

Combined Bleaching Technique Using Low and High Hydrogen Peroxide In-Office Bleaching Gel

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Clinical Relevance

A combined bleaching technique using at-home bleaching associated with 20% in-office hydrogen peroxide is an effective and stable technique and reduces the risk of tooth sensitivity compared with a protocol performed with 35% hydrogen peroxide.

SUMMARY

Objectives: The aim of this study was to evaluate the efficacy, color stability, risk, and intensity of tooth sensitivity (TS) of combined bleaching techniques performed with 20% or

35% hydrogen peroxide for an in-office protocol.

Methods: Thirty patients were randomly divided into two groups and submitted to a single 45-minute in-office bleaching session with 35% hydrogen peroxide or 20% hydrogen peroxide. At-home bleaching was performed with 10% carbamide peroxide for two hours daily over the course of two weeks. The color was evaluated with the value-oriented shade guide Vita Classical at different periods up to 12 months after bleaching. Patients recorded the intensity of TS using a five-point verbal scale. Color change data were submitted to a two-way repeated-measures analysis of variance and Tukey test ($\alpha=0.05$). The absolute risk and intensity of TS were compared with the Fisher exact test and Mann-Whitney test, respectively ($\alpha=0.05$).

Results: On average, an effective and similar whitening of three units in shade guide was observed for both groups, which remained stable for 12 months. When both protocols were compared, the one with hydrogen peroxide 35% showed a higher risk ($p=0.02$) and intensity of TS ($p=0.04$). In regard to the TS

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intensity, no significant difference was observed up to 48 hours after in-office bleaching ($p=0.09$) and during the at-home bleaching phase of the study ($p=0.71$).

Conclusion: The combined bleaching technique using at-home bleaching associated with in-office bleaching was effective and stable over the course of 12 months, regardless of the concentration of the hydrogen peroxide used for in-office bleaching. However, the protocol with 20% hydrogen peroxide produced lower risk and intensity of TS.

INTRODUCTION

Dental appearance is a determining factor in the attractiveness of a face and contributes decisively to the personal satisfaction of patients.^{1,2} With the increasing appeal of esthetic treatments in dentistry, the demand for tooth whitening has increased.³ Dental bleaching can be performed in vital teeth using at-home and in-office bleaching protocols.⁴

Tray-delivered, at-home bleaching usually employs carbamide peroxide in concentrations ranging from 10% to 22% or hydrogen peroxide in concentrations ranging from 4% to 10%.⁵ Satisfactory whitening results can be obtained in two to four weeks.⁶ On the other hand, in-office bleaching employs highly concentrated hydrogen peroxide gels (ranging between 20% and 38%) or 35% carbamide peroxide.⁷ The in-office protocol usually requires two or three clinical sessions with a duration of 30 to 50 minutes each and can produce effective whitening as long as at least two clinical sessions are performed.⁸⁻¹⁰

Tray-delivered, at-home bleaching with 10% carbamide peroxide is considered the gold standard for the treatment of discolored teeth.¹¹⁻¹⁴ However, the slow response to at-home bleaching in some cases and some patients' demands for faster ways to bleach their teeth have pushed clinicians to look for easier, safer, and quicker means of helping patients to obtain whiter teeth.

Within this context, and in an attempt to decrease the number of in-office bleaching sessions, some authors have proposed the combined bleaching technique.¹⁵⁻¹⁷ In this combined protocol, a single in-office bleaching session is performed at the beginning of the treatment and then followed by tray-delivered, at-home bleaching.¹⁵⁻¹⁷

Authors have reported that the combination of the techniques has reduced the risk of tooth sensitivity (TS) and gum irritation¹ and achieves satisfactory results in terms of whitening.¹⁵⁻¹⁷ So far, clinical

studies of the combined bleaching technique have used high hydrogen peroxide concentrations for the in-office phase of the protocol.¹⁵⁻¹⁷ The use of low concentrations of hydrogen peroxide gel for the in-office bleaching phase would have the advantage of reduced pulp aggression and, therefore, could also minimize the risk and intensity of bleaching-induced tooth sensitivity.¹⁰

Therefore, the aim of this study was to evaluate the efficacy, 12-month color stability, risk and intensity of TS of combined bleaching techniques using 20% or 35% hydrogen peroxide for the in-office phase and 10% carbamide peroxide gel for the at-home bleaching phase.

