase the risk for oral cancer, especially in regular users of mouthrinses containing 25% alcohol or more (Smigel 1991). Whether these concerns are scientifically valid, has not been established. At present, when correctly prescribed, the risk from the alcohol ingredient is probably minimal. This, however, does not exclude the possible risk from self-prescription, the chronic use of mouthrinses or the indigestion of alcoholic mouthrinses by children. Alcohol-free mouthrinses can be recommended in all patients but especially in patients for whom the use of alcohol is contraindicated (Leyes Borrajo et al. 2002). For instance, in recovering alcoholics, alcohol-containing mouthrinses could create the desire for alcohol. Also in patients taking metronidazole or disulfiram, as inadvertent swallowing of an alcohol-containing mouthrinse can cause gastrointestinal upset.

Alcohol-free CHX mouthrinses, are considered to cause fewer side effects, but they may also be less efficient. Alcohol has been added because it is important for the stability of the formulation and on the other hand for the prevention of cross contamination (Vigeant et al. 1998). New

Table 1. Mean overall plaque scores (Quigley & Hein 1962, scale 0–5) and patient perception of taste for each rinse after 72 h of plaque accumulation, standard deviation in parentheses

	CHX ⊕ Cpc	CHX ⊕ Alc	*p*-value*
N	19	20	
Plaque Index	0.97 (0.46)	0.78 (0.31)	0.14†
Taste	5.93 (0.50)	4.13 (1.92)	0.02
After-taste	7.24 (1.84)	5.39 (2.18)	0.04

*Mann–Whitney test.

†95% confidence interval $-0.07 < > 0.45$.

Question taste: What is your opinion concerning the taste of the mouthrinse?

Question after taste: How long did the taste of the mouthrinse remain after rinsing?

CHX ⊕ Cpc = 0.12% chlorhexidine solution with 0.05% cetyl pyridinium chloride basis (Perioaid®), CHX ⊕ Alc = 0.2% chlorhexidine solution with alcohol basis (Corsody®).

CHX mouthrinse formulations have been developed with alternative chemical agents in order to replace the alcohol. The CHX ⊕ Cpc formulation, used in the present study, has in recent years been marketed in Europe under the name Perioaid®. The added Cpc is known to have some antibacterial activity and many studies on Cpc formulations and products (Mandel 1988) confirm the activity of this antiseptic agent. However, the mere incorporation of Cpc in a CHX mouthrinse does not guarantee activity since modifications in the formulation could also affect its action (Addy et al. 1991, Harper et al. 1995). The short term study of Quirynen et al. (2001) indicated, however, that alcohol-free mouthrinses, especially the CHX ⊕ Cpc solution, were as efficient as those with an alcohol base on the inhibition of ''the novo'' plaque formation.

Recently, Herrera et al. (2003) investigated whether there are microbiological differences both ''in vivo'' and ''in vitro'', among 0.12% CHX commercial mouthrinses with and without alcohol. They observed that a 0.12% CHX formulation with alcohol was more active than a 0.12% CHX without alcohol but a favourable exception was however the formulation in which Cpc was added and which increased the antimicrobial activity. Earlier clinical and microbiological studies support the statement that alcohol-free mouthrinse solutions are effective in reducing plaque accumulation compared with a placebo solution (Eldridge et al. 1998, Arweiler et al. 2001, Leyes Borrajo et al. 2002). The absence of alcohol offers several advantages and Cpc appears to be a valuable alternative in order to maintain stability and antiplaque activity within the CHX mouthrinse. Whether in the present study Cpc actually contributed to the activity of the CHX was not assessed.

In a study of Ernst et al. (1998) approximately 33% of the people claim that alcohol-containing CHX mouthrinses are of poor taste. It has a reversible effect on the taste (intensity and quality) of NaCl and quinine-HCL and, to a lesser extend, on the taste quality of sucrose and citric acids (Helms et al. 1995). It has been proposed that the salt taste appears to be preferentially affected, leaving food and drinks with a rather bland taste (Lang et al. 1988). An alcohol-containing CHX mouthrinse may even alter the taste perception for up to 4 h after rinsing (Bolanowski et al. 1995). In the present study, a questionnaire was applied to evaluate the subject's attitude towards taste perception. The results showed that the CHX ⊕ Cpc was considered to taste better than the CHX ⊕ Alc, but the after-taste remained longer in the mouth. Quirynen et al. (2001) also demonstrated with CHX ⊕ Cpc reduced unpleasant side effects, especially for taste. One can question if it is the lower concentration of CHX or the shorter rinsing time, the absence of alcohol, the inclusion of Cpc, or perhaps even a combination of these factors, which are responsible for the better appreciation of the taste. Nevertheless, the new CHX formulation could have a positive effect on user's attitude toward compliance.

Conclusion

Within the limitations of this 72 h non-brushing study design, it can be concluded that rinsing with CHX ⊕ Cpc (Perio-Aid®) is not significantly different from rinsing with CHX ⊕ Alc (Corsodyl®). It appears that the subjects appreciated the taste of the CHX ⊕ Cpc better. However, the after-taste of this rinse remained longer in the mouth.

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