Desensitizing Agent Previously Applied During In-Office Bleaching: A Double-Blind Randomized Clinical Trial

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ABSTRACT

Objective: To compare the clinical effect of two desensitizing agents used before the application of a bleaching gel based on 35% hydrogen peroxide (HP). Material and Methods: 30 patients were selected, and two desensitizing agents with different mechanisms of action were applied: Fluorine Neutral 2% (FN), which acts by blocking dentinal canaliculi while Potassium Nitrate 5% with 2% Sodium Fluoride (PN/SF) that acts in nerve transmission and blockade. Desensitizers were used before the application of 35% HP. For whitening, three clinical sessions were performed, with an interval of seven days, with three applications of the bleaching gel for 15 minutes, totaling 45 minutes/session. Tooth sensitivity (TS) was assessed with the numerical analog scale, and a spectrophotometer was used to obtain the color variation (ΔE). ΔE were submitted to ANOVA and Tukey test (p<0.05), and TS data were submitted to a two-way ANOVA analysis. Results: For sensitivity experience, the Tukey test indicated differences between PN/SF and the placebo I, but there was no statistically significant difference between FN and the placebo II. The TS was lower when the desensitizing gel was used during the bleaching procedure compared to after treatment, regardless of the desensitizing agents. Conclusion: PN/SF before in-office tooth bleaching can reduce TS intensity, and the use of desensitizing gel before bleaching did not affect the bleaching efficacy.

Keywords: Tooth Bleaching; Hypersensitivity; Fluorides; Hydrogen Peroxide.
Introduction

Genetic diseases and fetal pathologies may cause intrinsic tooth staining or can be post-natal acquired [1,2]. Also, the extrinsic pigments result from the accumulation of chromatogenic substances on the external tooth surface [3]. Teeth bleaching has proven to be a conservative esthetic solution to remove intrinsic and extrinsic pigments [4] and involves oxidation of pigments in dental structures [5]. Thus, hydrogen peroxide reduces the long organic chains into colorless short chains by an oxidizing reaction [6].

Treatment efficacy is directly related to the whitening gel concentration and the contact time with the tooth surface [7]. The concentration depends on the chosen product and technique. At-home bleaching involves the use of a low concentration of whitening agent for approximately 4 hours, and in-office bleaching utilizes high concentrations of tooth-whitening agents for a period of 20 to 45 minutes [6].

However, the higher concentration of bleaching agents can produce more peroxide radicals for bleaching, which may increase the side effects. The main effect that patients report is tooth sensitivity [8], which may occur during or after the application of the bleaching gel, especially with the in-office technique [9]. This process can activate the nociceptors that innervate dentinal tubules, leading to the perception of dental pain [10-12].

Some clinical techniques may be used to decrease these side effects, such as concentration reduction of hydrogen peroxide, use of analgesic, anti-inflammatory [13], and desensitizing agents [9,14-16]. The mechanism action is based on the dentin tubules obliteration preventing dental fluid movement and assisting in dentin remineralization, and the second is due to the blockage of pulp enervation reducing nociceptor sensorial excitability [16]. Examples of each desensitization class are fluoride and potassium nitrate associated with sodium fluoride.

Previous studies [9,17] demonstrated that desensitizing agents, independently of the mechanism of action, do not influence dental bleaching. However, it is not possible to determine if its utilization reduces dental sensibility during treatment or post-operatively. According to Tay et al. [9] and Ajcharanukl et al. [18], utilizing desensitizing agents reduces the incidence and intensity of the sensibility. In contrast, other authors [14,17] did not obtain the same results. Therefore, the objective of this study is to assess the impact of pre-application of desensitizing agents on tooth sensitivity and whitening efficacy during in-office dental bleaching treatments. For this, Two hypotheses were proposed: the desensitizing agent would eliminate the pain resulting from tooth whitening, and the desensitizing agent would not influence the effectiveness of tooth whitening.

Material and Methods

Ethical Aspects and Human Subjects

The institutional review board of the University of Campinas - Piracicaba Dental School, Piracicaba, São Paulo, Brazil, reviewed and approved the study protocol with number 026/2014. In this clinical trial, the volunteers who participated were required to be at least 18 years old and have good overall and oral health. Additionally, they were required to have anterior teeth without any restorations and must have had central incisors of shade A2 or darker, as determined by a value-oriented shade guide. (VITA Zahnfabrink, Bad Säckingen, Germany). The exclusion criteria were volunteers who had undergone tooth-whitening procedures, smokers, volunteers with severe internal tooth discoloration, pregnant/lactating women, and participants with spontaneous sensibility.

