Study Protocol

Efficacy of Tooth Bleaching with 35% and 6% Hydrogen Peroxide in Primary Dentition: Study Protocol for a Randomized Controlled Clinical Trial

ABSTRACT

Background: The aesthetics of dental elements generates significant psychological and social impacts, both in primary and permanent dentition. One of the most employed techniques to visually improve the appearance of teeth is bleaching. In in-office whitening, the technique used consists of applying whitening gel to dental surfaces in concentrations ranging from 25% to 50% of hydrogen peroxide. However, recent studies showed that low and medium concentration bleaching agents based on hydrogen peroxide have been effective and present a lower risk of sensitivity to the patient. **Aims**: To carry out a controlled and randomized clinical trial to compare the effectiveness of dental bleaching in primary teeth with hydrogen peroxide at concentrations of 35% and 6%. **Methods:** In this study, 38 patients aged 3 to 6 years-old will be selected and allocated in 2 groups (G1 - Hydrogen Peroxide 35%, n=19 and G2- Hydrogen Peroxide 6%, n=19). Bleaching will be carried out in up to three sessions, with an interval of 7 days between each session. Evaluation of color and tooth sensitivity will be carried out 48 hours after each bleaching session. The color assessment will be measured with the aid of a digital spectrometer while the tooth sensitivity will be assessed by using the Pain Level Scale (Wong-Baker Faces®). **Discussion:** It is expected that there will be no significant difference between the groups in terms of color variation and that the low concentration bleaching group will have the lowest sensitivity index.

Keywords: Tooth Bleaching,Tooth Bleaching Agents, Hydrogen Peroxide, Primary Dentition, Tooth Deciduous.

1. INTRODUCTION

The aesthetic appearance of upper incisors, in both primary and permanent dentitions, is an important factor in the perception of a smile. Research has shown that a person's smile has significant social and psychological effects, directly influencing their quality of life [1]. In primary teeth, aesthetic issues are often linked to trauma, pulpal diseases, carious lesions, developmental disorders, fluorosis, opacities, and endodontic treatments performed with iodoform-based filling materials [1,2].

Dental stains are categorized into extrinsic and intrinsic types [3–5]. Intrinsic stains represent a particular challenge in Pediatric Dentistry because they often originate during the pre-eruptive stages of tooth formation and affect the majority of erupted primary teeth. These stains may result from systemic conditions, such as bilirubinemia, or the ingestion of certain substances, such as antibiotics (e.g., tetracycline) or excessive fluoride [6]. In clinical practice, intrinsic stains are complex to manage, as their removal or masking often does not achieve satisfactory aesthetic outcomes. Treatment methods

depend on the pulpal condition of the tooth: non-vital teeth are treated with internal bleaching, while vital teeth may require external bleaching, enamel microabrasion, or aesthetic rehabilitation using veneers [1,5].

In contrast, extrinsic stains are more manageable and often yield satisfactory results in dental practice [1,3,5,7]. Treatment approaches include professional cleaning with abrasive or bioactive pastes and the use of whitening agents.

Despite the widespread use of tooth whitening, few studies and standardized protocols focus on whitening procedures for primary teeth. Most available research consists of laboratory studies or case reports [3–5,8–10]. Among the various techniques, internal bleaching has been identified as the most effective for primary teeth in terms of cost-efficiency and minimal intervention. However, this method is limited by the requirement to devitalize the tooth.

Tooth whitening is considered a conservative and cost-effective treatment. Although this procedure has been practiced for nearly 150 years, the modern approach was introduced in 1984 to improve the aesthetic appearance of natural teeth [11]. Current methods include at-home kits and in-office treatments conducted by professionals, both of which are effective. However, potential side effects highlight the importance of professional supervision to ensure safe and effective outcomes [5,12].

