Long-term efficacy of in-office and at-home bleaching: A 2-year double-blind randomized clinical trial

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ABSTRACT: Purpose: This parallel, double-blind randomized clinical trial evaluated the 2-year bleaching efficacy and sensitivity produced by at-home (AH) and in-office (IO) bleaching therapies. Methods: 60 participants with tooth color darker than C2, without restorations in the anterior dentition and older than 18 years old, were randomly allocated into two groups to receive either IO with 35% hydrogen peroxide or AH with 16% carbamide peroxide. Color was recorded at baseline (BA); 1-week (1W); end of the treatment (ET); and 2 years (2Y) after bleaching, using the Vita Classical shade guide. The perception of TS was recorded on a 0-4 scale during and 2Y after bleaching. The variation in shade guide units (ΔSGU) from BA vs. 1W was compared to ΔSGU from BA vs. 2Y using paired t-test. The percentage of subjects who reported TS was evaluated by Fisher’s exact test. The intensity of TS was evaluated by a Mann-Whitney test (α=0.05). Results: Both bleaching techniques demonstrated equivalent and significant tooth color shade lightening. No significant color rebound occurred after 2Y for both techniques (P= 0.77 and 0.87, for AH and IO respectively). The absolute risk of TS was similar for IO and AH (P= 0.12), however the intensity of TS was significantly higher for IO (P= 0.001). No subjects reported sensitivity after 2Y. (Am J Dent 2012;25:199-204).

CLINICAL SIGNIFICANCE: In-office bleaching produced efficient and long-lasting whitening effect, as well as at-home bleaching, however the in-office bleaching protocol showed a higher intensity of sensitivity.

Introduction

Improvements in the standard of living have increased the number patients seeking cosmetic dentistry therapies. As whiter teeth are perceived as being associated with health and beauty, tooth bleaching has been widely performed by professionals for treatment of discolored teeth. Compared with other restorative treatments, such as porcelain veneers, crowns or composite bonding, this treatment is a very conservative approach.

Different techniques are available for tooth bleaching. Although at-home bleaching achieves a high success rate and it is the most widely taught bleaching technique in the USA, some patients do not adapt well to the at-home protocol as they prefer to use a bleaching tray or do not want to wait 2-3 weeks to see the results of the treatment. Besides that, the compliance of some patients to the daily use of a bleaching tray that is not under the dentist’s control may increase the treatment time and costs. In other clinical scenarios, such as the presence of extensive tissue recession or deep unrestored abfraction lesions, patients still need to be closely monitored. For these circumstances, the in-office bleaching protocol may be more adequate, since it allows close dentist control, avoidance of soft-tissue exposure and material ingestion, reduced total treatment time and greater potential for immediate results enhancing patient satisfaction and motivation.

Clinical trials have compared the performance of high and low-concentrated agents for at-home or in-office tooth bleaching and the majority has shown a similar whitening effect for both concentrations and techniques. Nevertheless, the incidence of tooth sensitivity or gingival irritation is more common when the agent concentration is higher.

As patients look for an effective esthetic treatment, they also expect that the treatment chosen will last for a long period of time. Although a regression of color over time has been reported for the at-home bleaching, there is a general perception among clinicians that at-home bleaching produces more long-lasting results than in-office bleaching without a substantial support of scientific evidence. Comparing 9-month clinical longevity of both bleaching therapies did not detect any significant difference among both protocols. Few randomized clinical trials have evaluated the longevity of the whitening produced by in-office bleaching and those available report only short-term results.

The present randomized clinical trial evaluated and compared the 2-year longevity of bleaching efficacy and sensitivity produced by at-home and in-office bleaching therapies. This study was prepared according to the Consolidated Standards of Reporting Trials (CONSORT) statement.

Materials and Methods

Experimental design - This clinical investigation was approved under protocol number 08272/08 by the Institutional Review Board of the local Ethics Committee of the State University of Ponta Grossa, Brazil. Based on pre-established criteria, 60 volunteers were selected for this study. Two weeks before the bleaching procedures, all the volunteers received a dental screening and a dental prophylaxis with pumice and water in a rubber cup. All subjects signed an informed consent form.