METHODS AND MATERIALS

This clinical investigation was approved by the committee for the protection of human subjects of the local university (protocol number 05530/09). This report follows the protocol established by the CONSORT Statement.

Based on preestablished criteria, 30 volunteers seeking dental bleaching were selected for this study. This study was performed from February 2011 to March 2012 in the city of Guarapuava (Paraná, Brazil). Two weeks before the bleaching procedures, all volunteers received dental prophylaxis with pumice and water in a rubber cup and signed an informed consent form. All participants were instructed to brush their teeth regularly using fluoridated toothpaste without hydrogen peroxide.

Study Design

This study was a randomized, parallel, and single-blind clinical trial with an equal allocation rate between groups.

Eligibility Criteria

Patients included in this clinical trial were at least 18 years old and had good general and oral health. Each subject had at least one central incisor with shade A2 or darker, assessed by comparison with a value-oriented shade guide (Vita Classical, Vita Zahnfabrik, Bad Säckingen, Germany).

Patients were excluded from the study if they had undergone previous teeth-whitening procedures or had anterior teeth with restorations on the labial surfaces, veneers or full crowns, gingival recession on anterior teeth, spontaneous tooth pain, endodontically treated anterior teeth, fluorosis, severe internal tooth discoloration, teeth with noncarious

Table 1: Details of the Brand, Composition, and Mode of Application of Each Bleaching Product According the Manufacturer		
Material/Brand	Composition	Mode of Application
HP Blue 20% (FGM)	Active ingredient: 20% hydrogen peroxide (after mixture of phases) Inactive ingredients: Thickeners, inert blue pigment, neutralizing agent, calcium gluconate, glycol, and deionized water	1. Attach the hydrogen peroxide syringe in the other side of the attachment appliance. 2 . Keep the set ready for mixture soon before application. 3. Mix the contents of both phases by alternately pressing the plungers of the syringes in opposite directions up to eight times. 4. Press the entire mixture content into one of the syringes. 5. Application of 40-50 minutes and a single application are done at each clinical appointment.
HP Blue 35% (FGM)	Active ingredient: 35% hydrogen peroxide (after mixture of phases) Inactive ingredients: Thickeners, inert violet pigment, neutralizing agent, calcium gluconate, Glycol, and deionized water.	
Whiteness Perfect 10% (FGM)	Carbamide peroxide, neutralized carbopol, potassium nitrate, sodium fluoride, humectant (glycol), deionized water	1. Press the syringe plunger and apply the bleaching gel into the dental tray. The small drop per tooth is sufficient to cover the teeth. 2. Place the tray on the teeth and press lightly so that the gel is distributed all over the dental surface. 3. Remove the excess gel with a finger or toothbrush. 4 . Use the gel for two hours. 5. Wash the tray well before storing it and using it.

cervical lesions, or bruxism habits. Pregnant and lactating women, smokers, and patients under orthodontic treatment or taking anti-inflammatory and/or analgesic drugs were also excluded.

Sample-Size Calculation

The primary outcome of this study was the absolute risk of TS. The absolute risk of TS was reported to be approximately 90%¹⁸⁻²¹ for the in-office bleaching. Thus, a minimum sample size of 28 patients was required to have an 80% chance of detecting (with an alpha of 5%) a decrease in the primary outcome measure from 90% in the control group to 45% in the experimental group.

Random Sequence Generation and Allocation Concealment

The randomization process was performed by coin toss immediately before the bleaching procedure to provide adequate allocation concealment.

