

Original Research Article

ONE-YEAR CLINICAL EVALUATION OF FOUR DESENSITIZING AGENTS IN THE MANAGEMENT OF CERVICAL DENTIN HYPERSENSITIVITY: A RANDOMIZED, PROSPECTIVE, BLINDED CLINICAL TRIAL

Abstract

Objective: The objective of this randomized, prospective, and blinded clinical study was to evaluate the efficacy of four desensitizing agents in the long-term treatment of cervical dentin hypersensitivity (HD) and their impact on the quality of life of the research volunteers. **Materials and Methods:** A total of 116 teeth were randomized and divided into 4 groups (n=29 teeth) according to the applied treatment: GD - Gluma Desensitizer; CV - Clinpro White Varnish; SB - Single Bond; AS - AdheSE. Sensitivity levels were assessed using the Visual Analog Scale (VAS) immediately after the application of each material, and at 7, 30, 60, and 360 days post-treatment. The patients completed a quality of life questionnaire. Data were analyzed using Kruskal Wallis test with the Dwass-Steel-Critchlow-Fligner post-test were used for intergroup evaluation ($p < 0.05$). **Results:** In the intragroup comparison, there was a statistically significant decrease ($p < 0.05$) in sensitivity from the initial period for the GD, CV, and AS groups. There was an improvement in the patients' quality of life. **Conclusion:** This clinical study demonstrated the effectiveness of the desensitizing agents in the long-term treatment of cervical dentin hypersensitivity, with the exception of SB. **Clinical relevance:** HD is a clinical condition that directly affects patients' quality of life. This study revealed three effective desensitizing agents for a prolonged period.

Key-words: Dentin Desensitizing Agents; Dentin Sensitivity; Dental Cavity Lining; Dentin-Bonding Agents

1. Introduction

Dentin hypersensitivity is characterized by an exaggerated response to stimuli applied to exposed dentin, particularly in the cervical facial region. The terms dentin sensitivity (DS) and dentin hypersensitivity (DH) are used interchangeably to describe this clinical condition [1,2]. Dentin can become exposed as a result of periodontal treatment, gingival recession, or enamel loss (abrasion, attrition, erosion), or a combination of these factors [3]. The condition predominantly affects women aged 40-50, with a higher prevalence in males. Premolar teeth are most commonly affected by hypersensitivity. A significant proportion of patients (10-25%) experience discomfort that significantly interferes with eating, drinking, oral hygiene, and sometimes even breathing. These symptoms have a substantial impact on patients' daily quality of life [4].

The Brännström Hydrodynamic Theory from the 1960s is the most widely accepted theory for explaining the mechanism of hydrodynamic (HD) pain. According to this theory, the exaggerated response of the pulp is caused by the movement of intratubular fluids [2,5,6]. Additionally, there is the Neural Theory, which suggests that nerve endings within the dentinal tubules directly respond to external stimuli. Another theory is the odontoblastic transducer theory, which proposes that odontoblasts can act as pain transducers [7].

For correct treatment, it is essential to know the risk factors and the etiology of DH [8]. Many therapies and material alternatives with different mechanisms of action have been proposed, either for home or office application [9,10]. Some studies report that self-etching adhesive systems decrease the DH for reducing tubular permeability due to producing a hybrid layer acid resistant, resulting in more lasting clinical efficacy [11]. Single-step Self-etching adhesive systems and dentin desensitizing agents may significantly decrease HD immediately and after 30 days of treatment [12,13]. However, there is a lack of studies for a follow-up period longer than 30 days.

One widely used product for treating dentin hypersensitivity is the varnishes containing sodium fluoride, which is responsible for the precipitation of insoluble calcium fluoride within dentinal tubules [14]. Clinpro White Varnish, in addition to 5% sodium fluoride, has modified tricalcium phosphate (TCP). According to the manufacturer, this product, in contact with saliva, releases calcium ions and fluorine, optimizing the formation of calcium fluoride. Despite the inherent ion exchange with the dental substrate, there is still no consensus in the literature regarding the clinical relevance of this material [15].

