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Clinical Research

Comparison of the Effects of In-office Bleaching Times on Whitening and Tooth Sensitivity: A Single Blind, Randomized Clinical Trial

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Clinical Relevance

This randomized clinical trial provides significant evidence that it is possible to obtain efficacy of whitening with lower tooth sensitivity when in-office bleaching is applied only two times for a period of 15 minutes during each bleaching session.

SUMMARY

Objectives: The objective of the present study was to compare the bleaching efficacy (BE) and tooth sensitivity (TS) of in-office bleaching applied under different time protocols.

Methods and Materials: Fifty-three patients were randomly distributed into three groups: the bleaching agent was applied in one (1×15), two (2×15), or three (3×15) 15-minute applications. The labial surfaces of the anterior teeth were bleached using a 35% hydrogen peroxide gel. Two bleaching sessions with a one-week interval between were performed. The shade evaluation was performed with a visual shade guide and spectrophotometer before and 30 days after bleaching. Participants recorded TS with a five-point verbal scale. Color change was analyzed by one-way analysis of variance and Tukey tests. The absolute risk of TS and TS intensity were evaluated by the Fisher exact and Friedman/Kruskal-Wallis tests, respectively ($\alpha = 0.05$).

Results: Significant whitening was observed in all groups, with statistically lower BE for the

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1×15 group ($p<0.05$). The absolute risk of TS (95% confidence interval) was lower for the 1×15 group than for the other groups ($p<0.05$). The TS intensity of the 3×15 group was statistically higher than that associated with the other protocols ($p<0.05$).

Conclusions: A single 15-minute application produced less TS but reduced BE. The protocol with 2×15 produced a degree of BE similar to that of the 3×15 group, but with reduced overall TS intensity.

INTRODUCTION

Nowadays, concerns about tooth discoloration have increased[1-3] as more emphasis is being placed on having a "beautiful smile" as an expression of health and vitality, mainly by media and dental manufacturers of tooth-whitening products.[4,5] This has increased the popularity of and demand for dental bleaching.[2,3,6]

Tooth bleaching is the most frequently requested procedure by patients because it is a highly effective and conservative way to improve the appearance of a patient's smile when compared to invasive restorative treatments.[2] Additionally, dental bleaching increases the oral health–related quality of life.[7,8]

In-office dental bleaching has been practiced for more than 100 years and has some advantages over at-home bleaching. In-office bleaching allows close dentist control, avoids material ingestion, and is associated with reduced total treatment time, with great potential for achieving some degree of whitening after one clinical appointment, which enhances patient satisfaction and motivation.[9,10]

However, tooth sensitivity (TS) is a very common adverse effect associated with in-office bleaching.[11-13] Although bleaching-induced TS is not fully understood,[14] it is hypothesized that it comes from the ability of hydrogen peroxide (HP), free radicals, and related by-products to penetrate tooth structure and, upon reaching the pulp,[15,16] produce dental inflammation.[17] At high HP concentrations, the antioxidant capacity of the pulp cells can be easily exceeded, producing oxidative stress and cell damage.[17,18] This explains the higher TS intensity of the in-office bleaching compared to at-home bleaching.[12,13]

In an attempt to reduce this side effect produced by bleaching products, several therapies have been proposed, such as the application of desensitizing agents, administration of analgesics or anti-inflammatory drugs, and the use of bleaching gels containing desensitizing agents[4,9,13,19-25] or the use of in-office bleaching gels with lower HP concentrations.[26,27]

In-office bleaching usually requires a longer application period with changes of the bleaching agent on the tooth surface in each clinical appointment to obtain optimum results.[28-31] In an attempt to reduce the amount of HP that reaches the pulp, researchers investigated whether reduced contact time of the bleaching gels could yield less-adverse effects while still being effective. This approach minimized the deleterious effects of HP to odontoblast-like cells[29-31] and dental pulp of rats[32] while not affecting the overall esthetic outcome in an *in vitro* study.[29-31]

To the best of the authors' knowledge, no clinical study to date has investigated the effectiveness (color change) and side effects (TS) of in-office bleaching performed with a reduced number of changes of the bleaching gel. The null hypotheses tested were that the changes in the in-office bleaching gel would not result in different degrees of 1) color change, 2) absolute risk of TS, or 3) intensity of TS.