In recent years, the interest of children and adolescents in tooth whitening has grown. The American Academy of Pediatric Dentistry has responded to this trend by establishing guidelines for whitening procedures in younger populations. According to these guidelines, tooth whitening is safe and beneficial when performed under professional supervision. Beyond improving aesthetics, whitening can enhance self-esteem. However, careful assessment and proper planning are essential prior to initiating any whitening protocol [13].

Research has demonstrated that low and medium concentrations of hydrogen peroxide used in in-office whitening are associated with a lower risk of sensitivity while maintaining whitening effectiveness comparable to high-concentration products. This makes lower-concentration products a safer alternative for patients [14]. In-office whitening involves the application of bleaching gels containing hydrogen peroxide or carbamide peroxide in concentrations ranging from 25% to 50%, with or without the use of light activation. Studies have shown that light activation does not significantly alter the final results of the treatment [15].

Based on this context, the present study aims to evaluate the effectiveness of in-office whitening in primary teeth using two different concentrations of hydrogen peroxide (high and low). The objective is to determine the most appropriate whitening protocol for primary teeth.

The hypotheses for this study are as follows:

1. The group using low-concentration hydrogen peroxide will experience less tooth sensitivity due to its alkaline and stable pH.
2. There will be no significant difference in the final whitening results between the two groups.

2. MATERIAL AND METHODS

2.1 Study design

This study protocol was designed as a randomized, controlled, blind, clinical trial according to the 2013 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement (Table 1) and the SPIRIT checklist can be found as an additional file.It will be conducted at the dental clinic of UniversidadeMetropolitana de Santos (UNIMES).

Table 1. Schedule of enrolment, interventions, and assessments of the study

	STUDY PERIOD											
	Enrolment	**Allocation**	**Post-allocation**									**Close-out**
TIMEPOINT*	***-t1***	**0**	***T1***	***T2***	***T3***	***T4***	***T5***	***T6***	***T7***	***T8***	***T9***	***T10***
ENROLMENT:												

Eligibility screen	X											
Informed consent	X											
Allocation		X										
INTERVENTIONS:												
[Bleaching 35% hydrogen peroxide gel]			X			X						
[Bleaching 6% hydrogen peroxide gel]			X			X						
ASSESSMENTS:												
[Clinical evaluation]		X	X	X	X	X	X	X	X	X	X	X
[First application]			X									
[Second application]												
[Third Application]									X			
[Wong-Baker FACES® Scale]		X		X	X		X	X		X	X	X
[Assessment of color]		X		X	X		X	X		X	X	X

* -t1 = before the Baseline, 0 = Baseline, T1 = 1ª application, T2 = immediately after 1ª application, T3 = 48 hours after 1ª application, T4 = 2ª application, T5 = immediately after 2ª application, T6 = 48 hours after 2ª application, T7 = 3ª application, T8 = immediately after 1ª application, T9= 48 hours after 1ª application, T10 = 4 weeks after the 1ª application.

2.1.2 Strengths and limitations of this study

- Tooth Bleaching consists of an aesthetic treatment whose main advantage is the preservation of the tooth structure.
- The darkening of teeth can interfere with the quality of life of children, due to the period of psychosocial development.
- Tooth bleaching, in addition to aesthetics, can also restore the child's self-esteem.
- The scarce literature on whitening protocols for primary teeth.
- This study can help professionals in decision-making in situations of darkened primary teeth with aesthetic complaints.

2.1.3 Hypotheses

The hypotheses for this study are:

- Lower levels of tooth sensitivity will be observed in the group using the low-concentration hydrogen peroxide whitening product, due to its alkaline and stable pH.
- There will be no significant difference in the final whitening results between the two groups.

2.2 Study Population

Thirty-eight teeth will be selected from healthy male and female children ranging from three to six years-old (no distinction in terms of ethnicity) enrolled for treatment at the pediatric dental clinic of UniversidadeMetropolitana de Santos

(UNIMES). At the first appointment, a form addressing the medical history of the patient will be completed. Next, the volunteers will be submitted to a clinical examination to assess their oral health status. Based on the information collected during this first appointment, the inclusion and exclusion criteria will be applied. Patients who meet the inclusion criteria and whose parents or guardians sign the informed consent form will be scheduled for a second appointment for treatment according to the allocation group.

