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Evaluation of several clinical parameters after bleaching with hydrogen peroxide at different concentrations: A randomized clinical trial

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ABSTRACT

Objective: This randomized double-blind clinical trial compared tooth sensitivity (TS), bleaching efficacy, and cytokine levels after applying in-office bleaching treatments containing 15% and 35% hydrogen peroxide (HP15% and HP35%, respectively).

Methods: Twenty-five volunteers were randomly assigned to receive HP15% or HP35% treatment. The bleaching agent was applied in three 15-min applications per session. Two bleaching sessions were separated by a 1-week interval. The participants scored TS using a visual analog scale and numerical rating scale. Bleaching efficacy was determined by subjective and objective methods. Gingival crevicular fluid was collected from three jaws sites per patient for the analysis of fluid volume. Flow cytometry was used to analyze gingival crevicular fluid levels of interleukin (IL)-1β, IL-2, IL-4, IL-6, IL-10, tumor necrosis factor, and interferon-gamma. All measurements were obtained before and after bleaching. All data were statistically analyzed ($\alpha = 0.05$).

Results: The absolute risk and intensity of TS was higher for HP35% than for HP15% ($p > 0.002$). One month post-bleaching, HP35% produced more bleaching than HP15% ($p = 0.02$). However patient perception ($p = 0.06$) and patient satisfaction ($p = 0.53$) with regard to bleaching were not significantly different. No significant differences existed in the gingival fluid volume ($p > 0.38$) or in any cytokine level ($p > 0.05$) for either HP concentration.

Conclusion: Treatment: with HP35% is more effective than HP15%, but generates a greater risk and intensity of TS. No inflammatory changes occurred despite the difference in the HP concentrations.

Clinical significance: Hydrogen peroxide at a lower concentration (e.g., 15%) should be considered a good treatment alternative for in-office bleaching because the higher concentration for in-office bleaching generates a greater risk and intensity of TS for patients.

1. Introduction

In-office tooth bleaching has become a widely used esthetic dentistry procedure because of patients' desire to obtain a faster whitening result and because some patients prefer not to use a bleaching tray (e.g., at-home bleaching) [1]. However, to achieve this goal, manufacturers indicate the use of high hydrogen peroxide (HP) concentrations (25%–35%) for in-office bleaching procedures. The more common adverse effects of the in-office procedures unfortunately are post-bleaching tooth sensitivity (TS) and gingival irritation [2]. The most acceptable hypothesis to explain the high prevalence of TS is the rapid diffusion of HP and degradation products inside the pulp chamber [3]. These products may also react with soft tissue and cause injuries such as gingival irritation, burns, and ulceration [4,5].

Several in vitro studies have shown that the higher the concentration of HP, the greater the damage to pulp cells [6–9]. This finding is in line with recent pooled data of 11 clinical trials of bleaching conducted by a research group our [10], which revealed that in-office bleaching was associated with an increased risk and intensity of TS, compared to at-home bleaching, primarily because at-home bleaching applies a

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lower concentration of HP during the procedure.

A close review of articles related to injuries to soft tissue caused by HP reveal controversial results [11–16]. However, a high concentration of HP has the potential to modify the histomorphological properties of teeth [17–19]. For instance, a recent study [17] showed increased activity by inflammatory cytokines and metalloproteinases when in-office bleaching gels were applied, which suggests that this treatment would affect the levels of these markers in the crevicular fluid, assuming that these substances would have spread to the periodontal tissues. Thus, a possible alternative would be to decrease the concentration of HP in-office bleaching gels. Several in vitro studies have shown that a reduction to approximately 15%–20% HP in an in-office bleaching gel resulted in effective bleaching and a significant reduction of HP diffusion to the pulp chamber, compared to the higher concentration used in in-office gels [7–9].

A lower HP concentration may generate less cytotoxicity and damage to the periodontal tissue, compared to a higher concentration of HP. In an effort to reduce this adverse effect, new low-concentration bleaching gels using 6%–20% HP were placed on the market. Several clinical studies evaluated TS and bleaching efficacy of low-concentration in-office HP gels, compared to high-concentration in-office HP gels, and demonstrated similar results. However, the application of 15%–20% HP is usually associated with light application [20–22].

