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Clinical Research

Combined Bleaching Technique Versus At-home Bleaching—A Single-blind Randomized Controlled Trial

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Clinical Relevance

Combined bleaching with reduction in the application time of 35% hydrogen peroxide and previous use of desensitizer is effective and stable but without reduction in the risk and intensity of dental sensitivity.

SUMMARY

Objective: To compare the efficacy, color stability, and tooth sensitivity (TS) of combined bleaching, using a modified protocol with at-home bleaching.

Methods: Eighty participants were randomized into two groups. In the combined group, a desensitizing gel was applied (10 minutes) prior to in-office bleaching (35% hydrogen peroxide (H_2O_2), 2×15 minute applications) and at-home bleaching (4% H_2O_2, 2×30 minutes for 21 days)

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started the next day. In the at-home group, only the at-home bleaching was performed. Color was recorded at the beginning and postbleaching with two scales (VITA Classical and Bleachedguide) and Easyshade spectrophotometer. The TS was recorded daily with a 0-10 visual analogue scale (VAS) and five-point numeric rating scale (NRS).

Results: A 40% lower risk (RR=1.4; 95% CI 1.1-1.9) was observed in the at-home group. Higher color change and intensity of TS [mean difference 2.3 (95% CI 1.3-3.3) in the VAS] was observed in the first week for the combined group. After the end of the protocol, a bleaching degree was detected for both groups, with no significant difference between both groups (p>0.05).

Conclusion: The combined group produced a slightly higher degree of color change than at-home bleaching but with a higher risk and intensity of TS.

INTRODUCTION

Dental bleaching has become increasingly sought by patients to improve the aesthetics of darkened teeth and the harmony of the smile.[1,2] For such purposes, there are two dentist-supervised categories—at-home and in-office, and both can be combined in so-called combined bleaching.[3]

At-home dental bleaching involves the use of individual trays with carbamide peroxide (CP) or low concentration hydrogen peroxide (H_2O_2) gels[4-6] It has the advantages of a lower risk and intensity of tooth sensitivity (TS),[7-9] and shorter chair time, although satisfactory results are obtained with 2-4 weeks of treatment.[10] In-office dental bleaching involves higher concentrations of H_2O_2[3,11-13] and, therefore, can provide faster results than at-home bleaching, with the disadvantage of generating a higher risk and intensity of TS during or after the bleaching session.[8,14,15]

H_2O_2 has a low molecular mass, which favors its penetration through the enamel, reaching the dentin and pulp tissue.[16] Upon penetrating these structures, their oxidizing components rapidly diffuse through the tissues, reaching the chemosensitive ion channel (TRPA1), which possibly directly activates the intradental nerve via TRPA1.[17] The first damaged cell is the odontoblast that is attached to the roof of the pulp chamber. When these cells undergo the action of oxidizing components of H_2O_2, they collapse due to oxidative stress but are subsequently replaced by newly differentiated mesenchymal cells.[18] However, all of these reactions lead to an inflammatory process that is directly responsible for generation of bleaching-induced TS.[17]

Although at-home bleaching with 10% CP is considered the gold standard,[19-21] the need for a long-lasting treatment when using in-office bleaching has led dentists and patients to seek a safer and faster dental bleaching protocol. A common clinical practice is the association of both in-office and at-home protocols to potentialize the bleaching effect[4] and maintain long-term color stability.[6,22]

In this context, in-office bleaching is performed during the first session to provide an initial "jump-start" bleaching effect.[3,6] Subsequently, the patient receives an individual bleaching tray to perform home bleaching, until the desired shade is obtained.[4,22] With the accomplishment of this technique, some authors have reported a reduction of the risk of TS[23] with satisfactory results.[4,22,24]

In an attempt to reduce TS[3,25] some alternatives have been proposed, such as a reduction of bleaching gel concentration,[26] the use of bleaching agents for shorter periods of time,[27,28] the use of drugs,[29-33] and topical use of desensitizing agents before or after bleaching.[34-38] However, studies combining drug use with dental bleaching reported no reduction in TS.[29-33] Among the topical desensitizing agents used are 2% sodium fluoride, 2-hydroxymethyl methacrylate with glutaraldehyde, and 5% potassium nitrate.[35,36,39] These topical agents have been reported as effective methods to reduce the risk and intensity of TS when applied before[35,37] or after bleaching.[38,40] Also, for in-office bleaching, reducing the number of applications of 35% H_2O_2 minimized the intensity of TS, as reported in the clinical trial published by Kose and others,[28] who found that two applications of 15 minutes was as effective as three applications of 15 minutes, but with a reduced intensity of TS.

