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Clinical Research

Comparison of the Effect of Agitation on Whitening and Tooth Sensitivity of In-Office Bleaching: A Randomized Clinical Trial

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Clinical Relevance

Although there is a common belief that agitation of the in-office bleaching gel with a microbrush should be applied to bring fresh bleaching gel into contact with the tooth surface, it seems to be unnecessary because no improvement in bleaching efficacy was observed.

SUMMARY

Objective: This single-blind, split-mouth, randomized trial was aimed at evaluating the bleaching efficacy (BE) and tooth sensitivity (TS) of a 20% hydrogen peroxide (HP) bleaching agent used under active or passive application.

Methods and Materials: Twenty-two patients with canines darker than C2 were selected. Teeth were bleached in two sessions, with a one-week interval between treatments. The bleaching agent was applied using active (HPactive) or passive (HPpassive) application. Each tooth in the HPactive-allocated hemiarch received bleaching gel with sonic activation after 10 and 30 minutes from the start of treatment, with rounded movements all over the buccal surface. The color changes were evaluated by subjective (Vita Classical and Vita Bleachedguide) and objective (VITA Easyshade Spectrophotometer) methods at baseline and 30 days after the second session. TS was recorded

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up to 48 hours after treatment using a 0-10 visual analog scale. Color change in shade guide units (SGUs) and ΔE was analyzed using a Wilcoxon test (α=0.05). The absolute risk and intensity of TS were evaluated using McNemar test and a Wilcoxon test, respectively (α=0.05).

Results: Significant whitening was observed in both groups after 30 days of clinical evaluation. The activation did not significantly influence BE (ΔSGU HPpassive=5.6 and HPActive=5.8; *p*=0.98; and ΔE HPpassive=10.6 and HPactive=10.3; *p*=0.83). Absolute risk of TS (HPactive=36.4% and HPpassive=31.8%; *p*=0.94) was similar for both groups (Fisher exact test). TS intensity (visual analogue scale) was higher during the bleaching sessions and up to 24 hours thereafter for both groups, with no differences between groups (two-way analysis of variance and Tukey).

Conclusion: The active application of a 20% HP gel did not improve BE and TS.

INTRODUCTION

Tooth bleaching is an easy, noninvasive alternative treatment for tooth discoloration that promotes excellent esthetic results.[1,2] It basically consists of the application of hydrogen peroxide (HP) to tooth surfaces using two techniques: at-home bleaching with carbamide peroxide (10%-22%) or HP (3%-10%) applied in an individual tray and in-office bleaching with higher-concentration HP (35%-40%).[3]

Although the at-home bleaching is the most frequently used treatment method for vital teeth, patients mostly ask for in-office bleaching due to its advantages, which include total control of the gel application, no need for tray use, and achievement of satisfactory results in one session.[4,5] However, tooth sensitivity (TS) is the most common side effect associated with in-office bleaching.[4,1] Such sensitivity is associated with the diffusion of HP molecules through dental tissues to reach the pulp, mainly when applied in higher concentrations.[6,7]

To improve bleaching safety, some manufacturers developed low-concentration HP (6%-20%) in-office gels. Use of low-concentration HP resulted in significant reduction in HP diffusion into the pulp chamber and, consequently, decreased its cytotoxic effects on pulp cells when compared with higher-concentration HP.[6,7] Some clinical trials also indicated lower risk of TS associated with low-concentration HP gels.[8-10] However, low-concentration HP gels have shown lower bleaching efficacy (BE) than those with high-concentration HP. [10,11]

There are ways to improve the dissociation of HP, mainly because HP acts as a strong oxidizing agent through the formation of free radicals, reactive oxygen molecules, and HP anions.[12] Light usually provides energy for this reaction.[2,13,14] However, another alternative is to agitate the bleaching gel during the application.[15-17] Several studies indicate that, during the in-office application, the clinician should frequently agitate the gel with a microbrush to bring fresh bleaching gel into contact with the tooth surface.[15-18]

Although several clinical studies evaluated the effects of various light sources on BE,[14,19-21] to the extent of our knowledge, no clinical studies have evaluated the effects of in-office bleaching gel agitation during application on BE and TS. Therefore, this single-blind, controlled, split-mouth, randomized clinical trial was aimed at evaluating the color change, risk, and intensity of TS of in-office 20% HP bleaching gel, with or without agitation. The null hypothesis was that bleaching gel agitation will not influence the 1) color change, 2) risk, and 3) intensity of TS.

