Chlorhexidine and the control of plaque and gingivitis

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Chapter 3

The anti-plaque efficacy of a chlorhexidine mouthrinse used in combination with toothbrushing with dentifrice

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Introduction

Adequate oral hygiene is an important part of maintaining oral health. The most common plaque removal procedure, at least in the Western society, involves a toothbrush and a dentifrice (Löe et al. 1965, Frandsen 1986). In situations in which plaque control is difficult or compromised, a 0.2% chlorhexidine (CHX) mouthrinse is generally prescribed to provide adjunctive oral benefits after toothbrushing with dentifrice (Addy 1986, Addy & Moran 1997). One of the most widely used synthetic detergents in dentifrice is sodium lauryl sulphate (SLS). Unfortunately, chlorhexidine (CHX) and (SLS) may counteract. Previous studies (Barkvoll et al. 1989, Owens et al. 1997) have shown that CHX and SLS are not compatible even when they are introduced separately in the oral cavity. Ever since, it has been recommended that the time between a CHX rinsing and toothbrushing with an SLS containing dentifrice should at least be 30 minutes, if reduction in the anti-microbial effect is to be avoided. To optimize the efficacy of a CHX rinse, toothbrushing with dentifrice should be suspended or toothbrushing should be performed with dentifrice formulations without antagonistic ingredients (Owens et al. 1997) or without dentifrice all together. Brushing with dentifrice followed by rinsing with CHX is probably the most common order as one would use these products in daily life. Barkvoll et al. (1989) showed that similar inhibitory effects were present when SLS was used 30 min before or after CHX. In addition, Owens et al. (1997) concluded that the actual inhibitory effect of dentifrice slurry on the efficacy of CHX was present, irrespective whether the rinse was used before or after the dentifrice slurry.

Recently, a clinical trial investigated the influence of toothbrushing with an SLS containing dentifrice on the anti-plaque efficacy of a CHX mouthrinse (Van Strydonck et al. 2004). The design of the study was conceived to establish, in a 4-days plaque accumulation model, the plaque inhibitory action of a 0.2% CHX rinse in one jaw, when used under the influence of toothbrushing with an 1.5% SLS containing dentifrice in the opposite jaw. Data showed that the level of plaque inhibition offered by a 0.2% CHX mouthrinse rinse was not reduced under the influence of a 1.5% SLS containing dentifrice. Consequently, the results of this study did not support the previous conclusions of Barkvoll et al. (1989) and Owens et al. (1997).

In the study of Owens et al. (1997), rinsing was supervised. In the previous study by Van Strydonck et al. (2004), brushing and rinsing were performed without supervision. However, the panelists were requested to fill out a rinsing diary to evaluate their compliance. Although the returned diaries indicated that the panelists followed the given instructions conscientiously, one can, however, not rule out that there could have been a chance that some panelists were not compliant.
Since to date no study has been conducted where the activity of a 0.2% CHX mouth-rinse was considered under the influence of an SLS-free dentifrice, the aim of the present study was to investigate, under supervised conditions, the inhibitory plaque effect of a CHX 0.2% pre-brushing mouthrinse in one jaw, under the influence of toothbrushing in the opposite jaw, either with an SLS-containing dentifrice or with an SLS-free dentifrice. In the present study three different dentifrices were tested. Two of them contained SLS in different concentrations (Colgate Total®, and Aquafresh Natural Whitening®, the other (Zendium®) did not contain SLS.

Materials and methods

Subjects
Thirty-five subjects, aged between 20 - 49 years, participated in the study. Subjects were in good general health without a medical history or medication that might interfere with the outcome of the study. All the subjects were dentate with at least 24 scorable teeth. They were excluded if they had fixed or removable orthodontic appliances or removable prosthesis, pockets > 5 mm or attachment loss > 2 mm. Twenty-two subjects, 10 males and 12 females, were found to be suitable for the study. On approval, all the volunteers received a personal instruction schedule, signed an informed-consent paper and, in order to participate, agreed to the following:

- Products would only be used under supervision of two dental assistants at set times.
- Appointments (days and hours) could not be changed.
- It was not allowed to perform another form of oral hygiene other than the one provided twice daily under supervision.
- It was not allowed to eat or rinse with water for 30 minutes after the rinsing and brushing exercise.
- Any change in medical status or medicine intake was to be reported.

