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Effect of Daily Usage Time of 4% Hydrogen Peroxide on the Efficacy and Bleaching-induced Tooth Sensitivity: A Single-blind Randomized Clinical Trial

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Clinical Relevance

Although color change was slightly lower in a 3-week 30-minutes/day protocol, than in the 120-minute protocol, this could be compensated by an extra week of bleaching. The advantage of the shorter protocol is the reduced daily application, making the procedure more comfortable for the patients.

SUMMARY

Objective: Compare the risk/intensity of tooth sensitivity (TS) and color change of a 30-minute vs. the recommended 120-minute application time of 4% hydrogen peroxide (HP) for at-home bleaching.

Methods: A single-blind, parallel, randomized clinical trial was conducted with 92 adult patients with caries and restoration-free anterior teeth A2 or darker, randomly allocated to two groups. Bleaching trays containing 4% HP were used for three-weeks. A four-week regimen was also

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offered to the patients for the 30-min group after the end of the 3-week protocol. The color change was assessed with the Vita Classical (VITA Zahnfabrik, Bad Säckingen, Germany) and Vita Bleachedguide shade guides (VITA Zahnfabrik) and the Vita Easyshade spectrophotometer (VITA Zahnfabrik) at baseline, weekly, and 30 days after the bleaching. The absolute risk and the intensity of TS were assessed daily using the 0-10 visual analogue scale (VAS) and 5-point Numerical Rating Scale (NRS) scale, and patient satisfaction was recorded with a Likert 0-7 scale. Risk of TS (Fisher's test), intensity of TS in NRS scale (Mann-Whitney test), VAS scale (*t*-test), and a color change (*t*-test) were compared.

Results: The 30-minute group saw color change of around 1 SGU inferior to the 120-minute group in all-time assessments ($p<0.05$). After an extra week of bleaching, mean color change was similar ($p>0.05$). Patient satisfaction was high for both groups ($p>0.05$).

Conclusions: A four-week protocol of at-home dental bleaching with 4% HP for 30 minutes/day whitened teeth similarly to the 120 minutes/day protocol, with low intensity of dental sensitivity and high patient satisfaction.

INTRODUCTION

The constant concern of contemporary society to obtain a bright and harmonious smile increased the popularity of dental bleaching, being nowadays one of the most requested clinical procedures of dentistry.[1] The bleaching process consists of reducing the saturation of the tooth, using bleaching gels based on peroxides, which provide a lighter-looking smile.[2] This treatment can be performed by two supervised techniques: at-home and in office.[3]

Among these techniques, at-home bleaching is the most used,[4] due to easy application, excellent esthetic result, lower cost than in-office bleaching, and full acceptance by patients, with efficacy extensively investigated in the literature.[2,5,6] The most frequently scrutinized at-home bleaching agent in the dental literature is 10% carbamide peroxide;[5,6] however, low concentrate hydrogen peroxide is also available for at-home use. Carbamide peroxide gels are used in concentrations between 10% and 22%,[7,8] both with 0.5% potassium nitrate and 0.11% fluoride ions while hydrogen peroxide is used in concentrations from 4% to 14%.[9–11]

Both dental bleaching agents are effective to whiten teeth,[12] but they vary in their recommended daily usage time. While carbamide peroxide is usually recommended for longer daily periods, hydrogen peroxide-based agents are recommended for shorter daily application times due to their different degradation kinetics.[13-15]

Despite the efficacy of at-home bleaching to whiten teeth, tooth sensitivity (TS) is a common and undesirable side effect. Tooth sensitivity results from the damage that hydrogen peroxide, which passes quickly through enamel and dentin, causes to the dental pulp.[16] Although for at-home bleaching TS is usually mild and transient, there are cases in which severe TS is reported, leading the patient to discontinue treatment.[16,17]

Higher gel concentration and contact time with the dental surface are known to be directly related to the higher prevalence of tooth sensitivity.[7,18-22] Indeed, Chemin & others[10] demonstrated that a 4% hydrogen peroxide bleaching gel had lower risk and intensity of TS than a 10% hydrogen peroxide product, even though approximately 40% of the participants from the 4% hydrogen peroxide group experienced some level of TS.