Although these alternatives have already been tested for in-office bleaching, it is still unknown if they can bring similar benefits when combined bleaching is used. The association of more than one attempt to reduce bleaching-induced TS may allow better acceptability in terms of reduced side effects. Therefore, the objective of this study was to compare the efficacy, color stability, and TS of a combined bleaching technique with a modified protocol to reduce bleaching-induced TS in adults with at-home bleaching.

METHODS AND MATERIALS

Trial Design, Settings, and Locations of Data Collection

This study was a randomized, parallel, single blind, and equivalence trial. Only the evaluator was masked to patient group assignment. The study was performed

from October 10, 2016, to June 7, 2017, in the clinics of the School of Dentistry State of the University of Ponta Grossa.

Recruitment

Participants were recruited through written advertisements placed on the university building walls. All participants signed an informed consent form before being enrolled in the study.

Eligibility Criteria

Volunteers included in the clinical trial were at least 18 years old, had good general and oral health, and did not report any type of TS. The volunteers were required to have six caries-free and restoration-free maxillary anterior teeth and healthy periodontal tissues. The central incisors had to be shade A2 or darker, as judged by comparison with a value-oriented shade guide (VITA Classical, Vita Zahnfabrik, Bad Säckingen, Germany).

Volunteers with anterior restorations or dental prosthesis, orthodontic apparatus, or severe internal tooth discoloration (tetracycline stains, fluorosis, pulpless teeth) were not included in the study. In addition, pregnant and lactating women, volunteers with any other pathology that could cause sensitivity (such as recession, dentinal exposure, visible cracks in teeth), taking anti-inflammatory or analgesic drugs, who smoked or had bruxism, or volunteers who had undergone tooth-bleaching procedures were excluded.

Sample Size Calculation

The absolute risk of bleaching-induced TS was previously reported to be 85%[6] when using 35% H_2O_2 associated with 10% carbamide peroxide. Considering an equivalence limit of 25% in the rate of bleaching-induced TS, a minimum of 80 volunteers would be required to detect such difference, if it exists, with a power of 90% and an alpha of 5%.

Randomization and Allocation Concealment

A third person who was not involved in implementation and evaluation steps performed a blocked randomization process (blocks of 2 and 4) using the website www.sealedenvelope.com. Block randomization was performed to allow groups with equivalent sample size. Details of the random sequence were recorded on cards, which were placed in sequentially numbered, opaque, and sealed envelopes.

The information contained in the envelope determined the group to which the volunteer would be assigned. Once the participant was eligible for the procedure and completed all baseline assessments, the allocation assignment was revealed by the third person opening this envelope immediately after implementation.

Study Intervention

Alginate impressions of each subject's maxillary and mandibular arch were made and filled with dental stone. No block-out material was applied to the labial surfaces of the stone model teeth. A 1 mm soft, acetate vinyl material provided by the manufacturer (FGM, Joinville, SC, Brazil) was used to fabricate the custom-fitted tray to hold the at-home bleaching gel. The bleaching tray was trimmed 1 mm beyond the gingival margin.

In the combined bleaching group, volunteers were submitted to a single clinical session of in-office bleaching with 35% H_2O_2 gel (Whiteness HP Maxx, FGM). A lip retractor (ArcFlex, FGM) was placed and a desensitizing gel based on potassium nitrate and sodium fluoride (Desensibilize KF 2%, FGM) was applied and left undisturbed for 10 minutes. The gel was removed with a disposable aspirator, and the teeth were cleaned with gauze. Then, the gingival tissue of the teeth to be bleached was isolated using a light-cured resin dam (Top Dam, FGM), and each tooth was light cured for 20 seconds (Radii Cal, SDI, Victoria, Australia). The in-office bleaching gel was applied in two 15 minute applications[28] and not in three 15 minutes applications, as recommended by the manufacturer.

