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A clinical, randomized, controlled study on the use of desensitizing agents during tooth bleaching

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ABSTRACT

Objectives: To evaluate the efficacy of experimental proposals of desensitizing agents during tooth bleaching.
Methods: 140 participants without tooth sensitivity (TS) received 16% carbamide peroxide (14 days-04 h each) (T1) or 35% hydrogen peroxide (single session-45 min) (T2). Participants used concomitantly (10 per group): desensitizing dentifrices (D1-experimental bioactive glass-ceramic; D2-commercial potassium nitrate; D3-commercial calcium and sodium phosphosilicate) in-home, daily and, desensitizing pastes (D4-experimental bioactive glass-ceramic; D5-experimental Bioglass type 45S5; D6-commercial calcium phosphate), in-office, immediately after the treatment and more 4 times. Participants in the control group did not use any desensitizing agent. We assessed TS with Visual Analogue Scale. Assessment point 1 was immediately after the first participant's exposure to the treatments; and points 2, 3, 4, and 5 were every 72 h along the period of the study. Two-way ANOVA (considering time and desensitizing as factors) and post-hoc Tukey test ($\alpha = 0.05$) analyzed the data.
Results: In the control group treated with 35% hydrogen peroxide, TS increased significantly on assessment points 1 and 2. The participants who used a 5% potassium nitrate dentifrice and in-office experimental pastes did not experience TS because of the 35% in-office bleaching treatment.
Conclusions: TS caused by 35% hydrogen peroxide in-office tooth bleaching was controlled by experimental products prepared as pastes D4-experimental bioactive glass-ceramic and D5-experimental Bioglass type 45S5, but not by D1-experimental dentifrice containing bioactive glass-ceramic.
Clinical significance: There is no a gold standard protocol for TS caused by tooth bleaching. The study of novel desensitizing agents that can obliterate the dentinal tubules in a faster-acting and long-lasting way may help meet this clinical need.

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1. Introduction

Tooth sensitivity (TS) is the most common side clinical effect of tooth bleaching [1–4]. TS caused by bleaching procedures usually results in mild and transient pain; however, it can occasionally cause significant discomfort [1] that is a main deterrent to patients successfully completing bleaching treatments [4].

Currently, the mechanism responsible for TS after tooth bleaching procedure is unclear. Literature explains this condition with the Hydrodynamic theory [5]. According to this theory, fluid movement inside dentin tubules is responsible for stimulating receptors in the pulpal dentin area, resulting in pain. However, Markowitz [2] noted that the mechanism of TS caused by tooth bleaching, which occurs in healthy teeth with no other provoking stimulus, differs from the mechanisms of other forms of TS, which usually occur when stimuli (cold or tactile) contact the surface of exposed dentin. It has been hypothesized that TS resulting from tooth bleaching occurs because peroxide penetrates the tooth structure and directly activates a neuronal receptor and not because of hydrodynamic effects. In addition, alteration caused by bleaching agents on the morphological enamel surface (increased surface porosity, depressions and superficial irregularities) [6,7] could leave to dentin less protected.

The application of desensitizing agents is usual in the attempt to reduce the TS that patients experience. They act via two different mechanisms of action: (1) reducing the excitability of the intradental nerve ending and (2) obliterating the dentin tubules [2]. Most clinical studies have shown that both approaches

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effectively reduce TS [4,8–11]. However, because neurogenic inflammation may play a role in TS resulting from tooth bleaching [2,10], we hypothesize that desensitizing products should prevent the bleaching product from reaching the pulp by obliterating the dentin tubules more quickly and consequently preventing the inflammation rather than by simply inhibiting the painful neural stimulus.

Because TS during bleaching treatment has been associated with morphological alterations of the enamel and dentin [7,12,13], bioactive materials have recently been used as desensitizing agents to repair the damaged tissues. In vitro studies of the desensitizing effects of bioactive materials have shown reduced dentine permeability, the occlusion of dentinal tubules and resistance to acid challenge [14] and have revealed remineralizing effects [14–18].