Control over the application time can also be an alternative to reduce or prevent bleaching-induced TS. In a study conducted with carbamide peroxide for at-home bleaching, the authors showed that reducing the application time from 8 hours to 1 hour daily reduced the risk and intensity of TS by half without jeopardizing color change.[23] Although this effect has been demonstrated for carbamide peroxide gels, randomized clinical trials with variations in the at-home protocol, mainly application times, are still scarce in the literature.

Many manufacturers recommend the application of 4% hydrogen peroxide gel for two hours daily; however, the amount of active agent available to react with tooth structure is known to drop by half in just 20 minutes,[15] which suggests that the use of the tray for prolonged periods may not offer benefits and may potentially increase the risk of adverse effects.

Therefore, the objectives of the present study were to evaluate the impact of reduced application time of a 4% hydrogen peroxide product from 120 minutes/day to 30 minutes/day on the efficacy and tooth sensitivity of at-home bleaching in adults. The null hypotheses tested were that the application of 4% hydrogen peroxide gel for 30 minutes would produce similar: 1) color change and 2) bleaching-induced tooth sensitivity compared to the recommended 2-hour application.

METHODS AND MATERIALS

Ethics Approval and Protocol Registration

The report of this clinical trial followed the Consolidated Standards of Reporting Trials (CONSORT) statements.

This study was registered in the Brazilian clinical trials registry (ReBEC) under the number RBR-96QPWN.

Trial Design, Settings, and Locations of Data Collection

This was a single-blind, parallel, randomized clinical trial, in which the evaluator was masked to the group assignment. The treatments proposed in this study were performed in the School of Dentistry clinic at the state University of Ponta Grossa, PR, Brazil, from November 2018 to July 2019.

Recruitment

The volunteers were recruited through local advertisements. All participants signed an informed consent form before the beginning of the study and received dental prophylaxis to remove extrinsic stains.

Eligibility Criteria

Volunteers were selected for this study according to the pre-established criteria. To be included in the study, they were required to be at least 18 years old, be in good general and oral health, and have the anterior maxillary teeth without restorations or caries lesions. They were required to present canine shade A2 or darker according to a value-oriented Vita Classical shade guide (Vita Zahnfabrik, Bad Säckingen, Germany).

Patients who had undergone previous bleaching procedures, with dental prosthesis or visible cracks of enamel, history of spontaneous tooth sensitivity (TS), severe tooth discoloration coming from dental pathologies or use of medications, were not included in the study. Pregnant or lactating women and patients under orthodontic treatment or taking any anti-inflammatory or analgesic medicines were also excluded.

Sample size

The sample size calculation was based on the primary binary outcome (absolute risk of TS) for a superiority trial. The absolute risk of TS for at-home bleaching using 4% hydrogen peroxide gel (White Class, FGM, Joinville, Brazil) was reported by Chemin & others[10] to be 38%. Thus, a minimum sample size of 44 subjects per group was required to have an 80% chance of detecting, as significant at the two-sided 5% level, a decrease in the primary outcome measure from 38% in the control group to 13% in the experimental group. A 5% increase in the sample size, considering potential loss or refusal, gave a total sample size of 92 subjects.

Randomization, Allocation Concealment, and Binding

The randomization process was performed on a website freely available online (http://www.sealedenvelope.com). Blocked randomization (block sizes of two and four) with an equal allocation ratio was used to form the allocation list for both treatment groups. The sequence was inserted into cards placed sequentially in opaque and sealed envelopes numbered from 1 to 92, prepared by a third person who was not involved in the research protocol. These envelopes were opened only at the moment of the intervention, ensuring the random sequence's concealment.

Participants and operators could not be blinded to the study groups, as they could easily identify the two protocols used. However, the evaluator who performed the color assessments was blinded to the treatments. To maintain evaluator blinding, the two protocols—30 minutes and 120 minutes per day with bleacching gel were explained to the patients by a researcher who was not an evaluator; the protocols were coded as either A or B. Only the research coordinator knew the coding system.

Bleaching Procedure

Alginate impressions (Plastalgin, Septodont Healthcare India Private Ltd., Raigad, Maharashtra, India) were taken of each subject's maxillary and mandibular arch, and after disinfection, stone molds were prepared (Asfer, Asfer Indústria Química Ltda, São Caetano do Sul, Brazil). Custom bleach trays were fabricated by heating 0.9 mm soft vinyl material (FGM Dental Products, Joinville, Brazil) in a special device (Plastivac P7, BioArt, São Carlos, SP, Brazil). The excess material on the buccal and lingual surfaces was trimmed 1 mm above the gingival junction.

