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Effectiveness of Bioactive Toothpastes against Dentin Hypersensitivity Using Evaporative and Tactile Analyses: A Randomized Clinical Trial

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Abstract: The objective of this study was to investigate and compare the effectiveness of toothpastes containing bioactives to relieve dentin hypersensitivity with that of a commercial desensitizing toothpaste containing REFIX technology, associated or not with a calcium booster. In this double-blind, randomized, parallel-group, multi-center clinical trial, thirty-two volunteers diagnosed with dentin hypersensitivity and qualified to participate were randomized into four groups: (1) Colgate Sensitive Pro-Relief; (2) Sensodyne Repair & Relief; (3) Regenerador Sensitive; and (4) Regenerador Sensitive, associated with a calcium booster. Evaporative and tactile tests were used to check for dentin hypersensitivity in the test subjects. The participants brushed their teeth with one of the toothpastes, and dentin hypersensitivity was immediately tested using a visual analogue scale (VAS), in which the pain was rated on a scale of 0 to 10. Dentin hypersensitivity was measured after one week and after one month of the subjects continuing to use the toothpaste three times per day. Data were statistically analyzed with a non-parametric Friedman test for dependent data ($\alpha = 0.05$). All toothpastes reduced dentin hypersensitivity. In the evaporative test, Sensodyne Protect & Repair and Regenerador Sensitive, associated with the calcium booster, exhibited faster and more effective results in reducing pain caused by dentin hypersensitivity, even after the first use. Colgate Sensitive Pro-Relief was effective only after one week of use. All toothpastes performed well in the tactile test for treating dentin hypersensitivity, and their performance improved over time. Sensodyne Repair & Protect presented the highest overall pain remission after one month (84.6%). The bioactive toothpastes reduced, to a different extent, the tooth hypersensitivity reported by the volunteers. Sensodyne Repair & Relief and Regenerador Sensitive, associated or not with a calcium booster, presented faster and more effective results in reducing pain caused by dentin hypersensitivity.

Keywords: clinical trial; dentin hypersensitivity; desensitizing; toothpaste

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1. Introduction

Dentin hypersensitivity is defined by an acute, short-lived, well-localized discomfort caused by exposed dentin, chemical, volatile, thermal, tactile, or osmotic stimuli and that cannot be attributed to another type of dental defect or pathology [1]. It is a problem that affects a large part of the world's population, causing pain and discomfort for patients [2]. Dentin hypersensitivity is more common in adults, is more common in people between

the ages of 20 and 40, and is more common at the end of the third decade of life, with an estimated prevalence of 11.5% in various populations, despite prevalence studies pointing to wide variation [3]. The typical pain of dentin hypersensitivity is acute and of short duration, persisting only during stimulus application [4]. The treatment is challenging, and studies generally use the keywords "control", "relief", or "improvement" regarding the clinical condition [5]. And in this sense, several therapies have been proposed, such as the application of agents to obliterate dentin tubules, the application of neural desensitizers such as potassium nitrate, and the use of high- and low-power lasers, in addition to more invasive alternatives, such as restorations and mucogingival surgery for root coverage, among other therapies [6].

In this context, toothpastes have also been used in the treatment of dentin hypersensitivity; as the oral hygiene products most used by the population, these may be the easiest and most comprehensive way to treat hypersensitivity [7]. Recently, a concept called biomimetic remineralization has drawn the attention of researchers as an alternative that mimics the natural process of dental mineralization [8]. This process is facilitated by the addition of different components in combination with fluoride application [9]. Products that perform this role are sources of calcium and phosphate, increasing the saturation of the oral environment in relation to hydroxyapatite [10]. Functionalized calcium phosphate, calcium glycerophosphate, and cyclophosphates have been used in association with fluoride as biomimetic remineralizing agents [11]. In this manner, these agents function as carriers of calcium and fluoride into the dental tissues, having a more effective mineralizing action, as they favor an increase in the size of hydroxyapatite crystals that become less soluble and porous [12]. Based on this concept, toothpastes for hypersensitivity can promote mineral deposition on dentinal tubules, providing an efficient and safe remineralizing strategy for the management of dentin hypersensitivity according to the precepts of minimally invasive dentistry.

Despite the extensive number of therapies, there is no standard treatment that is effective in all clinical situations [13]. Comparative investigations have shown that desensitizing toothpastes have varying effects on the inhibition of dentinal fluid mobility, which appears to reflect their efficiency in reducing dentin hypersensitivity [14]. In this manner, it becomes important to evaluate the effectiveness of toothpastes with different strategies for hypersensitivity treatment. The purpose of this clinical trial was to evaluate the effectiveness of different bioactive toothpastes in reducing dentin hypersensitivity reported by voluntary patients. The research hypothesis was that using this type of toothpaste will help to reduce/control the discomfort experienced by people with dentin hypersensitivity over time.

2. Materials and Methods

2.1. Experimental Design

This study was a double-blind, randomized, parallel-group, multi-center clinical trial to test the ability of toothpastes containing different bioactives to relieve the symptoms of dentin hypersensitivity. The primary outcome to be examined was the reduction in dentin hypersensitivity from baseline in response to evaporative and tactile tests for up to one month on a linear visual analog scale (VAS). The study was conducted at the School of Dentistry of the Universidade Anhanguera de São Paulo (UNIAN-SP, Brazil) and at the School of Dentistry of the Universidade Metropolitana de Santos (UNIMES, Santos-SP, Brazil). The factors under analysis were: I. Toothpaste, in 4 groups: (1) Colgate Sensitive Pro-Relief (n = 56); (2) Sensodyne Protect & Repair (n = 63); (3) Regenerador Sensitive (n = 53); (4) Regenerador Sensitive + calcium booster (n = 75); and II. Evaluation Time, in 4 groups: (1) baseline: before starting treatment; (2) immediately after the 1st brushing; (3) after 1 week of continuous use (3× a day); (4) after 1 month of continuous use (3× a day). As observed in several studies, the number of teeth presenting dentin hypersensitivity was highly distinguished among the selected patients, as were the baseline score and the response of each tooth to the treatment. Therefore, it was more appropriate to consider the

teeth as the experimental units instead of the number of patients, as in other studies [15–17]. So, teeth with dentin hypersensitivity served as the experimental units. The sample size was calculated using Sealed Envelope Ltd. (London, UK) [18], considering a significance level (alpha) of 5% and a power (1-beta) of 80%, and at least 48 teeth per group were included. Considering a possible dropout rate of 25%, a minimum of seven patients per group, with a minimum total of 48 teeth per group, were included in this study. This experimental design was based on previous studies, which also evaluated desensitizing products [19–21].