In particular, the use of a new glass-ceramic powder called Biosilicate has been proposed as a therapeutic agent for enamel and dentin regeneration because of the faster deposition of a hydroxyapatite layer where the product is applied [6,18,19]. Biosilicate particles appear to react rapidly with surrounding tissue inside the dentin microchannels [18] resulting in an effective clinical reduction in sensitivity by promoting the occlusion of dentin tubules [20]. When used immediately after bleaching treatment, Biosilicate can reduce or even prevent the demineralization effect of bleaching products and prevent the exposure of dentin tubules [6].

Nevertheless, to the best of our knowledge there is no information in the literature about clinical trials evaluating the use of this novel bioactive glass-ceramic with bleaching agents. Therefore, given that TS is the main side effect of tooth bleaching and the preliminary reports of the effectiveness of bioactive materials, the aim of this clinical study was to evaluate the efficacy of experimental desensitizing agents containing bioactive glass-ceramics powders for controlling TS caused by tooth bleaching. Our research hypothesis was that microparticulated Biosilicate powder could control TS caused by tooth bleaching. To test our hypothesis, we conceived a randomized, controlled, short-term, longitudinal clinical trial to compare experimental formulations containing Biosilicate and commercial desensitizing associated to at-home or in-office bleaching treatments.

2. Materials and methods

This study was a randomized, controlled, clinical trial that evaluated comparatively new proposals of desensitizing agents in TS caused by tooth bleaching treatments. The study followed the guidelines published by the Consolidated Standards of Reporting Trials—CONSORT. The Ethics Committee of the School of Dentistry of Ribeirão Preto, University of São Paulo, which follows the principles of the Helsinki Declaration, approved the study. The Clinical Trials identifier number was NCT02316080.

2.1. Sample size calculation

Sample size was calculated using the G Power software [21] considering 7 experimental groups, 6 longitudinal evaluations, an effect size of 25% (in accordance with Jorgensen and Carrol [1], and a pilot study conducted by the authors), a statistical test with a power of 80%, and a confidence level of 95%. Participants ($n = 140$) were considered the unit of the study. We randomly (via coin flip) distributed the participants according to the bleaching agent used (T1 or T2). Later, the participants allocated in T1 and T2 were distributed randomly into seven groups. Each patient was allocated into the desensitizing treatment by sorting one number from zero (control) to six that represented the desensitizing products described in Table 1.

2.2. Inclusion and exclusion criteria

To select participants, the inclusion criteria were as follows: adults aged 18 to 40 years in good general and oral health (when Plaque and Gingival Index scored zero) [22] with a minimum of 24 natural teeth and no TS at baseline examination.

The exclusion criteria were therapeutic drug history (chronic use); orthodontic appliance use; crowned, restored or abutted teeth; periodontal disease or poor oral hygiene; pregnancy or lactation; any condition that could cause tooth sensitivity (non-carious cervical lesions, dentin exposure); the use of desensitization therapy in the preceding 3 months; tooth color lighter than A2, B2, C2 or D2 on the shade guide (Vitapan Classical, Vita Zahnfabrik); and previous bleaching treatment.

2.3. Bleaching procedure

The selected participants signed the Term of Consent from the Ethical Committee and received one new soft-bristled toothbrush before procedures began.

2.4. At-home tooth bleaching (T1)

The participants assigned to this group received a treatment kit containing custom-made dental arch trays, one syringe (3 g) of bleaching gel containing 16% carbamide peroxide (CP) and the instruction to use the bleaching gel for four hours a day for 14 consecutive days in accordance with the days marked in the diary

Table 1
Products used in the study.