The bleaching gel used in this study for both groups was the 4% hydrogen peroxide agent (White Class, FGM). In the experimental group, the subjects used the bleaching tray for 30 minutes daily. In the control group, the tray was used for 120 minutes daily, following the manufacturer's instructions. Participants from both groups performed bleaching for three weeks. A four-week bleaching regimen was offered to the patients in the 30-minute group, after the one-month recall, if they did not reach the same bleaching efficacy of the 120-minute group. After the recommended daily period, the subjects were instructed to remove the trays, rinse with water and brush their teeth with a toothpaste free of bleaching agents or desensitizers. Both arches were bleached in the same way. All subjects received verbal and written instructions about the proper use of the bleaching agent and oral hygiene control.

Outcomes

Tooth Color Shade Evaluation—

The tooth color shade evaluation was recorded at baseline, weekly during the treatment, and one-month postbleaching, by two blinded calibrated evaluators (Kappa statistics measuring at least 85%). The evaluation was performed subjectively using value-oriented shade guide units and objectively using a dental spectrophotometer.[24] All recordings were made in the same room under D65 daylight fluorescent light with a luminescence intensity of between 1200 and 1600 lux.

Two shade guides were used for subjective evaluation: the Vita Classical (Vita Zahnfabrik) and the Vita Bleachedguide 3D-MASTER (Vita Zahnfabrik). The measurement area for shade matching was the middle third of the right upper canine's facial surface. If there were disagreements between the examiners during shade evaluation, a consensus was reached.

The Vita Classical scale was converted into numeric values arranged in 16 tabs from the highest (B1) to the lowest (C4) value. Although this scale is not linear in the most real sense, the scales' changes were treated as representing a continuous and approximately linear ranking, as already performed in prior published studies.[1,25,26] Thus, the lower the numeric value, the whiter the tooth. The Vita Bleachedguide 3D-MASTER contains lighter shade tabs, and it is already organized from the highest (0M1) to the lowest (5M3) value, by scores of 1 to 24. Shade guide units (SGU) were calculated by subtracting the individual recall times from those measured at baseline.

For objective evaluation, the Vita Easyshade spectrophotometer (Vita Zahnfabrik) was used. An impression of the maxillary arch was taken with high-putty silicone paste (Perfil, Coltene Holding, Altstätten, Switzerland), and a window on the labial surface of the silicone guide was created by using a metallic device with well-formed borders and 6-mm radius, which is precisely the diameter of the tip of the spectrophotometer, in the middle third of the right upper canine to standardize the area for color evaluation with the spectrophotometer.

The color parameters L*, a*, and b* were recorded. L* represented the luminosity, with values ranging from 0 [black] to 100 [white]), and a* represented color variations in the red-green axis, while b* represented color variations in the yellow-blue axis. Color change (ΔE) was given by the difference between baseline and each recall period, calculated by using the original CIELab (1976)[27] and also using the CIEDE2000, a formula based on the CIELab, which measures color difference and includes not only lightness, chroma, and hue weighting, but also an interactive term between chroma and hue differences for improving insight for small color differences.[28]

Tooth Sensitivity Evaluation—

The participants recorded TS daily during treatment using a Visual Analogue Scale (VAS) and a five-point Numeric Rating Scale (NRS).[22,25,26] For the VAS, the participants were instructed to place a line perpendicular to a 100 mm horizontal line with zero at one end indicating "no TS" and the other end indicating "severe TS." The distance between the marked line to the zero end was measured with the aid of a millimeter ruler.[1] For the NRS, the participants were instructed to indicate a numerical value (0 = none, 1 = mild, 2 = moderate, 3 = considerable and 4 = severe) that most represented their TS. These forms were returned to the researcher on the next clinical appointment.

The worst score from the NRS and the highest numeric value obtained in the VAS during the bleaching treatment were taken for statistical purposes. If the participant scored 0 (no sensitivity) in all-time assessments, this participant was insensitive to the bleaching protocol. We calculated the absolute risk of TS, representing the percentage of patients who reported TS at least once during treatment and the overall TS intensity for the two pain scales.

