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Is a Single Preliminary Session of In-office Bleaching Beneficial for the Effectiveness of At-home Tooth Bleaching? A Randomized Controlled Clinical Trial

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Clinical Relevance

A single session of in-office bleaching before home treatment yielded limited reduction in time to obtain a satisfactory bleaching effect compared with home treatment alone and could increase the risk and level of tooth sensitivity reported by patients.

Summary

Objectives: To evaluate the effect of combining in-office with at-home bleaching procedures in terms of the time required to obtain satisfactory tooth color, final color changes, and tooth sensitivity (TS) reported by patients.

Methods and Materials: Twenty-six patients enrolled in this study used 10% carbamide peroxide in a bleaching tray for 1 h/d until satisfactory tooth color was obtained. One-half of the participants underwent a preliminary session of in-office tooth bleaching with 35% hydrogen peroxide for 45 minutes. The time in days for the patients to obtain satisfactory tooth color by at-home bleaching procedures was recorded. The color change of the maxillary canines was assessed using the Vita Bleachedguide 3D Master scale and a spectrophotometer at 1 week and after the end of bleaching procedures. Participants' satisfaction with their smile was recorded using a

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visual analog scale, and TS was determined throughout the entire treatment. Data were analyzed by *t*-test, Mann-Whitney test, or Fisher exact test (α=0.05).

Results: The combined protocol reduced (by an average of 3.7 days) the time required to obtain satisfactory tooth color but increased the risk and level of TS. No difference in the final tooth color change (around 5.0 shade guide units; ΔE=11.6–14.9), or the level of patients' satisfaction with their smile, was observed.

Conclusions: A preliminary session of in-office bleaching reduced the time necessary to obtain satisfactory tooth color with at-home bleaching but increased the risk and level of TS.

INTRODUCTION

The increased demand for tooth bleaching as an esthetic treatment is a trend among patients, who desire not only well-aligned teeth but also whiter teeth. Previous studies have shown that more than 30% of Americans are dissatisfied with their tooth color,[1] while in United Kingdom this level reaches 20%.[2] Furthermore, such bleaching treatment can produce changes in patients' quality of life.[3,4] Usually, the procedure involves applying bleaching agents containing hydrogen peroxide or carbamide peroxide over the discolored tooth structure during in-office bleaching sessions or at home using customized trays.[5]

Regarding bleaching agents, hydrogen peroxide is an unstable substance with strong oxidizing properties. Usually, this compound is used at a high concentration (20%–40%) for in-office bleaching protocols.[5-7] On the other hand, carbamide peroxide is a white crystalline solid compound that breaks down into hydrogen peroxide and urea, with hydrogen peroxide being the active bleaching agent.[5] The concentrations used range from 10% to 35%, with concentrations of carbamide peroxide up to 22% recommended for at-home treatment.[6,7] Carbamide peroxide releases hydrogen peroxide at a ratio of 1:3. Therefore, for example, a product with 10% carbamide peroxide generates about 3.3% hydrogen peroxide.[8] Different concentrations of hydrogen peroxide affect the reactive oxygen species available to oxidize the organic structure of the dental tissues for color change[9] and can affect the effectiveness and speed of bleaching.[6,7] In general, products containing peroxides at higher concentrations tend to yield a faster bleaching effect.[10] However, high peroxide concentrations also produce increased activation of inflammatory receptors within the pulp chamber,[11,12] with increased risk of tooth sensitivity (TS) after the bleaching procedure.[6,7]

