Effect of a Toothpaste for Sensitive Teeth on the Sensitivity and Effectiveness of In-office Dental Bleaching: A Randomized Clinical Trial

MA Américo • FF Portella • R Zimmer • FR Garcia
DJ Porto • VL Barbosa • HJR Oballe • EG Reston

Clinical Relevance

The use of a desensitizing toothpaste containing arginine did not reduce sensitivity for in-office tooth bleaching.

SUMMARY

Objectives: The present study aimed to evaluate the desensitizing effect of toothpaste for sensitive teeth on patient tooth sensitivity and on bleaching efficacy of the 38% hydrogen peroxide bleaching agent used for in-office bleaching compared to a regular toothpaste in a randomized clinical trial.

Methods and Materials: Forty-eight patients having maxillary right central incisors with darkness greater than A1 were selected for the present double-blind randomized clinical trial. Patients were randomly allocated into two groups: the placebo group, which used regular toothpaste, and the experimental group, which

Michelle Azeredo Américo, DDS, MS, PhD, Postgraduate Program in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil

Fernando Freitas Portella, DDS, MS, PhD, Feevale University, Novo Hamburgo, Brazil

Roberto Zimmer, DDS, MS, Postgraduate Program in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil and Feevale University, Novo Hamburgo, Brazil

Filipe Reis Garcia, DDS, MS, PhD, Postgraduate Program in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil

Denner Jardim Porto, DDS, Undergraduate in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil

Viviane Leal Barbosa, DDS, MS, Postgraduate Program in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil

Harry Juan Rivera Oballe, DDS, MS, PhD, Postgraduate Program in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil

*Eduardo G. Reston, DDS, MSD, PhD, head of Postgraduate Program in Dentistry, Lutheran University of Brazil (Ulbra), Canoas, Brazil

*Corresponding author: Building 59, 3rd floor, Av Farroupilha, 8001 - São José, Canoas - Rio Grande do Sul, Brasil 92425-020; e-mail: ereston@dentalcore.com.br

used sensitivity toothpaste. The intervention consisted of applying toothpaste with the aid of an individual tray for a period of 4 minutes daily, starting one week before the first bleaching session and interrupting use immediately after the second session. After allocation to one of the groups, individuals received in-office dental bleaching with a 40-minute application of 38% hydrogen peroxide for two sessions with an interval of one week. The incidence and intensity of sensitivity were assessed using a visual analogue scale and a numeric analogue scale. Sensitivity was measured immediately before each session, 1 hour, 24 hours, and 48 hours after each bleaching session and four weeks after the second bleaching session. Tooth shade was evaluated using a spectrophotometer and by comparison with the VITA Classical Shade Guide (Vita Zahnfabrik, Bad Säckingen, Germany). Tooth shade was evaluated before the first bleaching session, one week after the first bleaching session, one week after the second bleaching session and four weeks after the second bleaching session. Participants and professionals who performed the bleaching, shade, and sensitivity assessments were blinded to the group of patients they were treating or assessing. For the incidence of hypersensitivity, the results were evaluated by comparing the groups at different evaluation times with the Mann-Whitney test for comparison between groups, the Friedman test for repeated measures, and the Tukey test for comparison of times. Shade change on the guide was analyzed using the Mann-Whitney test for comparison between groups and the Wilcoxon test for comparison between times. Shade change by the spectrophotometer was analyzed using the t-test for comparison between groups and the paired t-test for comparison between times. All analyses were performed with a significance level of 5%.

Results: There was no difference in the pattern of dental hypersensitivity between groups. For all shade measures, there was no difference between the bleaching results, and no statistically significant difference was observed between the study groups.

Conclusion: The use of arginine-based desensitizing toothpaste did not interfere with the bleaching ability of hydrogen peroxide and was not effective in reducing the sensitivity caused by in-office tooth bleaching.

INTRODUCTION

Hydrogen peroxide, when applied to the surface of teeth, diffuses through enamel and dentin since it has a low molecular weight and dissociates into hydroxyls, perhydroxyls and superoxides.[1] These radicals are capable of reacting with molecules that alter the shade of the dental structure present in the dentin, usually of high molecular weight, transforming them into smaller, lighter molecules.[1] Radicals derived from hydrogen peroxide can also react with the organic enamel matrix, making it more opaque.[2] As a result of this action, some adverse effects can occur when tooth bleaching is performed. Changes to the enamel surface, such as demineralization, the appearance of irregularities and porosity, reduced microhardness, and increased permeability can occur.[3-6] Although these events are transient and self-repairing,[7] they can contribute to the development of tooth sensitivity, which causes discomfort to the patient and often prevents the continuation of the bleaching treatment.[8]

Tooth sensitivity is the most frequently reported side effect associated with bleaching, particularly with in-office bleaching protocols that employ relatively high concentrations of hydrogen peroxide.[9,10] Even though the sensitivity is only transient and resolves a few days after the bleaching procedure is completed, it is an unpleasant experience[11,12] and can be severe and irritating enough to lead the patient to give up treatment.[13]