The literature is scarce regarding comparisons of in-office bleaching gels at different HP concentrations used without light [22,23]. For instance, Reis et al. [23] showed that faster bleaching occurred with a high-concentration gel (35% HP) than with a low-concentration gel (20% HP); however, TS was similar. Mena-Serrano et al. [23], also observed improved whitening with an in-office 35% HP gel than with an in-office 20% HP gel; however, their results were affected by the instruments used to evaluate color changes. In addition, the TS results were independent of the HP concentration. The absolute risk of TS was 22% in the Reis study [23], whereas the average percentage of patients with TS was approximately 72% in the Mena-Serrano study [22]. These conflicting results between the two studies in the percentage of TS, which is primarily related to differences between bleaching gel compositions, deserve further investigation. Therefore, this study aimed to evaluate the impact of HP15% and HP35% in-office bleaching procedures on TS, bleaching effectiveness, and a patient's perception of whitening. The levels of inflammatory markers were also evaluated. The null hypotheses tested were (1) the two HP concentrations would not result in different percentages of patients with TS; (2) the two HP concentrations would not result in different degrees of color change; (3) different HP concentrations would not result in different patient perceptions regarding the whitening effect; and (4) different HP concentrations would not result in different levels of inflammation.

2. Materials and methods

This clinical investigation was approved (protocol number 1.307.220) by the Research Ethics Committee of the Local University. The research protocol was registered in the Brazilian Clinical Trials Registry under the identification number RBR-4kkcd7. After obtaining approval, 25 volunteer graduate students with anterior teeth of shade A3 or darker—as judged by a comparison with a value-oriented shade guide (Vita Lumin; VITA Zahnfabrik, Bad Säckingen, Germany)—were enrolled to participate in this clinical trial. All participants received a dental screening and dental prophylaxis 1 week before the start of bleaching and signed an informed consent form before the study began.

2.1. Study design

This study was a randomized, double-blind, split-mouth clinical trial with an equal allocation rate of 1:1 for one of two treatments. The study was conducted at the clinic of the School of Dentistry of Local University from March 2016 to August 2016.

2.2. Inclusion and exclusion criteria

Patients included in this clinical trial were 18–40 years old and had good general health and oral health. The participants were required to have caries-free anterior teeth without restorations or periodontal disease. Each participant was required to have maxillary incisors that were shade A3 or darker, as determined by a comparison with a value-oriented shade guide (Vita Classical Shade Guide; VITA Zahnfabrik, Bad Säckingen, Germany), after undergoing the cleaning of all teeth using pumice and a slow-speed rotary brush/prophy cup.

The study excluded patients with poor oral hygiene; pregnant or lactating women; patients who had undergone tooth whitening treatment; smokers, and patients with restorations, root canal treatment or a dental prosthesis on the anterior teeth. Also excluded were patients with visible cracks, gingival recessions, carious cervical lesions or fractures, spontaneous TS, severe internal discoloration, bruxism, patients who were taking medications with an analgesic or anti-inflammatory effect, and patients with fixed orthodontic appliances.

2.3. Sample size calculation

The primary outcome of this study was the absolute risk of TS. Twenty-two patients were required to have an 80% chance of detecting a decrease in the primary outcome measure from 90% (i.e., the mean absolute risk of TS) [24–26] in the control group to 55% in the experimental group ($\alpha = 0.05$). Fifteen percent of patients were added for drop offs. The sample size was calculated on the website www.sealedenvelope.com. The present study was powered to detect a high significant effect.

2.4. Random sequence generation and allocation concealment

The randomization process was conducted by computer-generated tables prepared by a third person not involved in the research protocol. Blocked randomization was used for both treatment groups (block of 2; www.sealedenvelope.com). Details of the allocated group were recorded on cards contained in sequentially numbered, opaque, sealed envelopes. These envelopes were opened on the day of bleaching to prevent disclosure of the randomization scheme. For all patients, the left side received the treatment mentioned first on the randomization list, and the right side received the treatment mentioned second. Neither the participant nor the operator knew the group allocation—both were blinded to the protocol.

2.5. Study intervention

Before beginning the bleaching procedure, a third person not involved in the research protocol removed all commercial identifications from each product. Bleaching gels were identified by labels encoded as "A" and "B" to guarantee that the operator and patient were blinded. A single operator applied bleaching gels on the labial surface of the teeth. After prophylaxis and obtaining the initial registration of color, the bleaching procedure was performed. Before applying the whitening gel, the gingival tissue of the teeth to be bleached was isolated using a light-polymerized resin dam (Top Dam; FGM Prod. Odontol. Ltda., Joinville, SC, Brazil). The evaluated bleaching gels were Lase Peroxide Lite 15% ([i.e., HP15%] DMC Equip., São Carlos, SP, Brazil) and Lase Peroxide Sensy 35% ([i.e., HP35%] DMC Equip.). Each gel was applied in three applications with each lasting 15 min, but without using light (Table 1). Two bleaching sessions were performed with a 1-week interval between them. All participants were instructed to brush their teeth regularly using toothpaste without a desensitizing or bleaching agent.

2.6. Tooth sensitivity evaluation

The authors asked the volunteers to record whether they