As a result, many patients have chosen at-home bleaching with a customized tray as this technique provides satisfactory results with lower TS.[13] In spite of the overwhelming evidence for safe and effective results with at-home bleaching, many clinicians have combined both techniques as a means of seeking to accelerate the speed of the bleaching effect. The combined dental bleaching technique consists of a prior single session of in-office bleaching followed by at-home bleaching with a low peroxide concentration until a satisfactory tooth color is obtained.[14-19] In this regard, studies have usually compared the outcomes obtained with the combined tooth bleaching techniques with those from consecutive in-office bleaching sessions[14,16,19] or have evaluated different protocols of combined protocols.[15,17,18] Therefore, to the best of our knowledge, no prior study has compared the outcomes observed after combined tooth bleaching with those from at-home bleaching. Considering that the main rationale of the combined protocol is to accelerate the bleaching effect observed for the at-home protocol, this study aimed to evaluate the effect of a prior in-office bleaching session on the time required to achieve satisfactory tooth color resulting from the use of a customized tray containing 10% carbamide peroxide. Changes in tooth color, patients' perception, and TS caused by the combined or at-home protocols were also evaluated. The hypothesis of this study was that the combined protocol would reduce the time required to obtain satisfactory tooth color but would be associated with increased TS.

METHODS AND MATERIALS

Study Design

This study was a randomized, single-blind (evaluators), controlled clinical trial with a parallel design evaluating the effect of a single prior session of in-office dental bleaching on clinical outcomes obtained with at-home dental bleaching. The primary outcome to be assessed was the time (in days) of at-home bleaching required to obtain satisfactory tooth color. Changes in maxillary canine color, patients' satisfaction level with their smile, and risk and level of TS were also evaluated as secondary outcomes. The study was conducted by the School of Dentistry of the Federal University of Sergipe from May to June 2018.

Inclusion and Exclusion Criteria

The patients included in the study were older than 18 years and had maxillary canines darker than shade 2.5 M2 on the Vita Bleachedguide 3D Master (Vita-Zahnfabrik, Bad Säckingen, Germany). Patients were excluded if they were smokers, pregnant or lactating, or continuously (or currently) using anti-inflammatory or analgesic drugs. A prior clinical examination was also performed, and patients were excluded if they had restored and/or endodontically treated anterior teeth, prior TS, teeth presenting complex intrinsic staining (eg, tetracycline) or had any alteration in the enamel (eg, fluorosis), generalized periodontal disease, or fixed orthodontic appliances.

Sample-size Calculation

The sample-size calculation was based on the primary outcome, defined as the number of days performing at-home dental bleaching until a satisfactory tooth color was obtained. The calculation was performed for a continuous outcome and superiority trial, based on the expectation that the experimental treatment (combined protocol) would reduce the number of days. The mean (18.2 days) and standard deviation (2.8 days) from a prior study[20] evaluating at-home bleaching with 10% carbamide peroxide for 1 hour per day were used for calculation, and we determined a reduction of at least 4 days as clinically relevant. Therefore, a minimum of 26 patients was required for a 95% chance (power test) of detecting this difference with significance at the 95% level.[21]

Random Sequence Generation and Allocation Concealment

A randomized list was generated (www.sealedenvelope.com) by a person not involved in the intervention or evaluation. According to the list, the bleaching protocol (combined or at-home) was inserted into sealed envelopes numbered from 1 to 26. The patients were numbered according to the sequence of enrollment and received the treatment contained in the envelope with the corresponding number.

Baseline Measurements

A single, previously calibrated (Kappa coefficient >0.80) evaluator assessed tooth shade using the Vita Bleachedguide 3D Master scale during the experiment. The color evaluations were performed in the office under a light source with a Color Rendering Index above 90. The initial color of the maxillary canines was assessed based on a color match between the scale tabs and the middle third of the tooth crown. The shade tabs selected were converted to scores ranging from 1 (whiter shade – 0 M1) to 15 (darker shade – 5 M3), and the average between the scores recorded for each maxillary canine was calculated and used for statistical purposes. The maxillary canine color was also assessed using a spectrophotometer (Easy Shade Compact V4, Vita-Zahnfabrik). A silicone index containing a 6-mm hole for the placement of the spectrophotometer tip over the maxillary canine was used to standardize the readings. Data of lightness (L*) and chromaticity coordinates a* (red/green axis) and b* (yellow/blue axis) were recorded. Three assessments were performed on each tooth, and the mean was calculated. At this time, the participants recorded the satisfaction level with their smile using a 10-cm visual analog scale (VAS). The position of the satisfaction level was indicated with a pen along a continuous line between two end points (completely dissatisfied to completely satisfied) and the distance between the marking and the border corresponding to completely dissatisfied was recorded.