Alternatives to control tooth sensitivity caused by in-office bleaching have been studied but with little or no effectiveness. Some of the strategies already studied are reducing the concentration and time of application of peroxides, the use of analgesic or anti-inflammatory drugs prior to bleaching sessions, and the use of desensitizing agents.[8,14-17] In patients with dentin hypersensitivity or those undergoing non-surgical periodontal treatment, hypersensitivity has been managed with the use of desensitizing toothpastes containing 8% arginine in their composition.[18-21] It is believed that the action of these toothpastes is due to occlusion of the dentinal tubules by the precipitation of an arginine-calcium carbonate compound.[22] An evaluation of a toothpaste containing 8% arginine and calcium carbonate also showed that this combination was able to promote remineralization of early enamel caries lesions.[23]

Because sensitivity is one of the most common adverse effects during in-office tooth bleaching, the use of a desensitizing toothpaste containing arginine might be an alternative to control the adverse effects of the bleaching treatment. A recent randomized clinical trial[24] evaluated the effect of arginine application on hypersensitivity after in-office bleaching and showed a potential effect in

reducing sensitivity without compromising bleaching efficiency. Therefore, the present study evaluated the effect of applying a desensitizing toothpaste containing arginine in reducing sensitivity and on the outcome of the bleaching treatment. The hypothesis was that the use of the toothpaste would reduce sensitivity, both in incidence and intensity, without compromising tooth bleaching.

METHODS AND MATERIALS

Study Design

The present study was a randomized, double-blind clinical trial with an equal allocation rate between groups. All clinical steps were carried out on the premises of the dental clinics of the Universidade Luterana do Brasil campus, Canoas, between November 2019 and December 2021.

Participants and Sample Calculation

Participants who spontaneously requested dental bleaching at the clinics of the undergraduate course in dentistry, as well as individuals recruited through publicity for the study through posters strategically distributed in different locations on the university campus, were assessed for their eligibility for the research project.

The main outcome considered for the sample calculation was dental sensitivity, measured using a visual analogue scale of scores from 0 to 10. Considering a statistically significant difference to be 3 points on this scale, with a standard deviation of three, a study power of 80%, and a significance level of 5%, it was estimated that 17 patients were needed per experimental group. In order to contemplate a possible 40% loss in the follow-up of individuals, a sample size of 48 individuals was used.[25]

The present study was a double-blind clinical trial in which the patient and operator/rater were blinded to the group assignments. A third researcher, not involved in the implementation and evaluation process, was responsible for the randomization process and the filling of the white and opaque tubes containing the test and control toothpastes, which were numbered according to the randomization.

Eligibility Criteria

Participants were examined in a dental chair after dental prophylaxis with pumice and water to verify that they met the study eligibility criteria. To be included in the present study, participants must have been at least 18 years old, in good general and oral health, and willing to sign an informed consent form. In addition, they could not present any of the characteristics below (exclusion criteria):

- Caries or periodontal disease
- Maxillary anterior tooth shade of A1 or higher value
- Existing restorations on the anterior teeth
- Existing endodontic treatment of the anterior teeth
- Gingival recession, non-carious cervical lesions, or visible cracks in the anterior teeth
- Tetracycline staining or fluorosis

Training and Calibration

For shade measurement calibration purposes, 10 participants were selected and were not included in the study. The shade of the maxillary right central incisor was assessed by two examiners. The two examiners scheduled these patients and evaluated the shade of the tooth with the VITA Classical Shade Guide (Vita Zahnfabrik) at two time periods with an interval of seven days between evaluations. Both evaluators showed superior shade matching competence according to International Organization for Standardization (ISO)/TR 28642. This means that they had at least 85% agreement (Kappa statistic) before starting the study evaluation. If disagreements occurred during the assessment, the examiners needed to reach a consensus before the participant was dismissed.

Random Sequence Generation and Allocation Concealment

For the randomization of the present study, a research collaborator with extensive experience in this type of procedure and who was not involved with the experimental period of the study performed a list in consecutive Arabic numbers in an increasing order (01-48). Stratified randomization was performed using a specialized website (www.randomizer.org), separating participants by age groups. Subsequently, the participants were randomly allocated to one of the two experimental groups (placebo or experimental). The person responsible for the randomization put the random number in each brown envelope and inside it the name of the randomized participant, the type of toothpaste, the experimental group, and the participant's telephone number, to then be sealed and kept in a safe place. For the blinding of the study, the same collaborator in charge of the randomization filled white and opaque tubes with the test and control toothpastes, previously identified by the number that the randomization generated. This would allow keeping the main researcher and the participant blinded.

Study Intervention

To maintain allocation concealment before starting the bleaching procedure, an individual tray was made for all patients fabricated using the vacuum-forming method. To obtain the plaster models, impressions were taken with irreversible hydrocolloid. The individual trays were made from ethylene vinyl acetate copolymer using a vacuum laminator (Bio Art Equipamentos Odontologicos Ltda, São Carlos, SP, Brazil).

One week before the beginning of the intervention, supragingival scaling was performed in patients who needed it and prophylaxis with pumice and rubber cup was performed on all teeth in order to remove any extrinsic pigmentation. At that time the patients received instructions regarding oral hygiene to be used throughout the experimental period, as well as the application of toothpaste using trays.