Another desensitizing product used in the treatment of DH is Gluma Desensitizer, composed of glutaraldehyde and hydroxyl ethyl methacrylate (HEMA), among the commercially available desensitizing agents. Glutaraldehyde causes the coagulation of proteins and amino acids in the tubules and is also an effective disinfecting agent. HEMA can also effectively obstruct the dentinal tubules [16].

Despite the rapid reduction in HD, the duration of these desensitizing effects is still a critical factor, mainly because they do not have adequate adhesion to the dentin surface [13,17,18]. Therefore, the objective of this study was to evaluate, through a randomized clinical trial, the desensitizing efficacy among the Clinpro White Varnish, Gluma Desesititzer, and self-etching adhesive systems in a 1-year follow-up.

The utilization of different desensitizing agents, such as GD (Gluma Desensitizer), CV (Clinpro White Varnish), SB (Single Bond), and AS (AdheSE), in a randomized and blinded clinical study for the management of dentin hypersensitivity may result in significant differences in reducing dentinal sensitivity. It is expected that one or more of these agents will be more effective compared to the others, providing better treatment outcomes for the patients.

Materials and Methods

2.1 Ethics approval and protocol registration

The experimental design followed the Consolidated Standards of Reporting Trials (CONSORT) statement (Sarkis) and was registered in the Brazilian Clinical Trials Registry (REBEC - RBR-76cmjb). The study protocol was reviewed and accepted by the Local Ethics Committee on Investigations Involving Human Subjects (2.443.042). All patients who met the selection criteria were informed of the study's objectives, procedures, risks, and benefits and expressed consent to participate by signing the Terms of Free and Enlightened Consent.

2.2 Trial design, settings, and recruitment

This randomized, prospective, blinded, and parallel clinical trial was conducted between June 2018 and September 2019. This randomized clinical trial had dentin sensitivity as the outcome evaluated, and the variation factor was follow-up times. The participants were recruited through advertisements published in the local community.

2.3 Randomization, allocation concealment, and blinding.

This controlled clinical trial had an equal allocation rate to the groups. Based on the inclusion and exclusion criteria, the selected teeth were divided into four groups using block randomization (4 x 5) [19] of the Research Randomizer software version 4.0. During the application of the interventions experiments, the patient did not know to which experimental group belonged, not allowing this to interfere with the patient's perception of sensitivity. According to the CONSORT flow diagram, the distribution and dynamics of the groups are shown in Figure 1.

2.4 Eligibility criteria

Patients of both genders, aged between 18 and 70 years, were included. They had at least two teeth with cervical dentin hypersensitivity; at least one tooth with a result above 4 on the VAS scale; the presence of exposed dentin in the cervical region; at least two hemiarchs affected by the hypersensitivity condition.

Patients with the following conditions were excluded from the study: teeth covered by prosthetics or with endodontic treatment; patients in constant use or with a medical history marked by chronic use of analgesics; anti-inflammations and psychotropic drugs; patients with orthodontic appliances; patients who have used desensitizing products in the past three months; patients who have undergone restorative treatment on the sensitive element in less than a month ago; removable partial denture abutment teeth; the presence of lesions with great depth (>3mm) who needed pulp protection; the presence of carious cervical lesion; pregnant or lactating [20].

2.5 Sample size calculation

The G*Power program, version 3.1.9.2 (University of Düsseldorf, Germany) was fed from the data obtained in the pilot study. It obtained an effect size of 0.75, measured in the inter-group comparison, which resulted in 27 teeth per group obtaining power of 80%, with a significance level of α of 5%. For greater safety, 29 teeth were inserted in each group. Hence, the teeth were distributed into four groups (n=29) according to the desensitizing agent: GD - Gluma Desensitizer® (Heraeus Kulzer, Hanau, Alemanha); CV – Clinpro White Varnish® (3M ESPE, Minnesota, EUA); SB – Single Bond Universal® (3M ESPE, St.Paul, EUA) AS: AdheSE® (Ivoclar Vivadent, Schaan, Liechtenstein).