2.2. Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki (1964) and its later amendments and registered at Clinicaltrial.gov (RBR-36dr7t). Before enrolling in the study, all participants signed an informed written permission form after receiving accurate details about it. Before taking part in the study, each individual provided their informed consent for inclusion.

2.3. Patient Selection

This controlled clinical trial followed the CONSORT statement. For the present clinical study, 38 patients, both male and female, from private dental practices in Santos and São Paulo (Brazil) presenting dentin hypersensitivity were evaluated for eligibility (Figure 1). The inclusion criteria were subjects between 18 and 65 years old; in good health, with no history of allergies to dentifrice ingredients (essentially, preservatives and flavorings); classified, according to the American Society of Anesthesiology (ASA), in group I (healthy, without systemic alterations or making continuous use of medication); subjects with at least one tooth with an exposed root surface due to abrasion, abfraction, erosion, or gingival recession, which provoked a painful reaction to an air blasting stimulus, with a minimum baseline score of 2 [22]. Figure 1 displays a CONSORT diagram of the participant flow for this clinical trial.

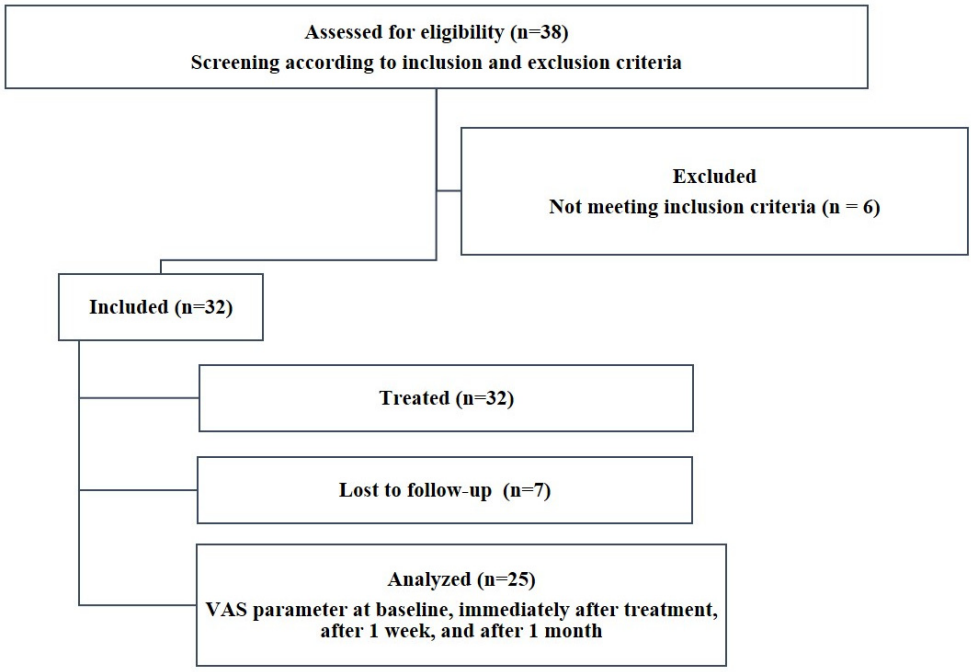

Figure 1. Trial flow diagram. Patients were selected according to the inclusion and exclusion criteria. Subjects claiming dentin hypersensitivity were recruited for the clinical trial.

Patients with physiological changes who were not classified as ASA I (pregnant women, patients with chronic diseases, or patients with infectious foci in the oral cavity);

patients with orthodontic appliances, moderate or advanced active periodontal disease, or soft or hard oral tissue tumors; and pregnant women were excluded from this clinical study. Patients who used analgesics or other medications that could potentially mask pain sensation (such as antihistamines, sedatives, anticonvulsants, antidepressants, anti-inflammatory drugs, tranquilizers, or daily analgesics) were also excluded, as were those who routinely used desensitizing toothpaste or any other desensitizing agent. Subjects who reported hypersensitivity in teeth with enamel cracks or flaws, cavitated caries, fractures, mobility, extensive or poor restorations, prosthetic crowns or veneers, or pulp involvement were also excluded from the study. Six of the thirty-eight patients initially chosen were excluded due to severe active periodontal disease, and one was excluded due to age (18 years old); thirty-two subjects were eventually included in the study (Figure 1). The distribution of patients and teeth per group can be observed in Table 1.

Table 1. Distribution of treated and lost patients (teeth) per group.

Treatment	UNIMES	UNIAN	Total	Dropouts
Colgate Sensitive Pro-Relief	5 (49)	1 (7)		3
Sensodyne Repair & Protect	3 (47)	2 (16)	5 (63) B	3
Regenerador Sensitive	4 (44)	2 (9)	6 (53) A	1
Regenerador Sensitive + Calcium Booster	4 (60)	4 (15)	8 (75) B	0

UNIAN-SP: Universidade Anhanguera de São Paulo; UNIMES: Universidade Metropolitana de Santos. Different capital letters for columns: significant, 5%.