The intervention in the present study consisted of applying toothpaste with the aid of an individual tray for a period of 4 minutes a day, starting one week before the first bleaching session and interrupting use immediately after the second session. Individuals were randomly allocated to a placebo group or a test group, which differed according to the toothpaste used:

- Placebo group: regular toothpaste (Colgate Total 12, Colgate-Palmolive Industrial Ltda, São Bernardo do Campo, SP, Brazil)
- Experimental group: a sensitivity toothpaste (Colgate Sensitive Pró-Alívio Repara Esmalte, Colgate-Palmolive)

After being allocated to one of the experimental groups, each individual received verbal and written instructions regarding the use of trays loaded with the intended toothpaste. The trays were to be loaded with the toothpaste in the region corresponding to the labial surface and then inserted and kept in the mouth for 4 minutes. This procedure was to be performed immediately after regular oral hygiene and after removing the tray. Individuals were then to rinse their mouths with water to remove any excess toothpaste. The procedure was performed once a day before going to bed.

At baseline participants also received regular toothpaste (Colgate Total 12), a soft-bristled toothbrush, and dental floss, which were used in all oral hygiene activities. All participants were instructed to brush their teeth at least three times a day.

Participants were instructed to maintain their oral hygiene routine (technique and frequency of brushing and flossing) but avoiding the use of mouthwashes. In addition, they were also instructed to record the use of analgesics and/or anti-inflammatories throughout the study period.

In the bleaching sessions, the protocol described below was followed and was repeated twice with an interval of 7 days:

1. Relative isolation with plastic retractor
2. Application of a photopolymerizable gingival barrier
3. Application of 38% hydrogen peroxide gel
4. Gel action for 40 minutes
5. Removing the gel using a suction and gauze
6. Removal of remaining gel with copious water rinsing
7. Removal of the gingival barrier
8. Removal of the plastic retractor

Evaluation of Outcomes

Two outcomes were evaluated at different times during the experiment. As a primary outcome, dentin sensitivity was assessed immediately before each bleaching session, 1 hour, 24 hours, and 48 hours after each bleaching session and 4 weeks after the second bleaching session. As a secondary outcome, shade was assessed before the first bleaching session, 1 week after the first bleaching session (immediately before the second bleaching session), 1 week after the second bleaching session, and 4 weeks after the second bleaching session.

Sensitivity Assessment (primary outcome)—The incidence and intensity of tooth sensitivity were evaluated using two analog scales, with the participant being asked to mark measures corresponding to the intensity of their sensitivity:

- Analog visual scale: scale consisting of a 10 cm horizontal line, the left end corresponding to "absence of sensitivity" and the right end corresponding to "severe sensitivity," in which the individual marked the region corresponding to their sensitivity with a vertical line. The distance from the left end to the vertical line was measured with a ruler.[8,25-27]

- Analog numeric scale: scale with scores from 0 to 4, ranging from no sensitivity (0), mild sensitivity (1), moderate sensitivity (2), considerable sensitivity (3) and severe sensitivity (4).[8,25]

Participants were asked to record their perceived sensitivity immediately before each bleaching session, 1 hour, 24 hours, and 48 hours after each bleaching session, and 4 weeks after the second bleaching session, using the analog numeric scale.

Shade Assessment (secondary outcome)—For the shade evaluation, the maxillary right incisor was determined, and the measurements were taken in the center of the labial face of the tooth. Shade was assessed subjectively

using the VITA Classical Shade Guide (Vita Zahnfabrik), and objectively using a spectrophotometer. Two experienced and calibrated dentists (Kappa statistic greater than 80% after previous calibration), who were not involved in the randomization procedures, performed clinical evaluations immediately before the first bleaching session, 1 week after the first bleaching session (immediately before the second bleaching session), 1 week after the second bleaching session and 4 weeks after the second session.

- Shade guide: evaluation based on the VITA Classical Shade Guide (Vita Zahnfabrik), organized from the highest to the lowest value,[8,25,28] constituting a score from 1 to 16, from the highest value (B1) to the lowest (C4): B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, and C4. Although this guide is not linear in the truest sense, the shade changes were considered to be continuous and linear changes, as seen in several clinical tooth bleaching studies.[27,29-32]

The examiner performed all evaluations in the same clinical room and maintaining the same light sources and evaluated the shade in the center of the labial surface of the maxillary central incisors.

- Spectrophotometer: shade was measured with a VITA Easyshade Advance 4.0 spectrophotometer (Vita Zahnfabrik). Shade values were collected according to the CIELab system, in which the value of "L" indicates brightness and "a" and "b" represent the red-green and yellow-blue chromatic axes, respectively. The shade variation (ΔE) between the different periods was calculated by the formula: $\Delta E = (\Delta L^2 + \Delta a^2 + \Delta b^2)^{1/2}$. Tooth shade was evaluated before the first bleaching session, 1 week after the first bleaching session, 1 week after the second bleaching session, and 4 weeks after the second bleaching session. The shade evaluation was carried out in a room under conditions of artificial lighting without interference from external light.

Statistical Analysis

For the incidence of hypersensitivity, the results were evaluated by comparing the experimental groups at different evaluation times with the Mann-Whitney test for comparison between groups, the Friedman test for repeated measures, and the Tukey test for comparison of times. Shade change as indicated by the guide was analyzed using the Mann-Whitney test for comparison between groups and the Wilcoxon test for comparison between times. Shade change as indicated by the spectrophotometer was analyzed using the t-test for comparison between groups and the paired

t-test for comparison between times. All analyses were performed using a significance level of 5%.

