A double blind randomized clinical trial of at-home tooth bleaching using two carbamide peroxide concentrations: 6-month follow-up

S.S. Meireles a, S.S. Heckmann b, I.S. Santos c, A. Della Bona d, F.F. Demarco a,∗

a Department of Operative Dentistry, Federal University of Pelotas, Pelotas, RS, Brazil
b Federal University of Pelotas, Pelotas, RS, Brazil
c Department of Epidemiology, Federal University of Pelotas, Pelotas, RS, Brazil
d School of Dentistry, University of Passo Fundo, Passo Fundo, RS, Brazil

ARTICLE INFO
Article history:
Received 24 April 2008
Received in revised form
3 July 2008
Accepted 8 July 2008

Keywords:
Carbamide peroxide
Tooth bleaching
Clinical trials
Randomized

ABSTRACT
Objectives: This double blind randomized clinical trial evaluated the longevity of the whitening effect (6-month follow-up) of two carbamide peroxide concentrations used in at-home vital bleaching.
Methods: Ninety-two volunteers with shade mean C1 or darker for the six maxillary anterior teeth were randomized into two balanced groups (n = 46) according to bleaching agent concentration: 10% (CP10) or 16% (CP16) carbamide peroxide. Patients were instructed to use the whitening agent in a tray for 2 h/day during 3 weeks. Shade evaluations were done with a value-oriented shade guide, and a spectrophotometer at baseline, and at 1-week and 6-month post-bleaching. Volunteers for both treatment groups had to answer questions related to dietary and oral hygiene behavior.
Results: At 6-month recall, tooth shade remained significantly lighter than at baseline, in both treatment groups, considering the color parameters: ΔL*, Δa*, Δb*, ΔE* (p < 0.0001) or the tooth shade median values (p < 0.001). Additionally, shade median relapse at 6-month follow-up was not statistically different between CP10 and CP16 groups using the spectrophotometer (p = 0.1) or the visual matching (p = 0.7) analyses. Overall, subjects from CP10 and CP16 reported high consumption of beverage and food stains, which was not different between groups (p = 0.5).
Conclusions: The whitening effect remained similar 6-month after the bleaching treatment for both carbamide peroxide concentrations tested. Additionally, the high consumption of staining beverages and foods reported by patients had no influence in the whitening effect longevity at 6-month.

© 2008 Elsevier Ltd. All rights reserved.

1. Introduction
Vital tooth bleaching is a treatment modality that has presented an exponential increase to treat tooth discoloration.1–3 Hydrogen peroxide or peroxide releasing agents, such as carbamide peroxide are the most common agents used for vital tooth whitening.4–6 Overall, when in contact with outer enamel surface, the peroxide-containing whiteners break
down into water and oxygen, which diffuses through the enamel, causing oxidation of organic pigments that are mainly located within dentine, resulting in a reduction or elimination of the discoloration.6,7

New products and a number of methods have been available for tooth vital bleaching, which vary according to peroxide concentration, bleaching agent formulation, mode of activation, exposure time, and application way.5,8–10 These characteristics determine if the bleaching has to be done in-office by the dentist using higher concentrations gels, or at-home by the patient using lower concentrations of whitening agents.3,11–13 At-home bleaching products include gels, rinses, gums, toothpastes, paint-on films, and whitening strips.1,14–16

At-home dentist-supervised tooth whitening with custom trays17 has become more popular than the in-office techniques.3,5,10 The benefits achieved with tray-based systems are widely known: lower incidence of tooth sensitivity or gingival irritation; less visits to the dental office; achievement of the same whitening results as higher concentrations agents; and safety and efficacy of 10% carbamide peroxide that has already been established in published clinical trials.10,11,14,18–20 In an attempt to increase the effectiveness and longevity of the whitening effect, manufactures have increased the concentrations of carbamide or hydrogen peroxide used for vital bleaching with trays.2,9,12,19 Yet, there is a lack of randomized, controlled clinical trials investigating the effect of increasing the whitening agent concentration on the efficacy and longevity of at-home tooth bleaching. Some of the reports on the longevity of the tray-based systems for home bleaching18,21–23 are relatively short-term followings.10–12,19,24,25 Unfortunately, the available studies have not reported the possible factors associated to shade relapse, such as dietary behavioral (e.g., beverage or food stains consumption). Additionally, most clinical studies on bleaching agents only use the visual assessment with a shade guides to measure the treatment outcome.5,15,19,23 Thus, the objectives of this randomized, controlled clinical trial were to evaluate the whitening effect, at 6-month post-bleaching, using two carbamide peroxide concentrations (10% or 16%), and to evaluate the influence of aspects from the diet and oral hygiene behavior on the longevity of the bleaching treatment.