Procedure
The study was based on the 4-days plaque accumulation model initially developed to compare the chemical plaque inhibitory properties of dentifrices (Addy et al. 1983), used in an earlier investigation (Van Strydonck et al. 2004). It was a single-blind, randomized, four-cell, cross-
over design. It compared three different oral hygiene regimens consisting of a combination of rinsing and brushing to a regimen of rinsing alone. Three different dentifrices were tested. Two of them contained SLS and one was free of SLS. A washout period of at least 7 days was introduced between the four crossover periods. At baseline (day 1) of each test period all subjects received a thorough dental prophylaxis to remove all stain, calculus and plaque. The subjects were randomly assigned to a sequence according to a 4 x 4 Latin square balanced for carryover effects (Newcombe, 1992a,b). Instructions for the allocated regimen were given to each subject in a sealed envelope. One jaw (upper or lower) was randomly assigned as the "study" jaw and was used to evaluate the level of plaque accumulation at the end of each 4-day period. The opposite jaw, called “the dentifrice” jaw, served to introduce the effect of toothbrushing with a dentifrice in the same mouth.

Four regimens were designed in which the panelists used the assigned products under supervision. In each regimen the subjects rinsed twice daily with 10 ml 0.2% CHX digluconate solution (Corsodyl®; GlaxoSmithKline, Zeist, The Netherlands) during 60 seconds. The CHX was to be expectorated directly after the rinsing. Immediately afterwards the subjects in the dentifrice regimens brushed for 2 minutes with a manual toothbrush and the assigned product in the randomly assigned “dentifrice” jaw (upper or the lower). After brushing, the dentifrice foam was expectorated and the oral cavity was rinsed with water during 3 seconds.

The four regimens included:

- **Regimen 1**: CHX rinsing + toothbrushing in the “dentifrice” jaw with 1 cm of a 1.5% SLS containing dentifrice (Colgate Total®; Colgate Palmolive)*. Colgate Total® dentifrice contains 1.5% SLS, 0.3% Triclosan, copolymer, and 0.32 NaF.
- **Regimen 2**: CHX rinsing + toothbrushing in the “dentifrice” jaw with 1 cm of a 1.1% SLS containing dentifrice (Aquafresh Natural Whitening®; GSK). Aquafresh Natural Whitening® (GSK) dentifrice contains 1.15% SLS, pyrophosphate, 0.24% NaF.
- **Regimen 3**: CHX rinsing + toothbrushing in the “dentifrice” jaw with 1 cm of an SLS free dentifrice (Zendium®; Kortman Intradal). Zendium® dentifrice contains glucoseoxidase, NaF and amyloglucosidase and is free of SLS.
- **Regimen 4**: CHX rinsing only, no brushing was allowed.
During the experimental regimens all other oral hygiene procedures were suspended. After 4 days of plaque accumulation, the teeth were scored for plaque in the study jaw, according to the modifications of Turesky et al. (1970) and Lobene et al. (1982) of the Quigley & Hein (1962) plaque index. After disclosing the teeth with erythrosine, the plaque was assessed at 6 sites around each tooth. During the washout period, subjects resumed their normal tooth cleaning habits. All clinical measurements were performed by one and the same, blinded examiner (D.V.S.) under the same conditions.

**Data analysis**

The mean plaque index was calculated for each individual after each experiment. To compensate for variation of the regimens over time, individual data were corrected by subtracting the overall mean value, per experimental period, from each individual value.

These acquired values were used to analyze differences between regimens using a Friedman test. To approximate differences between regimens, 95% confidence intervals of these differences were calculated using a mixed models analysis (BMDP 3 V).