Study Intervention

In the experimental group, patients were submitted to a single clinical session of in-office bleaching with 20% hydrogen peroxide gel (HP20; Whiteness HP Blue 20%, FGM, Joinville, Santa Catarina, Brazil). In the control group, patients were submitted to a single in-office bleaching with 35% hydrogen peroxide gel (HP35; Whiteness HP Blue 35%, FGM). In both groups, patients continued the bleaching with the at-home protocol using a tray-delivered 10% carbamide peroxide gel (Whiteness Perfect 10%, FGM). Details of the composition, mode of applica-

tion, and brand of the bleaching products are described in Table 1.

A lip retractor (ArcFlex, FGM) was placed in all patients. 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 10 seconds (Radii Cal, SDI, Victoria, Australia). The in-office bleaching gel was then applied in a single 45-minute session. After one week, the tray-delivered, at-home bleaching was initiated with 10% carbamide peroxide (Whiteness Perfect 10%, FGM). The patients were instructed to load the bleaching tray with the gel and wear it for two hours daily over the course of two weeks.

Color Evaluation

Two calibrated evaluators with an agreement of at least 85%, determined by weighted kappa statistics before the beginning of the study, recorded the color of each patient’s central incisor at different assessment points: 1) baseline, 2) one week after the in-office bleaching session, 3) after the end of the first and second weeks of at-home bleaching, 4) one month after bleaching, 5) six months after bleaching, and 6) 12 months after bleaching. In the event of disagreement between the examiners during shade evaluation, a consensus was reached.

Color evaluation was not performed immediately after the in-office bleaching session to avoid the effect of dehydration and demineralization on color measures. The color evaluation was performed with the value-oriented shade guide Vita Classical (Vita Classical, Vita Zahnfabrik). The 16 tabs of the shade

guide were arranged from highest (B1) to the lowest (C4) value. Although this scale is not linear in the truest sense, for the purpose of analysis, the changes were treated as though they represented a continuous and approximately linear ranking, as performed in most studies on dental bleaching.^{8,10,13,17,18,21-25}

The area of interest for the measurement of tooth color matching was the middle third of the facial surface of the anterior central incisors, according to the American Dental Association guidelines. Color changes were calculated from the beginning of the active phase through the individual recall times by calculating the change in the number of shade guide units (Δ SGU) that occurred toward the lighter end of the value-oriented list of shade tabs.

Tooth Sensitivity Evaluation

TS was evaluated at baseline, during in-office bleaching, up to 48 hours after in-office bleaching, and daily during the two weeks of at-home dental bleaching. The patient was asked to indicate the degree of TS at the different assessment points using a five-point verbal rating scale, where 0 = none, 1 = mild, 2 = moderate, 3 = considerable, and 4 = severe.

If the patient selected zero (no TS) for all the assessments, this patient was considered to be insensitive to the bleaching protocol. In all other circumstances, the patients were considered to have sensitivity to the bleaching procedure. This dichotomization allowed us to calculate the absolute risk of TS, which represents the percentage of patients who reported TS at least once during the treatment. We also calculated the overall TS intensity based on the worst score of pain reported by the patient in the different assessments.

If any patient reported severe TS, the researchers immediately helped the patient to reverse the pain with the use of desensitizing gels or analgesic/anti-inflammatory medications.^{18,19,26}

Statistical Analysis

Data from the 30 patients were used in this study according to the intention-to-treat analysis.²⁷ In case of missing data due to nonattendance at the recall visits; data from the last observation were carried forward. The data sets were plotted on histograms and inspected for normal distributions. Some data did not appear to be normally distributed and, therefore, nonparametric statistical tests were used to compare the various treatments.