METHODS AND MATERIALS

This was a randomized, single-blind (evaluators), split-mouth clinical trial with an equal allocation rate between groups. It was approved by the local ethics committee (protocol #49719715.2.00000.5020), and the protocol was also registered in a clinical trial website. This study took place within the dental clinics of the Universidade Federal do Amazonas dental school from January 2015 to February 2016.

Inclusion and Exclusion Criteria

Participants were examined in a dental chair after dental prophylaxis with pumice and water to determine whether they met the study's eligibility criteria. To be included in this study, participants had to be 18 years or older and have good general and oral health. Participants also had to have at least both canines whose coloration was shade C2 or darker as assessed using the value-oriented shade guide (VITA classical A1-D4 shade guide, Vita Lumin, Vita Zahnfabrik, Bad Säckingen, Germany) and at least six sound anterior maxillary teeth. Participants with restorations on the labial surface of their anterior teeth and noncarious cervical lesions, orthodontic devices, gingival recession, full crowns or veneers, endodontically treated teeth, or spontaneous tooth pain or who had internal tooth discoloration, had fluorosis or tetracycline stains, were pregnant or lactating, were using antioxidant or anti-inflammatory drugs, or had bruxism were excluded from the study.

Sample Size Calculation

The sample size calculation was based on the tooth color change measured with a spectrophotometer (ΔE), which was this study's primary outcome. Because the experimental design was split-mouth, the sample size was performed for a hemiarch. If there is truly no difference between the HPactive and HPpassive treatments, then 22 hemiarches are required to be 90% certain that the limits of a two-sided 90% confidence interval (CI) would exclude a difference in means of more than 3 (Δ shade grade units [SGU]) between the groups. Fifteen percent was added to account for any participants lost during the intervention periods, for a total of 25 patients.

Random Sequence Generation and Allocation Concealment

Twenty-five participants were selected according to the inclusion and exclusion criteria for bleaching (split-mouth) with Whiteness HP Blue 20% (FGM dental products, Joinville, SC, Brazil) with bleaching gel agitation or no agitation. A third operator who was not involved in the research protocol conducted the randomization procedure using computer-generated tables. We used blocked randomization (block sizes of two) with an equal allocation ratio (www.sealedenvelope.com). The same operator placed the identification groups in sequentially numbered, opaque, sealed envelopes. Once the participant was eligible for the procedure and had completed all baseline assessments, the operator opened the envelope. Neither the participant nor the operator knew the group allocation before this stage.

Random Sequence Generation and Allocation Concealment

Participants were submitted to two bleaching sessions with a seven-day interval between them. The gingival tissue was isolated with a light-cured resin dam (TopDam, FGM dental products). The 20% HP gel Whiteness HP Blue 20 (FGM dental products) was applied to all upper and lower central and lateral incisors, canines, and premolars for 50 minutes according to the manufacturers' instructions. At 10 and 30 minutes after the start of treatment, gel applied to hemiarches in the HPactive group was agitated with a sonic device (170Hz, 30 seconds, Smart Sonic Device, FGM dental products) applied directly to the central and lateral incisors and canine buccal surfaces with rounded movements, mainly in the regions of the oxygen bubble formation. In the HPpassive group, application lasted 50 minutes and was undisturbed. All participants were instructed to brush their teeth at least three times a day using fluoridated toothpaste with no desensitizing agents (Colgate, Colgate-Palmolive, SP, Brazil). 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.

Shade Evaluation

Tooth shade was recorded using an objective (VITA Easyshade spectrophotometer, Vident, Brea, CA, USA) and subjective (value-oriented shade guide Vita Classical) method before the bleaching procedure (baseline), before the second bleaching session, seven days after the end of the bleaching treatment, and 30 days after the end of the bleaching treatment. Color evaluation was performed in a room under artificial lighting conditions, under a color corrected light (Rite-Lite, AdDent, Inc, Danbury, CT, USA), as previously reported by Ontiveros and Pavarina.[22] For both devices, color was checked at the middle third of the canine. For the subjective method, the shade guide's 16 tabs were arranged from highest (B1) to lowest (C4) value (see Table 1). Although this scale is not linear in the truest sense, changes were treated as representing a continuous and approximately linear ranking for the purpose of the analysis. Two color evaluators assessed the tooth color of 10 patients not involved in the clinical trial three times each, and data were analyzed to check for accordance between them. Operators were only considered calibrated when they could obtain a weighted kappa of 85% in two consecutive readings of the same teeth in 10 patients.