Intervention

After initial prophylaxis, impressions of both dental arches were taken using alginate to obtain stone molds. Customized bleaching trays were built up with ethylene copolymer and vinyl acetate (Plates for Dental Trays Whiteness, FGM, Joinvile, SC, Brazil) for all participants, who were instructed to place a single drop of whitener (10% carbamide peroxide, Whiteness Perfect, FGM) over the buccal surface of each tooth in the trays, removing the excess after positioning them. We asked participants to use the trays containing the peroxide for 1 hour per day and to return once a week for evaluation and to receive new syringes of the whitener. The participants were also instructed to record the number of days using the trays and report any problems adversely affecting the at-home bleaching. The participants were to continue at-home bleaching until they reported that a satisfactory tooth color had been obtained, and the number of days (without limit) necessary to reach satisfaction was recorded. No additional instructions (eg, avoid staining drinks) were given to the participants. Additionally, the participants allocated to the combined protocol underwent a single prior session of in-office dental bleaching. During the in-office bleaching, a light-polymerized resin dam (Top Dam, FGM) was applied over the gingival tissue corresponding to the teeth to be bleached after

Table 1: *Characteristics of Participants Included in the Present Study*

	Bleaching Protocols		*p* Value
	Combined	At-home	
Age (y)[a]	29.5 (5.5)	31.3 (7.7)	0.490*
Gender (male/female)[b]	4/9	6/7	0.688**
Color of maxillary canines on the Bleachedguide scale (scores 0 to 15)[c]	10.5 (9.8/11.1)	11.0 (9.8/11.1)	0.815***
Color measured by spectrophotometer[a]			
L* (lightness)	74.0 (6.3)	78.0 (4.0)	0.090*
a* (+ red/ - green)	–1.2 (2.5)	–0.7 (3.0)	0.689*
b* (+ yellow/ - blue)	17.8 (6.6)	21.7 (4.1)	0.098*
Satisfaction level with his/her smile (0 to 10)[a]	5.4 (2.3)	6.7 (1.5)	0.119*

[a] *Mean (standard deviation).*
[b] *Ratio,*
[a] *Median (1st/3rd quartiles).*
* t *test; ** Fisher exact test; *** Mann-Whitney U Sstatistic.*

dental prophylaxis. A 35% hydrogen peroxide–based whitening agent (Whiteness HP Maxx, FGM) was mixed and applied over the surface of the teeth (both jaws through second premolar), remaining for 45 minutes without any replacement. Subsequently, the bleaching agent was removed, and the teeth were rinsed.

Evaluations

The TS reported by patients was recorded using a universal pain assessment tool. The participants self-assessed their level of sensitivity using a scale of 0–10 oriented by both verbal description and Wong–Baker facial grimace scales. For the participants allocated to the combined protocol group, the maximum level of TS was recorded during and up to 24 hours after the end of the procedure. During the at-home dental bleaching (for all participants), both occurrence and maximum level of TS were recorded daily. The color evaluation was repeated 1 week after ending the bleaching procedures. Color changes on the Bleachedguide 3D Master scale were calculated in shade guide units (SGUs) by subtracting the final mean scores from those measured at baseline. Furthermore, ΔE was calculated based on the following equation: $\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$. Changes in participants' satisfaction level with their smile were also assessed by subtracting the final value from those measured at baseline. All evaluations were performed by a single evaluator blinded to the allocation assignment.

Statistical Analysis

The statistician was blinded to the study treatments. Possible differences among the characteristics of participants included in the study were assessed at baseline by *t*-test (age, spectrophotometric data, and satisfaction level with their smile), Mann-Whitney U statistic (color of maxillary canines), or Fisher exact test (gender).

Data regarding the number of days of using the customized trays until a satisfactory tooth color was obtained was subjected to the *t*-test. The same test was used to analyze the tooth color changes (measured by SGU and ΔE) caused by bleaching protocols and to assess the changes in participants' satisfaction level with their smile 1 week after the end of tooth bleaching.