2.2.1 Inclusion criteria:

- Healthy children with no adverse systemic conditions;
- Age range: from 3 to 6 years-old;
- Vital teeth with severe to moderate discoloration;
- No active carious lesions;
- No lesions in the oral cavity;
- No report of previous tooth sensitivity.

2.2.2 Exclusion criteria:
Children with systemic diseases, Children who, during anamnesis, report allergies to dyes or latex, who withdraw from participating in the study, as well as those who do not attend the callbacks, will be excluded.

2.3 Sample size

To carry out the sample calculation, we assumed the study as non-inferiority design, with delta of 8.24 +-2.45 for color change in the control group [16]. The limit of non-inferiority was considered as -2.5 inferiority, power of 90% and significance level of 5%, which resulted in 17 teeth per group. 10% was added to this number due to possible sample losses, resulting in a sample of 19 primary anterior teeth per group, totaling 38 teeth.

2.4 Randomization and allocation

The type of treatment will be randomly determined for each tooth, through a draw before the intervention. The draw will follow the order electronically generated by the randomizer.org randomization website for a balanced distribution of all teeth between the groups. Thirty-eight vital primary teeth with severe to moderate discoloration will be selected; the teeth will be divided into two groups (Figure 1).

GROUP	Concentration of hydrogen peroxide	Chemical Composition	Material	Comercial Brand
G1 (N=19)	High Concentration	35% Hydrogen peroxide	Whiteness HP Automixx 35%	FGM Dental Group – Joinville-SC – Brazil
G2 (N=19)	Low Concentration	6% Hydrogen peroxide	Whiteness HP Automixx 6%	FGM Dental Group – Joinville-SC – Brazil

Figure 1. Distribution of Experimental Groups.

2.5 Interventions

Before starting the procedures, the color of the darkened tooth will be confirmed using the Vita Easyshade® digital spectrometer (Vita Easyshade®; VITA Zahnfabrik H. Rauter GmbH & Co., KG, Germany). The upper left canine will be used as a color reference because it is the most saturated tooth in the arch (greater dentin mass and greater amount of intrinsic pigments).

Group 1 - Hydrogen Peroxide 35%

In group 1, the following bleaching protocol will be performed:

1. Clinical examination and initial shade color assessment.

2. Sensitivity/pain recording using the Pain Level Scale (Wong-Baker Faces®)

3. Prophylaxis with a Robson brush (Color-Brush – Ultra-Soft; American Burns, Palhoça, SC, Brazil) and prophylactic paste (CleanJoy; Voco GmbH, Cuxhaven, Germany) to remove extrinsic pigments and bacterial plaque.

4. Application of lip balm (F&A, SP, Brazil) on the patient's lips;

5. Placement of the labial retractor (ArchFlex; FGM Dental Group, Joinville, SC, Brazil);

6. Application of the gingival barrier (Top Dam; FGM, Joinville, SC, Brazil) on the tissue free marginal gingival margin and the papillae between the upper right canine teeth and the upper left canine teeth. The gingival barrier material will be photopolymerized from 20 to 30 seconds using high power LEDs (Radii-Xpert; SDI Limited, Victoria, Australia);

7. Application of Whiteness HP Automixx 35% whitening gel (Whiteness HP Automixx 35%; FGM Dental Group, Joinville, SC, Brazil)

8. In the session, a single application of the gel will be carried out. It will remain in contact with the tooth for 15 min. With the aid of a micro-applicator (Cavibrush; FGM Dental Group, Joinville, SC, Brazil), the gel will be moved over the teeth frequently (every 5 minutes) to release oxygen bubbles and improve the contact between the gel and the teeth.