2.4. Clinical Procedures

The selected patients were given information on the etiology of dentin hypersensitivity (identifying predisposing factors, such as acid diet, excessive tooth brushing, occlusal trauma, and gingival recession) as well as all oral hygiene instructions to reduce gingiva trauma and increase plaque control efficiency, as well as dietary advice for dental erosion control and caries prevention. After that, the participants were told to clean their teeth three times a day with one of the toothpastes listed in Table 2 (random selection by draw). Each patient received an extra-soft toothbrush, a random toothpaste, and instructions on how to use them. The patients were told to only use the designated toothpaste and toothbrush and to stop using any other oral care products. The subjects were advised to clean their teeth for at least 90 s three times per day (morning, afternoon, and nighttime).

Table 2. Composition of the toothpastes selected for the study according to the manufacturers *.

Dental Gel	Composition
Colgate Sensitive Pro-Relief [a]	Arginine 8%, Calcium Carbonate, Sodium, Monofluorophosphate 1.1% (1450 ppm fluoride), Water, Sorbitol, Sodium Lauryl Sulfate, Aroma, Cellulose, Gum, Potassium Acesulfame, Sodium Silicate, Xanthan Gum, Sucralose, Titanium Dioxide
Sensodyne Repair & Protect [b]	1426 ppm sodium fluoride, Calcium Sodium Phosphosilicate 5% (NOVAMIN) Glycerin, PEG-8, hydrated silica, pentasodium triphosphate, sodium lauryl sulfate, flavor, titanium dioxide, polyacrylic acid, cocamidopropyl betaine, sodium saccharin
Regenerador Sentitive [c]	1450 ppm sodium fluoride, glycerin, silica, sorbitol, sodium lauryl sulfate, aqua, aroma, PEF-12, cellulose gum, phosphoric acid, xylitol, tetrasodium pyrophosphate, sodium saccharin, triclosan, menthol, mica, sodium benzoate, REFIX Technology
Calcium Booster [c]	5% calcium mix (calcium carbonate, tricalcium phosphate), silica, glycerin, CPC, saccharine, water)

* Manufacturers: [a] Colgate-Palmolive Manufacturing, São Bernardo do Campo, SP, Brazil; [b] GlaxoSmithKline, Philadelphia, PA, USA; [c] DentalClean, Londrina, PR, Brazil.

In the evaporative analysis, a 1 s burst of air from a triple 3-way syringe handpiece was administered to the exposed dentin surface at a distance of around 0.5 cm to assess discomfort. The participants were instructed to indicate the intensity of their discomfort on a 100 mm VAS scale ranging from no pain (score 0) to the greatest pain imaginable (score 10) [21,23]. The VAS pain scores were measured at baseline (before treatment),

immediately following the application of the desensitizing toothpaste, one week later, and one month later. The rate of pain severity following air blasting was observed immediately after the air stimulus.

For the tactile test, a conventional, sharp dental probe was passed lightly mesio-distally across the affected area, perpendicular to the long axis of the tooth over exposed dentin [24]. The test was repeated three times before the score was recorded. In both tests, participants reporting no or little pain relief after the 1-week treatment received an application of a high-fluoride-concentration varnish to the exposed area, and toothpastes were provided for continued use.

2.5. Statistical Analysis

The non-parametric Friedman test for dependent data with a significance level of 5% was selected to evaluate the effect of each dentifrice over time due to the nature of the data of the response variable (pain score). This test was selected for comparative evaluation of the decrease rate (%) of toothpaste pain after each evaluation period (after the first brushing, after 1 week, and after 1 month). This test was selected due to the lack of a normal data distribution.

3. Results

The average age of the patients was 35 years, and 68.75% of the 32 participants were female. In this clinical trial, there were seven dropouts (21.8%). Table 3 shows the mean pain levels based on the evaporative test evaluation periods.

Table 3. Means (standard deviations) of pain scores recorded in each assessment period of evaporative analysis according to the dental gel tested.

Dental Gel	Initial	First Brushing	1 Week	1 Month
Colgate Sensitive Pro-Relief	4.3 (2.9) B	3.8 (3.2) B	2.7 (2.7) A	2.1 (2.4) A
Sensodyne Repair & Protect	5.6 (3.0) C	3.2 (2.5) B	2.9 (2.2) B	1.3 (1.9) A
Regenerador Sensitive	5.9 (1.9) C	4.0 (2.9) B	2.6 (2.0) A	2.1 (2.4) A
Regenerador Sensitive + Calcium Booster	5.3 (2.3) D	3.9 (2.7) C	2.4 (2.1) B	1.0 (2.1) A

Different capital letters for rows: significant, 5%.

According to these results, it can be observed that all toothpastes were effective in controlling pain resulting from tooth hypersensitivity, since all demonstrated a significant reduction in pain scores after treatment ($p < 0.05$). Regenerador Sensitive caused a significant reduction in pain scores immediately after the first toothbrushing, followed by an even greater reduction after 1 week ($p < 0.05$), which was maintained after 1 month. When the calcium booster was associated with the Regenerador Sensitive, there was significant pain remission immediately after the first use; however, in this case, the reduction was progressive and significant over the evaluation periods ($p < 0.05$). For Sensodyne Repair & Protect, a significant reduction in pain scores was also observed after the first brushing, which was maintained after 1 week, and an even greater reduction after 1 month of continuous use ($p < 0.05$). For Colgate Sensitive Pro-Relief, a significant reduction occurred only after 1 week of use, remaining after 1 month. Table 4 displays the pain reduction rates according to the evaluation times with a comparative analysis of the toothpastes for the evaporative test.

Table 4. Means (standard deviations) of pain decrease rates (%) after different treatment times using evaporative analysis according to the dental gel tested.