METHODS AND MATERIALS

This clinical study was approved by the ethics committee of the local university. The experimental design followed the CONSORT statement.[33] Based on preestablished criteria, 53 volunteers were selected for this study. Two weeks before the bleaching procedures, all of the volunteers received a dental screening and a dental prophylaxis with pumice and water in a rubber cup and signed an informed consent form.

Study Design

This was a randomized, examiner-blind clinical trial with an equal allocation rate. The study took place in the clinics of the Dentistry School of the State University of Ponta Grossa from June 2011 to June 2012.

Inclusion and Exclusion Criteria

Patients included in this clinical trial were men and women between 18 and 30 years of age and had good general and oral health. Participants were recruited from the city of Ponta Grossa (Paraná, Brazil). The participants needed to have six maxillary and mandibular anterior teeth without caries lesions or restorations. The maxillary canine was shade A3 or darker as judged by comparison with a value-oriented shade guide (VITA Classical Shade Guide,

Vita Zahnfabrik, Bad Säckingen, Germany). Participants were excluded from the study if they presented with anterior restorations; had bruxism habits; were pregnant/lactating; were smokers; presented with severe internal tooth discoloration (tetracycline stains, fluorosis, pulpless teeth); were taking any drug with anti-inflammatory, analgesic, or antioxidant effect; or presented with recession and dentin exposure.

Sample Size Calculation

The primary outcome of this study was color change. It had already been reported that two bleaching sessions with the product Whiteness HP Maxx 35% (FGM Dental Products, Joinville, SC, Brazil) produce a whitening effect of around 7 ± 2 shade guide units (SGUs).[9,19,20,26] In order to detect a difference of 2 SGUs between means of any pair of the study groups, with a power of 80% and an alpha of 5%, a minimum sample size of 17 patients was required per group.

Study Intervention

Participants were randomly divided into three groups according to the number of changes of the bleaching gel in each clinical appointment: one 15-minute application (1×15 group); two 15-minute applications (2×15 group), and three 15-minute applications (3×15 group). The randomization process was performed in blocks of three and six using computer-generated tables. This procedure was performed by a third person who was not involved in the intervention procedures. The allocation sequence was placed in sealed and opaque envelopes and was only opened immediately before the beginning of the bleaching protocol.

The participant and the operator could not be blinded to the procedure, as the application of bleaching gel for different times could not be masked. However, the examiners who evaluated the color changes were not aware of which group the participant was assigned to. Before the start of the bleaching procedure, the color was confirmed using an Easyshade spectrophotometer (Vident, Brea, CA, USA), described in detail in the item color evaluation.

Bleaching Procedure

The gingival tissue of the teeth to be bleached was isolated using a light-cured resin dam (Top Dam, FGM Dental Products). In each clinical appointment, the 35% HP Whiteness HP Maxx (FGM Dental Products) was applied in a single (1×15) visit or via two (2×15) or three 15-minute (3×15) applications, following the manufacturer's directions. In the groups in which more than one application was performed, the product on the tooth surface was removed using an aspirating tip, and the product was applied again.

Two bleaching sessions, with one-week intervals between, were performed. All participants were instructed to brush their teeth regularly (four times a day) using fluoridated toothpaste (Sorriso Fresh, Colgate-Palmolive, São Paulo, SP, Brazil) provided by the study investigators.