Study design - This was a randomized, double-blind, clinical trial with an equal allocation rate to receive either one of two treatments. The study took place in the School of Dentistry of the State University of Ponta Grossa, Brazil, from October 2007 to August 2010.

Inclusion and exclusion criteria - Subjects included in this clinical trial were at least 18 years old and had good general
and oral health. A total of 202 participants were examined to check for the inclusion and exclusion criteria. Participants needed to have six caries-free maxillary anterior teeth without restorations on the labial surfaces, be willing to sign a consent form and have central incisors determined to be shade C2 or darker, according to a value-oriented shade guide [Vita Lumin Vacuum (now marketed as Vita Classical)]\textsuperscript{19}. Subjects were excluded from the study if they had undergone tooth-whitening procedures, had labial anterior restorations, were pregnant or lactating, had severe internal tooth discoloration (such as tetracycline stains, fluorosis, pulpless teeth), had bruxism habits or had any other pathology that could cause sensitivity (such as recession, dentin exposure).

**Sample size calculation** - Calculation of the sample size was based on data resulting from previous in-office and at-home bleaching studies.\textsuperscript{17,18} For both bleaching protocols, the primary outcome was the variation in shade guide units (ΔSGU). A sample size of 26 participants were required for both groups to detect a difference of 1 ΔSGU with a 90% statistical power using a standard deviation of 1.5 with a significance level of 5%. In order to account for follow-up losses, 30 participants were selected for each group.

**Study intervention** - Participants were randomly allocated into two experimental groups (n = 30) according to the bleaching technique: in-office or at-home bleaching. The simple randomization process was performed by computer-generated tables by a third person not involved in the research protocol. Once the participant was eligible for the procedure, and completed all baseline assessments, the allocation assignment was revealed by the third person. Neither the participant nor the operator knew the group allocation, being both blinded to the protocol.

The participants from the in-office bleaching received a prophylaxis of all teeth. The lips, cheeks and tongue were isolated using the ArcFlex\textsuperscript{5} lip retractor. The operators then isolated the gingival tissue of the teeth to be bleached by using a light-cured resin dam (Top Dam\textsuperscript{7}). They applied a 35% hydrogen peroxide gel (Whiteness HP\textsuperscript{8}) for a total of 45 minutes. Every 15 minutes during the 45-minute session, they refreshed the in-office bleaching agent. Participants repeated the in-office bleaching treatment 1 week later.

For participants assigned to the at-home group, an alginate impression of each subject’s maxillary arch was prepared and filled with dental stone. To produce study models, block-out material was not applied to the labial surfaces of teeth.\textsuperscript{15} A 1-mm soft vinyl material was used, provided by the manufacturer, to fabricate the custom-fitted tray for the whitening gel. The excess of labial and lingual surfaces was trimmed 1 mm from the gingival junction. The tray and 16% carbamide peroxide gel (Whiteness Standard\textsuperscript{3}) was delivered to each subject with oral instructions for use. All subjects were instructed to wear the tray with agent for at least 6 hours at night. In the morning, subjects were instructed to remove the tray, wash it and brush their teeth with the fluoride toothpaste. The subjects were instructed to wear the custom-fitted tray for 4 weeks. All participants were instructed to brush their teeth regularly with fluoridated toothpaste (Sorriso Fresh Gel\textsuperscript{16}).

**Shade evaluation** - The subjective evaluation of color was performed using a shade guide (Vita Lumina) in the same room under artificial lighting. The shade guide’s 16 tabs were arranged from highest (B1) to lowest (C4) value, making the color C2 as number 7. Although this scale is not linear in the truest sense, the changes were treated as representing a continuous and approximately linear ranking for the purpose of analysis. The measurement area of interest for shade matching was the middle one third of the facial surface of the anterior central incisor.

Two calibrated evaluators, blinded to the allocation assignment, recorded the shade of each participant’s teeth at baseline and immediately after the first and second appointments for the in-office bleaching. For the at-home protocol, the evaluators recorded the shade at baseline, and after 2 and 4 weeks of bleaching protocol. The two examiners were required to have an agreement of at least 85% (Kappa statistic) before beginning the study evaluation.