Color change was used to assess the efficacy of the bleaching treatment. The means and standard

deviations of the SGU at baseline and after different assessment points (baseline; after in-office bleaching; one week and two weeks after at-home bleaching; and one, six, and 12 months after bleaching) were calculated for each group. In order to evaluate whether the bleaching therapies were effective or not, the data from the SGUs of both groups were submitted to a two-way repeated measures analysis of variance (ANOVA) ($\alpha=0.05$). The Δ SGU of the baseline values vs the other assessment points was calculated, and a two-way ANOVA ($\alpha=0.05$) was used for statistical evaluation. In both cases, a post hoc analysis (Tukey test) was used to make pairwise comparisons ($\alpha=0.05$).

The absolute risk of TS of both treatments was compared using the Fisher exact test at a 5% level of significance at three different moments: during in-office bleaching, up to 48 hours after in-office bleaching, and during at-home bleaching. The risk ratio and the confidence interval for the effect size were calculated. The median of the TS intensity during the two weeks of at-home bleaching was used to summarize the TS intensity of each patient. For each of three assessment points for the risk of TS, a Mann-Whitney test ($\alpha=0.05$) was used to compare both treatment groups.

RESULTS

Characteristics of Included Participants

A total of 126 participants were examined in a dental chair to check if they met the inclusion and exclusion criteria. A total of 30 patients were included in this clinical study (Figure 1). All patients completed the bleaching protocols of this study and attended the one-month, six-month, and 12-month recalls.

The baseline color of the participants' teeth in SGUs (20% hydrogen peroxide: 5.3 ± 0.9 ; 35% hydrogen peroxide: 5.1 ± 0.3 ; Table 2) and the mean age (years) of the participants (20% hydrogen peroxide: 25.9 ± 8.1 ; 35% hydrogen peroxide: 24.0 ± 6.6) were similar between both groups. The age of the participants ranged from 18 to 44 years. Forty percent or 6 of the participants from the 20% hydrogen peroxide group and 60% or 9 of the participants from the 35% hydrogen peroxide group were female.

Color Evaluation

The color change results are described in Tables 2 and 3. The ANOVA test detected that only the factor assessment time was statistically significant for the SGU and Δ SGU ($p<0.001$). A whitening of about

