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Clinical Research

Effectiveness of and Dental Sensitivity to At-home Bleaching With 4% and 10% Hydrogen Peroxide: A Randomized, Triple-blind Clinical Trial

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Clinical Relevance

At-home dental bleaching with 4% hydrogen peroxide is as effective as with 10% hydrogen peroxide, but it produces a lower risk for and less intense tooth sensitivity.

SUMMARY

Objectives: To evaluate the risk for and intensity of tooth sensitivity and color change of at-home dental bleaching with 4% and 10% hydrogen peroxide (HP).

Methods: For this study, 78 patients were selected according to the inclusion and exclusion criteria and randomized into two groups: HP 4 (White Class 4%, FGM) and HP 10 (White Class 10%, FGM). In both groups, the at-home bleaching was performed for a period of 30 minutes twice a day for two weeks. The color was assessed by Vita Classical, Vita Bleachedguide 3D-MASTER and spectrophotometer Vita Easyshade (Vita Zahnfabrik) at baseline, during bleaching (first and second weeks) and after bleaching (one month). Patients recorded their tooth sensitivity using a numeric rating scale (0-4) and visual analog scale (0-10). Data from color change (DeltaE data) was submitted to two-way analysis of variance. The color change data in Delta SGU from the two shade guide units were compared with the Mann Whitney test. The risk of tooth sensitivity was evaluated by χ^2 test and the intensity of tooth sensitivity from both scales was evaluated by a Mann-Whitney test (α=0.05).

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Results: The absolute risk and intensity of tooth sensitivity was higher in the group that used HP 10 than the one that used HP 4. Data from change in the number of shade guide units and color variation after one month of bleaching for both groups showed significant whitening, with no difference between groups.

Conclusions: At-home bleaching is effective with 4% and 10% HP concentrations, but 10% HP increased the absolute risk and intensity of tooth sensitivity during at-home bleaching.

INTRODUCTION

Dental bleaching is a popular procedure for treatment of discolored teeth.[1-4] Among the dentist-supervised techniques, this procedure can be performed at home or in the office. At-home dentist-supervised bleaching with custom trays is more popular than the in-office techniques due to some widely known advantages: lower risk and intensity of tooth sensitivity[5,6]; fewer required visits to the dental office; and lower cost to achieve the same whitening results as those produced with agents of higher concentration used in the in-office bleaching protocol.[7,8]

Haywood and Heymann[1] first described the at-home bleaching technique in 1989. The active 10% carbamide peroxide (CP) ingredient was delivered in a custom bleaching tray and worn overnight by the patient for two to three weeks. This bleaching modality has shown satisfactory clinical results.[7-13] However, since its introduction, the original technique has undergone some modifications. Changes in tray material, tray design, active ingredient concentrations, time of custom-tray use, and type of active ingredients are examples of these modifications.[14,15]

Some of these changes, such as the increase in the active CP gel concentration and the introduction of low hydrogen peroxide (HP)–based products for at-home vital bleaching, were envisioned to shorten the clinical time required to reach satisfactory color changes.[11,12,16,17] Different from CP gels, HP-based products undergo a faster degradation rate[18-21] and therefore should be used for shorter periods of time. Whereas a 10% CP gel contains 64% of active HP after one hour,[18] a 3% HP at-home bleaching agent contains only 32% of active HP after one hour.[20] This can be seen as advantageous for those patients who do not want to wear the bleaching tray for prolonged periods of time.

Currently, there are various concentrations of CP or HP gels on the market, with CP gels ranging from 10% to 22% and HP gels ranging from 3% to 10% for at-home dental bleaching.[22-25] Some studies have already compared different concentrations of CP gels for at-home bleaching, and no significant differences in terms of color change were detected when both products were used for at least two weeks.[26-28]

However, to our knowledge, there is a lack of randomized, controlled clinical trials investigating the effect of varying concentrations of HP bleaching agents on the efficacy or the risk and intensity of tooth sensitivity of at-home bleaching. Therefore, the aim of this triple-blind, controlled and parallel, randomized clinical trial was to evaluate the color change and risk and intensity of tooth sensitivity of at-home bleaching performed with HP gel in concentrations of 4% and 10%.