Products	Group	Active composition	Manufacturer
Whiteness perfect®	T1	16% carbamide peroxide	FGM Dental Products, Joinville, SC, Brazil
Whiteness HP®	T2	35% hydrogen peroxide	FGM Dental Products, Joinville, SC, Brazil
Sorriso® dentifrice	Control	1500 ppm monofluorophosphate	Colgate-Palmolive Company, Brazil
Experimental dentifrice formulation containing 7.5% Biosilicate® particles	D1	Particles of glass-ceramic bioactive crystalline (1–10 μm) P_2O_5–Na_2O–CaO–SiO_2	Biosilicate® microparticles: Vitrovita, São Carlos, SP, Brazil Dentifrice: HELP Laboratory (Ribeirão Preto, SP, Brazil)
Sensodyne® dentifrice	D2	Potassium nitrate 5% and 1187 ppm monofluorophosphate	GSK, Glaxo Smith Kline, Brazil
Odontis RX® Sensi block dentifrice	D3	Calcium and sodium phosphosilicate	Daut Laboratories, Brazil
Paste 1:1 (Biosilicate® and distilled water)	D4	Particles of bioactive ceramic crystalline (1–10 μm)	Biosilicate® microparticles: Vitrovita, São Carlos, SP, Brazil
Paste 1:1 (Bioglass 45S5® and distilled water)	D5	Particles of bioactive bioglass (1–10 μm) P_2O_5–Na_2O–CaO–SiO_2	Bioglass microparticles type 45S5: Vitrovita, São Carlos, SP, Brazil
Desensibilize Nano P®	D6	Nanohydroxyapatite paste	FGM Dental Products, Joinville, SC, Brazil

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of treatment. Additionally, participants received detailed written instructions about the correct use of the bleaching gel.

2.5. In-office tooth bleaching (T2)

We followed the manufacturer's protocol for applying T2. The participants' teeth were cleaned and isolated from the gingival tissue with a light-polymerized resin dam before the single application of the 35% hydrogen peroxide (HP) for 45 min (the dentist refreshed the bleaching gel every 15 min).

2.6. Application of desensitizing agents

- For groups D1, D2 and D3: the participants brushed their teeth three times per day with the dentifrices listed in Table 1 according the standard oral hygiene procedure for 14 days when associated to at-home bleaching or 13 days associated to in-office bleaching.
- For groups D4, D5 and D6: the participants returned at assessment points 1, 2, 3, 4 and 5 to have the appropriate desensitizing agent reapplied by the dentist-authors. We applied the product to the bleached teeth of both arches. In groups D4 and D5, we treated the participants' buccal dental surfaces with a paste made from a powder (microparticles) of the appropriate biomaterial and distilled water (1:1); the paste was applied with a micro applicator and was kept in place for approximately 30 s. For group D6, the dentist applied the desensitizing product in accordance with the manufacturer's instructions using a micro applicator and used a felt disc to rub the product on the tooth surface for approximately 10 s. In order to standardize the oral hygiene, participants from group D4, D5 and D6 received the same dentifrice used in control group (regular 1500-ppm fluoride dentifrice) specified in Table 1.