Table 1: *Color Change Between Baseline and 1-Month Assessment (Means and Standard Deviations) for ΔSGU (Delta Shade Guide Units), ΔL, Δa, Δb, and ΔE for the Three Treatment Groups*[a]

	Groups		
	1 × 15 min	**2 × 15 min**	**3 × 15 min**
Subjective evaluation (ΔSGU)	4.2 ± 1.1 b	7.7 ± 1.3 a	8.0 ± 1.0 a
Objective evaluation (spectrophotometer–CIELab parameter)			
ΔL	0.4 ± 3.3 B	2.4 ± 1.4 A	2.0 ± 1.5 A
Δa	−0.3 ± 0.7 B	−1.5 ± 1.8 A	−1.2 ± 1.4 A
Δb	−5.1 ± 1.8 B	−7.3 ± 3.1 A	−8.3 ± 4.2 A
ΔE	4.5 ± 2.0 B	7.9 ± 2.1 A	8.4 ± 3.6 A

[a] *Comparisons are valid only within rows. Means identified with the same lowercase or uppercase letters are statistically similar (one-way analysis of variance [ANOVA] and Tukey test;* $p < 0.001$).

Color Evaluation

Shade evaluation was recorded before and 30 days after the bleaching treatment using two methods: subjective evaluation using a value-oriented shade guide (Vita Lumin, Vita Zahnfabrik) and an objective evaluation using the Easyshade spectrophotometer (Vident).[22-24]

For the subjective examination, the shade guide's 16 tabs were arranged from highest (B1) to lowest (C4) value. Although this scale is not linear in the truest sense, we treated the changes as representing a continuous and approximately linear ranking for the purpose of analysis. The measurement area for shade matching was the middle third of the facial surface of the anterior central incisor. This measurement was done at baseline and 30 days after bleaching, allowing for the calculation of means and standard deviations of the delta shade guide units (ΔSGUs) of each group.

For calibration purposes, five participants who we did not include in the sample participated in the training phase of this study. The two examiners, blinded to the allocation assignment, scheduled these participants for bleaching and evaluated their teeth against the shade guide at baseline and 30 days after the procedure. The two examiners were required to have an agreement of at least 85% (kappa statistic) before beginning the study evaluation. During the study, if disagreements arose, the examiners reached a consensus before dismissing the patient.

For the objective examination, the color measurement was done with the spectrophotometer Vita Easyshade (Vident). Before the spectrophotometer measurement, an impression of the maxillary arch was taken with dense silicone paste (Coltoflax e Perfil Cub, Vigodent, Rio de Janeiro, Brazil). The impression was extended to the maxillary canine and served as a standard for placement of the spectrophotometer probe in the same place during consecutive color evaluation. The measurement area of interest for shade matching was the middle one-third of the labial surface of the right maxillary canine. A window was created on the labial surface of the molded silicone guide for the central incisor to be evaluated. The window was made using a metallic device with well-formed borders, 3 mm in radius.

The measurement was done on all participants using the Vita Easyshade spectrophotometer (Vident) before and 30 days after the bleaching therapy by only one operator. The shade was determined using the parameters of the Easyshade device which indicated the following values: L*, (a*), and (b*), in which L* represents the value from 0 (black) to 100 (white) and a* and b* represent the shade, where a* is the measurement along the red-green axis and b* is the measurement along the yellow-blue axis. The shade comparison before and after treatment was given by the differences between the two shades (ΔE), which is calculated using the following formula:[22-24] $\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$. Three readings were done at each time period, and the shade detected at least twice in these three readings was considered for statistical purposes.

Tooth Sensitivity Assessment

The patients recorded their perception of TS during the first and second bleaching sessions using a five-point rating scale (0 = none, 1 = mild, 2 = moderate, 3 = considerable, and 4 = severe).[9,19] We asked subjects to indicate whether they experienced TS during the treatment and up to 48 hours postbleaching. As two bleaching sessions were performed, the higher score value obtained in both bleaching sessions was considered for statistical purposes. The values were arranged into two categories: overall percentage of patients who reported TS at least once during treatment (absolute risk of TS) and overall TS intensity in different periods (during treatment up to one hour; from one to 24 hours, and from 24 to 48 hours postbleaching). The patients were also instructed to record the painful tooth.

Statistical Analysis

The analysis followed the intention-to-treat protocol and involved all participants who were randomly assigned.[33] The color change (primary outcome) was used to determine the efficacy of the bleaching treatment. The ΔSGU (subjective measurement), ΔL, Δa, Δb, and ΔE (objective measurement) values of different groups were evaluated by one-way analysis of variance (ANOVA). The Tukey test was used for pairwise comparisons.