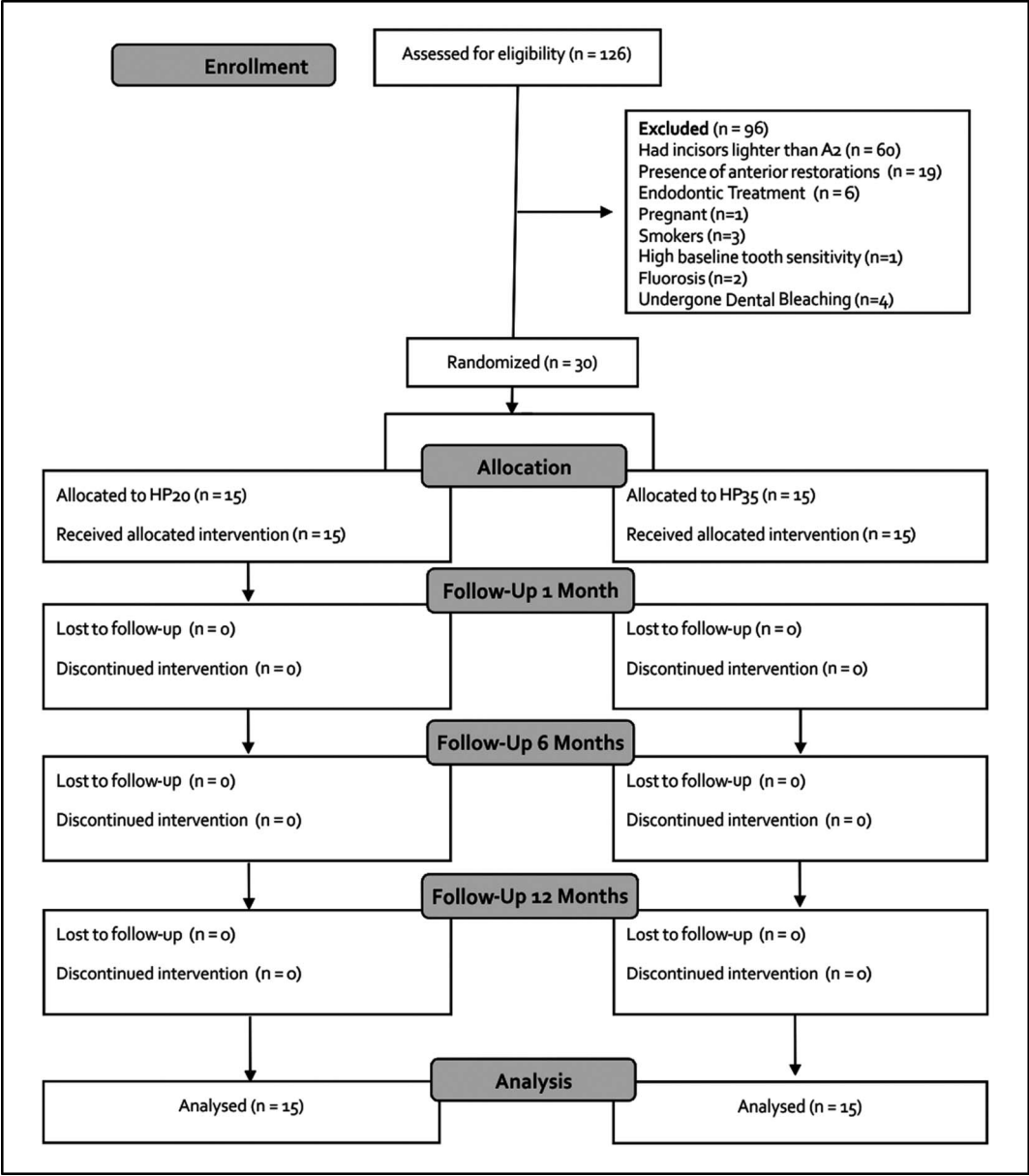


Figure 1. Flow diagram of the clinical trial, including detailed information on the excluded participants.

three units in the vita shade guide (Δ SGU) was observed for both groups (Table 3) after the end of the bleaching protocol.

Tooth Sensitivity

A significantly higher risk of TS was detected after the in-office bleaching with 35% hydrogen peroxide ($p=0.02$; Table 4). No significant difference was observed up to 48 hours after the in-office bleaching ($p=0.09$; Table 4) or during the at-home bleaching ($p=0.71$; Table 4).

Similarly, a higher intensity of TS was detected for the 35% hydrogen peroxide group during the in-office bleaching session ($p=0.04$; Table 5) and up to 48 hours after the in-office bleaching ($p=0.05$; Table 5). During at-home bleaching, no significant difference was detected between the two study groups ($p=0.27$; Table 5)

During recall visits for the evaluation of color rebound (one month, six months, and 12 months), the patients were asked about the presence of spontaneous TS, but none of them responded positively to this query.

Table 2: Means and Standard Deviations of the Color (Shade Guide Tab) Measured at the Different time Assessments for Both Study Groups^a

Periods	Groups	
	20% Hydrogen Peroxide	35% Hydrogen Peroxide
Baseline	5.1 ± 0.3 A	5.3 ± 0.9 A
One week after in-office session	3.6 ± 1.2 B	3.4 ± 1.8 B
After one week of at-home bleaching	2.3 ± 0.9 C	2.5 ± 0.9 C
After two weeks of at-home bleaching	1.3 ± 0.5 D	1.5 ± 1.0 D
One month after bleaching	1.4 ± 0.5 D	1.4 ± 0.6 D
Six months after bleaching	1.86 ± 1.3 C,D	1.78 ± 1.0 C,D
12 months after bleaching	1.93 ± 1.2 C,D	1.8 ± 1.0 C,D

^a Two-way analysis of variance and Tukey test. Means identified with the same letters indicate statistically similar values ($p > 0.05$).