**Results**

Twenty-one of the 22 subjects completed the study without any protocol violation. There was one withdrawal of the trial because of hospitalization due to an urgent surgical intervention which was not product related. In general, no side effects were noted. One individual complained once of a burning sensation in the mouth.

Table 1 shows the mean plaque-scores of the “study” jaws for rinsing with CHX followed by toothbrushing with one of the three dentifrices (regimen 1-3) and for rinsing with 0.2% CHX alone (regimen 4). The mean plaque index for the rinsing-brushing regimen CHX - Colgate Total® and Aquafresh Natural Whitening® was 1.8., for the rinsing-brushing regimen CHX - Zendium® was 1.9 and for the CHX rinsing alone regimen was 1.9. Statistical analysis showed no significant difference in overall plaque score between the four regimens. There were no differences in effects on those subjects receiving the treatment in the upper jaw as compared to those randomized for treatment in the lower jaw.
Table 1. Mean (SD) overall plaque scores for each regimen after 4 days of plaque accumulation.

<table>
<thead>
<tr>
<th>Plaque index</th>
<th>Regimen 1</th>
<th>Regimen 2</th>
<th>Regimen 3</th>
<th>Regimen 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHX - Colgate</td>
<td>CHX - Aquafresh</td>
<td>CHX - Zendium</td>
<td>CHX only</td>
</tr>
<tr>
<td>Overall</td>
<td>1.8 (0.64)</td>
<td>1.8 (0.57)</td>
<td>1.9 (0.45)</td>
<td>1.9 (0.53)</td>
</tr>
</tbody>
</table>

Regimen 1: CHX rinsing + toothbrushing in the “dentifrice” jaw with a 1.5% SLS dentifrice.
Regimen 2: CHX rinsing + toothbrushing in the “dentifrice” jaw with a 1.1% SLS dentifrice.
Regimen 3: CHX rinsing + toothbrushing in the “dentifrice” jaw with an SLS free dentifrice.
Regimen 4: CHX rinsing only.

CHX, chlorhexidine digluconate; SLS, sodium lauryl sulphate.

Friedman test on corrected individual values, \( p = 0.478 \).

Table 2 shows the 95% confidence intervals. The extend of the intervals is narrow and in none of the intervals “0” was near the boundaries. Also the estimated differences do not exceed a 0.1 unit of the plaque index.

Table 2. 95% CI for differences in plaque indices between regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Estimated differences</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 versus 2, 3, 4</td>
<td>0.082*</td>
<td>- 0.224 ↔ 0.060</td>
</tr>
<tr>
<td>2 versus 1, 3, 4</td>
<td>0.038*</td>
<td>- 0.104 ↔ 0.180</td>
</tr>
<tr>
<td>3 versus 1, 2, 4</td>
<td>0.037*</td>
<td>- 0.105 ↔ 0.179</td>
</tr>
<tr>
<td>4 versus 1, 2, 3</td>
<td>0.007*</td>
<td>- 0.135 ↔ 0.149</td>
</tr>
</tbody>
</table>

Regimen 1: CHX + SLS dentifrice.
Regimen 2: CHX + SLS dentifrice.
Regimen 3: CHX + non-SLS dentifrice.
Regimen 4: CHX alone.

CHX, chlorhexidine digluconate; SLS, sodium lauryl sulphate.

*Estimate differences when a particular regimen is compared to others (BMDP 3 V).
Discussion

Several studies have shown that SLS and CHX may act as antagonists (Bonesvoll et al. 1977, Kirkegaard et al. 1974, Rølla et al. 1970, Rølla & Melsen 1975, Barkvoll et al. 1989, Owens et al. 1997). However, Van Strydonck et al. (2004) showed, in a 4-day plaque accumulation model, that the plaque-inhibitory action of a CHX post-brushing rinse in one jaw, when used under the influence of toothbrushing with an SLS containing dentifrice in the opposite jaw, was not reduced. The rather unexpected outcome of this study (Van Strydonck 2004) could have been the result of poor compliance of the participants, the chosen brushing-rinsing order, and the concentration of SLS in the dentifrice or the presence of other dentifrice ingredients.