Dental Gel	After First Brushing	After 1 Week	After 1 Month
Colgate Sensitive Pro-Relief	15.5% (47.1) b	43.4% (47.0) a	36.7% (72.9) c
Sensodyne Repair & Protect	30.2% (77.7) a	33.5% (68.6) a	79.2% (33.7) ab
Regenerador Sensitive	27.4% (64.3) ab	51.0% (41.1) a	61.2% (53.1) bc
Regenerador Sensitive + Calcium Booster	30.3% (36.5) ab	47.7% (55.2) a	78.9% (57.6) a

Different lowercase letters for columns: significant, 5%.

It was demonstrated that, after the first brushing, the sensitivity reduction rate was around 30% for Regenerador Sensitive associated with a calcium booster and Sensodyne Repair & Protect; this rate of reduction was significantly higher than that provided by Colgate Sensitive Pro-Relief (15%). After 1 week, the rate of sensitivity reduction varied between 33 and 51%, and no significant differences among the toothpastes were observed. The rate of sensitivity reduction after 1 month was considerably higher for Regenerador Sensitive associated with the calcium booster and Sensodyne Repair & Protect compared to that of Colgate Sensitive Pro-Relief, which presented the worst results in terms of pain relief. Regenerador Sensitive presented intermediate results, not differing from either Sensodyne Repair & Protect nor Colgate Sensitive Pro-Relief. Additionally, it was observed that the calcium booster had a substantially positive effect on reducing sensitivity, as there was a considerable difference when comparing the association or not with Regenerador Sensitive.

Figure 2 displays the distribution of teeth according to pain relief in the evaporative test. It was observed that, immediately after the application of Regenerador Sensitive, 24.5% of the teeth obtained complete remission of sensitivity (score 0), and after 1 month of use, 37.7%.

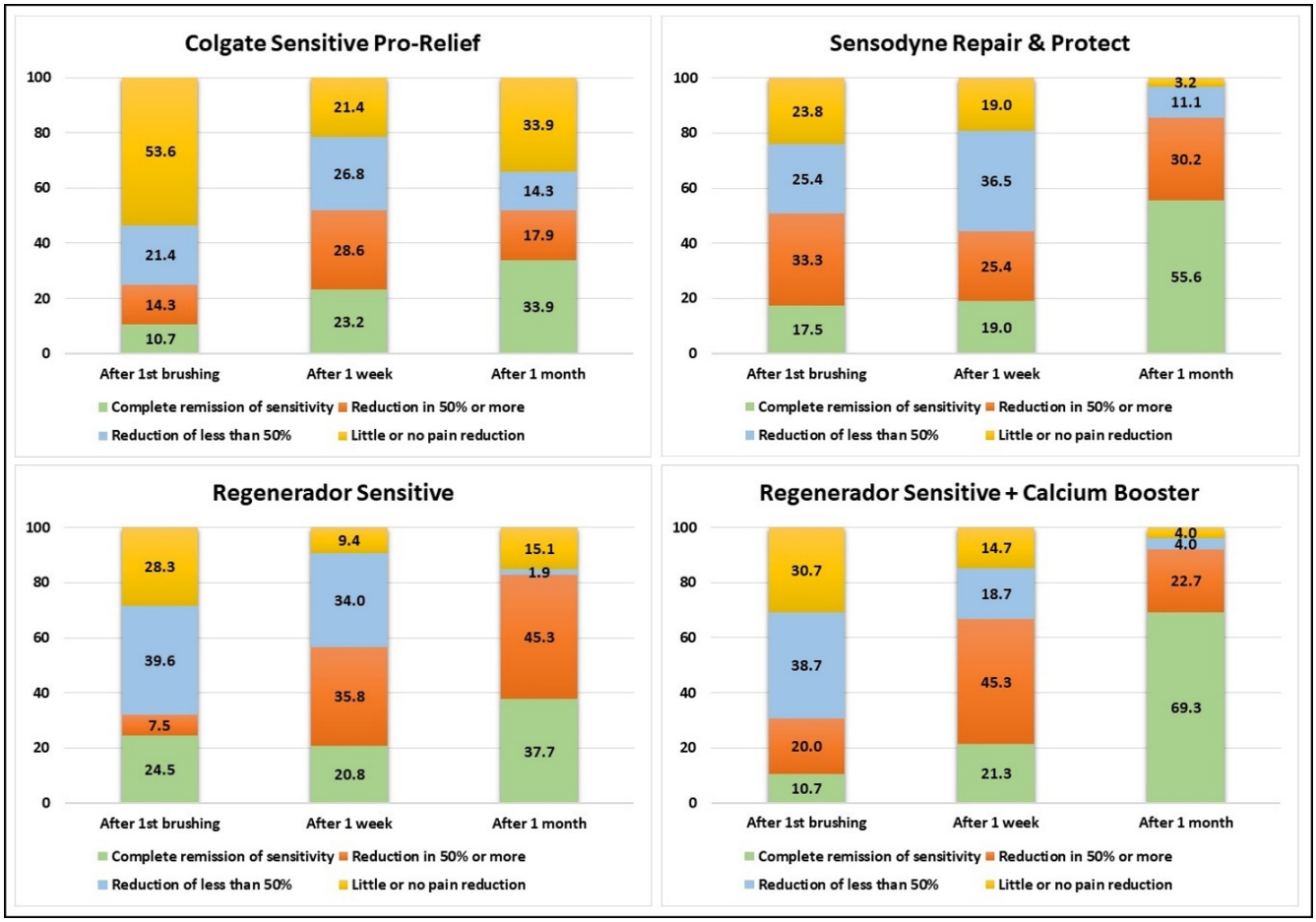

Figure 2. Distribution of teeth according to pain relief in the evaporative test after treatment with dental gels.