Assessment of Patients' Satisfaction—

Using a 7-point Likert Scale,[21] participants were asked to express how much they agreed to the statement that reflected their satisfaction with the bleaching treatment after the end of the treatment. For this purpose, the 7-point Likert scale was anchored by 1 (very dissatisfied) to 7 (very satisfied). Similarly, the participants used the same scale to express how much they would recommend the protocol to family and friends by anchoring 1 (would not recommend) and 7 (definitely recommend).

Statistical Analyses

The statistical analyses followed the intention-to-treat protocol according to CONSORT suggestion[29] and involved all the 92 participants who were randomly assigned. The statistical analyses were performed using the SigmaPlot for Windows version 12.0 (Systat Software) software, and in all statistical tests, the significance level was set at 5%.

The absolute risk of TS of both treatments was compared using Fisher's exact test. The relative risk and the confidence interval for the effect size were calculated. The comparison of the TS intensity (NRS and VAS) at the two different assessment points was performed

by using the Mann-Whitney test and the *t*-test for independent samples, respectively. Color changes (ΔSGU and ΔE) between groups at each assessment period were compared using a *t*-test. Comparisons between assessment periods and within groups were performed with the repeated measures one-way analysis of variance (ANOVA) and Tukey's test for pairwise comparisons. Data from the Likert scale from both groups were compared using a *t*-test for independent samples. In all statistical tests, the level of significance was set at 5%.

RESULTS

Characteristics of the Participants

A total of 146 participants were examined, but only 92 were eligible for the clinical trial (Figure 1). Reasons for exclusion are described in Figure 1. The demographic characteristics and the baseline color of the participants are described in Table 1. The distribution of the genders in both groups, as well as the baseline color parameters, were statistically similar, (p>0.05). The patients' ages ranged from 18 to 42 years, and most participants were White.

Adherence to the Protocol

Two participants from the 120-minute group did not return to the recall visits. We imputed the mean data of the group for the missing cells of these two participants.

One participant from the 30-minute group discontinued intervention because she was hospitalized for a reason not related to the intervention. The other two participants from the 120-minute group claimed lack of time and did not return for some recall visits. For these three participants, the last observation was carried forward for statistical purposes to keep the intention-to-treat analysis.[29]