RESULTS

A total of 79 participants were examined in a dental chair at the university clinic to determine whether they met the study inclusion criteria. A total of 48 participants were included in the present clinical study (Figure 1). The characteristics of the participants included at the beginning of the study and followed until the end of the study are described in Table 1. Comparable data can be observed between the groups, supporting the comparability of the baseline characteristics.

None of the participants presented with an intensity of sensitivity that prevented them from continuing in the study. No medication or desensitizer needed to be prescribed or used by the participants of the present study for the relief of tooth sensitivity induced by tooth bleaching.

A total of 11 participants discontinued the intervention, and among the dropouts, 2 participants underwent only the first bleaching session. Individuals who discontinued the intervention were contacted and asked about the reasons that led them to withdraw; five participants did not justify or return contact and six participants justified discontinuing the intervention due to change of place of residence or difficulty in commuting to appointments.

The relative risk of incidence of sensitivity did not differ between groups (Table 2). Table 3 presents intensity of sensitivity measured by the Likert scale and VAS scale according to the experimental group and study period. The values are also presented in graphic format (Figure 2). Both groups showed the same sensitivity pattern, with greatest sensitivity immediately after the bleaching sessions. The only difference found (p=0.035) occurred 24 hours after the first session when measured on the VAS scale. However, when a sensitivity analysis was performed including participants who discontinued the study or who only participated in the first bleaching session, this difference was not maintained (mean [standard deviation] sensitivity of the placebo group was 1.69 [2.54], and for the experimental group 1.79 [1.68], p=0.279).

For all shade measures, there was no difference between the bleaching results, and no statistically significant difference was observed between the study groups (Table 4).

DISCUSSION

The results of the present study show no significant difference in intensity of tooth sensitivity between the
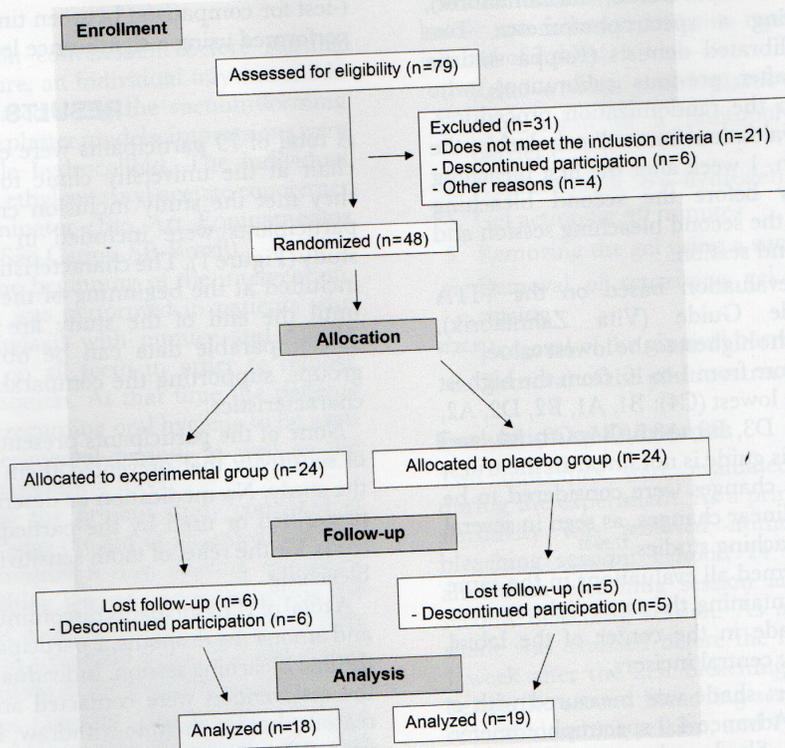
Figure 1. *The CONSORT flow diagram of study design phases including enrollment and allocation criteria.*

group that used desensitizing toothpaste and the group that used conventional toothpaste, both in trays, when used in conjunction with in-office bleaching.

Alternatives for controlling tooth sensitivity caused by in-office bleaching have been studied but have shown little or no effectiveness. Some of the strategies already studied are reduction in the concentration and time of application of peroxides, the use of analgesic or anti-inflammatory drugs prior to the bleaching sessions, and use of desensitizing agents; none of these have

shown differences in the reduction of sensitivity caused by bleaching or in bleaching efficacy.[8,14-17] In patients with dentin hypersensitivity or undergoing non-surgical periodontal treatment, hypersensitivity has been managed with the use of desensitizing toothpastes containing 8% arginine in their composition.[18-21] It is believed that the action of these toothpastes is due to the obliteration of the dentinal tubules through the precipitation of an arginine-calcium carbonate compound.[22] An evaluation of toothpaste containing

Table 1: *Characteristics of Participants Included (Randomized) at Baseline*		
Characteristics	**Placebo (24)**	**Experimental (24)**
Average age ± standard deviation*	28.7 ± 6.2	27.9 ± 6.2
Gender (masculine/feminine)	7/17	9/15
Characteristics of Included (Randomized) Participants Followed up Until the End of the Study		
Characteristics	**Placebo (19)**	**Experimental (18)**
Average age ± standard deviation*	29.1 ± 6.7	26.7 ± 5
Gender (masculine/feminine)	6/13	7/11
*t test for age p=0.252		

Table 2: *Incidences (Score 2 or Higher on the Likert scale) of Sensitivity During Bleaching Treatment*

Group	Number (%)	Relative Risk (95% CI)
Placebo (n=19)	13 (68.4)	1.14 (0.77-1.68)*
Experimental (n=18)	14 (77.8)	

Fisher test p=0.714.