The absolute risk of TS of both groups was compared using the Fisher exact test. The effect of period (during and up to one hour after procedure; from one to 24 hours after bleaching, from 24 to 48 hours after bleaching) was tested with the Friedman test. The effect of the group on the TS intensity at each period was compared using the Kruskal-Wallis and Mann-Whitney tests. In all statistical tests, the alpha was pre-set at 0.05.

RESULTS

A total of 101 participants were examined to select 53 participants (Figure 1). The mean age (years) of the participants was similar between groups (23.2±3.3, 21.2±4.0, and 25.6±2.4 years, respectively, for groups 1×15, 2×15, and 3×15). The majority of patients were male (58.5%, 72.2%, and 61.1%, respectively, for groups 1×15, 2×15, and 3×15).

Color Change

The mean baseline color of the participants from the three groups was similar between groups (10.4±1.5, 11.5±1.8, and 10.7±1.0, respectively for groups 1×15, 2×15, and 3×15). The subjective and objective evaluations showed a statistically significant higher degree of whitening after one-month postbleaching evaluation for the 2×15 and 3×15 groups compared with the 1×15 group (Table 1; $p<0.001$ for both methods). Whitening of approximately 7.7 and 8.0 SGUs was detected for the 2×15 and 3×15 groups, respectively, and a variation of 7.9 to 8.4 in the ΔE