Additionally, 45.3% of teeth experienced a higher decrease in sensitivity levels (more than 50%), and only 15.1% experienced no pain relief. The overall rate of decrease in pain after Regenerador Sensitive treatment was 61.2% (Table 4). The association of Regenerador Sensitive with a calcium booster exhibited high effectiveness in pain remission after 1 month of treatment, with 69.3% of the teeth achieving complete remission of sensitivity (score 0), 22.7% having a large decrease in sensitivity levels (more than 50%), 4.0% experiencing a

small decrease in sensitivity levels (less than 50%), and 4.0% experiencing no pain relief. The overall rate of decrease in pain after the treatment with Regenerador Sensitive associated with the calcium booster was 78.9% (Table 4). The treatment with Sensodyne Repair & Protect also demonstrated an effective pain remission after 1 month of treatment, so that 55.6% of the teeth had complete reduction in sensitivity (score 0), 30.2% had a large decrease in sensitivity levels (more than 50%), and only 3.2% obtained no pain relief, and, in this period, the overall rate of pain decrease was 79.2% (Table 4). The treatment with Colgate Sensitive Pro-Relief promoted total pain remission for only 33.9% of the teeth after 1 month of use, with 33.9% having no pain relief. In this context, with an overall pain reduction rate of around 36.7% (Table 4), this was the dentifrice that presented the worst results in controlling pain from dentin hypersensitivity. Thus, all the toothpastes tested were effective in the treatment of dentin hypersensitivity. Regenerador Sensitive, associated or not with a calcium booster, and Sensodyne Protect and Repair led to faster and more effective results in reducing pain. These toothpastes were effective in reducing sensitivity immediately after the first use, whereas the effectiveness of Colgate Sensitive Pro-Relief was observed only after 1 week. Additionally, the association of a calcium booster with Regenerador Sensitive was significantly more effective after 1 month, which seems to be the best indication for the treatment of tooth hypersensitivity.

Table 5 shows the mean pain levels based on the tactile test evaluation periods.

Table 5. Means (standard deviations) of pain scores recorded in each assessment period of tactile analysis according to the dental gel tested.

Dental Gel	Initial	First Brushing	1 Week	1 Month
Colgate Sensitive Pro-Relief	4.5 (2.6) C	2.9 (2.6) B	1.4 (2.1) A	0.9 (1.3) A
Sensodyne Repair & Protect	3.8 (2.2) B	1.3 (2.2) A	0.7 (1.9) A	0.4 (1.0) A
Regenerador Sensitive	6.1 (2.3) B	1.9 (2.4) A	1.4 (2.3) A	0.9 (1.6) A
Regenerador Sensitive + Calcium Booster	4.0 (2.9) B	1.3 (1.3) A	0.8 (1.6) A	0.6 (1.0) A

Different capital letters for rows: significant, 5%.

According to the analysis, a significant reduction in tooth hypersensitivity after the first brushing was observed in the teeth treated with the toothpastes Sensodyne Repair & Protect, Regenerador Sensitive, and Regenerador Sensitive associated with a calcium booster compared to the mean scores observed before the treatment ($p < 0.05$). For the teeth treated with the toothpaste Colgate Sensitive Pro-Relief, a significant reduction in tooth hypersensitivity occurred only after one week of use ($p < 0.05$). No significance was seen among the experimental groups after a week of use ($p > 0.05$).

Table 6 displays the pain reduction rates according to the evaluation times with a comparative analysis of the toothpastes for the evaporative test.

Table 6. Means (standard deviations) of pain decrease rates (%) after different treatment times using tactile analysis according to the toothpaste tested.

Dental Gel	After First Brushing	After 1 Week	After 1 Month
Colgate Sensitive Pro-Relief	33.5% (53.2) a	72.3% (43.4) a	74.2% (43.5) a
Sensodyne Repair & Protect	64.9% (57.2) b	82.9% (46.5) a	87.4% (32.7) a
Regenerador Sensitive	66.7% (38.3) ab	73.1% (39.1) a	85.6% (52.0) a
Regenerador Sensitive + Calcium Booster	58.0% (59.5) ab	87.2% (28.4) a	83.1% (30.4) a

Different lowercase letters for columns: significant, 5%.

It was demonstrated that the toothpaste Regenerador Sensitive, associated or not with the calcium booster, and Sensodyne Repair & Protect exhibited a significantly higher percentage of reduction in tooth hypersensitivity compared to that of Colgate Sensitive Pro-Relief ($p < 0.05$). After one week of use, no significant difference was observed comparing all the experimental groups. The higher percentage of reduction after one week of use compared to the initial use was observed for Regenerador Sensitive associated with the calcium booster, which demonstrated an increase of 58.0% to 87.2% in pain reduction. In

the same way, no significance was observed in terms of percent of pain reduction after one month of use when the results of the experimental groups were compared ($p > 0.05$).

Figure 3 displays the distribution of teeth according to pain relief in the tactile test. It can be observed that, immediately after the application of Regenerador Sensitive, the tactile analysis indicated that 39.3% of the teeth obtained complete remission of sensitivity (score 0), and after 1 month of use, 78.6%. Additionally, 35.7% experienced a higher decrease in sensitivity levels (more than 50%), and only 10.7% experienced no pain relief. The overall rate of decrease in pain after Regenerador Sensitive treatment was 85.6% (Table 5). The association of Regenerador Sensitive with a calcium booster exhibited high effectiveness in pain remission after 1 month of treatment, with 83.1% of the teeth achieving complete remission of sensitivity (score 0), 20.6% having a large decrease in sensitivity levels (more than 50%), 11.0% experiencing a small decrease in sensitivity levels (less than 50%), and none of the subjects experiencing no pain relief.