The volunteers were selected from random public places to obtain a heterogeneous sample. In total, 33 patients were examined. Three volunteers still need to meet the inclusion criteria. Two were smokers, and one
had restorations in the anterior teeth. The volunteers included in this study consisted of 12 men and 18 women between 18 and 41 years old. One week before starting the bleaching procedure, a run-in period was performed for all volunteers to standardize the toothbrush (Oral B Classic, Procter & Gamble, São Paulo, SP, Brazil) and 1500 ppm fluoride dentifrice (Colgate Máxima Proteção Anticáries, Colgate-Palmolive, São Bernardo do Campo, SP, Brazil) used.

Material

Researchers used two types of desensitizing agents, two types of placebos, and 35% hydrogen peroxide in the study (Table 1).

<table>
<thead>
<tr>
<th>Material</th>
<th>Composition</th>
<th>Manufacture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whiteness HP</td>
<td>35% hydrogen peroxide, thickening agent, red dye, glycol, and water.</td>
<td>FGM, (Joinville, SC, Brazil)</td>
</tr>
<tr>
<td>Desensibilize KF 2%</td>
<td>Potassium Nitrate 5% and sodium fluoride 2%</td>
<td>FGM, (Joinville, SC, Brazil)</td>
</tr>
<tr>
<td>Placebo I</td>
<td>2% of deionized water, glycerin, thickening, and neutralizing agent</td>
<td>Handling pharmacy</td>
</tr>
<tr>
<td>Flugel</td>
<td>Sodium fluoride 2%</td>
<td>DFL, (Rio de Janeiro, RJ, Brazil)</td>
</tr>
<tr>
<td>Placebo II</td>
<td>Gel without peroxide</td>
<td>Handling pharmacy</td>
</tr>
</tbody>
</table>

Experimental Design

This double-blind, split-mouth-designed study with four experimental groups. Based on pre-established criteria, 30 volunteers (in which each subject served as his own control) were evaluated for efficacy and the perception of the intensity of tooth sensitivity experience of in-office bleaching. There were four treatments: Potassium Nitrate 5% with 2% sodium fluoride (PN/SN) (Desensibilize KF 2%, FGM, Joinville, SC, Brazil) and their respective placebos (P1); 2% Neutral Fluoride (FN) (Flugel, DFL, Rio de Janeiro, RJ Brazil) and its respective placebo (P2). The variables were color change ($\Delta E$) and an analog pain scale.

The desensitizing agents and their respective placebos were randomly distributed between the upper and lower arches. In each arc, there was a subdivision in the hemi-arches for the distribution of active and placebo agents. Thus, each jaw received a desensitizing agent and the respective placebo. The experimental design can be seen in the experimental chart (Figure 1).

Bleaching and Desensitizing Procedures

The authors gave the desensitizing and placebo gels to the clinicians in unmarked syringes. The syringes were marked only with numbered codes that neither the clinicians nor the patients could identify. The clinicians isolated the gingival tissue of the teeth to be bleached by using a light-cured resin dam (Top Dam, FGM, Joinville, SC, Brazil). They applied a desensitizing gel corresponding to each group (PN/SN and Placebo I for 10 minutes; FN and Placebo II for 4 minutes) from the first right molar to the first left molar.

After the specified period, the products were removed with humidified cotton and abundant water. The bleaching procedure was performed with 35% hydrogen peroxide gel (Whiteness HP 35%, FGM, Joinville, SC, Brazil) in three 15-minute applications per the manufacturer's instructions. The volunteers repeated the in-office bleaching treatment one week later.

To evaluate the tooth sensitivity experience (quadrant), the authors asked subjects to record whether sensitivity after bleaching or in the days that followed (end of each bleaching session, before the second and third session, and one week after the bleaching protocol), using a following scale ranged from 0 to 4 (0 = no sensitivity,
1 = light sensitivity, 2 = moderate sensitivity, 3 = considerable sensitivity and 4 = severe sensitivity). Tooth sensitivity was defined as the pain intensity in each quadrant.

Figure 1. Experimental design.

Color Measurements

Color measurements were performed using a spectrophotometer (Easyshade, Vident, Brea, CA, USA). Color was evaluated with teeth in an entirely hydrated condition (Baseline) before the second and third sessions and one week after the bleaching protocol. The color was not soon assessed after each session in order to avoid the influence of dehydration that occurs with the bleaching procedure. For calibration purposes, a preliminary impression of both arches was made using dense silicon, and a window was created on the labial surface of the silicon guide for the middle third of the anterior central incisors.