1.6 Dentin hypersensitivity assessment

The stimulus adopted was the evaporative stimulus (triple syringe).and tactile (probing) stimuli. The Visual Analog Scale (VAS) with measurements

from 0 to 10 was used, in which the volunteer indicated their pain. Zero (0) refers to “no pain” and 10 corresponds to “unbearable pain” [21]. The clinical evaluation involved applying a triple syringe air jet perpendicular to the cervical region of the tooth, at a distance of 1 cm. This stimulus lasted for 2 seconds. Adjacent teeth were isolated using cotton rolls to prevent any interference with the measurement of the specific tooth. The tactile stimuli will be performed with the aid of an exploratory probe No. 5 under light manual pressure in the mesio-distal direction of the cervical dentin surface, by a single operator standardizing the force used. Immediately following the test, the patient indicated a single value of sensitivity experienced on a Visual Analog Scale (VAS), and this information was documented in the patient's clinical chart. The examiner responsible for assessing the level of cervical dentin hypersensitivity had undergone calibration prior to the evaluation.

All treatments were administered by the same researcher (operator 1). The stimuli and pain measurements were carried out by a previously calibrated examiner (operator 2). To minimize errors and prevent bias, operator 2, who was unaware of the treatments applied, assessed the response of each tooth to the air stimuli. Subsequently, the levels of dentin hypersensitivity were measured and recorded [22].

2.7 Interventions

After undergoing clinical examination and providing their consent to participate in the study, patients received treatment based on their assigned group. Two weeks prior to the start of the study, participants entered a wash-out period, during which they exclusively used oral hygiene products recommended by the researchers. These products were to be used consistently until the conclusion of the study. The oral hygiene kit included a soft toothbrush (Professional Lab Series, Colgate Palmolive Company), a fluoride toothpaste (Colgate Total 12, 1450 ppm F, Colgate Palmolive Company), and a dental floss (Colgate, Colgate Palmolive Company).

Prior to treatment, dental prophylaxis was conducted on all teeth using a rubber cup, 2% chlorhexidine, and a pumice stone. The area was subsequently rinsed with an air/water spray and dried using cotton. To ensure relative isolation, cotton rolls were used, and treatments were then administered based on the assigned groups. The group distribution, as well as the composition and usage instructions provided by each manufacturer, are presented in Table 1.

Table 01 - Distribution of patients and type of application in each group.

Group	Treatment	Application	Composition
GD	Gluma Desensitizer [®] (Heraeus Kulzer, Hanau, Germany Lot # K010512)	Prophylaxis, relative isolation, dry the area, apply a minimum amount of material with the aid of a disposable brush, leave for 30 to 60 seconds, then carefully dry the surface with an air jet until the liquid	2-hydroxyethyl methacrylate, Glutaraldehyde, purified water.

CV	Clinpro White Varnish® (3M ESPE, Minnesota, USA Lot # N875861 2)	disappears. Rinse. Open the single-dose package and distribute the contents on a surface that facilitates handling. Use an applicator brush to thoroughly mix the product. Apply a thin layer evenly to the surface to be treated. After application, instruct the patient to close his mouth, so the material can set and stick when it comes in contact with saliva.	Colophony resin, n-Hexane, ethyl alcohol, sodium fluoride, xylitol, thickener, flavoring, modified tricalcium phosphate (TCP).
SB	Single Bond® (3M ESPE, St. Paul, USA Lot # 3210663)	Prophylaxis, relative isolation, dry the area, apply Single Bond by rubbing for 20 sec., light jets of air for 5 sec., light curing for 10 sec. with the Bluephase led curing light (Ivoclar Vivadent, Barueri, São Paulo, Brazil) with light intensity of 1200 mW / cm ² .	HEMA, ethanol, water, initiators, silane, filler, Dimethacrylate, MDP, Vitrebond Copolymer.
AS	AdheSE® (Ivoclar Vivadent, Schaan, Liechtenstein Lot # U26216)	Prophylaxis, relative isolation, dry the area, apply AdhESE Primer for 15 sec. and brush the surface for another 15 sec., disperse the primer with a strong jet of air. Apply AdhESE Bond, disperse with a weak jet of air. Light cure for 10 seconds with the Bluephase led light cure (Ivoclar Vivadent, Barueri, São Paulo, Brazil) with light intensity of 1200 mW / cm ² .	Methacrylates, ethanol, water, highly dispersed silicon dioxide, initiators and stabilizers.