9. The gel must be removed from the teeth with a dental suction device and the teeth cleaned with gauze.

10. Sensitivity/pain recording using the Pain Level Scale (Wong-Baker Faces®)

11. The second bleaching session will be carried out 7 days after the first one and, if necessary, a third session can be carried out 7 days after the second one.

Group 2 - Hydrogen Peroxide 6%

In group 1, the following bleaching protocol will be performed:

1. Clinical examination and initial shade color assessment;

2. Sensitivity/pain recording using the Pain Level Scale (Wong-Baker Faces®) [17]

3. Prophylaxis with a Robson brush (Color-Brush – Ultra-Soft; American Burns, Palhoça, SC, Brazil) and prophylactic paste (CleanJoy; Voco GmbH, Cuxhaven, Germany) to remove extrinsic pigments and bacterial plaque.

4. Application of lip balm (F&A, SP, Brazil) on the patient's lips;

5. Placement of the labial retractor (ArchFlex; FGM Dental Group, Joinville, Brazil);

6. Application of the gingival barrier (Top Dam; FGM, Joinville, SC, Brazil) on the tissue free marginal gingival margin and the papillae between the upper right canine teeth and the upper left canine teeth. The gingival barrier material will be photopolymerized from 20 to 30 seconds using high power LEDs (Radii-Xpert; SDI Limited, Victoria, Australia);

7. Application of Whiteness HP Automixx 6% whitening gel (Whiteness HP Automixx 6%; FGM Dental Group, Joinville, SC, Brazil)

8. In the session, a single application of the gel will be carried out. It will remain in contact with the tooth for 15 min. With the aid of a micro-applicator (Cavibrush; FGM Dental Group, Joinville, SC, Brazil), the gel will be moved over the teeth frequently (every 5 minutes) to release oxygen bubbles and improve the contact between the gel and the teeth.

9. The gel must be removed from the teeth with a dental suction device and the teeth cleaned with gauze.

10. Sensitivity/pain recording using the Pain Level Scale (Wong-Baker Faces®)

11. The second bleaching session will be carried out 7 days after the first one and, if necessary, a third session can be carried out 7 days after the second one.

2.6Outcome assessment

Clinical evaluations will assess tooth color and sensitivity.

2.6.1 Assessment of color

The initial color will be determined by using Vita Easyshade® digital spectrometer (Vita Easyshade®; VITA Zahnfabrik H. Rauter GmbH & Co., KG, Germany) before the rubber cup polishing at the first bleaching session. The spectophotomer measurement will be performed again at 48 hours after the first bleaching section, one week after the end of bleaching and 4 weeks after the beginning of the bleaching treatment.

The tooth shade will be determined using the parameters of the spectrophotometer device, according to the study of Pierote et al 2020 [12]. This study assessed the following values: L*, a*, and b*. L* parameter represents the tooth value on a scale from 0 (black) to 100 (white), a* is the measure along the red (a* positive) and green (a* negative) axes and b* is the measure along the yellow (b* positive) and blue (b* negative) axes. The color will be estimated by the equation ΔE = ((ΔL*)2+(Δa*)2+(Δb*)2)1/2. This assessment will be performed to verify the effectiveness of the bleaching treatment.

2.6.2 Assessment of of tooth sensitivity

Tooth sensitivity assessment will be performed with the aid of Wong-Baker FACES® Pain Rating Scale (Figure 2). This scale was created to help children communicate about their pain. Nowadays, the scale is used for 3-year-old children and above. The assessment will be performed according to the instructions provided by the Wong-Baker FACES Foundation (www.WongBakerFACES.org), as follows. The professional will explain that each face represents a person with no pain, or some pain, or a lot of pain. Face 0 doesn't hurt at all. Face 2 hurts just a little bit. Face 4 hurts a little bit more. Face 6 hurts even more. Face 8 hurt a whole lot. Face 10 hurts as much as you can imagine, although you don't have to be crying to have this worst pain. After the explanation, the patient will be asked to choose the face that best depicts the pain that they are experiencing [17].