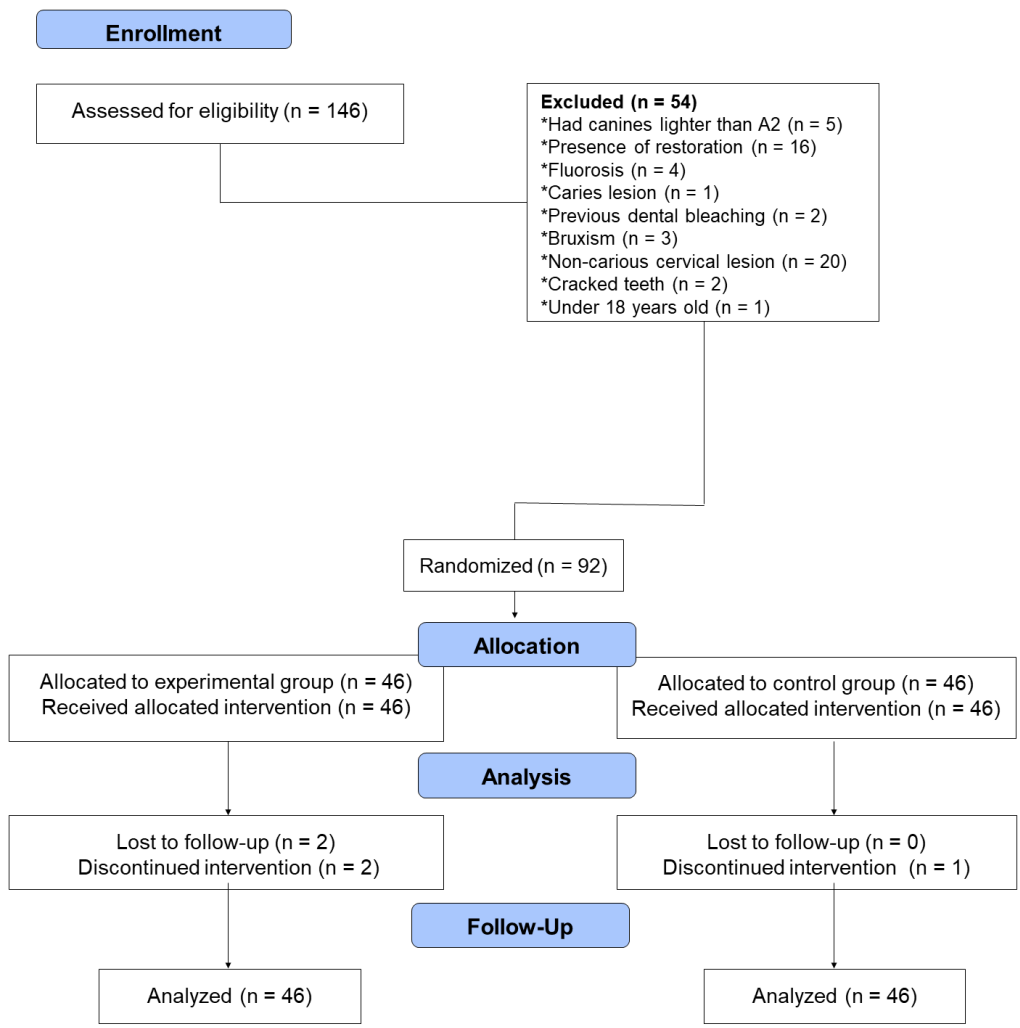

Figure 1. *Flow diagram of study design phases including enrollment and allocation criteria*

Table 1: *Baseline Characteristics of the Participants*

Characteristics		30-min	120-min	*p*-value
Baseline color, (mean ± SD)	SGU Vita Classical	11.0 ± 2.5	11.1 ± 2.4	0.417†
	SGU Vita Bleachedguide	20.3 ± 2.4	20.3 ± 2.8	1.0†
	L*	82.0 ± 3.4	82.7 ± 3.4	0.362†
	a*	-1.3 ± 1.7	-1.4 ± 2.3	0.793†
	b*	24.6 ± 3.9	24.8 ± 4.5	0.886†
Age (years; mean ± SD)		25 ± 6.4	23 ± 5.8	0.133†
Gender (female; %)		76.1	76.1	0.807††
Race	White (%)	73.9	78.2	0.879††
	Black (%)	2.2	2.2	
	Other (%)	23.9	19.6	

Abbreviations: a, color variations in the red-green axis; b*, color variations in the yellow-blue axis; L* luminosity, with values ranging from 0 [black] to 100 [white]); SGU, shade guide unit.*
†t-test for independent samples.
††Chi-square test.

All other participants, except those five, attended all recall visits up to one month after the treatment. Figure 1 depicts the participant flow diagram in the different phases of the study design.

Tooth Sensitivity

Table 2 demonstrates the number of participants who experienced TS during the bleaching treatment in each group. There was no significant difference between the two groups (Fisher test, p=0.34). The relative risk (95% confidence interval) crosses the null value 1, showing that reducing the application time of bleaching gel does not seem to reduce TS.

Table 3 shows data from the TS intensity obtained by NRS and VAS scales. No significant difference in the intensity of TS between groups was observed in any pain scale (p=0.32 and p=0.11 for NRS and VAS, respectively).

Color Evaluation

The descriptive data from bleaching obtained after three weeks of treatment can be seen in Tables 4 and 5. A higher degree of whitening was observed in participants from the 120-min in all-time assessments when the color change was evaluated with shade guide units (p<0.05). Participants from the 30-minute group performed an extra week of bleaching. The four-week 30-minute bleaching regimen achieved the same bleaching efficacy of the three-week 120-minute bleaching regimen (p>0.05).

For DE_{76}, significant differences between groups were observed (p<0.05) in some time assessments, while others were at borderline significance. For DE_{00}, non-significant results were obtained in all-time assessments, being borderline at the 1-month post- bleaching time. Similar results between the two groups were detected when the 30-minute group received an extra week of bleaching (p>0.05).

The mean L* values increased while the mean values of a* and b* decreased in both treatment groups (data not shown). These data suggest that the color change occurred towards an increase in lightness and reduction in the chroma, making teeth less yellow and less saturated.