8% arginine and calcium carbonate also showed that this combination was able to promote remineralization of early enamel caries lesions.[23]

The cause of bleaching-induced tooth sensitivity is not completely understood. According to the "hydrodynamic hypothesis,"[33] thermal and tactile stimuli are effective to assess tooth sensitivity when dentin is exposed, and many authors consider bleaching-related pain as a form of dentin sensitivity.[34] However, key differences distinguish bleaching-related pain from dentin hypersensitivity. Although sensitivity in bleached teeth can be evoked by thermal or other stimuli, most patients complain of tingling or sharp pain.[9] Pain during and after bleaching treatments can affect intact teeth without dentin exposure, in stark contrast to dentin sensitivity, in which pain occurs in teeth with exposed dentin.

Markowitz[12] has presented an alternative hypothesis related to tooth sensitivity induced by bleaching. In the sensitivity caused by tooth bleaching, pain can occur in intact and healthy teeth without any provocative stimulus. Currently, the mechanism of activation of nociceptors in the sensitivity generated by bleaching is unknown. A more common form of sensitivity is dentin sensitivity, which occurs when cold or tactile stimuli come into contact with areas of exposed dentin in healthy teeth. In dentin sensitivity, stimulation of the dentin results in fluid shifts in the dentinal tubules, which activate mechanosensitive nerve endings in the dentin and pulp. Since many aspects of the symptoms of bleaching sensitivity and dentin sensitivity differ, it is assumed that the pain generation mechanism differs for these two conditions. In the sensitivity generated by bleaching, hydrogen peroxide would be a mechanism for activating nociceptors located in the dental pulp. According to Carlos,[35] tooth sensitivity induced by bleaching appears as a consequence of peroxide penetration into the tooth structure, causing direct activation of a neuronal receptor, and not by the hydrodynamic mechanism.

This clinical finding, combined with the current need to report patient-centered results, led the authors of the present study to use self-reported pain, as used in clinical bleaching trials that assess tooth sensitivity as a primary outcome.[8,26,35-40] However, one cannot overlook the fact that there are other methods described in the literature to assess tooth sensitivity that are not used in the present study, and this can be considered one of the limitations of the study. Among them, we can mention the Schiff Cold Air and Yeaple Probe Tactile methods, commonly used in studies that evaluate dentin

Table 3: *Intensity of Sensitivity Measured by the Likert Scale and VAS Scale According to the Group and Study Period[a]*

Time of Assessment	Likert Scale (0-4) Median (minimum/maximum)		VAS Scale (0-10) Average ± Standard Deviation	
	Placebo	Experimental	Placebo	Experimental
Before the first session	0 (0/2) ABa	0 (0/1) Ba	1.10±1.83 ABa	0.53±0.62 Ba
1 h after the first session	1 (0/3) Aa	1 (0/3) Aa	2.46±2.67 Aa	2.93±2.65 Aa
24 h after the first session	1 (0/3) ABa	1 (0/2) ABa	1.10±1.94 ABb	1.94±1.67 Aa
48 h after the first session	0 (0/2) ABa	0.5 (0/2) ABa	0.70±1.08 Ba	0.84±1.09 ABa
Before the second session	0 (0/3) ABa	0 (0/1) Ba	0.66±1.17 ABa	0.54±0.90 Ba
1 h after the second session	1 (0/3) Aa	1 (0/4) Aa	1.60±1.30 Aa	2.54±2.49 Aa
24 h after the second session	1 (0/2) ABa	1 (0/2) ABa	1.84±2.37 Aa	1.33±1.36 Aa
48 h after the second session	0 (0/2) ABa	1 (0/2) ABa	0.79 ± 1.17 ABa	0.42±0.77 Ba
28 d after the second session	0 (0/1) Ba	0 (0/1) Ba	0.30 ± 0.60 Ba	0.42±0.62 Ba

[a]Mann-Whitney test for comparison between groups (lowercase); Friedman test for repeated measurements with Tukey for comparing times (uppercase).
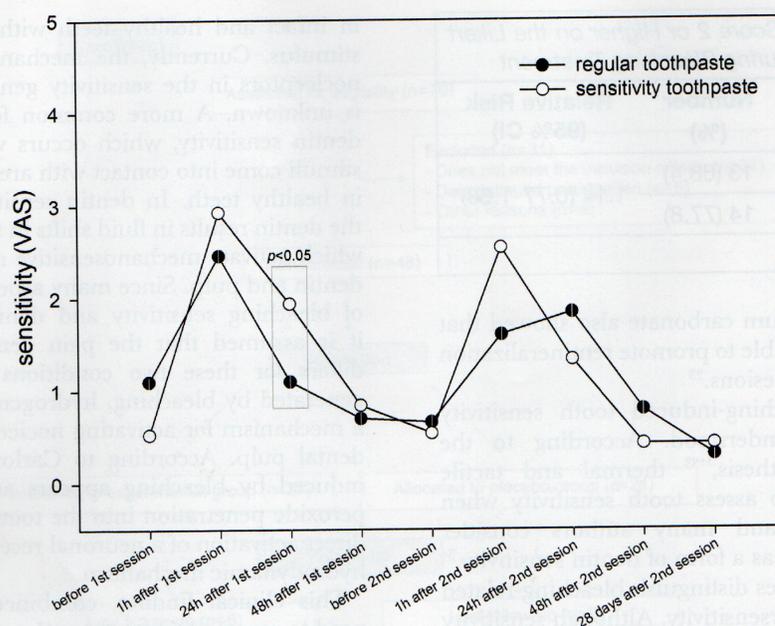
Figure 2. Sensitivity (mean of VAS scale) according to time.

hypersensitivity.[41,42] To the best of our knowledge, they have not yet been used in bleaching studies, but need to be included in future bleaching studies to determine if they can add useful information.