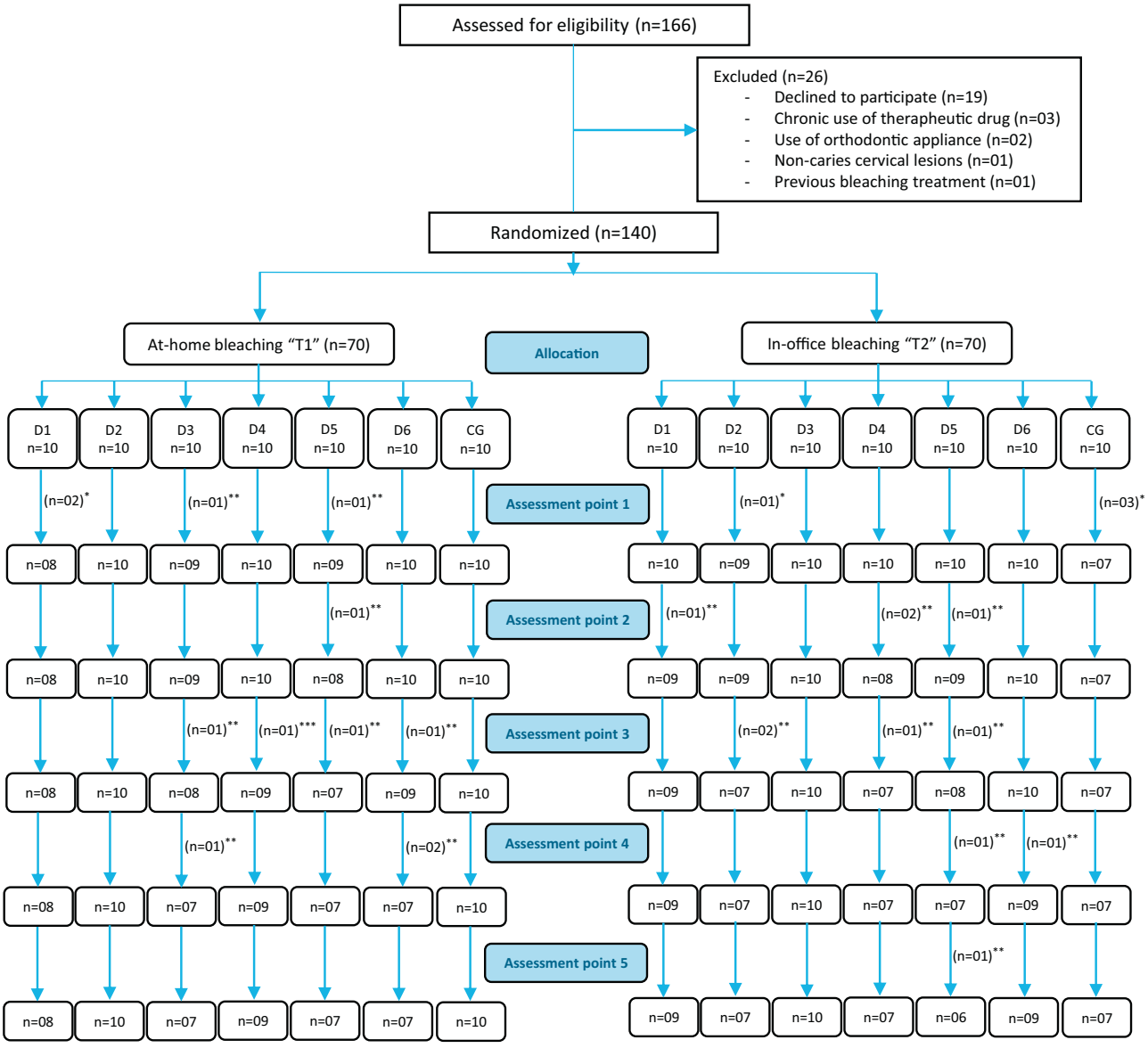

Fig. 1. The Consort flow chart.
*Declined.
**Lost contact.
***Excluded by presence of Aphthous stomatitis.

2.7. Assessment points

We observed the participants' TS on points 1, 2, 3, 4 and 5 during the study. Because the 16% CP and 35% HP treatments and the desensitizing therapies involve different procedures, it is important to detail the chronology of the study.

For T1, we established assessment point 1 as 24 h after the visit at which the participants received the treatment kit, when they received practical instructions from the dentist-authors about how to apply the bleaching gel to the trays and place the trays in the arches. The participants left the first visit using the custom trays filled with 16% CP. Consequently, 24 h later, at assessment point 1, all of the participants in T1 had used 16% CP for 4 h. The T1 participants in subgroups D1, D2 and D3 had brushed their teeth with the desensitizing dentifrices at their homes, and the participants in groups D4, D5 and D6 received the in-office desensitizing therapy immediately before the TS measurement. This procedure aimed to guarantee that at assessment point 1, all of the participants had completed one cycle with the 16% CP and the desensitizing therapies. The subsequent assessment points (2, 3, 4, and 5) were every 72 h thereafter, for a total of 14 days.