**Tooth sensitivity evaluation** - Participants were asked to record, on a daily basis, their tooth sensitivity, according to the 5-point Numerical Rating Scale,\textsuperscript{17,18} with the following criteria: 0 = none, 1 = mild, 2 = moderate, 3 = considerable and 4 = severe. These values were averaged for statistical purposes and grouped into two categories: the overall percentage of subjects with tooth sensitivity and the overall intensity of tooth sensitivity. At the 2-year recall subjects were also asked to record their tooth sensitivity.

All participants were evaluated at baseline, 1 week after the end of the treatment and 2 years after bleaching. A standardized questionnaire related to diet and oral hygiene behavior was used specifically for the participants at the 2-year recall appointment. Subjects were asked about the usage of whitening toothpaste after bleaching; if they underwent another bleaching treatment after the active treatment was completed; and the daily intake frequency and type of staining beverage and food, such as coffee, tea, wine, cola, artificial juices, chocolate, beetroot or spinach, and smoking habits.

**Statistical analysis** - The analysis followed the intention-to-treat protocol and involved all participants who were randomly assigned, even those that were not able to be analyzed in the scheduled recall visits.\textsuperscript{16} In this case, we filled in the missing data carrying the last observed value of such patient. The statistician was blinded to the study groups. The agreement between examiners was evaluated using the Kappa statistic.

Tooth shade changes were determined by calculating the shift in the number of ΔSGU that occurred toward the lighter end of the scale. Two ΔSGU were calculated: one taking the baseline color vs. the color 1 week after the end of the bleaching protocol (ΔSGU 1 week) and the other taking the baseline color vs. color taken at the 2-year recall (ΔSGU 2 year). A paired Student t-test was used to compare the ΔSGU 1 week and ΔSGU 2 year for each bleaching therapy. A Student t test for independent data was used to compare the bleaching efficacy (ΔSGU) at each assessment point for both therapies. The least square mean differences as well as the confidence interval were calculated.

The relative risks of tooth sensitivity for both bleaching therapies were compared using the Fisher’s exact test (α = 0.05). The median of the tooth sensitivity intensity experienced by each patient throughout the 4-week at-home and the 2-week in-office therapies was used for statistical purposes. The intensity of tooth sensitivity of both bleaching therapies were compared using the Mann-Whitney test (α = 0.05).
Fig. 1. Flow diagram of the clinical trial including detailed information on the excluded participants.

Table 1. Change in tooth shade (mean and standard deviation) between assessment points for the two treatment groups (*).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ΔSGU (Baseline vs 1 wk)</th>
<th>ΔSGU (Baseline vs 2 yrs)</th>
<th>Least square mean difference (95% CI)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>At-home (n=30)</td>
<td>6.27 ± 1.5</td>
<td>6.02 ± 1.4</td>
<td>0.77</td>
<td>0.25 (-0.5 – 1.0)</td>
</tr>
<tr>
<td>In-office (n=30)</td>
<td>5.62 ± 0.9</td>
<td>5.32 ± 0.7</td>
<td>0.87</td>
<td>0.30 (-0.1 – 0.7)</td>
</tr>
</tbody>
</table>

P-value** 0.51 0.47

* Paired t-test; ** unpaired t-test; CI: Confidence interval.

Results

Figure 1 depicts the participant flow diagram. All 60 participants who began the study, completed it. The mean ages of the participants were 21 ± 3.8 and 21 ± 3.2 years for at-home and in-office groups respectively. Males comprised 47.8 and 26.6% of participants in the at-home and in-office groups, respectively.

Table 1 depicts the ΔSGU calculated after each assessment point for both bleaching protocols. Both techniques yielded a whitening of approximately five to six shade guide units. No significant darkening occurred by the 2-year recall (P< 0.77 and P< 0.87 respectively, for at-home and in-office techniques). The bleaching efficacy of at-home and in-office bleaching was not statistically significant either 1 week after the end of treatment (P< 0.51) or 2 years later (P< 0.47).

Table 2 shows the number of subjects who reported tooth sensitivity during bleaching treatment. Statistically similar (P = 0.12) absolute risk of tooth sensitivity was reported by subjects from the in-office and at-home bleaching. None of the participants from either bleaching technique complained of tooth sensitivity at 2 years (P = 1.0).