Regarding shade assessment, the results of the present study showed significant lightening at the end of the bleaching protocol in both groups, using two different instruments; this is in line with the findings of several other clinical trials that evaluated shade change.[25,26,36,43] For all shade measures, there was no difference in bleaching outcome, and no statistically significant difference was observed between groups. In the present study, the shade measurement was performed only on the maxillary right central incisor since this tooth has a flat labial surface that allows the standardization

of the area for shade evaluation. This guarantees a correct angle for placement of the spectrophotometer tip in all the recall periods of the present study and allows a more sensitive assessment of shade change. It is noteworthy that at least two previously published clinical studies did not show significant variations in shade measurement with the spectrophotometer when measured in the incisors or canines.[44,45]

Adequate randomization control, allocation concealment, and blinding, factors not seen in some of the previous studies that investigated this issue, put this study at low risk of bias. Taken together, these factors increase the reliability of the current study's findings but do not preclude the need for more well-designed randomized, controlled trials on this issue.

Table 4: Shade Variation Before Bleaching and 30 Days After				
	Objective Evaluation[a] (Spectrophotometer)		Subjective Evaluation[b] (VITA Classical Shade Guide)	
	Placebo	Experimental	Placebo	Experimental
Before	5.51±3.28 Aa	5.08±2.23 Aa	4.84±3.24 Aa	3.50±1.82 Aa
After	4.41±2.78 Aa	4.54±1.84 Aa	1.16±0.38 Ba	1.33±0.69 Ba
[a]Objective evaluation t test for comparison between groups (lowercase); Objective evaluation Paired t test for comparison between times (uppercase). [b]Subjective evaluation Mann-Whitney test for comparison between groups (lowercase); subjective evaluation Wilcoxon test for comparison between times (uppercase).				

Finally, the use of a tray for applying the toothpaste has an advantage over brushing since it allows a possible potentiation of the effect and standardization of use by the patient. A study by Pierote[46] clinically evaluated the influence of desensitizing dentifrices applied through a plastic tray in reducing sensitivity to pain and shade variation caused by in-office tooth bleaching. After each bleaching session, the volunteers used a plastic tray containing different dentifrices, including two with desensitizing components (arginine and potassium nitrate). The use of desensitizing dentifrices with arginine and calcium carbonate or 5% potassium nitrate in a plastic tray was effective in reducing pain sensitivity without reducing the effectiveness of bleaching. This effect was not observed in the present study, and this difference can be explained by the different protocols used. In Pierote's study, the bleaching session consisted of three 15-minute applications of hydrogen peroxide, and the application of toothpaste via trays occurred only once, for 4 hours on the day of bleaching. Possibly the longer action time of the gel compared to the present study (3x15 min versus 2x20 min) represented a greater challenge to the tooth structure, contributing to greater sensitivity, as well as the longer contact time of the toothpaste (1x4 hours versus 7x4 minutes), represented a minor antisensitivity benefit.

Considering these findings, it seems reasonable that for desensitizing toothpastes to be effective in reducing the sensitivity caused by in-office bleaching, their use for a prolonged period is necessary, especially in the period of greatest sensitivity (24 hours), with more frequent exposure (daily use) unnecessary.

CONCLUSIONS

The present study demonstrated that the application of arginine-based desensitizing toothpaste was not effective in reducing tooth sensitivity caused by in-office tooth bleaching. Likewise, the use of toothpaste for sensitive teeth did not affect the effectiveness of the bleaching treatment.

Acknowledgments

Regulatory Statement

This study was conducted in accordance with all the provisions of the human subjects oversight committee guidelines and policies of the Ethics Committee of the Universidade Luterana do Brasil. The approval code issued for this study is 03850118.0.0000.5349.

Conflict of Interest

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

REFERENCES

1. Carey CM (2014) Tooth whitening: What we now know *Journal of Evidence-Based Dental Practice* **14**(Supplement) 70-76.

2. Eimar H, Siciliano R, Abdallah MN, Nader SA, Amin WM, Martinez PP, Celemin A, Cerruti M, & Tamimi F (2012) Hydrogen peroxide whitens teeth by oxidizing the organic structure *Journal of Dentistry* **40**(Supplement 2) e25-e33.

3. Tanaka R, Shibata Y, Manabe A, & Miyazaki T (2010) Microstructural integrity of dental enamel subjected to two tooth whitening regimes *Archives of Oral Biology* **55**(4) 300-308.

4. Abouassi T, Wolkewitz M, & Hahn P (2011) Effect of carbamide peroxide and hydrogen peroxide on enamel surface: An *in vitro* study *Clinical Oral Investigations* **15**(5) 673-680.