Source: Manufacturer

The treatments were carried out in one session. The effectiveness of the products was evaluated immediately after each treatment session using the Visual Analog Scale (VAS). Participants were scheduled for follow-up visits at 7, 30-, 60-, and 360 days post-treatment, during which the VAS level was assessed using the same evaporative and tactile stimuli.

2.8 Statistical methods

The analysis followed the intent-to-treat protocol and involved all participants, who were randomly divided (Figure 1). The statistician was also blinded to the groups. The sensitivity data reported by the patients in this study were tabulated in a digital spreadsheet (Microsoft Excel Windows 2010) and subsequently analyzed using the Jamovi 2.3.16 software (Project Jamovi). Considering the variables ordinal qualitative of this study, the Kruskal Wallis test with the Dwass-Steel-Critchlow-Fligner post-test were used for intergroup evaluation ($p < 0.05$); for intragroup analysis, the Friedman test was applied ($p < 0.05$).

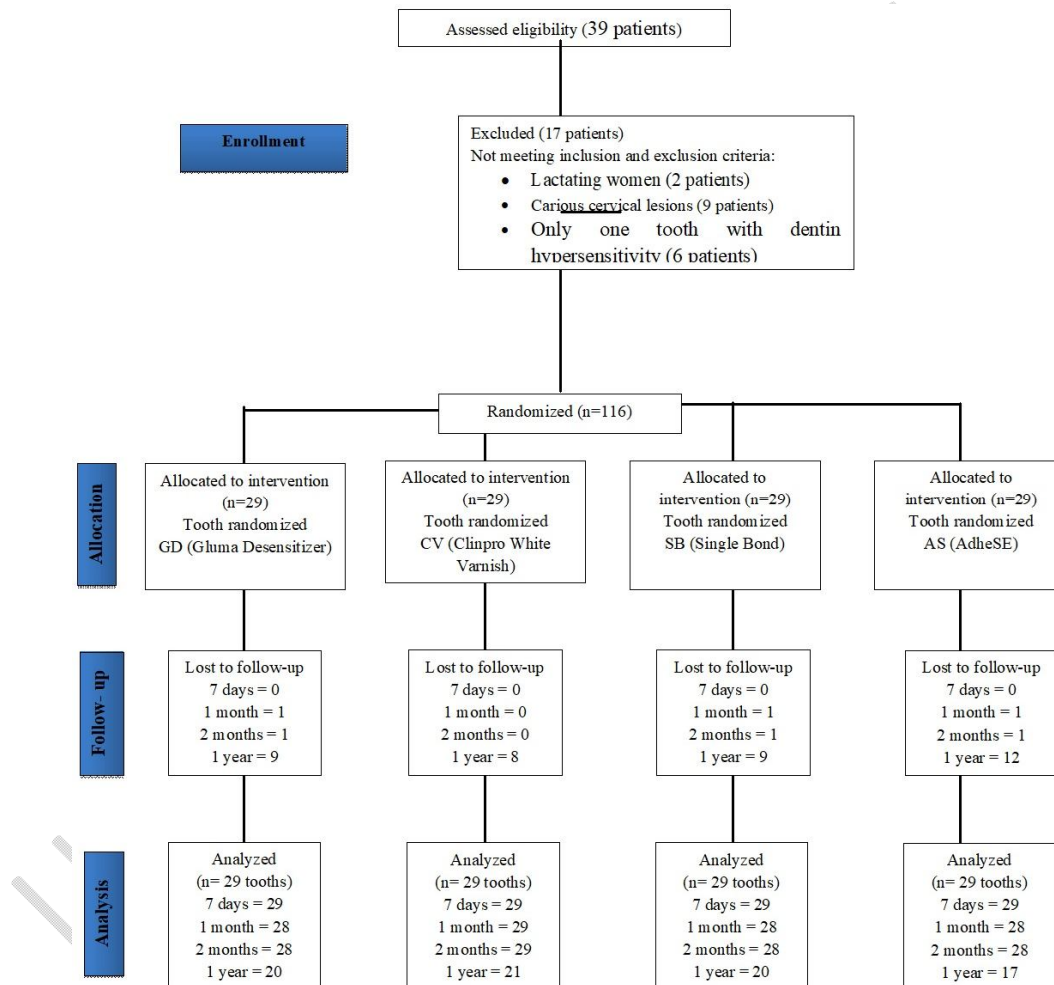


Figure 01 – CONSORT Flow Diagram

3. Results

Table 02 shows the intragroup and intergroup results over the periods. In the intragroup comparison over the periods, it was possible to observe a statistically significant decrease ($p < 0.05$) from the initial period (T0) to all other periods for the groups treated with AS, CV, and DG. Regarding the intergroup comparison, at the first evaluation, there were no statistically significant differences between the different desensitizing agents; thus, the baseline was the same for all the groups evaluated. Statistically significant differences

($p < 0.05$) were observed between the different desensitizing agents only in the period of 7 days (T7) for SB; in the 1-year reassessment (T1) it showed a significant increase when compared to T7 and T30, the sensitivity levels approached the initial pre-treatment values.

Table 02- Representative results of the median (\pm inter-quartile deviation) for the degree of dentinal sensitivity of each group by period evaluated.

	Initial (T0)	Immediate (T1)	7 days (T7)	30 days (T30)	60 days (T60)	1 year (T1Y)
SB	9 (± 4.00) Aa	0 (± 0.00) Ab	0 (± 0.00) Ab	0 (± 1.00) Abc	0 (± 3.00) Abc	2 (± 3.00) Ac
AS	7 (± 4.00) Aa	0 (± 0.00) Ab	0 (± 2.00) Bb	0 (± 3.00) Ab	0 (± 1.00) Ab	0 (± 2.00) Ab