METHODS AND MATERIALS

Ethics Approval and Protocol Registration

This clinical investigation was approved by the ethics committee from the local university (Protocol Number 1.009.881), and it was registered in the Brazilian clinical trials registry under the identification number RBR-45xmzj. We prepared this article using the protocol established by the Consolidated Standards of Reporting Trials statement.[29]

Trial Design, Settings, and Locations of Data Collection

This was a triple-blind, controlled, parallel, randomized clinical trial, in which the patient, operator and evaluator were blinded to the group assignment. This study was performed between March 2015 and September 2015 in the clinics of the school of dentistry at the local university.

Recruitment

Two weeks before the bleaching procedures, all the volunteers, who were patients and students seeking treatment at the clinic of the dental school, received dental prophylaxis with pumice and water in a rubber cup and signed an informed consent form. Recruitment was performed by placing a written advertisement on the university walls.

Eligibility Criteria

Patients included in this clinical trial were at least 18 years old and had good general and oral health. The participants had six caries-free maxillary anterior teeth, without restorations and with no periodontal disease. The superior central incisors

were shade A2 or darker as judged by comparison with a value-oriented shade guide (Vita Classical, Vita Zahnfabrik, Bad Säckingen, Germany). Two calibrated investigators performed this evaluation. They were required to have an agreement of at least 85% (κ statistic) before beginning the study evaluation.

Participants with anterior restorations or a dental prosthesis, orthodontics apparatus, or severe internal tooth discoloration (tetracycline stains, fluorosis, and pulpless teeth) were not included in the study. In addition, pregnant/lactating women, participants with any other pathology that could cause sensitivity (such as recession, dentin exposure, or the presence of visible cracks in teeth), smokers, bruxers, or participants who had previously undergone tooth-whitening procedures were also excluded.

Sample Size Calculation

The primary outcome of this study was the absolute risk of tooth sensitivity (TS). A preliminary study with 20 patients using the 10% hydrogen peroxide gel (White Class Calcium, FGM, Joinville, Brazil) showed an absolute risk of TS of 70%. Thus, a minimal sample size of 38 participants per group were required to have a 90% chance of detecting, as significant at the two-sided 5% level, a decrease in the primary outcome measure from 70% to 35% using a low-concentration HP gel.

A secondary sample size calculation for the secondary outcome color change was also performed. For color variation (ΔE) a minimum of 33 participants per group would be required to exclude a mean difference of 3.0 in the ΔE, with 90% power and 5% α, considering that the standard deviation of ΔE is approximately 3.5 units. This limit of equivalence (difference of means) was because only a ΔE greater than 3.0 is considered clinically perceptible.

Randomization and Allocation Concealment

We used blocked randomization (block sizes of two and four) with an equal allocation ratio to form the allocation list for the two comparison groups. The randomization list was prepared in a software program freely available online (http://www.sealedenvelope.com). Opaque, sealed, and consecutively numbered envelopes containing the identification of the groups were prepared by a third person who was not involved in the research protocol. An envelope was only opened immediately before the beginning of the bleaching procedure.

Study Intervention

Alginate impressions (Avagel, Dentsply, Petrópolis, Brazil) were made of each participant's maxillary arch, and after disinfection these were filled with dental stone (Asfer, Asfer Indústria Química Ltda, São Caetano do Sul, Brazil). A 0.9-mm soft vinyl material (Whiteness Placas para Moldeiras, FGM) was used to fabricate the custom-fitted tray that would hold the whitening gel in the Plastivac P7 (BioArt, São Carlos, Brazil). The excess material from the labial and lingual surfaces was trimmed to 1 mm from the gingival junction.

At this time, group assignments were revealed and each patient received the bleaching tray and his or her respective bleaching product. We instructed all participants to wear the tray with the bleaching agent for 30 minutes twice a day for 14 days. We instructed the participants to remove the tray after each bleaching period, wash it with water, and brush their teeth as usual.

As a measure of adherence to the experimental protocol, participants were given a diary in which they were asked to take note of the number of times they used the tray during the treatment. If they had worn the bleaching tray 28 times, this would result in a 100% adherence to the protocol. We also provided verbal instructions about oral hygiene, encouraging participants to brush their teeth regularly with fluoridated toothpastes without whitening components.

Color Evaluation

Two calibrated evaluators with agreement of at least 85% determined by weighted κ statistics recorded the shade of each participant's teeth at baseline, during treatment (after the first and second week of bleaching treatment), and one month postbleaching. In the event of disagreements between the examiners during shade evaluation, a consensus was reached through discussion.