5. Sun L, Liang S, Sa Y, Wang Z, Ma X, Jiang T, & Wang Y (2011) Surface alteration of human tooth enamel subjected to acidic and neutral 30% hydrogen peroxide *Journal of Dentistry* **39**(10) 686-692.

6. Magalhães JG, Marimoto AR, Torres CR, Pagani C, Teixeira SC, & Barcellos DC (2012) Microhardness change of enamel due to bleaching with in-office bleaching gels of different acidity *Acta Odontologica Scandinavica* **70**(2) 122-126.

7. Sa Y, Sun L, Wang Z, Ma X, Liang S, Xing W, Jiang T, & Wang Y (2013) Effects of two in-office bleaching agents with different pH on the structure of human enamel: An *in situ* and *in vitro* study *Operative Dentistry* **38**(1) 100-110.

8. de Paula EA, Loguercio AD, Fernandes D, Kossatz S, & Reis A (2013) Perioperative use of an anti-inflammatory drug on tooth sensitivity caused by in-office bleaching: A randomized, triple-blind clinical trial *Clinical Oral Investigation* **17**(9) 2091-2097.

9. Haywood VB (2005) Treating sensitivity during tooth whitening *Compendium of Continuing Education in Dentistry* **26**(9 Supplement 3) 11-20.

10. Nathanson D (1997) Vital tooth bleaching: Sensitivity and pulpal considerations *Journal of American Dental Association* **28**(Supplement) 41S-44S.

11. Hewlett ER (2007) Etiology and management of whitening-induced tooth hypersensitivity *Journal of California Dental Association* **35**(7) 499-506.

12. Markowitz K (2010) Pretty painful: Why does tooth bleaching hurt? *Medical Hypotheses* **74**(5) 835-840.

13. do Amaral FL, Sasaki RT, da Silva TC, Franca FM, Florio FM, &

Basting RT (2012) The effects of home-use and in-office bleaching treatments on calcium and phosphorus concentrations in tooth enamel: An *in vivo* study *Journal of American Dental Association* **143(6)** 580-586.

14. Bonafé E, Loguercio AD, Reis A, & Kossatz S (2014) Effectiveness of a desensitizing agent before in-office tooth bleaching in restored teeth *Clinical Oral Investigations* **18(3)** 839-845.

15. Rezende M, Bonafé E, Vochikovski L, Farago PV, Loguercio AD, Reis A, & Kossatz S (2016) Pre-and postoperative dexamethasone does not reduce bleaching-induced tooth sensitivity: A randomized, triple-masked clinical trial *Journal of the American Dental Association* **147(1)** 41-49.

16. Rezende M, Chemin K, Vaez SC, Peixoto AC, Rabelo JF, Braga SSL, Faria-E-Silva AL, Silva GRD, Soares CJ, Loguercio AD, & Reis A (2018) Effect of topical application of dipyrone on dental sensitivity reduction after in-office dental bleaching: A randomized, triple-blind multicenter clinical trial *Journal of the American Dental Association* **149(5)** 363-371.

17. Vaez SC, Faria-e-Silva AL, Loguércio AD, Fernandes MTG, & Nahsan FPS (2018) Preemptive use of etodolac on tooth sensitivity after in-office bleaching: A randomized clinical trial *Journal of Applied Oral Science* **26** e20160473.

18. Docimo R, Montesani L, Maturo P, Costacurta M, Bartolino M, DeVizio W, Zhang YP, Cummins D, Dibart S, & Mateo LR (2009) Comparing the efficacy in reducing dentin hypersensitivity of a new toothpaste containing 8.0% arginine, calcium carbonate, and 1450 ppm fluoride to a commercial sensitive toothpaste containing 2% potassium ion: An eight-week clinical study in Rome, Italy *Journal of Clinical Dentistry* **20(1)** 17-22.

19. França-Grohmann IL, Sallum EA, do Vale HF, Casati MZ, Sallum AW, & Stewart B (2015) Efficacy of a combined in-office/home-use desensitizing system containing 8% arginine and calcium carbonate in reducing dentin hypersensitivity: An 8-week randomized clinical study *American Journal of Dentistry* **28(1)** 45-50.

20. Pepelassi E, Rahiotis C, Peponi E, Kakaboura A, & Vrotsos I (2015) Effectiveness of an in-office arginine-calcium carbonate paste on dentine hypersensitivity in periodontitis patients: A double-blind, randomized controlled trial *Journal of Clinical Periodontology* **42(1)** 37-45.

21. França-Grohmann IL, Sangiorgio JM, Viana Casarin RC, Casati MZ, Sallum AW, & Sallum EA (2016) Dentin hypersensitivity reduction using an arginine-based approach after non-surgical periodontal treatment *American Journal of Dentistry* **29(5)** 271-276.

22. Cummins D (2009) Dentin hypersensitivity: From diagnosis to a breakthrough therapy for everyday sensitivity relief *Journal of Clinical Dentistry* **20(1)** 1-9.

23. Wang Y, Mei L, Gong L, Li J, He S, Ji Y, & Sun W (2016) Remineralization of early enamel caries lesions using different bioactive elements containing toothpastes: An *in vitro* study *Technology and Health Care* **24(5)** 701-711.