Then, the participants received the bleaching tray and the 4% H_2O_2 gel (White Class with Calcium 4%, FGM). Participants were instructed to start the at-home bleaching the day after the in-office session using the bleaching tray with gel daily for 30 minutes, for 21 days.

In the at-home bleaching group (control), volunteers only performed the at-home bleaching with the 4% H_2O_2 gel (White Class with Calcium 4%, FGM) following the same protocol as described above.

Outcomes

Tooth Sensitivity—Tooth sensitivity (TS) in the combined bleaching group was evaluated immediately after the bleaching and during the 21 days of at-home bleaching. In the at-home group, TS was evaluated daily during the 21 days of treatment. In both the groups, TS was assessed using a 0–10 visual analogue scale (VAS) and five-point numeric rating scale (NRS).

The VAS is a 10-cm horizontal line with scores of 0 and 10 at the ends, with 0 meaning no sensitivity and 10 meaning severe TS. The patient marked the TS intensity with a vertical line across the horizontal line

of the scale. Then, the distance in millimeters from the zero end was measured with the aid of a millimeter ruler.[31,32] Using the five-point NRS, where 0 = none, 1 = mild, 2 = moderate, 3 = considerable, and 4 = severe, the participants were instructed to indicate the numerical value of the degree of sensitivity.[6,37,41] During the 21-day treatment period, patients scored the intensity of TS once daily. If the patient did not have pain, he or she was instructed to mark a zero on both the scales.

If the participant scored 0 (no sensitivity) in all time assessments, he or she was considered to be insensitive to the bleaching protocol. In all other circumstances, the participants were considered to have bleaching-induced TS. This dichotomization allowed us to calculate the absolute risk of TS, which is the percentage of patients who reported TS at least once during treatment.

To calculate the TS intensity, we took the worst score from the NRS scale and the highest numerical value obtained in the VAS scale reported by each patient so that only a single value per patient was taken from the whole bleaching period.

Color Change—Two experienced and calibrated dentists (kappa statistic greater than 80% after previous calibration) who were not involved in the randomization procedures performed assessments at baseline, after 1, 2, and 3 weeks of treatment, and 1 week, 1 month, and 6 months after bleaching for both the groups. The color of the patient's teeth was not evaluated immediately after the in-office bleaching session, to avoid the effects of dehydration and demineralization on color measurements.

The subjective color evaluation was performed with a VITA Classical shade guide (VITA Classical, Vita Zahnfabrik) and VITA Bleachedguide 3D-MASTER shade guide (Vita Zahnfabrik). An objective color evaluation was also performed using a VITA Easyshade (VITA Zahnfabrik, Bad Säckingen, Germany) spectrophotometer.

The VITA Classical shade guide (VITA Classical, Vita Zahnfabrik) is composed of 16 color guide tabs organized from the highest (B1) to the lowest value (C4). The VITA Bleachedguide 3D-MASTER (Vita Zahnfabrik) scale contains clearer color tabs already organized from the highest (0M1) to the lowest value (5M3).

The area of interest for the measurement of tooth color matching was the middle-third of the facial surface of the anterior central incisors. Color changes were calculated from the beginning of the active phase up to the individual recall times by calculating the change in the number of shade guide units (ΔSGU), which occurred toward the lighter end of the value-oriented list of shade tabs. In the event of disagreement between the examiners during shade evaluation, a consensus was reached.

Objective color evaluation was performed using a VITA Easyshade spectrophotometer (Vita Zahnfabrik) according to the CIELab system. In order to standardize the region of the tooth that was measured, the upper arch of all patients was impressed with condensation silicone (Perfil Cub, Vigodent, Rio de Janeiro, Brazil) for the preparation of a guide. The guide was perforated in the vestibular region in the middle-third of the right upper central incisor with the aid of a 5-mm diameter circular scalpel (Biopsy Punch, Miltex, York, Pennsylvania, USA) similar to the active tip of the appliance. Color change was evaluated by the researchers at the same time as assessments reported for the shade guides. The spectrophotometer was always calibrated daily before measurements.