The color evaluation was performed with the use of two value-oriented shade guide units: Vita Classical (Vita Zahnfabrik)[30,31] and Vita Bleached-guide 3D-MASTER (Vita Zahnfabrik)[6,32,33] and with the aid of a spectrophotometer (Easyshade, Vita Zahnfabrik).[25,31]

For color evaluation with the Vita Classical scale, the 16 tabs of the shade guide were arranged from the 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 approx-

imately linear ranking. The Vita Bleachedguide 3D-MASTER contains lighter shade tabs and is already organized from the highest (0M1) to the lowest (5M3) value. The measurement area of interest for shade matching was the middle one-third of the facial surface of the anterior central incisor.

The two examiners, blinded to the allocation assignment, scheduled these patients for bleaching and evaluated their teeth against the shade guide at the different time assessments. Color changes were calculated from the beginning of the active phase through 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.

For the color evaluation with spectrophotometer Vita Easyshade (Vita Zahnfabrik), an impression of the maxillary arch was taken with dense silicone paste (Speedex Putty, Coltene, Rio de Janeiro, Brazil). The impression was extended to the maxillary canine and served as a standard color measurement guide for the spectrophotometer. For each dental component to be evaluated, a window was created on the labial surface of the molded silicone guide using a metal device with a radius of 6 mm and well-formed borders. The shade was determined using the parameters of the Easyshade device where it indicated the following values: L*, a*, and b*, in which L* represented the value from 0 (black) to 100 (white) and a* and b* represented the shade, where a* was the measurement along the red-green axis and b* was the measurement along the yellow-blue axis. The color comparison before and after treatment was given by differences between the two colors (ΔE), which was calculated using the formula: $\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$ (Commission Internationale de l'Eclairage).

TS Evaluation

Participants were asked to keep a daily record of whether they experienced sensitivity. The patient was asked to indicate the numerical value of the degree of sensitivity using a 5-point numeric rating scale (NRS) where 0 = *none*, 1 = *mild*, 2 = *moderate*, 3 = *considerable*, and 4 = *severe* [6,28,34] and also to express their pain intensity using a visual analog scale (VAS).[6,35,36] This scale was a 10-cm horizontal line with scores of 0 and 10 at the ends, where 0 = *no sensitivity* and 10 = *severe sensitivity*. The patient marked, with a vertical line across the horizontal line of the scale, the intensity of the TS. Then, the distance in millimeters from the zero end was measured with the aid of a millimeter ruler.

The worst score from the NRS and the highest numeric value obtained in the VAS during all bleaching treatments were considered for statistical purposes, so that only a single value was taken from the two-week treatment. The values were arranged into two categories: absolute risk of TS, which represented the percentage of patients who reported TS at least once during treatment, and the overall TS intensity.

Blinding

This was a triple-blind study in which the operator, patient, and evaluator were not aware of the group assignment. To maintain blinding, the two bleaching products (4% [HP 4] or 10% [HP 10] HP [White Class, FGM]) were transferred to identical whitening syringes of the same color and were identified as codes "A" or "B." Only the research coordinator knew the coding system.

Statistical Analysis

The analysis followed the intention-to-treat protocol and involved all participants who were randomly assigned (Figure 1).[29] The statistician was blinded to study groups. The absolute risks of bleaching-induced TS were compared by χ^2 test. The intensity of TS from both pain scales were compared using the Mann-Whitney test.

At each time assessment, the color change data in ΔSGU from the two shade guide units were compared with the Mann Whitney test. The ΔE data (groups vs assessment time) were submitted to a two-way repeated measures analysis of variance with the assessment time being the repeated factor. After this, the post hoc Tukey test was used for pairwise comparisons. In all statistical tests, the significance level was 5%.

RESULTS

Characteristics of Included Participants

A total of 251 participants were examined according to the inclusion and exclusion criteria (Figure 1), but only 78 participants remained for the clinical trial. The baseline color of the participants' teeth was similar in shade guide units as was their mean age in years (Table 1). The distribution of the genders in both groups was quite similar (Table 1). No hypothesis testing was performed for baseline features because any difference between these features is attributed to chance alone.