Table 2: *Comparison of the Number of Patients who Experienced Tooth Sensitivity During the Bleaching Regimen in Both Groups Along with Absolute and the Risk Ratio*

Groups	Tooth Sensitivity (Number of Patients)		Absolute Risk (95% CI)†	Risk Ratio (95% CI)
	Yes	No		
30 min	32	14	70 (55-80)	0.9 (0.7-1.1)
120 min	37	9	80 (67-89)	

Abbreviations: CI, confidence interval.
†Fisher test (p=0.34).

Table 3. *Tooth Sensitivity Intensity Using Both Pain Scales, as well as the* p*-value from the Statistical Analysis*

Pain Scales	Means and Standard Deviations		Mean Difference (95% CI)	Medians and Interquartile Range		*p*-value
	30-min	120-min		30-min	120-min	
NRS (0-4)	0.9 ± 0.9	1.1 ± 0.9	0.2 (-0.2-0.6)	1 (0-1)	1 (0-1)	0.32†
VAS (0-10)	0.9 ± 1.3	1.5 ± 2.1	0.6 (-0.1-1.3)	0.4 (0-1.4)	0.8 (0.1-1.8)	0.11††

Abbreviations: CI, confidence interval; NRS. numeric rating scale; VAS; visual analogue scale.
†Mann-Whitney test
††t-test

Patient Satisfaction

Data from the Likert scale can be seen in Table 6. Patients in different bleaching groups gave similar scores (p=0.063) when evaluating their satisfaction after the end of the bleaching treatment (three-week regimen). They were quite satisfied with the overall bleaching treatment. The high and similar ratings between groups indicate that participants from both groups would undoubtedly recommend the same bleaching treatment to their family or friends (p=0.129).

DISCUSSION

A significant color change occurred after the end of the three-week protocol for both groups. However, this study showed that the recommended application time of 120-minutes produced a slightly higher whitening degree on tooth shade subjective evaluation (around one shade guide unit in all-time assessments) than that achieved with a daily 30-minute application when a 4% HP gel was employed. This is evidence that the color change occurring during bleaching is time-dependent,

Table 4: *Means and Standard Deviations of ΔSGU Obtained with the Vita Classical and Vita Bleachedguide 3D-MASTER at Different Periods*[a]

ΔSGU (Vita Classical)				
Periods	**30-min**	**120-min**	**Mean Difference (95% CI)**	***p*-value†**
One week	2.3 ± 2.0 A	3.1 ± 1.7 A	0.8 (0.03 to 1.57)	0.045
Two weeks	4.3 ± 2.2 B	5.9 ± 2.4 B	1.6 (0.65 to 2.55)	< 0.001
Three weeks	5.6 ± 2.4 C	6.8 ± 2.4 C	1.2 (0.21 to 2.19)	0.013
1 month post bleaching	5.3 ± 2.4 C	6.7 ± 2.5 C	1.4 (0.38 to 2.42)	0.006
3-week (120-min) vs. 4-week (30-min)	6.1 ± 2.6	6.8 ± 2.4	0.7 (-0.34 to 1.74)	0.157
ΔSGU (Vita Bleachedguide 3D-MASTER)				
Periods	**30-min**	**120-min**	**Mean Difference (95% CI)**	**p-value†**
One week	2.7 ± 1.9 A	3.7 ± 1.7 A	1 (0.25 to 1.75)	0.015
Two weeks	4.7 ± 2.1 B	5.8 ± 2.1 B	1.1 (0.23 to 1.97)	0.013
Three weeks	6.0 ± 2.3 C	7.1 ± 2.6 C	1.1 (0.08 to 2.12)	0.028
1 month post bleaching	5.6 ± 2.1 C	6.9 ± 2.8 C	1.3 (0.27 to 2.33)	0.013
3-week (120-min) vs. 4-week (30-min)	7.0 ± 2.5	7.1 ± 2.6	0.1 (-0.96 to 1.16)	0.870

Abbreviations: ΔSGU, change in shade guide units; CI, confidence interval.
[a]Comparisons within time assessments are valid only within each column. Different letters mean statistically different averages (repeated measures one-way ANOVA, p*<0.05).*
†t-test for independent samples.