Figure 2 Wong-Baker FACES® Pain Rating Scale

In this study, tooth sensitivity will be assessed before the first bleaching session, immediately after the bleaching section, 48 hours after the end of each bleaching section, one week after the end of the bleaching treatment and 4 weeks after the beginning of the bleaching treatment.

2.7 Statistical Analysis

Descriptive analyses will consist of calculations of mean and standard deviation. According to previous studies[12], pain sensitivity data can be subjected to multivariate analysis of variance (MANOVA) with repeated measures and Wilks' Lambda test ($p<0.05$). For shade variation analysis, a completely random analysis of variance will be applied ($p<0.05$).

3. DISCUSSION

The systematic review and meta-analysis conducted by Pontes et al. (2020) selected 14 studies for qualitative analysis and seven for quantitative analysis. A total of 649 patients were evaluated, with follow-up periods ranging from one week to 12 months. The study concluded that lower concentrations of hydrogen peroxide in tooth bleaching gels result in reduced tooth sensitivity and greater efficacy in objective color change, as measured by a spectrophotometer. However, no significant differences were observed between high and low concentrations regarding subjective color change, as measured by a shade guide [18].

Similarly, Maran et al. (2020) performed a systematic review and meta-analysis to address the following research question: "Do low-to-moderate concentrations of hydrogen peroxide used for in-office bleaching in patients with permanent dentition achieve similar color changes and bleaching sensitivity compared to high concentrations of hydrogen peroxide?" Their findings confirmed that low-concentration hydrogen peroxide products could achieve comparable color change efficacy while offering the advantage of reduced bleaching sensitivity in terms of both risk and intensity [15].

A randomized, split-mouth, double-blind clinical trial evaluated the efficacy of in-office bleaching using 6% hydrogen peroxide in adolescents, analyzing different application tips, tooth sensitivity, and aesthetic self-perception. Regardless of the application tip used, 6% hydrogen peroxide demonstrated effective bleaching outcomes and improved aesthetic self-perception. However, the use of a brush tip was associated with a reduced risk of tooth sensitivity [19].

Another split-mouth, double-blind, randomized clinical trial by Carneiro et al. (2024) assessed gingival irritation, color change, and the impact of oral health conditions on quality of life following in-office bleaching with 6% hydrogen peroxide, with and without a gingival barrier, in adolescents. The study concluded that using or not a gingival barrier yielded equivalent results for gingival irritation and bleaching efficacy. Furthermore, improvements were observed in the impact of oral health conditions on quality of life [20].

To date, no standardized bleaching protocols for primary teeth have been described in the literature. Low-concentration hydrogen peroxide bleaching agents exhibit excellent thixotropy, optional gingival barrier use, and an alkaline, stable pH. These properties suggest that such products could be a suitable choice for bleaching primary teeth.

4.**Conclusion**

The conclusion will be drawn after completing the study.

CONSENT AND ETHICAL APPROVAL

The study will be conducted in accordance with the ethical precepts determined in the Declaration of Helsinki (World Medical Association Declaration of Helsinki, 2008). The protocol for this study was approved by the Human Research Ethics Committee of UniversidadeMetropolitana de Santos - UNIMES (certificate number: 68431023.5.0000.5509/ 6.019.284 - Approval date: April 24, 2023). All information will be detailed and specified in the statement of informed consent, in accordance with Resolution 196 of the National Board of Health (Health Ministry, Federal District, Brazil, March 10, 1996). This is the first version of a protocol that was registered in ClinicalTrials.gov, under the registration number: NCT05789004, first posted on March 29, 2023, and last updated on October 31, 2024.

The legal guardians of the children will agree to participate by signing a statement of informed consent; two copies will be signed – one for the legal guardian of the child and one for the researchers. The participants will be informed that they may withdraw from the study at any time for any reason if they so desire. The researchers may also remove participants from the study, if deemed necessary.

Disclaimer (Artificial intelligence)

The authors hereby declare that NO generative AI technologies, such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators, were used during the writing or editing of this manuscript.

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