Absolute and relative risks of TS and 95% confidence intervals were calculated based on the number of scores different from 0. Possible statistical differences in the absolute risk were analyzed by Fisher exact test. Maximum levels of TS observed for each of the protocols were compared using the *t*-test. This last analysis was performed using the overall data and those measured only during the at-home bleaching. The percentage of days presenting any TS was calculated. These data did not present a normal distribution (Shapiro-Wilk test, $p<0.05$) and were therefore compared using the Mann-Whitney U statistic. All statistical analyses were performed considering a significance level of 95%.

RESULTS

The characteristics of participants at baseline are presented in Table 1. Age of participants allocated to the combined (29.5 years) and at-home (31.3 years) bleaching protocols were similar ($p=0.490$). Thirty-eight percent of participants enrolled in the study were males, and there were no significant difference

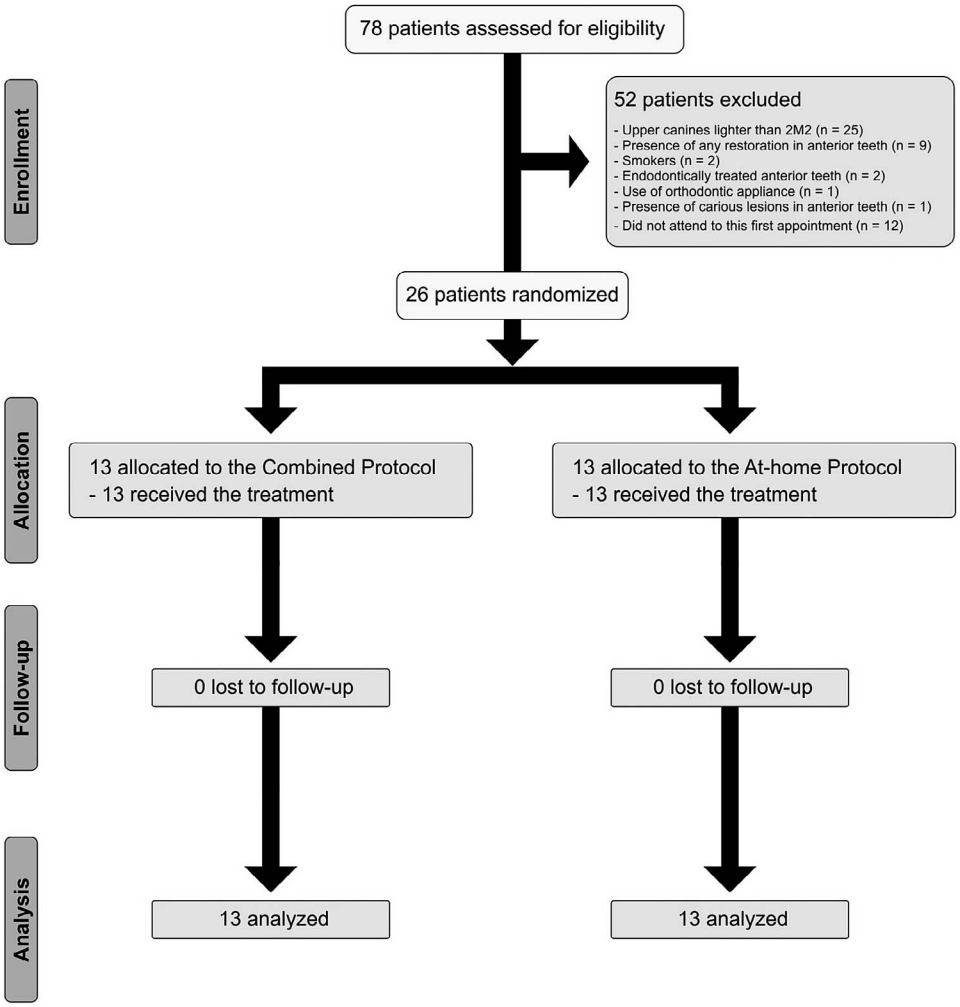

Figure 1. *Flow diagram of the clinical trial.*

(p=0.688) between the combined (31%) and at-home (46%) protocols. Half of the participants enrolled had an average maxillary canine color between the tabs 3M2 and 4M2, and there was no difference between the bleaching protocols (p=0.815). Similarly, no difference in the maxillary canine color was observed with regard to the parameters L* (p=0.090), a* (p=0.689), and b* (p=0.098). Participants' satisfaction level with their smile before the bleaching procedures was also similar (p=0.119) between those allocated to the combined (average of 5.4) and at-home (average of 6.7) protocols. A flowchart of the trial is shown in Figure 1.

Results of the color evaluations and participants' satisfaction level with their smile are shown in Table 2. Combining in-office and at-home bleaching procedures reduced (p=0.040) the mean time required to obtain a satisfactory tooth color by 3.7 days. Despite the difference in time, similar color changes were observed following both protocols, when evaluated using either the Bleachedguide 3D Master scale (p=0.544) or the spectrophotometer (p=0.093). A mean reduction of 5 SGUs was observed for both protocols, and in over 75% of participants, the color of their maxillary canines was similar or whiter than 1.5 M2. Similar improvements in participants' satisfaction level with their smiles were also observed between the protocols (p=0.208).

The results of TS assessments are shown in Table 3. The combined protocol increased the overall risk of TS by 71%, and this higher risk was statistically significant according to the calculated confidence interval, but not when data were analyzed by Fisher exact test (p=0.073). On the other hand, no difference (p=1.000) in the risk of TS was observed between the protocols when only the sensitivity reported by participants during the use of customized trays was used. Regarding the level of TS, combined protocols resulted in a higher level of TS (average of 1.7 cm on the VAS, p=0.021) when the