Table 5: *Means and Standard Deviations of ΔE Obtained by Spectrophotometer (Vita Easyshade) at Different Periods*[a]

ΔE 1976				
Periods	**30-min**	**120-min**	**Mean Difference (95% CI)**	***p*-value**[†]
One week	5.8 ± 2.5 A	6.9 ± 3.1 A	1.1 (0.03 to 2.17)	0.061
Two weeks	7.6 ± 2.8 B	9.0 ± 3.5 B	1.4 (0.09 to 2.71)	0.039
Three weeks	8.4 ± 3.1BC	9.9 ± 4.2 C	1.5 (-0.03 to 3.03)	0.061
1 month post bleaching	8.9 ± 3.2 C	10.7 ± 4.2 D	1.8 (0.25 to 3.35)	0.030
3-week (120-min) vs. 4-week (30- min)	9.7 ± 3.4	9.9 ± 4.2	0.2 (-1.38 to 1.78)	0.816
ΔE 2000				
Periods	**30-min**	**120-min**	**Mean Difference (95% CI)**	**p-value**[†]
One week	3.8 ± 1.7 A	4.4 ± 2.0 A	0.6 (-0.17 to 1.37)	0.118
Two weeks	5.0 ± 1.9 B	5.7 ± 2.2 B	0.7 (-0.15 to 1.55)	0.077
Three weeks	5.5 ± 2.0 BC	6.2 ± 2.6 C	0.7 (-0.26 to 1.66)	0.134
1 month post bleaching	5.8 ± 2.1 C	6.8 ± 2.6 D	1 (0.02 to 1.98)	0.053
3-week (120-min) vs. 4-week (30- min)	6.2 ± 2.2	6.2 ± 2.6	0 (-1 to 1)	0.979

Abbreviations: ΔSGU, change in shade guide units; ANOVA, analysis of variance; CI, confidence interval.

[a]*Comparisons within time assessments are valid only within each column. Different letters mean statistically different averages (repeated measures one-way ANOVA,* p< *0.05).*

[†]t-*test for independent samples.*

since the 30-minute time is enough to bleach teeth but in a slightly whitening degree (approximately 1.2 units of ΔSGU and 1.5 units of ΔE 1976). Thus, the first null hypothesis was rejected.

Such results are consistent with previous studies demonstrating that the color change achieved during bleaching is directly related to the amount of time that the agent is in contact with the dental structure.[23,30,31]

However, the significant difference in color change in the 30-minute group was compensated by longer treatment time. Although not specified in the research protocol, we performed an extra week of bleaching in the participants from the 30-minute group (four-week protocol), and we observed that the color change reached the same level of that achieved in the three-week 120-minute protocol.

Regarding TS, literature findings led us to hypothesize that a shorter application time of a low concentrate product (4% HP) could reduce TS. A previous in vitro study has already demonstrated that diffusion of HP, cell viability, cell morphology alterations, oxidative stress, and cell membrane damage occurs in a concentration-time dependent fashion.[32] In agreement with those findings, clinical studies have also recommended reduced application times to minimize bleaching-induced TS.[20,23,33,34]

Contrary to our expectation, the present study did not show any difference in the risk and intensity of

Table 6: *Patient Satisfaction and Patient's Recommendation Using a 7-point Likert Scale*[a]

7-point Likert Scale	**Means and Standard Deviations**		**Medians and Interquartile Range**		***p*-value**[†]
	30-min	**120-min**	**30-min**	**120-min**	
Patient satisfaction	6.0 ± 0.9	6.4 ± 0.9	6 (5-7)	7 (6-7)	0.063
Patient recommendation	6.4 ± 0.9	6.7 ± 0.7	7 (6-7)	7 (7-7)	0.129

[a]*Maximum of 7 points.*

[†]Mann-Whitney statistical analysis.

TS between the two application times of 4% HP. Approximately 70% to 80% of the participants from both groups experienced pain at least once during bleaching, and the intensity of TS was very low in both cases. Thus, the second null hypothesis was not rejected.

The differences between the present and earlier clinical studies are ascribed to their use of high concentrate products and more extended application periods than those used in the present investigation. For instance, Kose & others employed a 35% HP in-office product[20] showing lower TS when the product was applied for 30 minutes rather than the recommended 45-minute protocol. Cardoso & others[23] employed a low concentrate 10% carbamide peroxide; however, they compared a short application time of one-hour versus an overnight use (at least 7-hour difference between the groups) showing a lower risk of TS for the shorter application period.