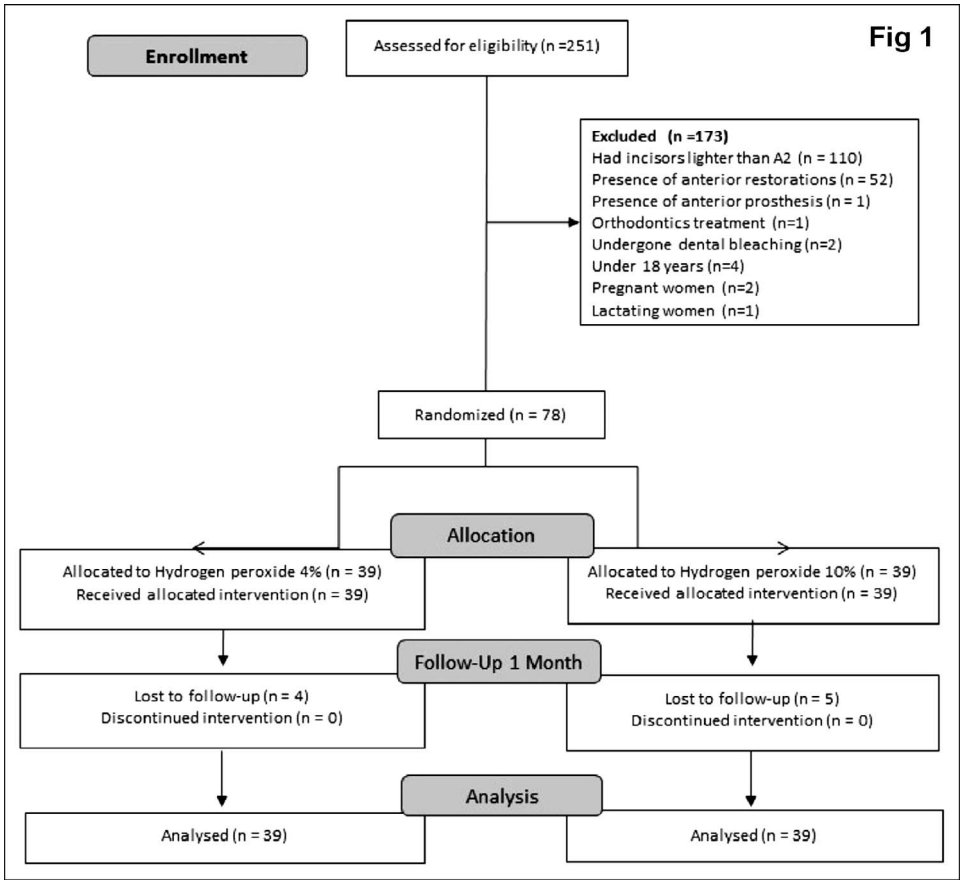

Figure 1. *Flow diagram of study design phases including enrollment and allocation criteria.*

Adherence to the Protocol

The adherence to protocol was 88% in the HP 10 and 85% in the HP 4, meaning that patients did not use the bleaching tray at times during the two-week protocol. All participants attended the recall visits during the bleaching protocol. Nine participants did not attend the one-month recall visit. For these participants, the last observation was carried forward for statistical purposes to keep the intention-to-treat analysis.[29] Figure 1 depicts the participant flow in the different phases of the study design.

Tooth Sensitivity

In regard to the absolute risk of bleaching-induced TS, a significant difference was observed between groups as seen in Table 2 (χ^2 test, p=0.04). In HP 10, there were 25 patients who reported tooth sensitivity of some degree during bleaching, and in HP 4, only 15 patients reported some degree of pain during treatment. The risk ratio, along with the 95% confidence interval, is also evidence that the use of the HP 10 produced significantly higher risk of bleaching-induced TS than did HP 4.

According to the NRS pain scale, two patients from HP 10 reported severe TS, whereas none from HP 4 reported this degree of pain. The highest level of TS

Table 1: *Demographic Characteristics of the Participants*

	HP 10	HP 4
Baseline color, SGU (mean ± SD)	5.6 ± 0.9	6.2 ± 2.0
Age, y (mean ± SD)	23.6 ± 5.9	24.3 ± 9.1
Gender (female; %)	64.1	53.8

Abbreviations: HP 4, group with 4% hydrogen peroxide; HP 10, group with 10% hydrogen; SGU, shade guide unit measured by Vita Classical.