Color change in ΔE was determined using the CIELab* parameters[42] L^*, a^*, and b^*, where L^* represents brightness ranging from 0 (black) to 100 (white), and a^* and b^* represent the chromatic axes, where a^* is the measure along the red–green axis, and b^* is measured along the yellow–blue axis.

The color variation (ΔE^*_{ab} and ΔE_{00})[43,44] before and after the treatment was calculated by the formulas: $\Delta E^*_{ab} = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)2]^{1/2}$ and ΔE_{00} (CIEDE2000) = $[(\Delta L/\mathrm{KlSL})^2 + (\Delta C/\mathrm{kCSC})^2 + (\Delta H/\mathrm{kHSH})^2 + \mathrm{RT}\,(\Delta C^*\Delta H/\mathrm{SC^*SH})^{1/2}$.

Statistical Analysis

Data from 80 patients were used in this study, according to the intention-to-treat analysis.[45] In case of missing data due to nonattendance at the recall visits, data from the last observation were carried forward. The absolute risk of TS in both the groups was compared using Fisher's exact test at a 5% level of significance. The relative risk as well as the 95% confidence interval was also calculated.

The TS intensity data obtained with the NRS scale were analyzed using Mann–Whitney (NRS). For this scale, comparison between assessment times within each group were performed using the Friedman test. Data of TS intensity obtained with the VAS scale were analysed with a two-way ANOVA with repeated measures.

For each instrument of color assessment (ΔSGU in both scales, ΔE^*_{ab} and ΔE_{00}), the color change of groups were compared using a two-way repeated measures ANOVA (groups *vs.* assessment time). Tukey test was used for pairwise comparisons. In all statistical tests, the significance level was 0.05. We performed all the analyses by using the software SigmaPlot version 11.0 (Systat Software).

RESULTS

Characteristics of Included Participants

A total of 121 volunteers were examined in a dental chair to check if they met the inclusion and exclusion criteria. A total of 80 patients were included in this clinical study (Figure 1). Seventy-eight patients completed the bleaching protocols of this study and attended the 1-week, 1-month, and 6-month recalls. Only two patients discontinued intervention.

Similar baseline features were observed between the two study groups. The baseline color of the participants in SGU was 5.7 ± 1.4 for the combined bleaching group and 6.0 ± 1.7 for the at-home bleaching group. The mean age (years) of the participants was 23.2 ± 4.9 for the combined bleaching group and 22.9 ± 4.8 for the at-home bleaching group. Females represented 62.5% of the combined bleaching group and 52.5% of the at-home bleaching group.

Color Change

For the VITA Classical shade guide (Table 1), the mean difference (95% CI) for the groups was 0.4 (−0.3-1.0), while for the spectrophotometer the mean difference for the ΔE^*_{ab} was −0.4 (−2.6-1.8; Table 2) and ΔE_{00} was −0.5 (−2.13-1.13; Table 3). For all these measures of color evaluation, only the main factor time ($p<0.001$) was statistically significant, meaning that a significant color change occurred over time irrespective of the group. At the end of the bleaching protocol, bleaching of approximately 4 SGU was detected; a ΔE^*_{ab} of 9.0 units and ΔE_{00} of approximately 7.0 units were detected for both the groups (Tables 1-3).

In the VITA Bleachedguide shade guide, the main factors time ($p<0.001$) and group ($p=0.04$) were statistically significant. Bleaching increased over time for both groups, and a statistically greater color change was observed for the combined bleaching group. The mean difference of color change was 1.2 (0.0-2.4), which can be clinically detected by a calibrated operator (Table 4).