24. Moharam LM, Khadr S, Abdou A, & Nagi SM (2022) Effect of arginine and nano-hydroxyapatite application on the hypersensitivity and color change of bleached enamel: A randomized controlled clinical trial *Journal of Clinical and Experimental Dentistry* **14(6)** 499-505.

25. Rezende M, Loguercio AD, Kossatz S, & Reis A (2016) Predictive factors on the efficacy and risk/intensity of tooth sensitivity of dental bleaching: A multi regression and logistic analysis *Journal of Dentistry* **45** 1-6.

26. Charakorn P, Cabanilla LL, Wagner WC, Foong WC, Shaheen J, Pregitzer R, & Schneider D (2009) The effect of preoperative ibuprofen on tooth sensitivity caused by in-office bleaching *Operative Dentistry* **34(2)** 131-135.

27. Mehta D, Venkata S, Naganath M, Linga Reddy U, Ishihata H, & Finger WJ (2013) Clinical trial of tooth desensitization prior to in-office bleaching *European Journal of Oral Sciences* **121(5)** 477-481.

28. Bernardon JK, Sartori N, Ballarin A, Perdigão J, Lopes GC, & Baratieri LN (2010) Clinical performance of vital bleaching techniques *Operative Dentistry* **35(1)** 3-10.

29. Alomari Q, & El Daraa E (2010) A randomized clinical trial of in-office dental bleaching with or without light activation *Journal of Contemporary Dental Practice* **11(1)** e017-e024.

30. de Paula EA, Kossatz S, Fernandes D, Loguercio AD, & Reis A (2014) Administration of ascorbic acid to prevent bleaching-induced tooth sensitivity: A randomized triple-blind clinical trial *Operative Dentistry* **39(2)** 128-135.

31. Tay LY, Kose C, Loguercio AD, & Reis A (2009) Assessing the effect of a desensitizing agent used before in-office tooth bleaching *Journal of the American Dental Association* **140(10)** 1245-1251.

32. Tam L (2001) Effect of potassium nitrate and fluoride on carbamide peroxide bleaching *Quintessence International* **32(10)** 766-770.

33. Brännström M (1986) The hydrodynamic theory of dentinal pain: Sensation in preparations, caries, and the dentinal crack syndrome *Journal of Endodontics* **12(10)** 453-457.

34. Swift EJ Jr (2005) Tooth sensitivity and whitening *Compendium Continuing Education in Dentistry* **26(9 Supplement 3)** 4-10.

35. Carlos N, Bridi E, Amaral F, França F, Turssi C, & Basting R (2017) Efficacy of home-use bleaching agents delivered in customized or prefilled disposable trays: A randomized clinical trial *Operative Dentistry* **42(1)** 30-40.

36. Matis B, Cochran M, & Eckert G (2009) Review of the effectiveness of various tooth whitening systems *Operative Dentistry* **34(2)** 230-235.

37. Pale M, Mayoral JR, Llopis J, Vallès M, Basilio J, & Roig M (2014) Evaluation of the effectiveness of an in-office bleaching system and the effect of potassium nitrate as a desensitizing agent *Odontology* **102(2)** 203-210.

38. Leonard RH, Smith LR, & Caplan DJ (2004) Desensitizing agent efficacy during whitening in an at-risk population *Journal of Esthetic and Restorative Dentistry* **16(1)** 49-55.

39. Özcan M, Abdin S, & Sipahi C (2014) Bleaching induced tooth sensitivity: Do the existing enamel craze lines increase sensitivity? A clinical study *Odontology* **102(2)** 197-202.

40. Haywood VB, Cordero R, Wright K, Gendreau L, Rupp R, Kotler M, Littlejohn S, Fabyanski J, & Smith S (2005) Brushing with a potassium nitrate dentifrice to reduce bleaching sensitivity *Journal of Clinical Dentistry* **16(1)** 17-22.

41. Trushkowsky RD & Garcia-Godoy F (2014) Dentin

hypersensitivity: Differential diagnosis, tests, and etiology *Compendium of Continuing Education in Dentistry* **35**(2) 99-104.

42. Gillam DG (2013) Current diagnosis of dentin hypersensitivity in the dental office: An overview *Clinical Oral Investigation* **17**(Supplement 1) 21-29.

43. Wang Y, Gao J, Jiang T, Liang S, Zhou Y, & Matis BA (2015) Evaluation of the efficacy of potassium nitrate and sodium fluoride as desensitizing agents during tooth bleaching treatment—A systematic review and meta-analysis *Journal of Dentistry* **43**(8) 913-923.

44. Wetter NU, Branco EP, Deana AM, & Pelino JE (2009) Color differences of canines and incisors in a comparative long-term clinical trial of three bleaching systems *Lasers in Medicine Science* **24**(6) 941-947.

45. Ontiveros JC, Eldiwany MS, & Paravina R (2012) Clinical effectiveness and sensitivity with overnight use of 22% carbamide peroxide gel *Journal of Dentistry* **40**(Supplement 2) e17-e24.

46. Pierote JJ, Barbosa IF, Prieto LT, Lima DA, Paulillo LA, & Aguiar FH (2019) Effects of desensitizing dentifrices on the reduction of pain sensitivity caused by in-office dental whitening: A double blind controlled clinical study *Clinical, Cosmetic and Investigational Dentistry* **11** 219-226.