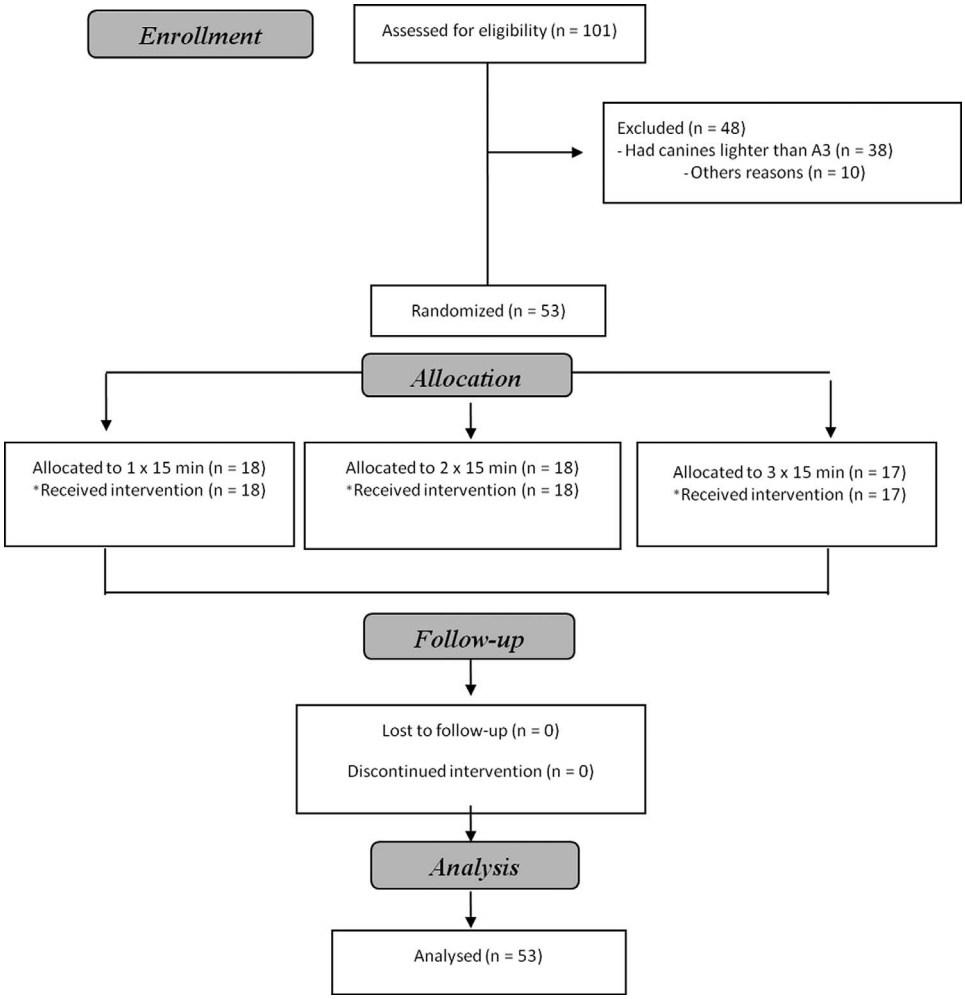

Figure 1. *Flow diagram of the clinical trial including detailed information on the excluded participants.*

was observed for the 2×15 and 3×15 groups, respectively (Table 1; $p>0.32$). On the other hand, only 4.2 SGUs and 4.5 ΔE were observed for the 1×15 group, respectively, in subjective and objective evaluations. The results of the subjective (visual shade guide) and the objective evaluations (spectrophotometer) matched the hypothesis of difference between the groups one month after bleaching ($p<0.001$ for both methods).

Tooth Sensitivity

In regard to the absolute risk of TS, a significant difference was observed between groups (Table 2; $p=0.02$), with the 1×15 group presenting the statistically lowest TS risk. Most of the TS complaints occurred within the first 24 hours after bleaching (Table 3). Only six participants from group 1×15, 9 from group 2×15, and 15 from group 3×15 complained about TS 24 hours after bleaching. The intensity of TS was the highest for the 3×15 group within the first 24 hours (Table 3; $p=0.001$)

DISCUSSION

As a result of the difficulty of measuring color clinically, in the present study we used a shade guide and a spectrophotometer. However, it is also difficult to make a comparison of color change after bleaching, according to previously published literature, because of the different color scales and devices of measurement, as well as the different units of measurement used.[2] Regardless, all in-office bleaching techniques investigated in this randomized clinical trial showed significant color change after two bleaching sessions, which is in agreement with the findings of a recently published literature review[2,34] and clinical trials, mainly for the 2×15 and 3×15 groups after two bleaching sessions,[12,20,24-26,35] which led us not to reject the first null hypothesis.

The whitening effect is related to the concentration, application time, and the number of changes of in-office bleaching gel.[26,29-31,36-38] Despite the find-

Table 2: *Comparison of the Number of Patients Who Experienced Tooth Sensitivity at Least Once During the Three Different Bleaching Regimens Along With Absolute Risks and the Statistical Comparison*[a]

Groups	Tooth Sensitivity, No. of Participants		Absolute Risk (95% Confidence Interval)
	Yes	No	
1 × 15 min	11	07	61 (39-80) A
2 × 15 min	15	03	83 (60-94) AB
3 × 15 min	16	01	94 (73-98) B

[a] *Fisher exact test. Means identified with the same letters are statistically similar ($p<0.05$).*

ings of a recent study[38] that reported that after a single 45-minute application there are still substantial concentrations of HP, this amount may not be enough to sustain the same degree of bleaching obtained in the first 15 minutes, a period during which the availability of HP might be much higher than it is after 45 minutes.[37]

In the present study, there is an association between the effects of application time vs number of gel changes. In the 3×15 group, the gel was maintained for a period that was three times longer, and the gel was refreshed twice more than in group 1×15. The significantly lower amount of gel applied on the tooth surfaces of patients from the 1×15 group can explain the lower whitening effect of this group in comparison to the other groups.[34,39]

Interesting results were found when the bleaching gel was refreshed only twice (2×15), as it reached a similar degree of whitening as was obtained by the conventional 3×15 application suggested for the bleaching gel used. This has an important clinical implication, as it reduces the total chair time and also the amount of bleaching gel required for bleaching, which favors the clinicians' preference for simplification.