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

Treatment	Tooth Sensitivity (Number of Patients)		Absolute Risk (95% CI)	Risk Ratio (95% CI)
	Yes	No		
HP 10	25	14	64 (48–77)	0.6 (0.38–0.95)
HP 4	15	24	38 (25–54)	

Abbreviations: HP 4, group with 4% hydrogen peroxide; HP 10, group with 10% hydrogen.
** χ^2 test (p=0.04).*

Table 3: *Means and Standard Deviations and Medians (Interquartile Range) of the Tooth Sensitivity Intensity Using Both Sensitivity Scales as Well as Statistical Analysis*

Pain Scales	Means and Standard Deviations		Medians and Interquartile Range		*p*-value*
	HP 10	HP 4	HP 10	HP 4	
Numeric rating scale (0-4)	0.8 ± 0.9	0.5 ± 0.8	1 (0 – 1)	0 (0 – 1)	0.02
Visual analog scale (0-10)	1.2 ± 2.1	0.7 ± 1.5	0.5 (0 – 1.3)	0 (0 – 0.65)	0.03

Abbreviations: HP 4, group with 4% hydrogen peroxide; HP 10, group with 10% hydrogen.
** Mann-Whitney test.*

reported in the HP 4 group was considerable and was reported by two patients. Regarding the TS intensity (Table 3), significant differences between the two groups were observed with the two pain scales used in this study ($p=0.02$ and $p=0.03$, for NRS and VAS, respectively), showing greater intensity of TS for HP 10.

Color Evaluation

Significant whitening was observed in both study groups under the subjective and objective evaluation methods. Most of the whitening occurred within the first week of bleaching, as can be observed by the three different instruments used for evaluation of color changes (Table 4). The subjective results (Vita Classical: $p=0.38$; Vita Bleachedguide: $p=0.11$) and the objective evaluation with the spectrophotometer ($p=0.27$) indicates that there was no significant difference between groups after bleaching (Table 4).

Although the three tools used for color evaluation did not produce identical results, they tended to show a higher whitening degree for the HP 10 in the first week of bleaching (Vita Classical and Vita Bleachedguide) and/or the second week of bleaching (Vita Bleachedguide and spectrophotometer) than the HP 4. However, at one-month postbleaching, no significant difference was observed between both products for any of the instruments used for color evaluation, meaning that at the end of the bleaching protocol, similar color changes could be achieved with the two HP concentrations ($p>0.05$).

DISCUSSION

We have used three different tools for evaluation of color changes in the present study to obtain a more reliable evaluation of the whitening changes that occurred during bleaching. The Vita Classical shade guide is widely used in clinical studies of dental bleaching and therefore allows comparison of the results with earlier clinical trials in this field. It was already demonstrated to be a valid method, with good reliability for differentiating between dark and light colors.[37] However, this shade guide was not specifically designed for tooth whitening assessment: The tabs in the shade guide are nonlinear and it lacks color uniformity, and some overlap between similar colors provides little resemblance to reality.[25,38]

That is why we have also used the more recent Vita Bleachedguide 3D-MASTER scale, developed

Table 4: *Means and Standard Deviations of ΔSGU Obtained With the Vita Classical and Vita Bleachedguide 3D-MASTER and ΔSGU Obtained With the Spectrophotometer Vita Easyshade at Different Periods as Well as the Statistical Analysis*

	Periods	HP 10	HP 4	Mean difference (95% CI)	*p*-value*
ΔSGU (Vita Classical)	1 wk	3.7 ± 1.2	3.0 ± 1.3	0.7 (0.13 to 1.27)	0.01
	2 wk	4.2 ± 0.9	4.0 ± 1.3	0.2 (−0.31 to 0.71)	0.24
	1 mo postbleaching	4.1 ± 0.9	4.1 ± 1.3	0.0 (−0.51 to 0.51)	0.38
SGU (Vita Bleachedguide 3D-MASTER)	1 wk	5.1 ± 2.3	3.7 ± 1.6	1.4 (0.49 to 2.31)	0.006
	2 wk	6.6 ± 2.6	5.3 ± 1.8	1.3 (0.28 to 2.32)	0.03
	1 mo postbleaching	6.1 ± 2.5	5.0 ± 2.3	1.1 (0.00 to 2.20)	0.11
ΔE	1 wk	7.4 ± 3.6	6.5 ± 3.2	0.9 (−0.06 to 2.46)	0.23
	2 wk	9.0 ± 4.2	6.8 ± 3.0	2.2 (0.53 to 3.87)	0.01
	1 mo postbleaching	8.4 ± 3.5	7.9 ± 4.5	0.5 (−1.34 to 2.34)	0.27