For objective shade evaluation, color measurement was performed using a VITA Easyshade (Vident) spectrophotometer. Prior to color measurement, an

Table 1: *Vita Classical Scale Organized in Order of Descending Value*

Color	B1	A1	B2	D2	A2	C1	C2	D4	A3	D3	B3	A3.5	B4	C3	A4	C4
Reference number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16

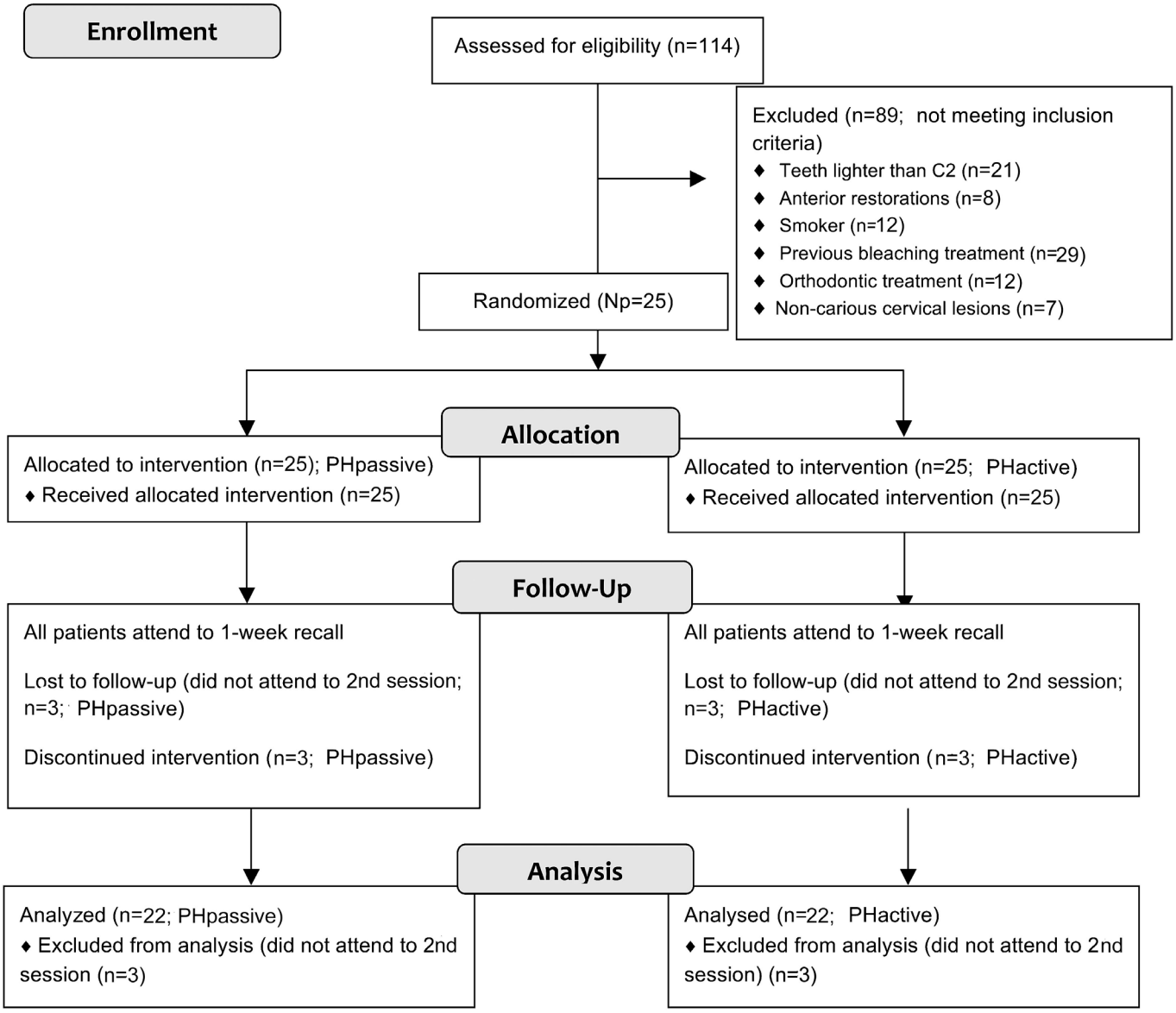

Figure 1. *Flow diagram of the clinical trial including detailed information on the participants.*

impression of the maxillary arch was taken with high-putty silicone paste (Clonage, Nova DFL, Rio de Janeiro, RJ, Brazil), and a window was created on the labial surface of the silicone guide using a 6-mm-radius metal device. The purpose of this was to standardize the area for color evaluation with the spectrophotometer in all recall periods. Color was determined using the parameters of the digital spectrophotometer, on which the following values were indicated: L*, a*, and b*, where L* represents luminosity (the value from 0 [black] to 100 [white]) and a* and b* represent color along the red-green axis and the color along the yellow-blue axis, respectively. The difference between the baseline and each recall period (ΔE*) was calculated using the following formula: $\Delta E^* = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$.