Table 2: *Results for Tooth Color Measurements and Satisfaction Level of Participants' Smile*

	Bleaching Protocols		Difference (95% CI)	*p* Value
	Combined	At-home		
Number of days using the tray until obtaining satisfactory teeth color[a]	16.1 (4.6)	19.8 (4.2)	–3.7 (–7.4 to –0.2)	0.040*
Changes in SGU (1 to 15)[a]	–5.2 (1.0)	–5.5 (1.2)	–0.3 (–1.2 to 0.6)	0.544*
ΔE[a]	14.9 (5.0)	11.6 (4.8)	3.4 (–0.6 to 7.4)	0.093*
Changes in satisfaction level with his/her smile (0 to 10)[b]	2.4 (1.6/ 6.2)	2.1 (1.8/3.2)	-	0.208**

Abbreviation: CI, confidence interval.
[a] *Mean (standard deviation).*
[b] *Median (first/third quartiles).*
* t *test; ** Data did not present normal distribution and was analyzed by Mann-Whitney U statistic.*

entire treatment was evaluated. However, similar and lower levels (around 1.2 cm on the VAS) of TS were reported for both protocols during at-home bleaching procedures (p=0.935). Moreover, irrespective of the protocol, 75% of participants did not report any TS in more than 88% of days using the customized tray. No other adverse event caused by tooth bleaching was reported during the study.

DISCUSSION

Tooth bleaching is an esthetic and conservative treatment for discolored teeth that is largely performed by clinicians and produces excellent color change results when well indicated. Despite improvements in tooth color that positively affect the quality of life, the occurrence of tooth pain during or after tooth bleaching procedures is commonly reported by patients and can negatively affect their daily performance.[22] TS has been related to diffusion of peroxides and their by-products through the hard dental tissues, reaching the pulp chamber and activating the receptor TRAP1 (transient receptor potential cation channel with ankyrin domain-type 1) by oxidizing cysteine residues and Fe2+ via the Fenton reaction.[12] Therefore, the at-home bleaching protocol using a low concentration of peroxides results in reduced TS[7,23,24] and has become the technique most recommended by dentists.[25] Furthermore, at-home tooth bleaching is a simpler technique than the in-office procedure because it reduces chair time, thus lowering costs. Regarding the bleaching agents used for at-home protocols, 10% carbamide peroxide has been demonstrated to be a safer concentration than typical in-office bleaching gels, resulting in reduced adverse effects yet still yielding satisfactory final color.[26,27] The main concern regarding the use of this low concentration of peroxide is related to the possible longer time required to obtain satisfactory color, and some dentists prefer to increase the concentration of carbamide peroxide or the daily treatment time (up to 8 hours) or to begin the bleaching protocol with a single session of in-office bleaching (combined protocol).