Table 3: *Tooth Sensitivity Intensity (Medians and Interquartile Ranges) at the Different Assessment Points for Both Study Groups and the Statistical Comparison*[a]

Assessment Periods	Groups		
	1 × 15 min	2 × 15 min	3 × 15 min
During bleaching up to 1 h	0 (0/1) Aa	1 (0/2) Cb	2 (0/2) Eb
From 1 to 24 h after bleaching	0 (0/1) Ac	0 (0/1) Bc	2 (0/1) Ed
From 24 h to 48 h after bleaching	0 (0/0) Ae	0 (0/0) Be	0 (0/0) De

[a] *Uppercase letters indicate comparisons within groups for the different assessment periods (Friedman test). Lowercase letters indicate comparisons within each assessment period for the different groups (Kruskal-Wallis and Mann-Whitney tests). Similar letters indicate statistically similar medians.*

The absolute risk of TS was greater than 50% in all study groups. The literature reports that TS is a common side effect of bleaching treatments,[11-13,20] and this was confirmed in the present study. HP has a low molecular mass, which favors its rapid diffusion into enamel prisms and interprismatic spaces.[40,41] When it reaches dentin, the HP can easily travel to the pulp chamber through dentinal tubules.[15,16] At high concentrations, HP causes reduction of cell proliferation, metabolism, and viability,[18] and it reduces the pulp-reparative capacity.[42] Additionally, sites of tissue necrosis in teeth with reduced dimensions, such as mandibular incisors, have already been reported.[17] Taken together, these factors may be responsible for the bleaching-induced TS reported by most patients who have undergone bleaching procedures.[11-13,20]

Although a high prevalence of TS was reported in all study groups, the absolute risk and the overall TS intensity were significantly different among them, which led us not to reject the second and third null hypotheses. *In vitro* studies have reported that three consecutive applications of a highly concentrated HP (group 3×15) led to higher amount of HP in simulated pulp chambers,[29-31] with a consequent increase in toxicity to cultured odontoblast-like cells.[29,30] This was much less pronounced with a single 15-minute application (group 1×15).[29,30]

It seems that the bleaching-induced damage of the dental tissue is cumulative and proportional to the amount of HP that reaches this tissue. For instance, Cintra and others[32] evaluated pulp tissue in rats after several bleaching sessions. Significant bleaching-induced changes were observed after one bleaching session with three 15-minute applications, but the extent and intensity of these changes became more severe as more bleaching sessions were performed. Thus, the difference in the amount of the HP that reaches the pulp chamber in the three bleaching protocols might explain the differences in the absolute risk and intensity of TS observed in this study.

Despite the better results in terms of TS in the 1×15 group, this group was not as effective as the others in terms of whitening degree with only two bleaching sessions. However, this does not mean that effective bleaching cannot be achieved. In an *in vitro* protocol, Soares and others[30] demonstrated that five bleaching sessions of a single 15-minute

application can gain the same level of whitening produced by the conventional two bleaching sessions with three 15-minute applications each, with considerably fewer adverse effects. Future clinical studies should attempt to investigate bleaching effectiveness and adverse effects of this shorter protocol of a single 15-minute application for as many bleaching sessions as needed to achieve the patient's satisfaction.

At first glance, multiple bleaching sessions of a single 15-minute application have the problem of increasing the bleaching costs, but this drawback may be outweighed by the reduction in the damage produced in the pulp tissue[29-31] and the reduction in the risk and intensity of TS that arises from this shorter clinical protocol. In addition, a protocol comprising multiple bleaching sessions of a single 15-minute application may play an important role in pulp-dentin stimulation and healing.[43,44]

CONCLUSIONS

Within the limitations of this study, a single 15-minute application of an in-office bleaching gel significantly decreased the risk and intensity of TS but yielded a lower whitening degree after two bleaching sessions. Two 15-minute applications did not reduce the risk of TS but minimized its intensity and whitened to the same extent as did the conventional three 15-minute applications.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the State University of Ponta Grossa. The approval code for this study is 44/2011.

Conflict of Interest

No, the authors have no proprietary, financial, or other personal interest of any interest in any product, service, and/or company that is presented in this article.

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