For T2, we established assessment point 1 as the moment immediately after the application of the tooth bleaching procedure and the use of the desensitizing agent. Consequently, at assessment point 1, the participants in T2 had just received 35% HP. The T2 participants in subgroups D1, D2 and D3 brushed their teeth in the dental office before the TS measurement. The T2 participants in subgroups D4, D5 and D6 received the desensitizing therapy from the dentist-author immediately after the bleaching procedure was performed and before the TS measurement. This procedure was followed to guarantee that at assessment point 1, all of the participants had completed one cycle with the 35% HP and the desensitizing therapies. Similarly, assessments points 2, 3, 4, and 5 occurred every 72 h thereafter, for a total of 13 days.

2.8. Tooth sensitivity measurement

We evaluated TS using a visual analogue scale (VAS) [9,23]. Each participant placed a mark on a 0–10 scale (on which 0 referred to 'no pain' and 10 referred to 'intolerable pain') after the application of a cold air stimulus from a triple syringe placed about 1.0 cm from the tooth surface to the cervical region of the selected teeth (upper central incisors, lower lateral incisors, upper and lower canines and upper and lower first premolars) for 3 s and the application of a tactile stimulus (a dental explorer) to the cervical area of each tooth [24].

The TS evaluations occurred at baseline to ensure that the participants had no TS before treatment and at assessment points 1, 2, 3 4, and 5 during (T1) or after (T2) the bleaching procedure.

2.9. Diary of treatment

In order to control compliance, the participants received before the beginning of the study a "Diary of Treatment" in which they were asked to daily record TS when chewing, drinking or talking (yes or no). In addition, they recorded the times of tooth-brushing (0, 1, 2, 3, or more), if they got sick (description), abnormalities in diet (description) and satisfaction with the treatment (yes or no). In the last case, if we had a "no", for ethical reasons, the participant was excluded from the clinical trial and the researchers provided them a satisfactory solution.

2.10. Statistical analysis

The unit of this longitudinal short-term study was the participant. Therefore, at each assessment point, the authors obtained a TS mean for each participant (based on the VAS values reported in response to the cold stimulus) considering the 12 teeth measured. We calculated the mean for each group using each participant's TS means.

For each treatment (T1 and T2), we compared the TS values statistically using two-way analysis of variance (ANOVA) and the post-hoc Tukey's test ($\alpha = 0.05$), considering the desensitizing agents and time as factors. The software Prism, version 6.0 (GraphPad, CA, USA) was used to analyze the data. We focused on the differences between the desensitizer groups and the control group at the same assessment point and on the within-group differences along the assessment points.

3. Results

Of the 140 randomly assigned participants who participated in this study, we lost 27 participants (12 in the T1-16% CP group and 15 in the T2-35% HP group) because desistance (06), lost contact (20) and excluded by presence (T1-D4) of Aphthous stomatitis (01). Thus, 113 participants completed the study, including 58 participants in group T1 (41 women and 17 men) and 55 participants in group T2 (39 women and 16 men) ranging in age from 18 to 38 years (mean age 23.9 years). Fig. 1 is the Consort flow chart for the study.

At baseline, as established in the inclusion criteria, TS was zero for all of the participants.

3.1. At-home tooth bleaching (T1)

Regarding the time factor, the statistical analyses revealed that TS did not increase significantly over the days of treatment for the participants in groups D1, D3, and D6, and the control group. TS increased significantly at point 1 for the participants treated with D2 and D5. At point 2, TS was significantly different from baseline

Table 2
Mean and standard deviations for tooth sensitivity assessed with a VAS for groups treated with desensitizing agents during tooth bleaching with 16% carbamide peroxide, at-home (T1).