In this study, combining in-office and at-home bleaching protocols reduced the number of days

Table 3: *Results of Risk and Level of Tooth Sensitivity Measured During the Entire Treatment or Only During the At-home Bleaching*

	Bleaching Protocols		Relative Risk (95% CI)	Difference (95% CI)	*p* Value
	Combined	At-home			
Risk of tooth sensitivity during the entire treatment (95% CI)	0.92 (0.67 to 0.98)	0.54 (0.29 to 0.77)	1.71 (1.01 to 2.90)		0.073*
Risk of tooth sensitivity during the at-home bleaching only (95% CI)	0.46 (0.23 to 0.71)	0.54 (0.29 to 0.77)	0.86 (0.40 to 1.86)		1.000*
Maximum level of tooth sensitivity during the entire treatment[1]	3.0 (2.2)	1.3 (1.3)		1.7 (–3.2 to –0.3)	0.021**
Maximum level of tooth sensitivity during the at-home bleaching only (95% CI)	1.2 (2.0)	1.3 (1.3)		–0.1 (–1.3 to 1.48)	0.935**
% of days presenting any tooth sensitivity during at-home bleaching[2]	0.0 (0.0/11.1)	4.8 (0.0/10.0)			0.978***

Abbreviation: CI, confidence interval.
[a] *Mean (standard deviation).*
[b] *Median (first/third quartiles).*
* *Fisher exact test; **t test; *** Data did not present normal distribution and was analyzed by Mann-Whitney U statistic.*

required to obtain a satisfactory tooth color according to participants' perception, but the overall risk and level of TS were higher for the combined protocol. Consequently, the hypothesis of the study was accepted. The rationale for performing a preliminary in-office session is to jump-start the bleaching effect and shorten the time required for at-home treatment to achieve a satisfactory tooth color. The color change caused by the in-office bleaching alone was not assessed in the present study because the at-home bleaching began on the following day, and any rebound effect would hinder a correct measurement of the real color change achieved.[28] However, a prior study using the same protocol for in-office bleaching (35% hydrogen peroxide for 45 minutes uninterrupted) found a reduction of 3.5 SGUs on the Bleachedguide 3D Master scale 1 week after the first session.[29] Considering that the average final color change for the combined protocol was 5.2 SGUs, the further color change required to obtain this value was 1.7 SGUs, which is approximately a third of the overall color change achieved using only the at-home procedure (5.4 SGUs). However, it is important to emphasize that the combined protocol caused a reduction of only 3.7 days in the mean time required to obtain satisfactory tooth color using only the at-home bleaching. This number of days is slightly lower than that used in the sample-size calculation as clinically relevant (4 days), and it is unclear whether this shorter time is worth the additional cost of an in-office bleaching procedure. Furthermore, considering that the patients allocated to the combined protocol were subjected to an additional day of in-office bleaching, the mean difference between the two protocols until a satisfactory tooth color was reached is shorter than 3 days.

Despite accelerating the bleaching effect, combining in-office and at-home procedures resulted in an overall higher risk of TS. This increased risk was mainly related to the high incidence of TS reported by participants during the first 24 hours after the in-office bleaching. Over 90% of participants allocated to combined tooth bleaching reported some TS, and the level of pain reported was more than twofold higher than observed during the at-home bleaching (for both protocols). This increased risk and level of pain caused by in-office bleaching is related to the higher concentration of peroxide reaching the pulpal tissue, causing an inflammatory reaction.[7,11,12,30] However, it is important to emphasize that the mean TS caused by in-office bleaching was 3.0 according to the universal pain assessment tool. This level of pain is between moderate, which can interfere with tasks or sleep, and mild, when the pain can be ignored.