2. Materials and methods

2.1. Examiners calibration

This double blind randomized, controlled clinical trial was approved by the local Ethics Committee. Prior to enrollment, each volunteer received an informed consent form containing all the information about the risks and benefits of the treatment. All participants signed the informed consent form.

Before starting the study, two examiners were calibrated on shade determination of the anterior teeth in 16 volunteers. The shade was recorded using a digital spectrophotometer (Vita Easysmile, Vita Zahnfabrik, Bad Säckingen, Germany) by the study supervisor, and a value-oriented shade guide (Vitapan; Classical, Vita Zahnfabrik) by the two examiners. These shade selections were carried out in the afternoon with sunlight and room illumination without any communication between the examiners.26

The visual evaluation was made by comparing the shade tabs with the middle third of the maxillary canines and incisors. The 16 shade tabs in the guide were numbered from 1 (highest value, B1) to 16 (lowest value, C4) for statistical analysis. The digital spectrophotometer (Vita Easysmile, Vita Zahnfabrik) analysis was adopted as the gold standard. At each evaluation period, the shade of the upper six anterior teeth was measured three times, with the active point of the instrument in the middle third of each tooth, and the spectrophotometer automatically averaged the three readings for each tooth. The digital spectrophotometer measures the shade of teeth based on the CIEL*a*b* color space system, allowing the determination of color in the three-dimensional space. This system was defined by the International Commission on Illumination, in 1967, and is referred to as CIELAB. The L* represents the value (lightness or darkness). The a* value is a measure of redness (positive a*) or greenness (negative a*). The b* value is a measure of yellowness (positive b*) or blueness (negative b*). The difference between the color coordinates was calculated as: \( \Delta E^* = \sqrt{(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2} \) (CIE, Commission Internationale de L’Eclairage 1978).27 The whitening occurs mainly by a yellowness reduction (lower b*), and to a lesser extent, by an increasing of lightness (higher L*) and a redness reduction (lower a*).14,27 This study was started when the examiners achieved agreement with the gold standard at a level higher than 70% according to the grouping by chroma.26

2.2. Sample size

The calculation of the sample size was carried out based on a previous study Kihn et al.19 To detect the bleaching effect with a statistical power of 90%, when the significance level was 5% (one-tailed test), a sample size of \( n = 80 \) volunteers would be necessary. A 15% addition in volunteer number, taken in consideration potential loss or refusal, gave a total sample size of \( n = 92 \) volunteers. The individuals were invited to participate in this clinical trial through advertisement in local newspapers, radio stations and University website.

2.3. Eligibility criteria, randomization and blinding

Prior to dental examination, each volunteer filled out a medical history sheet and a complete dental prophylaxis was performed to remove extrinsic stains. One hundred eighty-three volunteers were examined to obtain 92 individuals who met the inclusion/exclusion criteria described below. Patients were 18–55 years of age and, all were in good general and dental health. To be included, the six maxillary anterior teeth had to be present, with a shade mean C1 or darker (Vitapan; Classical, Vita Zahnfabrik) and, should not have more than 1/6 of their buccal surface covered with a restorative material. Patients with active caries, periodontal disease, previous hypersensitivity, and orthodontic treatment or with tetracycline-stained teeth were excluded from the study. Patients who have used tooth whiteners within the past 3 years, patients without schedule availability or smokers, pregnant or lactating also were excluded (Fig. 1).20
After initial evaluation, the baseline tooth shade determination was performed as described above using the Vita shade guide and the digital spectrophotometer, similar to the protocol of the calibration exercise. Then, the participants were randomly assigned into two experimental groups (n = 46) according to the bleaching agent concentration: 10% (CP10) or 16% (CP16) carbamide peroxide (Whiteness Perfect, FGM Dental Products, Joinville, Brazil). A randomization table to allocate the participants in each study group was prepared in advance by an epidemiologist, not directly involved with the clinical part of the study.