Assessment point	Groups						
	Control group	Home-use desensitizing			In-office desensitizing		
		D1	D2	D3	D4	D5	D6
Baseline	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}
1	0.1 ± 0.2^{aA}	0.3 ± 0.4^{aA}	0.9 ± 1.5^{bA}	0.1 ± 0.3^{aA}	0.6 ± 0.6^{abA}	1.0 ± 1.6^{bA}	0.6 ± 0.9^{aA}
2	0.3 ± 0.3^{aAB}	0.3 ± 0.4^{aAB}	0.4 ± 0.4^{abAB}	0.2 ± 0.4^{aA}	0.9 ± 1.8^{bAB}	1.3 ± 1.7^{bcB}	0.4 ± 0.4^{aAB}
3	0.2 ± 0.2^{aA}	0.3 ± 0.5^{aAB}	0.6 ± 0.5^{abAB}	0.3 ± 0.4^{aAB}	0.2 ± 0.2^{abA}	1.2 ± 1.7^{bcB}	0.2 ± 0.2^{aAB}
4	0.4 ± 0.4^{aA}	0.3 ± 0.4^{aA}	0.6 ± 0.7^{abA}	0.3 ± 0.4^{aA}	0.4 ± 0.6^{abA}	0.8 ± 1.2^{abA}	0.2 ± 0.1^{aA}
5	0.4 ± 0.5^{aA}	0.3 ± 0.4^{aA}	0.7 ± 0.9^{bA}	0.2 ± 0.3^{aA}	0.1 ± 0.2^{abA}	0.3 ± 0.4^{aA}	0.3 ± 0.3^{aA}

VAS: Visual Analogue Scale.
The same lowercase letters indicate statistically similar means within columns. The same uppercase letters indicate statistically similar means within rows ($P > .05$).

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in the participants treated with D4 and D5, and this difference persisted at point 3 for D5. At the end of study (point 5), TS was significantly different from baseline only for the participants who were treated with D2; in all of the other groups, TS at point 5 was not significantly different from baseline.

Regarding the desensitizing agent, the statistical analysis showed that the participants in group D5 presented significantly higher VAS means for TS compared with D3 at point 2 and compared with control group and group D4 at point 3 (Table 2).

3.2. In-office tooth bleaching (T2)

When comparing the VAS means along the different assessment points, the data analysis showed that for the control group, TS increased significantly at points 1 and 2 compared with the baseline values; however, the values for the last three TS assessment were similar to the baseline values. The participants in groups D1 and D3 also showed a statistically significant increase in TS at point 1 compared with baseline values; in group D6, TS increased significantly only at point 2. For the participants allocated to the D2, D4 and D5 groups, TS did not increase significantly over the study period.

The multiple comparisons of the desensitizing treatments revealed that the participants in control group showed the highest VAS means for TS. TS in the control group was significantly higher compared with TS in the participants in groups D4 and D6 (at point 1), indicating that these two desensitizing agents controlled the TS increase immediately after the procedure. TS was significantly higher in the participants in the control group compared the participants in groups D1, D2, D3, D4, and D5 (at point 2), suggesting that most of the evaluated desensitizing agents controlled TS after the bleaching procedure. At the subsequent assessment points (3, 4, and 5), no difference was observed among the desensitizing agents (Table 3).

3.3. Diary of treatment

All patients who concluded the study recorded in the diary that they were satisfied with the treatment. During the period of the study, no patient recorded disturbances in health, abnormalities in diet or diminished frequency of tooth brushing (three times per day, on average). Interestingly, all patients (from the control, D1, D2, D3, and D6 groups) who recorded TS in T2 noticed it on day 1 (24 h after treatment). For groups D4 and D5, 70% and 80% of the patients, respectively, marked that they had TS on day 1. Still for T2, on day 2 (48 h after treatment), TS was recorded in the control group (30%) and in groups D2 (20%), D3 (10%), and D6 (10%). On the other days, no TS was recorded. Patients in T1 who were treated with 16% carbamide peroxide did not record TS on any day.

4. Discussion

The use of desensitizing agents to control TS during tooth bleaching is a relevant subject of study in a society where some level of pain is culturally acceptable to achieve a given standard of beauty. Such study becomes more important when people request tooth bleaching in their 20s because such early use of bleaching indicates that it is considered part of a beauty routine. In this context, we evaluated the effect of an experimental desensitizing formulation containing a microparticulated powder of bioactive glass and a glass-ceramic (Biosilicate) to treat TS in 113 participants using at-home or in-office tooth bleaching agents. The results of this study confirmed our research hypothesis; experimental formulations containing Biosilicate appeared to control TS caused by tooth bleaching.

According to Dalh and Pallensen [25] TS is a common site effect observed in 15–78% of patients. Clinical trials [9,26–29] have shown that participants experienced any level of TS during the bleaching period.