DISCUSSION

In the present study we opted for 10% carbamide peroxide bleaching gel for the at-home technique because this product has been extensively studied and its safety and effectiveness are well documented in the literature.^{8,28-31} For the in-office bleaching, we selected a calcium-containing bleaching gel, as previous studies have already reported reduced risk and intensity of TS compared with other calcium-free products.^{10,23,32} Additionally, the selected in-office bleaching gels have a very friendly protocol, as they do not require product refreshment during the 45-minute application.

Although we employed two different concentrations of hydrogen peroxide gel for the in-office bleaching, one being approximately 40% lower than the traditional 35% hydrogen peroxide, this difference did not affect the overall color change achieved after a single in-office bleaching. Although an earlier study showed that the degree of whitening was dependent on the concentration of the in-office bleaching product, this was less pronounced after a single bleaching session.¹⁰ Additionally, the constant delivery of the at-home bleaching gel for the next two weeks compensated for the lower hydrogen peroxide concentration of the in-office bleaching, producing a similar overall whitening degree after the end of the bleaching protocol.

In general, we observed a whitening of approximately three SGUs in both groups. This is lower than the change of eight to nine SGUs observed by Deliperi and others,¹⁷ who performed combined bleaching using 35% and 38% hydrogen peroxide

Table 3: Means and Standard Deviations of the Color (Change in Shade Guide Unit) at the Different Time Assessments Vs Baseline for Both Study Groups^a

Periods	Groups	
	20% Hydrogen Peroxide	35% Hydrogen Peroxide
Baseline vs one week after in-office session	1.4 ± 1.2 A	1.9 ± 1.3 A
Baseline vs one week after at-home bleaching	2.8 ± 1.0 B	2.8 ± 0.9 B
Baseline vs two weeks after at-home bleaching	3.7 ± 0.5 C	3.8 ± 0.6 D
Baseline vs one month after bleaching	3.7 ± 0.5 C	4.0 ± 1.0 C
Baseline vs six months after bleaching	3.2 ± 1.1 B,C	3.3 ± 1.2 B,C
Baseline vs 12 months after bleaching	3.1 ± 1.0 B,C	3.2 ± 1.0 B,C

^a Two-way analysis of variance and Tukey test. Means identified with the same letters indicate statistically similar values ($p > 0.05$).

followed by 10% carbamide peroxide. This difference can be attributed to the differences in the baseline color of the participants in both studies. The pooled data from several studies of bleaching revealed that baseline color has a significant effect on the overall whitening efficacy; the darker the teeth, the higher the degree of whitening.^{33,34} In the present study, we employed participants with lighter teeth (A2 or darker), while the study by Deliperi and others¹⁷ recruited patients with darker teeth (A3 or darker). Another possible reason could be the use of the Vita classic shade guide. If the patient is A2, the maximum SGU difference measurable is four SGUs, limiting the detectable whitening change that may have occurred.

The similar overall bleaching efficacy of both groups can be viewed with enthusiasm as the protocol with the lower in-office hydrogen peroxide concentration showed less TS sensitivity during the active phase of in-office bleaching using 35% hydrogen peroxide; this percentage was only 35% for the participants bleached with 20% hydrogen peroxide.