Unlike earlier studies, we used a very low concentration of HP and a slight difference in daily time regimen, which explains the similar TS risk and intensity of both time regimens in the present study. The extra amount of radical oxygen species (ROS) that may reach the pulp in the 120-minute regimen may not surpass the pulp defense system, contrary to what occurs when high concentrate products are applied for longer times.[32]

However, we could observe that even in the shorter application time of 30 minutes, the 4% HP product was capable of triggering TS. Due to its relatively low molecular mass (34 g/mol), HP crosses enamel and dentin very fast, and it takes approximately 15 minutes for the hydrogen peroxide to reach the pulp chamber.[31]

Clinical trials of bleaching protocols are essential as they allow the identification of optimum concentration and application times to keep HP penetration in the pulp chamber minimal without compromising bleaching efficacy. In this way, other time regimens than the one recommended by manufacturers should be investigated to find the shortest application time that yields similar color change.

We used shade guide units and a spectrophotometer for color change evaluation. The spectrophotometer is an objective method capable of quantifying differences in color and its dimensions.[24] The color dimensions can be quantified using either the CIELab 1976 formula (ΔE_{ab}) or the CIEDE2000 formula (ΔE_{00}). While shade guide units and the CIELab 1976 formula reached the same conclusions in most of the time assessments, the CIEDE2000 was less sensitive in detecting the slight changes between the groups under investigation. Kury & others[35] also found differences between the methods of an objective assessment; in their study, ΔE_{00} was also unable to detect a significant difference between groups.

The fact that some color change instruments detected significant differences while other instruments did not, cannot be seen as a limitation of the present study. These findings do reflect that the differences observed between the daily regimens were subtle and not substantial. Had they been expressive, all methods of a color change would yield statistically significant results. Similar results between the study groups were also observed with another recently developed index used to compare the bleaching efficacy of treatments, called whitening index (WI_D).[36] Its calculation is straightforward, and it is based on the L*, a*, and b* parameters from baseline and after bleaching. After an extra week of bleaching for the participants from the 30-minute group (4-week), these values were statistically similar to the three-week 120-min protocol.

Perceptibility (PT) and acceptability (AT) thresholds are very relevant in clinical dentistry.[37] Paravina & others[38] found that the PT and AT values were 1.2 and 2.7, respectively, for the CIELab system and 0.8 and 1.8, for the CIEDE2000 system. These values can be used as a reference for the evaluation of color changes after dental bleaching.

In our study, the ΔEab and ΔE_{00} values for whitening treatments were above the 50%:50% perceptibility thresholds and 50%:50% acceptability thresholds (AT) in dentistry for both groups, indicating that color change was perceptible for most observers.

The results of patients' satisfaction are in line with the subtle differences observed. Despite the statistical difference in the whitening degree between groups after three weeks of treatment for most tools employed, this difference was, in average, only one shade guide unit and did not affect patients' satisfaction or treatment recommendation. As important as using objective tools for color change evaluation is, the use of patient-centered outcomes to assess the efficacy of any given treatment[39] is just as important.

The literature has shown that there are differences between patients' and dentists' expectations with dental bleaching treatment,[40] but patients' opinion is more important than the dentists' perception. This is why patient-reported outcomes, which place patients' values, needs, and beliefs in the center of the healthcare field, seem to be of greater importance than evaluator-centered outcomes.[41]

The choice of the two application times investigated in this study did not impact patients' satisfaction. The chosen protocol for any patient may be based on other features, such as patients' time availability to wear the bleaching tray and patients' comfort.

In short, the reduction in daily use time of the whitening tray with a low HP concentrate gel produced a slightly lower whitening degree than the recommended 120-minute application time and the same risk and intensity of TS. However, both protocols resulted in high patient satisfaction.

CONCLUSIONS

The 30-minute application time of 4% HP for three weeks treatment can result in complete patient satisfaction. However, this treatment protocol does not produce the same whitening degree as the 120-minute protocol. This difference is not noticed when the treatment time of the 30-minute group is extended to four weeks. Tooth sensitivity was low in both protocols.

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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 Scientific Review Committee from the State University of Ponta Grossa (protocol number 2.971.337).

Conflict of Interest

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

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