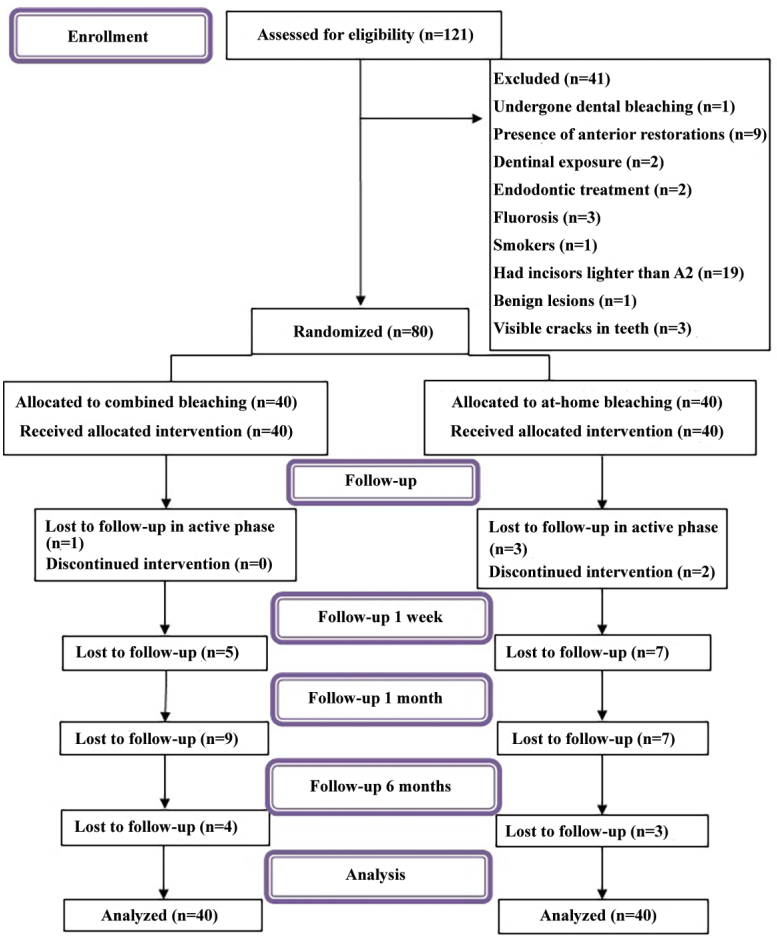

Figure 1. Flow diagram of the clinical trial, including detailed information on the excluded participants.

Table 1: *Means and Standard Deviations of ΔSGU Values in the Vita Classical Scale, For the Two Groups, at the Different Time Assessments*[a]

Periods	Combined Bleaching	At-home Bleaching	Main Factor Time	Mean Difference (95% CI)
Baseline vs 1st week	3.7 ± 1.6	3.0 ± 1.7	3.4 ± 1.6 a	0.7 (–0.0-1.4)
Baseline vs 2nd week	4.1 ± 1.4	3.6 ± 1.4	3.8 ± 1.4 b	0.5 (–0.1-1.1)
Baseline vs 3rd week	4.4 ± 1.3	4.4 ± 1.5	4.4 ± 1.4 c	0.0 (–0.6-0.6)
Baseline vs 1st week after	4.4 ± 1.3	4.0 ± 1.4	4.2 ± 1.4 c	0.4 (–0.2–1.0)
Baseline vs 1 month after	4.4 ± 1.3	4.0 ± 1.3	4.2 ± 1.4 c	0.4 (0.2-1.0)
Baseline vs 6 months after	4.4 ± 1.3	3.9 ± 1.7	4.1 ± 1.5 c	0.5 (–02-1.2)
Main factor group	4.2 ± 1.4 A	3.8 ± 1.5 A	—	0.4 (–0.3-1.0)

Abbreviations: CI, confidence interval; SGU, shade guide units.
[a] *Uppercase letters indicate statistical similarity between groups and lowercase letters indicate statistical similarity among times of assessment.*

Table 2: *Means and Standard Deviations of the ΔE Values Obtained by the Vita Easyshade Spectrophotometer, for the Two Groups, at the Different Time Assessments*[a]

Periods	Combined Bleaching	At-home Bleaching	Main Factor Time	Mean Difference (95% CI)
Baseline vs 1st week	8.8 ± 6.2	8.8 ± 4.0	8.8 ± 5.1 a	0 (–2.3-2.3)
Baseline vs 2nd week	8.8 ± 4.8	8.6 ± 4.8	8.7 ± 4.8 ab	0.2 (–1.9-2.3)
Baseline vs 3rd week	10.1 ± 5.1	9.8 ± 5.2	9.9 ± 5.1 ab	0.3 (–2-2.6)
Baseline vs 1st week after	8.4 ± 4.0	8.8 ± 4.7	8.6 ± 4.3 ab	–0.4 (–2.3-1.5)
Baseline vs 1 month after	9.7 ± 5.2	12.0 ± 6.4	10.8 ± 5.8 b	–2.3 (–5-0.3)
Baseline vs 6 months after	9.3 ± 4.6	9.6 ± 4.6	9.4 ± 4.6 b	–0.3 (–2.3-1.8)
Main factor group	9.2 ± 5.0 A	9.6 ± 4.9 A	—	–0.4 (–2.6-1.8)