Regarding tooth sensitivity intensity (Table 3), there was a statistical difference between the bleaching therapies (P = 0.001). Most of the participants from the at-home group experienced none to mild sensitivity, while most in the in-office bleaching group experienced mild to moderate sensitivity. Figure 2 shows the levels of sensitivity (%) perceived by the participants for both groups during the treatment. At 2 years, none of the participants reported tooth sensitivity.

Ten subjects (33.3%) from the in-office group and 18 subjects (60%) from the at-home group consumed at least one kind of staining beverage every day. Only one subject from the in-office group and three subjects from the at-home group were daily smokers. From the in-office group, one subject reported using a new bleaching agent after treatment and none of them...
used tooth whitening paste, while in the at-home group none of the subjects reported using a new bleaching agent, and four (13.3%) subjects used a whitening toothpaste. Details of the daily frequency of staining beverage and subject behavior are shown in Table 4.

**Discussion**

Investigators have used different methodological approaches to assess tooth shade and changes in tooth shade resulting from bleaching treatments. Recently, digital systems (spectrophotometers, colorimeters or digital cameras) have been used to measure tooth shades. These systems express color in three-dimensional specifications and allow for more accurate assessments. These digital systems are precise instruments that produce highly reliable, easily evaluated results. High cost and complex operation could be unique disadvantages for some of these methods.

A recent study evaluating the validity and reliability of visual assessment of tooth color using a commercial shade guide (Vitapan Classical shade guide) reported that despite its subjectivity such visual assessment was a valid method, with good reliability in differentiating between dark and light colors. Other clinical studies comparing the color change after different bleaching techniques using a subjective method (shade guide) and an objective method (spectrophotometer) usually reported similar outcomes with both evaluation methods. In the present study, the shade guide was used for color change evaluation because it is an easy, fast and reliable method supported by the literature.

The results of the present investigation showed that both techniques were effective and reached similar results when used following their respective protocols. At the end of the treatment, a mean variation of 6.2 and 5.6 SGUs was observed for the in-office and at-home techniques, respectively. Auschill et al showed that at-home bleaching with 10% carbamide peroxide gel and in-office bleaching with 35% hydrogen peroxide lightened teeth six shades on the Vita color scale, which is in line with the present investigation and other studies.

The efficacy of a bleaching technique depends on the concentration of the hydrogen peroxide and the application duration. However, the relationship between hydrogen peroxide concentration and application time is not linear but exponential. This explains why for the 16% carbamide peroxide (~5% hydrogen peroxide) a 4-week treatment with at least a 6-hour daily use (~ a total of 168 hours) was required to reach the same whitening effect produced by an overall 1.5-hour treatment time using of the 35% hydrogen peroxide gel. This exponential relation was recently demonstrated in a laboratory setting and means that bleaching gels with a higher peroxide concentration needed fewer applications/reduced time to produce a similar bleaching effect.

To the extent of the authors' knowledge, no study has evaluated the longevity of whitening produced by bleaching with 35% hydrogen peroxide for prolonged periods, i.e. more than 1 year. Previous findings have already reported color rebound for at-home bleaching. Ritter et al reported that 38 months after the end of at-home bleaching treatment, 62% of the participants reported slight darkening. Leonard et al found a color rebound of two shade guide units over a period of time ranging from 6 to 47 months with 10% carbamide peroxide, which was similar to the findings of other clinical trials. It is widely reported that with in-office bleaching the color reverses in a few days. This ΔE reversal was shown to be of the order of 51% and 65% after 1 and 6 weeks post-bleaching, respectively for eight in-office products. Many aspects may account for this long-term color reversal. The effect of staining produced by beverages and food is usually believed as explanation for the slight darkening that follows bleaching over time. However one should consider that this staining is usually extrinsic and although it may affect the overall perception of whiter teeth, this can be easily removed by professional cleaning. In the present investigation none of the consumption parameters were shown to be associated with the longevity of the treatment. These findings do not necessarily mean that these parameters do not influence the longevity of the whitening, since the study design was not planned to detect such association. Further studies should address this question.

Color rebound can also result from reversal of oxidative reactions so that the shorter and lighter molecules produced by the bleaching therapy return to their original configuration and yellower color. Another explanation for the color rebound is the fact that as teeth get older, there is a continuous deposition of secondary dentin by the pulp. As the dentin thickness increases, teeth appear yellower. Unfortunately, the length of time that it takes to change one Vita shade tab due to deposition of secondary dentin is unknown and may take longer than the period of 2 years of the current study. Future studies need to be done to test this hypothesis.