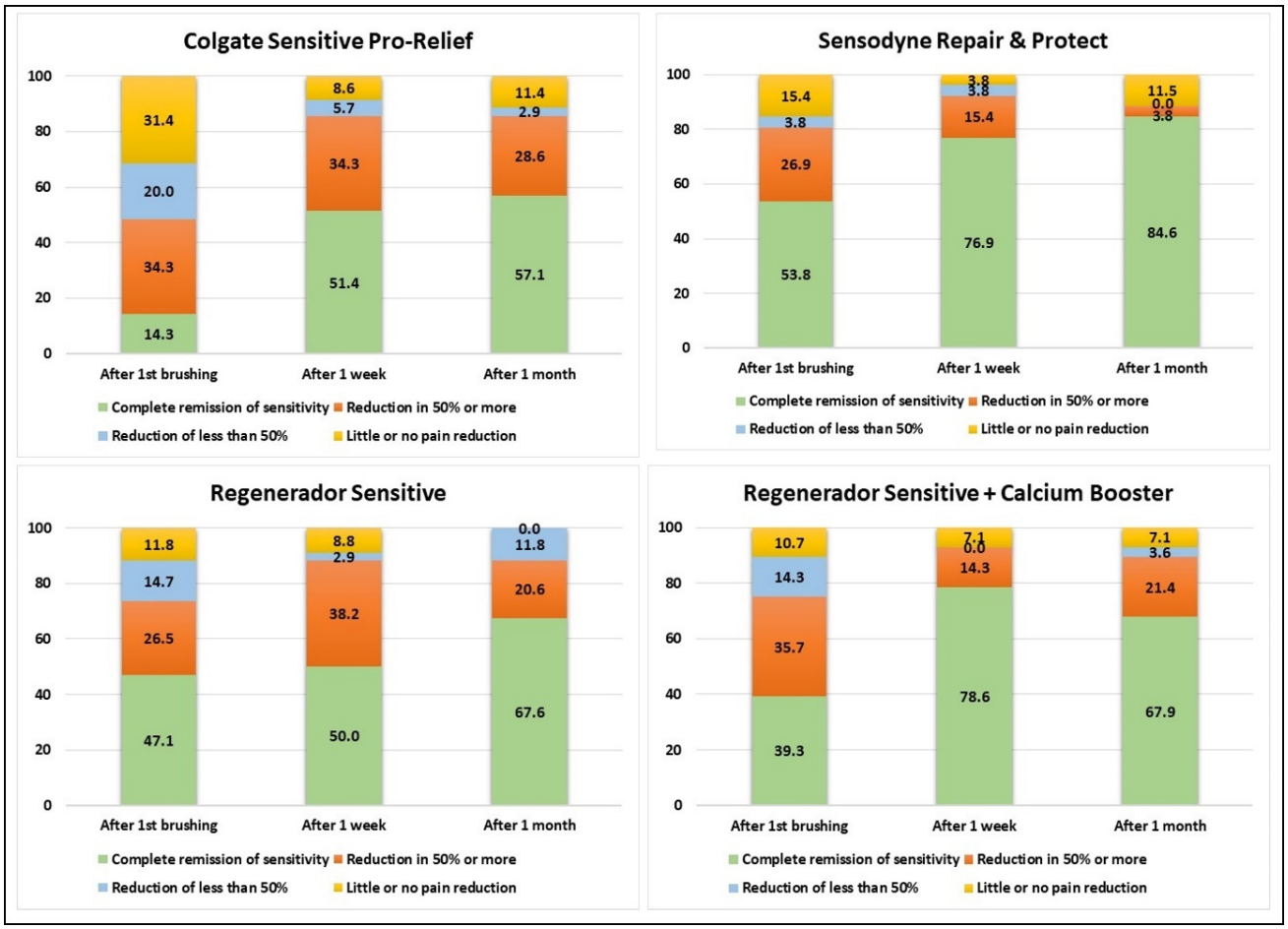

Figure 3. Distribution of teeth according to pain relief in the tactile test after treatment with the dental gels.

The overall rate of decrease in pain after the treatment with Regenerador Sensitive + calcium booster was 67.9% (Table 6). The treatment with Sensodyne Repair & Protect demonstrated the highest percentage of pain remission after 1 month of treatment (84.6% with score 0) and only 3.0% with no pain relief. The overall rate of pain decrease was 87.4% (Table 6). The treatment with Colgate Sensitive Pro-Relief promoted total pain remission for 57.1% of the teeth after 1 month of use, with 11.4% with no pain relief. The overall rate of decrease in pain after the treatment with Regenerador Sensitive + calcium booster was 67.9% (Table 6). The treatment with Sensodyne Repair & Protect demonstrated the highest percentage of pain remission after 1 month of treatment (84.6% with score 0) and only 3.0% with no pain relief. The overall rate of pain decrease was 87.4% (Table 6). The treatment

with Colgate Sensitive Pro-Relief promoted total pain remission for 57.1% of the teeth after 1 month of use, with 11.4% experiencing no pain relief. The overall pain reduction rate was 74.2% (Table 6), with no statistical significance when compared to other toothpastes. In this manner, all the toothpastes tested were effective in the treatment of dentin hypersensitivity when analyzed with the tactile test. In this analysis, it seems that the toothpastes Colgate Sensitive Pro-Relief, Sensodyne Repair & Protect, and Regenerador Sensitive presented an increasing effectiveness with time; the effectiveness of Sensodyne Repair & Protect was at a higher extent, with the highest overall pain remission after one month (84.6%). Additionally, the association of a calcium booster with Regenerador Sensitive was also effective after 1 month, but its effectiveness in terms of pain remission was reduced when comparing the evaluation times after one week and one month. Conversely, when Regenerador Sensitive was used alone, it was the only toothpaste which demonstrated a complete pain remission in all of the teeth tested.

4. Discussion

All the toothpastes were successful in treating dentin hypersensitivity. The research hypothesis was accepted because it predicted that, over time, the use of the toothpastes would lessen the pain experienced by patients with dentin hypersensitivity. Colgate Sensitive Pro-Relief desensitizing toothpaste, developed with the technology ProArgin, was based on the role that saliva plays in the natural reduction in dentin hypersensitivity. Its essential ingredients are calcium carbonate and 8% arginine. Together, the main claim of this product is the promise of "immediate and lasting action against dentin hypersensitivity". However, according to this study, the pain relief was not immediate, and a significant reduction in pain was observed only after 1 week.