Abbreviations: CI, confidence interval.
[a] *Uppercase letters indicate statistical similarity between groups and lowercase letters indicate statistical similarity among time assessments.*

Table 3: *Means and Standard Deviations of the ΔE_{00} Values Obtained by the Vita Easyshade Spectrophotometer, for the Two Groups, at the Different Time Assessments*[a]

Periods	Combined Bleaching	At-home Bleaching	Mean Difference (95% CI)	Mean Difference (95% CI)
Baseline vs 1st week	6.5 ± 4.4	6.5 ± 3.0	6.5 ± 3.7 a	0 (–1.68-1.68)
Baseline vs 2nd week	6.3 ± 3.5	6.5 ± 3.6	6.4 ± 3.5 ab	–0.2 (–1.78-1.38)
Baseline vs 3rd week	7.1 ± 3.6	7.1 ± 3.8	7.1 ± 3.7 b	0 (–1.65-1.65)
Baseline vs 1st week after	6.1 ± 3.1	6.5 ± 3.3	6.3 ± 3.2 ab	–0.4 (–1.83-1.03)
Baseline vs 1 month after	7.0 ± 3.8	8.9 ± 5.0	7.9 ± 4.4 b	–1.9 (–3.88-0.08)
Baseline vs 6 months after	6.7 ± 3.2	6.9 ± 3.5	6.8 ± 3.4 ab	–0.2 (–1.69-1.29)
Main factor group	6.6 ± 3.6 A	7.1 ± 3.7 A	—	–0.5 (–2.13-1.13)

Abbreviation: CI, confidence interval.
[a] *Uppercase letters indicate statistical similarity between groups and lowercase letters indicate statistical similarity among time assessments.*

Table 4: *Mean and Standard Deviations of ΔSGU Values on the Vita Bleachedguide Shade Guide, for the Two Groups, in the Different Evaluation Periods*[a]

Periods	Combined Bleaching	At-home Bleaching	Main Factor Time	Mean Difference (95% CI)
Baseline vs 1st week	4.5 ± 2.9	2.7 ± 2.5	3.6 ± 2.7 a	1.8 (0.6-3.0)
Baseline vs 2nd week	5.5 ± 2.6	3.7 ± 2.4	4.6 ± 2.5 b	1.8 (0.7-2.3)
Baseline vs 3rd week	6.0 ± 3.2	4.8 ± 2.8	5.4 ± 3.0 c	1.2 (–0.1-2.5)
Baseline vs 1 week after	6.0 ± 3.3	4.8 ± 2.8	5.4 ± 3.0 c	1.2 (–0.2-2.6)
Baseline vs 1 month after	5.7 ± 2.8	5.0 ± 2.0	5.4 ± 2.4 c	0.7 (–0.4-1.8)
Baseline vs 6 month after	5.5 ± 2.8	4.8 ± 2.8	5.1 ± 2.8 c	0.7 (–0.5-1.9)
Main factor time	5.5 ± 2.9 A	4.3 ± 2.5 B	—	1.2 (0-2.4)

Abbreviations: CI, confidence interval;SGU, shade guide units.
[a] Uppercase letters indicate statistical similarity between groups and lowercase letters indicate statistical similarity among time assessments.

Tooth Sensitivity (TS)

A significantly higher risk of TS was observed for the combined bleaching (90%; 95% CI 77-96) than at-home bleaching (63%; 95% CI 47-76) (Table 5, p=0.008). Regarding TS intensity, a statistical difference between the groups in the first week of bleaching was detected (Tables 6 and 7, p<0.001).

TS intensity was higher for the combined bleaching group in the first week of bleaching. The magnitude of the difference in pain intensity was 2.3 (95% CI 1.3-3.3) VAS units (Table 7). After the first week, no significant difference in TS intensity between the groups was detected. In general, TS intensity decreased significantly over time for both groups (Tables 6 and 7, p<0.05).