Tooth Sensitivity Evaluation

Patients were asked to record their perceptions of TS during the first and second bleaching sessions and 30 days after bleaching using the visual analogue scale (VAS). This scale uses a 10-cm horizontal line with the words *no pain* at one end and *worst pain* at the other end. Subjects were asked to record their TS experience during the treatment and up to one hour after bleaching, from one hour to 24 hours after bleaching, and from 24 to 48 hours after bleaching. They were also asked to record

whether they experienced TS during the 30-day period after bleaching. After the two bleaching sessions, the VAS scores obtained for both sessions were considered for statistical purposes.

Statistical Analysis

The statistician was blinded to the study groups. The analysis followed the intention-to-treat protocol and involved all participants who were randomly assigned. Color change was used to determine the primary outcome (BE). Color change based on subjective (ΔSGUs) and objective (ΔE) evaluations was analyzed using a Wilcoxon test. The absolute risk of TS was compared using the McNemar test. The confidence interval of the effect size was calculated. TS intensity between assessment points (during and after the bleaching process) within each group was analyzed using a Wilcoxon test. The alpha in all the statistical tests was preset at 0.05.

RESULTS

A total of 114 patients were examined, and only 25 patients were selected. Eighty-nine patients were excluded mainly due to color (shades lighter than C2 or previous bleaching) or because they did not meet some inclusion criteria (Figure 1).

The participants' mean age (years) and baseline SGU are described in Table 2. Comparable data were obtained among treatment groups by ensuring the comparability of baseline features (not shown data). Three patients discontinued the intervention due to schedule limitations, and no patients presented adverse effects during the intervention. No medication or desensitizer had to be prescribed or applied to this study's participants for the relief of bleaching-induced TS.

Shade Evaluation

Table 3 shows a whitening of approximately 5.8 SGUs at the ΔSGU evaluation, and a variation in ΔE of approximately 10 was detected for both groups when the baseline and results from 30 days after bleaching were compared (Table 3). No statistically significant difference was observed between the study groups (p>0.83).

Tooth Sensitivity Evaluation

Absolute risk (%) of TS was 36.4 (95% CI: 19-57) for the HPactive group and 31.8 (95% CI: 16-52) for the HPpassive group, with no statistical difference (p=0.94; Table 4). TS intensity means remained higher during the first 24 hours after bleaching but diminished noticeably between 24 and 48 hours after bleaching (Table 4; p=0.02). However, there was no difference between the groups (p=0.35; Table 5).

DISCUSSION

The results of the present study indicate that in-office bleaching gel applied with or without agitation achieved significant tooth whitening compared with the baseline color. Usually, 5.5-SGU and 10-ΔE color variations were observed for both groups after two bleaching sessions. These results are in agreement with previously reported studies in the literature in which low-concentration HP gel was also applied for in-office bleaching.[10,11,23]

The whitening effect is highly dependent on HP concentration.[11,23-25] For instance, Reis and others[11] showed that a stronger whitening effect was obtained only when high-concentration HP gel was applied in comparison to low-concentration HP gel. These authors hypothesized that three bleaching sessions, rather than two, might be necessary for low-concentration HP gel to achieve a BE similar to that of high-concentration HP gel.

Other clinical alternatives to improve the BE of low-concentration HP gel include associated at-home bleaching[26] or using light during the bleaching gel application.[23,27] However, in these techniques, additional procedures or sessions might be necessary, which is contrary to the need for simplified clinical procedures. Regarding light, a recent published systematic review showed that no available lamps showed any improvement in the BE, even when a low-concentration HP gel was used.[14]

This is the main reason for evaluating the effects of agitation in the present study. HP acts as a strong oxidizing agent through the formation of free radicals, reactive oxygen molecules, and HP anions.[28] Clinically, this can be observed from the formation of oxygen bubbles on the surface of the bleaching gel.