In this study, the control participants treated with 16% CP showed no significant alterations in TS during bleaching treatment. Thus, one could assume that any desensitizing agents tested would help to reduce TS. At this regard, Matis et al. [8] evaluated the effect of bleaching gels (15% and 16% CP) containing 5% potassium nitrate and amorphous calcium phosphate as desensitizing agents and found no alterations in TS during 14 days of bleaching for either bleaching agent. Despite the safety reported in the literature and the absence in our study of significant TS in participants who used 16% CP without a desensitizing agent (control group), the participants who used D2, D4, and D5 presented significant TS at different assessment points. We interpreted the reports TS in the D2 (commercial potassium nitrate dentifrice), D4 and D5 (in-office bioactive pastes) groups as resulting caused by the in-home, participant-dependent profile of the treatment. Indeed, some of the participants claimed that they used more bleaching gel at the second assessment point of the study, indicating an incorrect mode of use despite the explanations and instructions provided.

In contrast, the control group participants who received in-office treatment with 35% HP presented significant TS, mainly at assessment point 1 and 2, after the single-session bleaching. This result probably can be associated with the concentration of the bleaching treatment [30]. Similarly, a clinical study [31] that evaluated TS in patients treated with different bleaching techniques found that the highest TS values occurred with in-office bleaching using 35% HP (two sessions, 45 min each) compared with at-home bleaching with 10% CP (8 h daily for two weeks). In contrast, Reis et al. [28] showed that TS after two in-office bleaching sessions with two concentrations of HP was relatively low; however, this result can be because the tested products contained 2% calcium gluconate as a desensitizing agent.

Table 3
Mean and standard deviations of tooth sensitivity assessed with a VAS for groups treated with desensitizing agents after bleaching with 35% hydrogen peroxide, in-office (T2).

Assessment point	Groups						
	Control group	Home-use desensitizing			In-office desensitizing		
		D1	D2	D3	D4	D5	D6
Baseline	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}	0.0 ± 0.0^{aA}
1	1.5 ± 1.2^{bcA}	0.9 ± 1.5^{bAB}	0.6 ± 0.5^{aAB}	0.7 ± 0.6^{bAB}	0.1 ± 0.2^{aB}	0.5 ± 0.5^{aAB}	0.3 ± 0.4^{aB}
2	1.7 ± 1.8^{bA}	0.5 ± 1.0^{abB}	0.3 ± 0.3^{aB}	0.4 ± 0.6^{abB}	0.4 ± 0.6^{aB}	0.5 ± 0.3^{aB}	0.9 ± 1.0^{bAB}
3	0.8 ± 1.3^{acA}	0.3 ± 0.6^{abA}	0.3 ± 0.3^{aA}	0.4 ± 0.5^{abA}	0.4 ± 0.6^{aA}	0.4 ± 0.4^{aA}	0.7 ± 0.7^{abA}
4	0.6 ± 1.9^{aA}	0.2 ± 0.3^{aA}	0.1 ± 0.1^{aA}	0.2 ± 0.3^{abA}	0.1 ± 0.2^{aA}	0.4 ± 0.4^{aA}	0.6 ± 0.5^{abA}
5	0.3 ± 0.4^{aA}	0.1 ± 0.2^{aA}	0.1 ± 0.2^{aA}	0.1 ± 0.3^{abA}	0.0 ± 0.0^{aA}	0.2 ± 0.3^{aA}	0.4 ± 0.4^{abA}

VAS: Visual Analogue Scale.
The same lowercase letters indicate statistically similar means within columns. The same uppercase letters indicate statistically similar means within rows ($P > .05$).