Since in-office bleaching with a high concentration of peroxide causes some inflammatory processes in the pulpal tissue,[11,30] it has been advocated that intervals between sessions should range from 2 to 7 days to allow the inflammation to subside and to eliminate TS.[31] For that reason, it is reasonable to assume that some level of pulp inflammation was present in the teeth subjected to the combined protocol when the at-home bleaching began, and additional TS could be caused by using trays filled with carbamide peroxide. However, no difference was observed between the protocols evaluated regarding the risk and level of TS measured during the at-home bleaching. This finding can be justified due to the low concentration of peroxide used for the daily application time of 1 hour. This short daily application time was chosen based on results from a prior study evaluating different times for 10% carbamide peroxide,[20] which demonstrated that increasing the daily application time from 1 to 8 hours resulted in a reduction of only 2 days in the mean time necessary to obtain a satisfactory tooth color. However, increasing the daily application time caused a higher level of TS.[20] An important matter was that using 10% carbamide peroxide for 1 hour daily caused some TS in approximately half of participants, but 75% of participants did not report any sensitivity on more than 88% of the days when using the customized tray. Moreover, the average maximum level of sensitivity reported during the at-home bleaching was 1.2–1.3 according to the universal pain assessment tool, which corresponds to an intermediate level between mild (can be ignored) and no pain.

In addition to TS and the time necessary to obtain satisfactory tooth color, the final color was also evaluated. We chose to assess the maxillary color due to the usually increased chromaticity of these teeth facilitating the analysis bleaching effectiveness. Both bleaching protocols yielded results with most participants presenting maxillary canines whiter than 1.5 M2 on the Bleachedguide 3D Master scale at the end of the study. The tooth color changes achieved in this study—reduction of approximately 5 SGUs, corresponding to mean ΔE between 11.6 and 14.9 (at-home and combined, respectively)—are similar to the bleaching effect described in previous studies.[7] Despite the relevance of clinician-centered outcomes of color measurement, the use of patient-reported outcomes has

gained importance in clinical trials seeking to better understand the patients' perception regarding the treatments performed.[32,33] In the present study, a VAS was used to assess the level of participants' satisfaction with their smile before and after the bleaching procedures. The results of this evaluation demonstrated that most participants indicated a moderate (around 6 on the VAS) level of satisfaction prior to bleaching. Irrespective of protocol used, achieving whiter teeth resulted in significant improvements in participants' satisfaction level with their smile, and an average of 9.0 on the VAS (close to the maximum of 10.0) was observed at the end of the bleaching procedures. Indeed, it has been demonstrated that tooth color is an important factor affecting patients' perception of their smile, and whiter teeth positively affect patients' quality of life.[22,34] However, although the VAS is widely used to assess patient-reported outcomes, this tool presents some limitations due to the ceiling effect, dependence on the instruction level, and prior experience of participants.[35]

The outcomes of the present study demonstrate that combining in-office and at-home bleaching procedures might accelerate the bleaching effect, even though both protocols result in similar final color changes. On the other hand, the preliminary in-office bleaching session increased the risk and maximum level of TS reported during the entire treatment. However, a low concentration of carbamide peroxide for only 1 hour per day was used during the at-home bleaching, and the results of the present study cannot be extrapolated to other bleaching agents or daily application times. Moreover, further studies with patient-reported outcomes could determine how many days of at-home bleaching are clinically relevant for patients.

CONCLUSIONS

A single preliminary in-office bleaching session with 35% hydrogen peroxide for 45 minutes reduced (by 3.7 days) the mean time necessary to obtain a satisfactory tooth color using 10% carbamide peroxide for 1 hour per day at home. However, the combined protocol resulted in an increased incidence of risk and level of TS without affecting the final color changes and level of patients' satisfaction with their smile.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the Research Ethics Committee of the Federal University of Sergipe. The approval code for this study is: 83162318.4.0000.5546. The study protocol was registered at clinicaltrials.gov under the number NCT03514797. All patients enrolled signed the informed consent form.

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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