The shade was determined using the parameters of the Easyshade device, where indicated the following values: L*, (a*), and (b*). L* represents a value from 0 (black) to 100 (white), and (a*) and (b*) represent the shade where a* is the measurement along the red-green axis and b* is the measurement along the yellow-blue axis. The color comparison before and after the weeks of treatment was determined by the differences between the two colors (ΔE), which was calculated using the formula: \[ \Delta E = ((\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2)^{1/2}. \]

The color variation (ΔE) was obtained by comparing three different times: baseline x 1st week of bleaching (ΔE1), baseline x 2nd week of bleaching (ΔE2), and baseline x 3rd week of bleaching (ΔE3). The data were submitted to a one-way (ANOVA). A post-hoc analysis (Tukey test) was used to make pairwise comparisons.
Statistical Analysis

Pain intensity was submitted to a two-way ANOVA (time and desensitizing agent). Because the data was not homogeneous, the data was transformed (Box and Cox 1964). For decision-making, a probability of 5% (p<0.05) was considered significant. The SAS ESTAT program was used for statistical analyses.

Results

A total of 30 volunteers were selected for the study, 28 were evaluated and completed the study. Two volunteers decided to drop out of the bleaching treatment, so we excluded these patients from the analysis. These volunteers were not considered in the statistical tests.

The ANOVA results indicated that the desensitizing products used before the treatment did not influence the final treatment efficacy. All patients who completed the three bleaching sessions had significant color changes (p=0.0031). ΔE3 (mean 0.868A) was significantly different from ΔE1 (mean 0.632B) but was not substantially different from ΔE2 (mean 0.765AB). ΔE2 was not different from ΔE1 (Table 2).

| Table 2. Statistical analysis (Tukey) from color variation (ΔE). |
|---|---|---|
| **Color Variation** | **N** | **Mean** |
| ΔE3 | 28 | 0.868A |
| ΔE2 | 28 | 0.765AB |
| ΔE1 | 29 | 0.632B |

Similar capital letters indicate statistically similar in each column (p<0.05).

All patients experienced some sensitivity in this study. The ANOVA demonstrated a significant difference for desensitizing agents (p=0.028) and time (p<0.001). The statistical analyses revealed that the interaction of the two factors was not statistically significant (p=0.969). The Tukey test indicated differences between Desensibilize KF 2% and the placebo. There was no significant difference between neutral Fluorine 2% and the placebo (Table 3).

| Table 3. Statistical analysis (Tukey) from desensitizing agents. |
|---|---|---|
| **Treatment** | **N** | **Mean** |
| Desensibilize KF 2% (D1) | 168 | 0.916A |
| Neutral Fluoride (D2) | 168 | 1.041AB |
| Placebo II (P2) | 168 | 1.101AB |
| Placebo I (P1) | 168 | 1.166AB |

SD: Standard Deviation; Similar capital letters indicate statistically similar in each column (p<0.05).

The pain intensity was lower when using the gel during the bleaching compared to the days after the treatment, regardless of the desensitizing agent used (Table 4).

| Table 4. Statistical Analysis (Tukey) from pain intensity over time. |
|---|---|---|
| **Time** | **N** | **Mean** |
| T3 | 112 | 0.571A |
| T5 | 112 | 0.607A |
| T1 | 112 | 0.848AB |
| T6 | 112 | 1.276RC |
| T2 | 112 | 1.303RC |
| T4 | 112 | 1.732CE |

SD: Standard Deviation; Similar capital letters indicate statistically similar in each column (p<0.05).

Discussion
The current study evaluates two mechanisms of action of two desensitizing agents when applied before bleaching. Prior studies evaluating these desensitizing agents used a control and experimental group. However, sensitivity is a subjective factor unique to each person. Therefore, it is necessary to use volunteers as their control [19]. Despite the limitations of a split-mouth study, the desensitizing agents have a gel consistency. Thus, the dentist can confine their action to the tested teeth, as demonstrated in other studies evaluating dentin hypersensitivity.

Sensitivity is the most common adverse side effect of tooth whitening and is the main impediment to successfully completing treatment [9,17]. In this study, 7% of patients (n = 2) discontinued the treatment due to hypersensitivity, as described by Basting et al. [16]. Dentists have used different techniques to reduce sensitivity during bleaching treatment, such as reducing the application time of the bleaching gel and decreasing session frequency. Additionally, studies [9,17] have shown that using fluoride or potassium nitrate before bleaching can effectively reduce tooth sensitivity. Thus, the hypothesis that the desensitizing agent would eliminate the pain resulting from tooth whitening was rejected.

The etiology of hypersensitivity is complex and may be related to the amount of hydrogen peroxide that reaches the pulp [16,17,20,21]. Fluoride occludes dentinal tubules [22] with precipitation of calcium fluoride crystals on the dentin tubules, reducing their diameter and thus reducing the movement of pulpal fluid [23].