Table 5: *Comparison of the Number of Patients Who Reported TS During Bleaching Treatment with Absolute and Relative Risks*[a]

Treatment	Tooth Sensitivity (Number of Patients)		Absolute Risk (95% CI)	Relative Risk (95% CI)
	Yes	No		
Combined bleaching	36	4	90 (77-96)	1.4 (1.1-1.9)
At-home bleaching	25	15	63 (47-76)	

Abbreviations: CI, confidence interval; TS, tooth sensitivity.
[a] Statistical comparison between groups was performed with Fisher exact test (p=0.008).

DISCUSSION

In this study, a significant statistical difference was found for the risk and intensity of TS reported by the volunteers among the groups evaluated. At-home bleaching produced a lower risk and intensity of TS, when compared to the associated bleaching, being in agreement with other studies in the literature.[6,9,46] This difference may be directly correlated with the low concentration of H_2O_2 used in the at-home technique. By using low-concentration products, a smaller amount of H_2O_2 reaches the pulp chamber within the time of application.[19,47]

The study by Soares and others[48] demonstrated reduced aggression of the pulp cells when bleaching was performed with low-concentration products. The at-home bleaching agent also contains potassium nitrate and sodium fluoride as desensitizing agents, as

Table 6: *Medians (Interquartile Range) of TS Intensity Obtained with the NRS Scale*[a]

Periods	NRS (0-4)		*p*-Value (*)
	Combined Bleaching	At-home	
1st week	2 (1/3) A	1 (0/1) A	<0.001
2nd week	0 (0/0) B	0 (0/1) A	0.28
3rd week	0 (0/0) B	0 (0/2) A	0.21

Abbreviations: NRS, numeric rating scale.
[a] Statistical comparison between groups were performed with Mann–Whitney test (*). Comparison of the different assessment times within each group were performed with the Friedman test (p<0.05), and significant differences are represented by different uppercase letters.

Table 7: *Means, Standard Deviations and Mean Difference (95% Confidence Interval [CI]) of TS Intensity Obtained with the VAS Scale*[a]

Periods	VAS (0-10)		Mean Difference (95% CI)	*p*-Value
	Combined Bleaching	At-home		
1st week	3.2 ± 3.0 A	0.9 ± 1.3 A	2.3 (1.3-3.3)	<0.001
2nd week	0.4 ± 0.7 B	0.8 ± 1.7 AB	–0.4 (–1.0-0.2)	0.48
3rd week	0.3 ± 0.5 B	0.5 ± 1.0 B	–0.2 (–0.6-0.2)	0.38

Abbreviations: VAS, visual analogue scale.

[a]*Mann–Whitney test. The assessment times within each group were compared with the Friedman test (p<0.05), and significant differences are represented by different uppercase letters.*

well as calcium,[49] which has been claimed to reduce the risk and intensity of TS of at-home products.

The absolute risk of TS from at-home bleaching in this study was 62%. Other studies in the literature evaluated similar concentrations of H_2O_2, such as those of Myers and others,[50] which found an absolute risk of TS of 48%, and Chemin and others,[26] which reported TS risks varying from 25% to 54% with the same at-home bleaching protocol as used in this study. The low absolute risk and intensity of TS observed in the at-home bleaching of this clinical trial appear to be further evidence of the correlation between the H_2O_2 concentration and the risk and intensity of TS. Studies comparing the risk and intensity of TS in at-home bleaching versus in-office bleaching also reported favorable results for the at-home protocol.[3,9,35,51,52]

The higher risk and intensity of TS of in-office bleaching[6] explains why the combined bleaching of this study showed a higher risk and intensity of TS than the at-home protocol. We expected that by using only two 15 minute applications, instead of the recommended three 15 minute applications, and the preliminary application of potassium nitrate, bleaching-induced TS caused by in-office bleaching could be minimized, but these alternatives were shown to be unfruitful.