According to a previous study, the combination of 8% arginine and calcium carbonate was developed based on the blocking action of a protective glycoprotein composed of calcium and phosphate transported by saliva, a process favored under alkaline pH conditions [25]. The alkalinity of arginine and calcium carbonate allows greater absorption of calcium and phosphate ions present in saliva, which are then deposited on the dentin surface, forming plugs that contain arginine, calcium, phosphate, and carbonate [26]. Calcium carbonate is one of the abrasive components most frequently found in toothpastes, with the potential to obliterate tubules by its abrasives or, indirectly, by the formation of a smear layer during brushing [26]. Thus, it has been identified as an ingredient with a beneficial capacity for oral health. That said, studies found in the literature reported that a combination of arginine bicarbonate and calcium carbonate is capable of creating a layer rich in calcium on the dentin surface, sealing the dentinal tubules, and physically blocking the sensitivity mechanism. In addition to these ingredients, other components can also be found in the composition, such as hydrated silica, glycerin, water, bicarbonate, cellulose gum, and sodium saccharin. In a previous clinical trial, the authors concluded that 8% arginine and calcium carbonate were able to successfully reduce tooth hypersensitivity during an 8-week trial [22]. However, in another study, greater effectiveness of commercial products containing arginine was observed for the treatment of dentin hypersensitivity only in response to stimuli with air jets [27]. Conversely, it was observed that arginine was effective in minimizing dentin hypersensitivity after tactile and cold stimuli, showing beneficial effects when compared to fluoride, but without complete evidence it was not possible to conclude that arginine had effectively significant results [28]. Concerns have been expressed over the effectiveness of arginine considering the inconsistency when the results of direct and indirect evaluation are compared, thus not demonstrating definitive scientific evidence in the different studies analyzed in meta-analysis [28]. Based on the results of the present study evaluating the effectiveness of Colgate Sensitive Pro-Relief, it promoted a significant pain reduction only after 1 week of use (43.4%), which remained at a lower extent after 1 month (36.7%), according to the results of the evaporative test.

Indicated for the control of dentin hypersensitivity, the toothpaste Sensodyne Repair & Protect is reported to form a protective layer on the sensitive areas of exposed dentin

areas by means of NovaMin technology. It comprises an amorphous inorganic material classified as particulate bioactive glass with an average particle size of less than 20 µm [29]. Sensodyne Repair & Protect also contains two bioactive components, sodium and calcium phosphosilicates, that, when in contact with the tooth surface, initiate the enamel remineralization process based on ionic exchange. It has been reported that NovaMin binds to the collagen fibers in the exposed dentin, acting as a reservoir of minerals such as phosphate and calcium and forming a robust and repairing layer similar to hydroxyapatite on the exposed dentinal tubules. In summary, the instantaneous contact of the components in an aqueous medium with saliva promotes the release of calcium and phosphate, forming an insoluble remineralizing hydroxyapatite carbonate on the enamel surface [30]. NovaMin is thus a highly water-reactive phosphosilicate consisting of fine powder particles that can physically obstruct dentinal tubules, demonstrating broad clinical efficiency in the enamel remineralization process [31]. In a six-week clinical study, the effectiveness of a NovaMin-containing technology was compared to the action of two other dentifrices (one commercial and the other placebo) [32]. After the evaluation period, it was observed that, after stimulation with a blast of air, 58% of subjects treated with NovaMin reported improvement in sensitivity, while 26% of the group treated with a commercial product and 20% of the placebo group did so. The results obtained demonstrate that the toothpaste containing NovaMin technology was more effective in reducing sensitivity compared to a commercial dentifrice and a placebo control.

According to the results of the present study, it was possible to verify in the evaporative test that Sensodyne Repair & Protect promoted an effective pain remission after 1 month of treatment, so that 55.6% of the teeth had complete remission of sensitivity (score 0), 30.2% had a large decrease in sensitivity levels (more than 50%), and only 3.2% obtained no pain relief, and, in this period, the overall rate of pain decrease was 79.2% (Table 4). In the tactile test, Sensodyne Repair & Protect demonstrated the highest percentage of pain remission after 1 month of treatment (84.6% with a score of 0) and only 3.0% with no pain relief. The overall rate of pain decrease was 87.4% (Table 6), the highest percentage compared to the other treatments.

The treatment of tooth hypersensitivity with the toothpaste Regenerador Sensitive led to an immediate remission of sensitivity in 24.5% of the teeth after the application (score 0), and after 1 month of use, 37.7% (Figure 2). Additionally, 45.3% experienced a higher decrease in sensitivity levels (more than 50%), and only 15.1% experienced no pain relief (Figure 2). The rate of decrease in pain treatment was the highest after one week of treatment with Regenerador Sensitive (51.0%), which increased to an overall rate of 61.2% after one month (Table 4). Regenerador Sensitive was developed based on the REFIX technology, reported to be a "fluoride phosphate complex that, in combination with calcium from saliva and dental structures, allows the formation of new minerals; this interaction can lead to pain relief caused by dentin sensitivity" (manufacturer's information). It comprises a so-called acidified bioactive complex, which comprises salts, organic compounds, and ingredients with an association with silicon and phosphates [8,33–35]. According to the manufacturer, this relationship promotes the creation of fluoridated apatite and the formation of a silicate layer, which is also formed deeper in the enamel tissues and open dentin tubules. This alleged ionic alteration promotes a decrease in hydroxyapatite solubility, a decrease in dentin fluid flow, and an improvement in dentin mechanical characteristics. As a result, this mechanism protects against the consequences of dentin hypersensitivity [21]. In a previous in vitro study [33], it was demonstrated in a morphological analysis that a mineral layer formed on the treated enamel surface; the layer had a consistent uniform thickness of ~14 µm. These results were corroborated in another study, which also demonstrated the formation of a silicon-enriched mineral layer on the enamel and dentin surfaces. In the latter, the dentinal tubules were progressively occluded until a complete tubule occlusion occurred after 7 days [8]. These results were also corroborated in a previous clinical study, which demonstrated an immediate effect after the first use, where the pain reported by the subjects reduced to mild pain according to a visual analogue scale (VAS). After