Abbreviations: ΔE, change in color; ΔSGU, change in shade guide units; HP 4, group with 4% hydrogen peroxide; HP 10, group with 10% hydrogen; SGU, shade guide units.
** Mann-Whitney test.*

for bleaching research purposes. This newer scale has more tabs lighter than B1, which expands the degree of measurements of the shade guide. Although Vita Bleachedguide 3D-MASTER was developed in 2007, only a few studies have used this new shade guide for bleaching research.[6,33,39-42] In the present study, the use of Vita Bleachedguide 3D-MASTER seemed to be more sensitive because it was the only color measurement tool able to detect the subtle but significant differences between the groups after one and two weeks of at-home bleaching and one month postbleaching. The spectrophotometer provides an objective, consistent and reliable monitoring of color change that is less affected by observer training and variability.[38,43]

These three instruments used for color evaluation were not unanimous in their findings. They showed variations in their results. However, an overall trend could be observed. When differences were detected between groups during the first and second week of bleaching, HP 10 showed a higher degree of whitening, meaning that a higher HP concentration may initially boost the whitening outcome. However, this initial advantage is lost during the two-week treatment because all color measurement instruments demonstrated the same degree of color change for the two bleaching products after the 2-week protocol, with a bleaching of approximately four and six units of color on the Vita Classical and Vita Bleachedguide scale, respectively, and a ΔE color variation of approximately eight units when a spectrophotometer was used.

This corroborates with the results of several clinical trials[12,28,44] that compared different concentrations of CP. For example, in the study of Meireles and others,[28] no difference in effectiveness between 10% and 16% CP were observed after a three-week protocol, but teeth exposed to 16% CP became whiter first after the first week of treatment. The same was observed by Braun and others[44] and Krause and others.[13] In both studies, the authors observed faster whitening when 17% CP was used, but at the end of the bleaching treatment in a one-week protocol, the 17% CP showed the same degree of whitening produced by the 10% CP.[13,44]

In both groups, though at different rates, bleaching-induced TS was observed. HP can pass easily through the enamel and dentin, and this phenomenon results in pulp inflammation, with release of inflammatory mediators and pulp sensory nerve stimuli.[45] The kinetics of degradation of delivered HP is a very fast process, mainly because HP-based products are very unstable and release the majority of their active HP in 60-75 minutes.[20,21]

However, one could observe that the application of 10% HP produced a higher risk of TS than did 4% HP. The absolute risk of TS of the HP 10 group was 64%, which is approximately double the one detected with the HP 4 group. As expected, the higher the initial concentration of bleaching agent, the higher the amount of HP that reaches the pulp chamber and the aggression to the pulp cells.[46,47] That is why in-office bleaching gels have a higher overall TS intensity than at-home bleaching products[6] and why highly concentrated CP bleaching agents (20%-22%) yielded higher levels of TS when compared with the traditional 10% CP.[7,11,12]

Unfortunately, most of the information we obtain from the literature about HP bleaching agents for at-home bleaching is from bleaching strips and not products for tray delivery, which prevents us from further comparisons.[32,48-51] In a recent systematic review that compared CP and HP bleaching products for at-home bleaching,[52] nine of the 13 selected papers used strip-based HP products. Although the HP concentration in strips and in a tray delivery system can be the same, the amount of HP that contacts the enamel is smaller when delivered in strips than in trays, and therefore this may yield different risks of TS.[53,54] However, further clinical trials comparing HP-based products with same concentrations in strips and in a tray delivery system should be conducted.

Despite the promising results presented in this study, more clinical studies are needed to evaluate the clinical effectiveness and adverse effects using protocols with shorter application times and lower HP concentrations for at-home bleaching.

CONCLUSIONS

It can be concluded that both HP concentrations (4% and 10%) were equally effective after two weeks of at-home bleaching. The gel with 4% HP showed lower risk and intensity of TS.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the State University of Ponta Grossa, Brazil. The approval code for this study is 1.009.881.

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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