Besides, 5% potassium nitrate with 2% sodium fluoride inhibits nerve repolarization after initial depolarization. The nerve impulses that travel through the neuron are electrical and result from changes in the electrical charges of the surfaces of the cell membrane. The membrane of a neuron at rest has a positive charge on the outside due to sodium ions and a negative charge on the inner side due to potassium. A chemical, mechanical, or electrical stimulus may change the neuron’s membrane permeability, allowing sodium entry into the cell and potassium output [24]. Therefore, a reversal of charges occurs around the membrane that generates pain transmission. This depolarization spreads throughout the neuron, characterizing the painful nervous impulse [24]. The application of potassium nitrate provides a high concentration of extracellular potassium ions to the sensory nerve, causing an electrochemical change that reduces the excitability of the nerve and the nerve’s ability to transmit pain [25-29].

These mechanisms of desensitizing agents support the results found in this study. Neutral fluoride was not significantly different compared to the placebo. However, potassium nitrate with fluoride was significantly different compared to the placebo, confirming other studies [9,14].

The precipitation of calcium fluoride would reduce the penetration of hydrogen peroxide to the pulp [17] and reduce sensitivity. However, this mechanism only occurs when fluoride is applied directly to the exposed dentin, which did not occur in this study (enamel application) [9]. Furthermore, calcium fluoride is approximately 0.05 micrometers and is too small to block the dentinal tubules. Therefore, precipitates resulting from the action of fluoride with the dental structure cannot decrease the permeability of dentin with a single application. Thus, the application of fluoride before the bleaching was not effective in reducing hypersensitivity [30-33].

The NP applied before the bleaching treatment reduced the intensity of tooth sensitivity. This reduction in pain sensitivity was more effective because even with the arrival of free radicals to the pulp, the pain was reduced by nervous system site lock [17]. Other studies that assessed the effectiveness of the treatment on post-bleaching sensitivity also demonstrated a reduction in pain intensity [14], which agrees with the results obtained in this study.
Regardless of the desensitizer, the tooth sensitivity at 1, 3, and 5 was lower than at 2, 4, and 6. The odd numbers represent pain assessment immediately after each bleaching session, and the even numbers represent sensitivity during one-week intervals between sessions. Thus, the sensitivity immediately after bleaching was lower than the interval between bleaching sessions. This result demonstrates that the desensitizing agent reduced the pain intensity when applying hydrogen peroxide. This proves that the use of desensitizing topical gel has a short duration, allowing the return of pain sensitivity approximately 20 minutes after treatment [18].

A return to average potassium ion concentrations can explain the rapid recovery of sensitivity after treatment with desensitizing agents. This rapid decrease in concentration occurs when the pressure on the tooth surface returns to normal due to the removal of the gel (regulating the normal physiological flow of fluid in the dentinal tubules) [18].

The application of whitening gel increases the pressure through the intertubular oxygen molecules released from hydrogen peroxide [34-36]. These molecules can diffuse and accumulate on the enamel and dentin, occupying an intratubular space, which increases the pressure on pain receptors present in the pulp [9] and prevents intertubular fluid movement. Thus, removing the bleaching agent by washing the gel removes the oxygen ions and consequently decreases the pressure on the dentin, allowing intertubular flow to return. Furthermore, removing the gel also removes potassium ions, and their action is limited to the time of gel application.

The second hypothesis, which considers that the desensitizing agent would not influence the effectiveness of tooth whitening, was corroborated by clinical findings. The desensitizing agents do not interfere with bleaching efficacy with hydrogen peroxide at 35%, as previously reported by other studies [9,14-17,19].

Due to the fluoride mechanism of action, the diffusion of hydrogen peroxide could be impaired and reduce the bleaching effectiveness. However, free radicals from hydrogen peroxide have a low molecular weight and can pass through the interstitial space between the dentinal tubules and among the calcium phosphates formed by fluoride deposition [9]. A dental color change was observed at the end of each session. The color change was more significant after the third session. Greater contact time of the bleaching gel allows for a higher concentration of free radicals, which first oxidizes the pigments in the enamel before reaching the deep dentin, where tooth whitening occurs. Therefore, although office bleaching results in an immediate color change after the first session, a satisfactory result and no color rebound effect are achieved when more than one session is performed [9].

Conclusion

The use of neutral fluorine (2%) prior to the in-office tooth bleaching does not reduce tooth sensitivity. Also, the use of a desensitizing gel based on 5% potassium nitrate and 2% sodium fluoride minimizes the intensity of bleaching-induced tooth sensitivity, and desensitizing gel prior to the tooth bleaching procedure does not affect the whitening effectiveness.

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All authors declare that they contributed to a critical review of intellectual content and approval of the final version to be published.
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None.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

References