The concentration seal for each bleaching gel syringe was removed in order to mask treatment groups. To mask the tubes half of their plungers were covered with white adhesive tape. The same member responsible for volunteer allocation did this procedure. Therefore, the examiners and patients were blinded to the agent concentration that was being delivered.

2.4. Bleaching procedure

Two alginate impressions (Jeltrate regular set, Dentsply International Inc., Milford, DE, USA) were taken per patient and stone molds were prepared. The buccal surfaces of the anterior teeth on each mold were blocked out with five coats of nail polish, starting approximately 1.0 mm above the gingival margin. This area created a reservoir in the tray (about 1.0 mm of thickness) for the bleaching gel. The custom trays were fabricated using a 3-mm thick soft vinyl material (FGM Dental Products) and a vacuum-formed process. The excess on the buccal and lingual surfaces was trimmed just short of the gingival margin.

Patients were recalled in another clinical session to receive the trays and three bleaching gel tubes. They were instructed to use dispensed gel at night for a period of 2 h/day, during 3 weeks. Both arches were bleached at the same time. All the patients received a hands-on practical demonstration and written instructions concerning the proper use of the bleaching agents and on diet and oral hygiene control during the course of the treatment. Subjects also received toothbrushes and dentifrices without whitening agents aiming to standardize their oral hygiene regimen.

Each subject was instructed to record tooth sensitivity on a daily basis during the 3-week treatment. Patients who experienced more than a moderate degree of sensitivity received potassium nitrate desensitizing gel (Desensibilize KF 2%, FGM Dental Products). Subjects were instructed to place the desensitizing gel in their tray and wear it for 20 min once a day, as recommended by the manufacturer.

Patients were evaluated at the following times: baseline, 1 week and 6 months post-bleaching. Examiners were blind to the status of participants in regard to the study group they belonged. At each evaluation period, tooth shade determinations were made following the same protocol that was conducted at the baseline. At the 6-month recall, shade changes for each subject in both treatment groups were compared to the tooth shade determined at the baseline and, at 1-week post-bleaching. Two examiners applied a standardized questionnaire related to diet and oral hygiene behavior. Subjects for both treatment groups were questioned regarding to: (1) whitening toothpaste use; (2) re-bleaching after the end of the active treatment phase and, (3) amount, frequency and type of beverage and food staining intake, such as: coffee, tea, wine, fruit or artificial juices and cola-containing beverages, and natural colorant foods (i.e., beetroot, carrot and lettuce) or industrialized foods.

2.5. Statistical analysis

Tooth shade medians, median shade change and color parameters were analyzed within the same treatment group.
by Wilcoxon Signed Rank test and by the Mann–Whitney U-test for statistical comparison between the two groups at the different evaluation periods. Chi-squared tests were used to compare the significant differences in categorical variables. Differences were considered statistically significant when \( p < 0.05 \).

3. Results

Eighty-nine of the original 92 subjects enrolled in the study (96.7%) were recalled at 6-month follow-up. One subject from CP16 group failed to continue the treatment, complaining about an unpleasant taste from the whitening agent and tooth sensitivity in the first day of application. Demographic characteristics of the sample and, results of the study at 1-week post-bleaching have been reported previously. At 6-month follow-up, two subjects were lost (one from each group). The participant from CP10 group moved to another Country and the other from CP16 started orthodontic treatment.

3.1. Spectrophotometer data

Results of the study from \( L^* \), \( a^* \) and \( b^* \) values at the baseline and at 1-week recall have been reported previously. At 6-month recall, both treatment groups remained significantly lighter than at baseline, as for the color parameters: lightness improvement (\( \Delta L^* \)), reduction of redness (\( \Delta a^* \)), reduction of yellowness (\( \Delta b^* \)), overall color change (\( \Delta E^* \)) (\( p < 0.0001 \)) as for the tooth shade median values (\( p < 0.001 \)). Although at 1-week post-bleaching evaluation the CP16 group has showed a significant reduction for \( \Delta b^* \) (\( p = 0.05 \)) compared to CP10 group, this difference disappeared after adjusting for \( b^* \) parameter at baseline. At 6-month follow-up, comparisons between the CP10 and CP16 groups did not showed significantly different values for means in \( \Delta L^* \), \( \Delta a^* \), \( \Delta b^* \) and, \( \Delta E^* \) (Table 1).