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We noted that the participants in groups D2, D4, and D5 (which used Sensodyne dentifrice, Biosilicate paste, and Bioglass type 45S5 paste, respectively) in the in-office tooth bleaching did not show significant difference TS during the evaluation period. Despite their different mechanisms of action and application methods, these treatments maintained VAS scores that were statistically similar to baseline values. Sensodyne® is a potassium nitrate-containing dentifrice that decreases the ability of the nerve fibers in the dental pulp to re-polarize after an initial repolarization caused by pain sensations; consequently, it leads to a minimal sensation of TS [8]. The study conducted by Thiesen et al. [11] suggested that the use of a dentifrice containing 5% potassium nitrate for 14 days can reduce the TS induced by 35% HP. In another study, Tay et al. [4] showed the efficacy of potassium nitrate for relieving TS intensity when used prior to in-office bleaching. Despite the efficacy of potassium nitrate for reducing the TS caused by in-office bleaching, we want to suggest that avoiding a pulp inflammatory process (or the pain caused by it) by blocking the dentin tubules as quickly as possible should be the gold standard protocol for TS pain caused by tooth bleaching.

In this sense, we proposed the use of microparticles from a bioactive glass-ceramic material to reduce TS by obliterating the dentinal tubules and the formation of hydroxyapatite crystals [8]. In a previous in vivo study, Tirapelli et al. [20] indicated that micron-sized particles of Biosilicate may provide immediate and long-lasting relief of dentin hypersensitivity caused by such factors as abfraction, gingival recession, and attrition. In our present study, the use of an experimental dentifrice, containing microparticles of Biosilicate did not lead a significant difference from the control group at assessment point 1 after the application of 35% HP. However, the in-office use of an experimental formulation containing Biosilicate (D4) showed a positive performance at assessment point 1, as suggested by the fact that the group that received this treatment had the lowest TS values compared with the other groups and TS values that were significantly lower than those of the control group. The in vitro study conducted by Pinheiros et al. [6] suggested that the association of remineralizing products with bleaching agents could diminish the number of opened dentin tubules. According to those authors, bioactive materials may facilitate the deposition of calcium and phosphate ions that are lost during the bleaching treatment precipitating in the form of amorphous calcium phosphate and forming a new layer crystallized by the reaction with hydroxyl, carbonate and fluoride from the oral cavity.

In addition to discussing the performance of desensitizing agents, we would like to say that in our study, the highest medium value was 1.7, based on VAS data (Table 2). Similarly low TS values have been shown in previous studies [32,33]. On a zero-to-ten scale, 1.7 is closer to no pain than to intolerable pain. Statistically, we can affirm that TS in the control group (who were treated with 35% HP) was significantly higher at assessment points 1 (immediately after treatment) and 2 (72 h after treatment) compared with the groups that received desensitizing agents; however, from a clinical point of view, this result can raise some discussion and needs to be considered carefully.

The diary of treatment indicated that, especially for those patients who were treated with 35% HP, TS was also present on days 1 and 2 (24 and 48 h after treatment). Nevertheless, the diaries show that no patient declared that TS made the treatment unpleasant, which reveals that TS was a tolerable discomfort. Indeed, this result suggests that TS manifested differently among the groups that were treated with 35% HP and that the desensitizing agents likely played a role in this difference, especially in the first 72 h. Nonetheless, health professionals still need to be cautious about the side effects of tooth bleaching, such as demineralization and/or pulpal reaction, by using reliable products that address the pain or discomfort perceived by the patient.

Despite the recommendations and the appropriate use of the desensitizing agents, this study was limited because it did not control the participants' oral hygiene or eating habits during the study period. In addition, although the experimental formulations showed good results for controlling TS, this study did not assess whether these formulations could interfere with bleaching effectiveness. Therefore, further studies will be needed to assess this variable.

5. Conclusions

TS did not vary from baseline thought the assessment points for participants that used 16% CP without desensitizing agents.

In the first 72 h after a single session of in-office bleaching with 35% HP, TS was higher in patients that did not use desensitizing agents.

When in-office bleaching with 35% HP was associated to D2, D4, and D5 no TS alteration occurred along of the period of the study.

TS caused by 35% HP in-office tooth bleaching was controlled by experimental products prepared as pastes D4-experimental bioactive glass-ceramic and D5-experimental Bioglass type 45S5, but not by D1-experimental dentifrice containing bioactive glass-ceramic.

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