In the previous study (Van Strydonck et al. 2004), the panelists were requested to fill out a rinsing diary to stimulate their compliance. Although the returned diaries indicated that the panelists followed the given instructions conscientiously, it has recently been shown that the use of manually completed brushing diaries at home may not provide an accurate reflection of patient compliance with toothbrushing instructions (McCracken et al. 2002). Consequently, the present study was conducted using the products under strict supervision. Even under these conditions, the present study shows no influence of toothbrushing with a dentifrice on the plaque inhibition of CHX.

The brushing and rinsing order has been the subject of previous studies. Barkvoll et al. (1989) showed that the use of an aqueous solution of SLS before rinsing with CHX had an inhibiting effect on the efficacy of a CHX mouthrinse. Similarly Owens et al. (1997) showed that an SLS-containing dentifrice-slurry, used before the CHX, resulted in a reduced plaque inhibition. Recently, Van Strydonck et al. (2004) had the panelists brush their teeth with an SLS containing dentifrice followed by rinsing with CHX, as one would in daily life. No inhibition was observed in this design. Barkvoll et al. (1989) also did one experiment in reverse order, having subjects use the CHX 30 min. before rinsing with SLS aqueous solution. Again, he observed inhibition of the CHX. This was confirmed by Owens et al. (1997), who had the panelists rinse with an SLS containing dentifrice-slurry, immediately after the CHX mouthrinse. The present study with a design similar to Van Strydonck et al. (2004), but in a reverse order (rinsing-brushing), questioned the proposed inhibiting effect of the SLS in a dentifrice. Once more, no difference in plaque inhibition of CHX under the influence of toothbrushing with a dentifrice was observed.

Toothbrushing with another brand of dentifrice may have yielded a different result. SLS may not be present in equal concentration or equally available in the formula of the
dentifrice. In the previous study by Van Strydonck (2004), the influence of one SLS containing dentifrice on the anti-plaque efficacy of a 0.2% CHX mouthrinse was investigated. The concentration of SLS in the chosen dentifrice (Colgate bi-fluor\textsuperscript{®}) was 1.5%. In the present study, 2 dentifrices were tested with different SLS-concentration and one free of SLS. No difference in plaque inhibition of CHX under the influence of toothbrushing with or without SLS was observed.

In the present study, Colgate Total\textsuperscript{®} dentifrice was used which, besides SLS, contains Triclosan. This ingredient is supposed to have a supplementary inhibiting effect on plaque growth as has been shown in other studies (Svatun et al. 1989, Stephen et al.1990, Jenkins et al. 1991a, b,). It is possible that the existing inhibiting effect of the SLS ingredient of the dentifrice on the anti-plaque action of CHX is compensated by the addition of the anti-microbial effect of Triclosan. However, Aquafresh Natural Whitening â, containing SLS but no Triclosan, showed similar results as Colgate Totalâ. Moreover, the results of the combination of Colgate Total\textsuperscript{®} and CHX in the present study were also comparable with CHX and Zendium\textsuperscript{®}, a dentifrice which does not contain SLS and Triclosan.

As has been suggested in the previous study (Van Strydonk et al. 2004), the most likely explanation for the observed absence of a reduction of the inhibitory plaque effect of the CHX rinse seems to be a lower intra-oral SLS-concentration and a shorter contact time of SLS in our studies as compared to that in the studies of Barkvoll et al. (1989) and Owens (1997). In the latter studies the oral cavity was not cleared from SLS after rinsing with the aqueous solution or dentifrice slurry, whereas in our studies the panelists expectorated and rinsed with water immediately after brushing with dentifrice.

In conclusion, within the present study design, based on the present results and those of the previous study of Van Strydonck et al. (2004), the anti-plaque effect of a CHX mouthrinse does not appear to be reduced under the influence of a normal toothbrushing exercise with a dentifrice, irrespective if the dentifrice contains SLS, or was used before or after the rinse.

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...in combination with toothbrushing with dentifrice.
References