Although some loss of the lightening effect could be noted at 6-month recall, changes in \( \Delta L^* \), \( \Delta a^* \), and \( \Delta E^* \) for CP10 and, changes in \( \Delta L^* \), \( \Delta a^* \), \( \Delta b^* \), and \( \Delta E^* \) for CP16 group were not statistically different from 1-week post-bleaching (Table 1). However, the CP10 group had a statistically significant reduction in \( \Delta a^* \) (\( p = 0.03 \)) (reduction in redness represents a color improvement).

At 6-month follow-up, the tooth shade median remained significantly lighter for CP16 than CP10 group (\( p = 0.04 \)), however, the shade median relapse was not significant different comparing the treatment groups (\( p = 0.1 \)) or within the same treatment group, CP10 (\( p = 0.3 \)) and CP16 (\( p = 0.7 \)) (Table 2).

3.2. Visual assessment with a shade guide

The visual evaluation showed that tooth shade medians for both bleaching treatment groups remained significantly lighter at 6-month recall than at baseline (\( p < 0.001 \)), but the shade change from baseline was not statistically different between groups (\( p = 1.0 \)). At 6-month follow-up, the shade regression for teeth treated with CP10 was not significantly different from teeth that received CP16 (\( p = 0.7 \)) (Table 2). However, we found significant difference in shade relapse compared to at 1-week post-bleaching in both CP10 (\( p = 0.05 \)) and CP16 (\( p = 0.03 \)) groups.

3.3. Diet and oral hygiene behavior

None of the participants reported bleaching their teeth during the 6 months after treatment. Regarding the use of whitening toothpaste, 31 (68.9%) subjects from CP10 and 28 (63.6%) from CP16 group reported the use of non-whitening toothpaste.

### Table 1 – Means change from baseline for \( \Delta L^* \), \( \Delta a^* \), \( \Delta b^* \) and \( \Delta E^* \) at 1-week and 6-month recall for groups treated with 10% or 16% carbamide peroxide

<table>
<thead>
<tr>
<th>Color parameters</th>
<th>Evaluation periods: means (±S.D.) change from baseline</th>
<th>p-Value1-week-6-month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>1-week</td>
</tr>
<tr>
<td>( \Delta L^* )</td>
<td>CP10</td>
<td>77.4 (±4.1)</td>
</tr>
<tr>
<td></td>
<td>CP16</td>
<td>78.5 (±2.7)</td>
</tr>
<tr>
<td></td>
<td>p-Value10-16</td>
<td>0.2</td>
</tr>
<tr>
<td>( \Delta a^* )</td>
<td>CP10</td>
<td>-0.2 (±1.0)</td>
</tr>
<tr>
<td></td>
<td>CP16</td>
<td>-0.5 (±1.0)</td>
</tr>
<tr>
<td></td>
<td>p-Value10-16</td>
<td>0.7</td>
</tr>
<tr>
<td>( \Delta b^* )</td>
<td>CP10</td>
<td>0.2 (±1.7)</td>
</tr>
<tr>
<td></td>
<td>CP16</td>
<td>1.1 (±1.5)</td>
</tr>
<tr>
<td></td>
<td>p-Value10-16</td>
<td>0.02</td>
</tr>
<tr>
<td>( \Delta E^* )</td>
<td>CP10</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CP16</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>p-Value10-16</td>
<td>0.5</td>
</tr>
</tbody>
</table>

* At baseline, \( L^* \), \( a^* \), \( b^* \) means were showed in absolute values.
* Adjusted for \( b^* \) parameter at baseline.
Only 8 (17.8%) subjects from CP10 group and 10 (22.7%) from CP16 group used whitening toothpaste, while 6 volunteers for each treatment group were not able to recall if the toothpaste had or not whitening agents in the composition.

Overall, individuals from both treatment groups reported a high rate of beverage or food staining consumption. Also, more than 50% of the participants from each group reported of drinking staining beverages more than twice daily. Such intake was not different between groups ($p = 0.5$). Information on daily intake of staining beverages and foods is shown in Table 3.