Table 2: *Baseline Characteristics of the Participants Included in This Clinical Trial*

Characteristics	HPactive	HPpassive
Age (mean ± SD, years)	26.5 ± 7.1	26.1 ± 7.1
Baseline color (mean ± SD, SGU)	11.9 ± 2.0	11.7 ± 2.2

Abbreviations: HP, hydrogen peroxide; SGU, shade guide units

Table 3: *Color Change in Shade Guide Units (SGU) and ΔE (Means ± SD) Between Baseline vs 30 Days After Bleaching for the Two Treatment Groups*

Color Evaluation Tools	HPactive	HPpassive	*p*-Value[a]
ΔSGU (Vita Classical)	5.8 ± 2.3 A	5.6 ± 2.4 A	0.98
ΔE	10.3 + 6.0 a	10.6 ± 5.9 a	0.83

Abbreviations: HP, hydrogen peroxide.
[a]Wilcoxon test. Means identified with the same capital or lowercase letters are statistically similar.

Table 4: *Number of Participants Who Experienced Tooth Sensitivity (at least once) During the Bleaching Regimen for the Two Treatment Groups*

Bleaching Treatment	Number of Participants		Absolute Risk (95% CI)[a]	Relative Risk (95% CI)
	Yes	No		
HPactive	8	14	36.4 (19-57)	87.5 (38-199)
HPpassive	7	15	31.8 (16-52)	

Abbreviations: CI, confidence interval.
[a]McNemar test (p=0.94)

Table 5: *Tooth Sensitivity Intensity (mean ± SD) in Different Time Intervals for the Two Treatment Groups[a]*

Interval	VAS Scale	
	HPactive	HPpassive
Up to 1 h	2.2 ± 6.0 A,B	3.0 ± 6.7 A,B
1-24 h after bleaching	4.1 ± 8.1 B	2.7 ± 5.7 B
24-48 after bleaching	0.4 ± 1.2 A	0.4 ± 1.2 A

Abbreviations: HP, hydrogen peroxide; VAS, Visual Analogue Scale
[a]Wilcoxon-paired test (p=0.02). Means identified with the same capital letters are statistically similar.

It was expected that agitating the gel with a microbrush moved away oxygen bubbles from the tooth surface. Therefore, more oxygen bubbles would be released because molecular agitation increases the rate of the oxygen decomposition and produces more oxygen-free radicals. At first glance, gel agitation appears to renew and maximize the gel's contact with the dental surface.[15-17] Unfortunately, gel agitation did not produce better whitening results, which leads us to accept the first null hypothesis. It is probable that 20% HP alone produces enough free radicals to oxidize the organic component of dentin. Thus, the increase in free radicals produced by gel agitation might be useless.

In addition, gel agitation did not significantly increase the absolute risk and intensity of TS. Thus, the second and third null hypotheses were also accepted. If the fact that the most common adverse effect of bleaching (TS) is taken into consideration, a more plausible hypothesis for this adverse effect is that the excess HP penetrates the enamel or dentin and reaches the pulp tissue.[29] The brushing motion of the applicator under agitation imparts energy to the HP in contact with the dental structure. This agitation creates pressure waves and shear forces in the HP, decreasing the gel's viscosity.[30] Unfortunately, little attention[31,32] has been afforded to the rheological properties of whitening gels. Only recently, Kwon and others[32] showed that, although bleaching effects were similar, a higher amount of HP was found in the pulp chamber when using a low-viscosity gel compared to a high-viscosity gel. However, this did not occur in our study. Future studies must be conducted to evaluate the effects of agitation on the viscosity of various in-office bleaching gels.

It is worth mentioning that relatively few patients (32%-36%) reported TS related to in-office bleaching, as was the case in previously reported studies.[11,24,33] This could be directly related to the low-concentration HP used (20%). Usually, more than 60% of patients report TS when high-concentration HP gels are used.[4,1,34,35] However, HP concentration might not be solely responsible for the lower TS pattern. Several recently published studies indicated that alkaline and calcium-containing digluconate exhibited lower HP penetration than acidic and desensitizer-free bleaching agents.[36-39] Consequently, a lower percentage of TS is expected.[11,26,33] Therefore, future studies must be conducted to evaluate the effects of agitation on in-office bleaching gels with varying pH levels.

CONCLUSION

The active application of a 20% HP in-office bleaching gel did not improve BE and TS when compared to passive application.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the human subjects oversight committee guidelines and policies of the Federal University of Amazonas. The approval code issued for this study is 49719715.2.00000.5020.

Conflicts of Interest

Prof Alessandro Loguercio and Prof Alessandra Reis are inventors of the SMART device.

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