In the combined bleaching, we used a high-concentration 35% H_2O_2, which has been attributed to a higher risk and intensity of TS than in-office bleaching with 20% H_2O_2.[6] Perhaps the high concentration of H_2O_2 in the combined bleaching protocol followed by the daily use of the tray in the at-home protocol overrode the benefits achieved by the reduction in the number of applications and prior use of a desensitizing agent. Additionally, recent well-designed and well-powered randomized clinical trials have reported that application of potassium nitrate before and after bleaching does not have the benefits otherwise shown in earlier and small clinical trials.[35,53,54] Perhaps false positive results were obtained in these earlier trials, which were not confirmed by other studies.[34,37,39]

For color change evaluation, we used three different instruments. The VITA Classical shade guide is widely used in clinical trials of bleaching and, therefore, allows comparison of results with previous clinical studies. Although it consists of a valid method, with good reliability to differentiate between dark and light colors,[19] it was not designed for bleaching studies and lacks uniformity between different color tabs, leading to some overlaps between similar colors. This reduces the sensitivity of this tool to detect color changes.[55,56] Another instrument used was the VITA Bleachedguide 3D-MASTER scale, developed for the purposes of dental bleaching evaluation. Different from the VITA Classical, this new shade guide contains shades lighter than B1, which expands its sensitivity to detect subtle differences in the bleaching process.[32,57,58] The VITA Easyshade spectrophotometer apparatus provides an objective and consistent assessment of color change that is less affected by observer training and variability.[55,59]

In the present study, in addition to the conventional CIELab 76 system (ΔE^*_{ab}), other systems were used including the CIEDE2000 system (ΔE_{00}).[60,61]. This new system allowed for better adjustment than the CIELab formula did in estimating the visual perception of color and allowed a better evaluation of the color-difference thresholds.[62,63] Although CIEDE2000 is more advanced, no difference among groups or assessment times were observed when CIELab 76 system or CIEDE2000 system were used. Actually, as the vast majority of previously published bleaching studies still report their findings using ΔE^*_{ab}, it is important to ensure that the present data will be able to be compared with the previous literature. This justified the presentation of data using both formula (ΔE^*_{ab}, and ΔE_{00}).

It is worth mentioning that, for all spectrophotometer measurements, a colored impression material was used

as a guide to assure that the spectophotometer tip was put in the same position and in intimate contact with the dental surface during all color measurements. However, some studies used a transparent impression material, mainly because the authors expected a color interference from the colored impression material in the color measurement.[3,41,46,51] The colored impression material used in the present study has been used in several studies, and none of them describe a color interference.[2,6,26,28,32,53,54] However, to the extent of the author's knowledge, no study was found evaluating this hypothesis. Therefore, future studies need to be done regarding this topic.

In the present study, the VITA Bleachedguide 3D-MASTER shade guide was the only tool that detected a subtle difference between groups throughout the dental bleaching period. A difference in color change of approximately 1.2 units of the 3D-MASTER Bleachedguide was detected. All patients were exposed to 4% H_2O_2 30 minutes daily for 21 days; however, patients from the combined group received an extra 30 minute application of 35% hydrogen in the first clinical appointment. This may be the reason why a higher degree of bleaching was detected for the combined protocol. Had the at-home bleaching continued for an extra week, similar results might have been obtained.

Combined bleaching was suggested to potentiate the bleaching effect[4] and improve color stability.[6,22] The efficacy of bleaching was detected using the three instruments used for color evaluation, according to previous studies in the literature, both for at-home bleaching[26,48,64-66] and combined bleaching.[6,9,46] Although a small but significant higher degree of bleaching was detected using the 3D-MASTER Bleachedguide, this also reduced the risk of pain.

Further well-designed and well-powered randomized clinical trials of combined bleaching should be conducted in order to find a protocol that provides faster bleaching and low risk and intensity of TS.

CONCLUSIONS

Both the combined and at-home bleaching protocols yielded an effective and stable color change 6 months posttreatment. The combined bleaching not only showed a slightly higher degree of bleaching but also a higher risk and intensity of TS.

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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 Committee for the Protection of Human Participants of the State University of Ponta Grossa. The approval code issued for this study is protocol number 1.879.340. It was registered in the Brazilian Clinical Trials Registry (REBEC) under identification number RBR-9GNHTH.

Conflict of Interest

The authors of this article certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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