## Table 2 – Final median shade and, median shade changes from baseline and 1-week post-bleaching evaluation to 6-month recall evaluation for groups treated with 10% or 16% carbamide peroxide

<table>
<thead>
<tr>
<th>Shade methods evaluation/treatment groups</th>
<th>Baseline</th>
<th>1-Week</th>
<th>6-Month</th>
<th>6-Month–Baseline</th>
<th>6-Month–1-week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectrophotometer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CP10</td>
<td>8.5</td>
<td>2.7</td>
<td>3.0</td>
<td>−5.5</td>
<td>0.3</td>
</tr>
<tr>
<td>p 10–16</td>
<td>0.8</td>
<td>0.04</td>
<td>0.04*</td>
<td>0.06</td>
<td>0.1*</td>
</tr>
<tr>
<td>CP16</td>
<td>8.8</td>
<td>2.3</td>
<td>2.4</td>
<td>−6.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Shade guide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CP10</td>
<td>8.7</td>
<td>2.3</td>
<td>2.5</td>
<td>−6.2</td>
<td>0.2</td>
</tr>
<tr>
<td>p 10–16</td>
<td>0.2</td>
<td>0.01*</td>
<td>0.06</td>
<td>1.0</td>
<td>0.7*</td>
</tr>
<tr>
<td>CP16</td>
<td>8.0</td>
<td>2.0</td>
<td>2.3</td>
<td>−5.7</td>
<td>0.3</td>
</tr>
</tbody>
</table>

* Difference statistically significant between groups ($p < 0.05$).

** Adjusted for shade median at 1-week post-bleaching.

### 4. Discussion

The 10% carbamide peroxide has been considered by ADA $^{14}$ the “standard” concentration for at-home vital tooth bleaching. $^{1,8,18,21,23}$ This study was designed to compare the whitening effect of 10% and 16% CP and its longevity considering important diet and oral hygiene aspects. At 6-month follow-up, the visual and spectrophotometric analyses showed that both treatment groups continued to have teeth lighter than five shades, according to value-oriented Vita
shade guide, when compared with the baseline\textsuperscript{14,20} and, based on CIEL*a*b* system, the ΔE* values also remained with efficacy levels established by ADA.\textsuperscript{14} The lightening effect obtained at 1-week post-bleaching\textsuperscript{20} was maintained after 6 months for both groups and the shade relapse was not statistically significant between groups.

Generally, studies have been performed in order to evaluate the efficacy and longevity of at-home tooth whitening using 10% carbamide peroxide\textsuperscript{18,22,23} or when comparing this concentration with similar hydrogen peroxide concentrations.\textsuperscript{3,8,28,29} Few investigations compared the efficacy and longevity of the concentrations tested in this study. One study\textsuperscript{19} verified that tooth whitened by a 15% CP agent were significantly lighter than tooth treated with 10% CP, and the bleaching effect was higher for 15% CP after 2 weeks of treatment. In opposite, other study did not detect significant differences neither at the end of the study nor 4 weeks post-treatment for groups treated with 10% or 15% CP.\textsuperscript{11} The post-treatment evaluation period in both studies was very short, which make it difficult to detect some loss of lightening.

It was observed a reduction in Δa* mean values for group treated with 10% CP when compared with the values obtained at 1-week post-treatment period. The reduction in redness (Δa*) represents, in a minor extent, a color improvement, once that the reduction in b* occurs more rapidly and to a great extent.\textsuperscript{30} However, it is recommended to perform longer follow-up to effectively determine if higher bleaching concentrations can really increase the longevity of the lightening effect.

There is a lack of information in the literature regarding the association of high consumption of staining beverages and foods with tooth whitening longevity. Only one study, comparing the clinical efficacy and tolerability of two self-applied whitening systems contain 6% hydrogen peroxide or 10% CP, reported a high consumption of coffee, tea, cola or tobacco use.\textsuperscript{8}

The present data showed that the intake of staining beverages and foods was very high in the diet of all subjects from both treatment groups. Although the staining diet has been associated with the tooth darkening, it appeared not to have influenced the bleaching effect durability in the present study. Further long-term clinical trials are needed to provide additional information about the bleaching effect longevity and the factors involved with shade relapse.

5. Conclusions

The whitening effect evaluated by visual shade matching and digital spectrophotometer remained similar after 6 months of bleaching treatment using any of the carbamide peroxide concentrations tested. Additionally, the high consumption of staining beverage and food had no influence in the whitening effect longevity.

REFERENCES