The high risk of TS in the group using 35% hydrogen peroxide in this study is in accordance with previous findings in the literature.¹⁸⁻²¹ Few studies have attempted to evaluate the clinical efficacy and TS of a low hydrogen peroxide gel without light activation for in-office bleaching, but the few studies available comparing low and high hydrogen peroxide concentrations for in-office bleaching revealed that less-concentrated products

Table 4: Absolute Risk of Tooth Sensitivity, Along With the Risk Ratio, for Both Groups at the Different Assessment Points ^a						
Periods	Group	Number of Patients With TS		Absolute Risk (95% CI)	Risk Ratio (95% CI)	P Value ^a
		Yes	No			
During in-office session	35% hydrogen peroxide	17	3	85.0 (64.0-95.0)	1.8 (1.1 – 3.2)	0.02
	20% hydrogen peroxide	7	8	47.0 (25.0-69.0)		
Up to 48 hours after in-office session	35% hydrogen peroxide	13	7	65.0 (43.2-81.9)	2.0 (0.9 –4.3)	0.09
	20% hydrogen peroxide	5	10	33.3 (15.2-58.3)		
During at-home bleaching	35% hydrogen peroxide	5	15	25.0 (11.2-46.9)	1.3 (0.5 –3.8)	0.71
	20% hydrogen peroxide	5	10	33.3 (15.2-58.3)		
Abbreviations: TS, tooth sensitivity; CI, confidence interval.						
^a Fisher exact test.						

cause less TS than the conventional 35% hydrogen peroxide gel.^{10,32,35}

This difference may be directly correlated with the reduced amount of hydrogen peroxide that reaches the pulp chamber within the application time. Using a higher hydrogen peroxide concentration may allow for the arrival of larger amounts of reactive species to the pulp, leading to a more intense inflammatory response and greater TS. High hydrogen peroxide concentrations increase the enamel permeability and release more free radicals that reach the pulp.^{36,37} A previous *in vitro* study demonstrated that the cytotoxicity of hydrogen peroxide bleaching gels was dose dependent, with the highest concentration causing the most intense cytopathic effects to the cultured cells.³⁸⁻⁴⁰

The low absolute risk and intensity of TS observed in the at-home bleaching phase of this clinical trial seem to be further evidence of the correlation between hydrogen peroxide concentration and risk

and intensity of TS. Studies comparing the risk and intensity of TS of at-home vs in-office bleaching also reported results favoring the at-home protocol.^{8,18,41,42}

In regard to color stability, the present study revealed that both techniques produced stable color after 12 months, which is in agreement with more recent studies that evaluated the color stability of in-office and at-home bleaching.^{9,43,44} Although some color rebound is expected to occur over time due to the continuous deposition of secondary dentin as well as the deposition of extrinsic stains from colored foods and drinks on the enamel surface, this process probably takes longer than one to two years to occur.

In summary, the present study demonstrated that the use of a combined bleaching technique using a low hydrogen peroxide concentration for the in-office bleaching phase is an excellent clinical technique as it whitens teeth as effectively and stably as the combined technique using 35% hydrogen peroxide yet has the advantage of causing less TS.

CONCLUSION

The combined bleaching technique using at-home bleaching associated with in-office bleaching was effective and stable over the course of 12 months, regardless of the concentration of the hydrogen peroxide used for the in-office phase of the study. However, the use of a lower hydrogen peroxide concentration for in-office bleaching resulted in lower risk and intensity of TS.

Acknowledgement

The authors would like to thank FGM Dental Products for the donation of the bleaching gel used in this investigation.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee

Table 5: Medians (First and Third Interquartile) of Tooth Sensitivity Intensity for Each Group in the Different Periods of Evaluation			
Periods	Groups	Tooth Sensitivity Intensity	P Value ^a
During in-office session	35% hydrogen peroxide	1 (1-1)	0.04
	20% hydrogen peroxide	0 (0-1)	
Up to 48 hours after in-office bleaching	35% hydrogen peroxide	1 (0-2)	0.05
	20% hydrogen peroxide	0 (0-1)	
During at-home bleaching	35% hydrogen peroxide	0 (0-0)	0.27
	20% hydrogen peroxide	0 (0-1)	

^a Mann-Whitney test.

guidelines and policies of State University of Ponta Grossa located in Guarapuava, Paraná, Brazil. The approval code for this study is: 21 05530/09.

Conflict of Interest

The authors of this manuscript 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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