one week of consistent use, the pain score was significantly reduced, with most participants reporting no pain, proving the effectiveness of REFIX-containing toothpaste against dentin hypersensitivity [21]. Although some of the toothpastes were previously evaluated in previously published studies, this was the first time that the effectiveness of the toothpaste Regenerador Sensitive, associated or not with the calcium booster, was clinically tested in comparison with commercial products with the same indication.

Considering the association of Regenerador Sensitive with a calcium booster, it was observed that 10.7% of the teeth had complete pain remission immediately after the first application (score 0), whereas 20.0% of the teeth had more than 50% pain and 30.7% had no pain relief immediately after the first application. The overall rate of pain decrease was 30.3%, according to Table 4. Conversely, after 1 month of continuous use, 69.3% of the teeth achieved complete remission of sensitivity (score 0), 22.7% had a large decrease in sensitivity levels (more than 50%), 4.0% had a small decrease in sensitivity levels (less than 50%), and only 4.0% of the teeth had no pain relief in the evaporative test. In the tactile test, the association of a calcium booster with Regenerador Sensitive was also effective after 1 month, but its effectiveness in terms of pain remission was reduced when the means after one week and one month were compared (78.6% and 67.9%, respectively). In the evaporative test, both groups achieved a similar percentage of pain remission after one week (around 21%), but after one month, this toothpaste achieved the highest percentage of pain remission (69.3%) compared to the treatments with other toothpastes. When comparing the treatment with Regenerador Sensitive alone with that associated with the calcium booster, both achieved similar results in the tactile test after one month (around 68%). In spite of this similarity, the association of the calcium booster allowed a higher percentage of pain remission after one week (78.6%) when compared to Regenerador Sensitive alone (50%).

The calcium supplement is characterized by increasing the availability of calcium in the oral environment and accelerating the enamel remineralization process mineral formation. That said, it was possible to assess, after the different treatment times, that the association of the calcium booster with the REFIX technology had an immediate positive effect on the sensitivity reduction rate, calculated at 30.3%, and maintained the progression after one month of continuous use, reaching 78.9%. The results were even more significant in relation to the number of sensitive teeth treated with "pain elimination" after one month of use (69.3%), and only 4% of teeth achieved "no pain reduction", as shown in Table 5. In a previous study [36], it was observed that a considerable mineral change occurred following 5 days of treatment with a booster/silicon-rich toothpaste, forming a protective silicon-enriched mineral layer on both enamel and dentin surfaces. In vitro studies have shown that a fluoride-silicon-rich toothpaste combined with a calcium booster regenerates dental tissues by remineralizing the enamel structure and occluding dentin tubules [36].

In a previous study [37], it was stated that calcium silicate can transform and provide significant protection to sound enamel against acid attacks. Although fluoride treatments are known to be effective in preventing enamel demineralization and enhancing remineralization, researchers have continued to work to increase their efficacy, particularly by incorporating calcium salts or substances containing calcium in oral care products that may increase the distribution and retention of fluoride in the oral cavity, increasing their efficacy [38]. Furthermore, calcium salts or compounds can act as an additional source of calcium to promote enamel remineralization or reduce demineralization processes. Inspired by the concept of bioactive materials for repair and regeneration of mineralized tissue, such as bioglass, and, in particular, calcium silicate-type materials, they have potential for benefits to enamel health and are a growing research area [38].

Given the limitations of the present clinical research, the lack of a negative control for comparative purposes appears to have influenced the interpretation of the results. A negative control was not added for ethical reasons. Furthermore, experimental designs for assessing desensitizing drugs in an open, single-group clinical treatment trial have already been documented [19,20]. Other limitations include the subjectivity of VASs for recognizing pain and the patients' knowledge as clinical study participants. The responses

of the participants had no influence on compliance bias because they had no personal relationship with the investigator and no incentives were presented to the participants. On the other hand, an examination of the rapid relief of pain caused by exposed dentin in response to various stimuli following the administration of this pain-relieving product is recommended. This could be credited to a score of 2 to validate a treatment's efficacy. This can introduce bias into results because the chances of entirely stopping the pain after a single application of a toothpaste are greater.

5. Conclusions

All the toothpastes tested were successful in treating dentin hypersensitivity. In the evaporative test, the calcium-booster-associated Sensodyne Protect and Repair and Regenerador Sensitive showed faster and more effective effects in alleviating pain brought on by dentin hypersensitivity. Sensodyne Repair & Protect and Regenerador Sensitive toothpastes, associated or not with a calcium booster, were effective in lowering sensitivity as soon as they were used; however, Colgate Sensitive Pro-Relief's benefit was not shown until one week after use. The results of the evaporative test demonstrated that the association of the calcium booster with the toothpaste Regenerador Sensitive significantly reduced the pain sensitivity after one month (69.3%). In the tactile test, all the toothpastes tested were similarly effective. Colgate Sensitive Pro-Relief, Sensodyne Repair & Protect, and Regenerador Sensitive presented increasing effectiveness with time. The effectiveness of Sensodyne Repair & Protect was higher, with the highest overall pain remission after one month (84.6%).

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are contained within the article.

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Conflicts of Interest: Fabiano Vieira Vilhena has a classified patent pending and was employed by the company Trials, Research and Development. Paulo Henrique Perlatti D'Alpino was employed by the company Triplet Biotechnology Solutions. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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