Surprisingly, however, the present investigation reported that both techniques achieved stable results at the 2-year recall. A 2-year follow-up may be a short recall time to detect the effects of continuous deposition of secondary dentin on the outcome of bleaching.

Another interesting finding of the present investigation was that this study challenged the widespread concept that the at-home bleaching may produce more long-lasting results than in-si...
Tooth sensitivity is the most common adverse side effect of remineralization and rehydration that occurs after each bleaching session. It does not mean ineffective bleaching, since it is due to demineralization and rehydration that occurs after each bleaching session. It is known that isolation can cause the teeth to dehydrate, and it takes at least 30 minutes for teeth to rehydrate. Also, most of the bleaching gels possess an acidic pH ranging from 2.4 to 6.2 and therefore teeth are also demineralized by the bleaching gels.

In order to gather more stable results with less color reversal, more than one clinical session may be required and this seems to be the key feature for the long-lasting results of the present study. According to Shethri et al., only a second session of in-office bleaching treatment, tooth lightness improved significantly. Therefore, a single in-office treatment with 35% hydrogen peroxide seems to be not enough to bleach teeth to the same rate of the well-accepted at-home technique.

Tooth sensitivity is the most common adverse side effect of bleaching and according to Leonard et al., 25-75% of subjects receiving the active bleaching ingredient experience tooth sensitivity. In the present study it was observed that the incidence of tooth sensitivity in the at-home and in-office bleaching was similar, which is in agreement with others. However, significant differences were observed between techniques when the intensity of tooth sensitivity was compared as well as in a previous study. While most of the participants from the at-home bleaching experienced none to mild sensitivity, most of the participants from in-office group reported mild to moderate sensitivity.

Cooper et al. showed that a very fast passage of hydrogen peroxide occurs through the dental structure; within 15 minutes after application, hydrogen peroxide can be detected at the pulp. Thus, using a higher hydrogen peroxide concentration, there may be larger amounts of reactive species arriving to the pulp, leading to a more intense inflammatory response and tooth sensitivity. A previous laboratory study demonstrated that the cytotoxicity of carbamide peroxide bleaching gels was dose-dependent, with the highest concentration causing the most intense cytotoxic effects to the cultured cells.

None of the participants from both bleaching techniques reported tooth sensitivity in the 2-year recall. Generally, tooth sensitivity caused by at-home bleaching occurs in the first 2 weeks of treatment, often in the first few days and decreases as the teeth are accustomed to the procedure, but occasional single-day episodes of sensitivity may occur over the course of the treatment. For in-office bleaching, tooth sensitivity usually occurs within the 24 hours following the bleaching protocol. The lack of tooth sensitivity after long-term evaluation seems to be consistent in the literature. Most of the studies that evaluated the longevity of tooth bleaching reported that subjects did not report tooth sensitivity after the end of the bleaching.

In the present study tooth sensitivity was assessed using a 5-point numerical rating scale (NRS) as this has been used for tooth sensitivity evaluation in the great majority of the clinical trials involving bleaching and therefore allows comparison with the earlier results. The other common scale for tooth sensitivity evaluation is the visual analog scale (VAS). Although we have not found in the bleaching literature any study that compared the VAS and 5-point NRS, some earlier studies pointed out that both scales yield similar results. This lack of comparison between these two scales should be the focus of future investigations regarding tooth sensitivity from bleaching therapies.

It is worth mentioning the limitations of the present study. The fact that the participants were taken from a convenient sample (participants seeking professional dental treatment) may lead to bias, since they are much more motivated than participants taken from outside the school. In addition, most of the participants were young adults, which affect the generalizability of the findings of the present investigation to the overall population.

In summary, both techniques were effective to whiten teeth and produced long-lasting and satisfactory results. Thus, the choice of the bleaching technique depends on the professional as well as patient preferences. At-home and in-office bleaching are effective protocols for vital teeth bleaching, however a higher intensity of tooth sensitivity was reported for in-office bleaching.

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c. Colgate-Palmolive Company, São Paulo, SP, Brazil.

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