CV	8 (± 4.00) Aa	0 (± 0.00) Ab	0 (± 3.00) Bb	1 (± 2.00) Ab	0 (± 2.00) Ab	1 (± 4.00) Ab
GD	8 (± 3.00) Aa	0 (± 1.00) Ab	1 (± 2.00) Bb	0 (± 2.00) Ab	0 (± 3.00) Ab	1 (± 5.00) Ab

* Different letters indicate statistical difference.

Capital letters – Inter-group analysis

Lowercase letters – Intra-group analysis.

In the 1-year (T1Y) intergroup assessment, there was no difference between the desensitizing agents for the hypersensitivity reported by patients using the VAS scale. In the intra-group comparison of 1 year (T1Y), there was a difference in the hypersensitivity reported by the patients through the VAS between all the periods evaluated compared to the initial period, except for the SB group. Thus, in the AS, CV, and GD groups, hypersensitivity was reduced when compared to the reported pre-treatment (T0), and this result remained stable during the 1-year reassessment (T1Y).

4. Discussion

Dentin hypersensitivity is short, acute pain due to exposed dentin in response to thermal, tactile, osmotic or chemical stimuli [23]. It was observed in this study that all the desensitizing agents tested were able to decrease DH, probably by satisfactorily occluding the dentinal tubules exposed in the cervical dentinal region.

A systematic review carried out in 2019 evaluated the effectiveness and duration of treatments available for cervical dentin hypersensitivity and demonstrated positive levels in the reduction of DS through studies with different materials and mechanisms of action [24]. However, the authors claim that there is a minority of studies with an evaluation period longer than 6 months to compare long-term effects, justifying the conduct of this clinical research for a period of 1 year-follow-up.

Based on the results obtained, we can accept the hypothesis that the desensitizing agents GD, CV, and AS are effective in reducing dentin hypersensitivity and improving patients' quality of life. However, it is important to note that the initial hypothesis did not address the desensitizing agent SB, for which no statistically significant reductions in dentin hypersensitivity were observed.

It was found in the present study that the most significant desensitizing effect in the seven days occurred for the group in that the Universal Single Bond adhesive was applied. Perhaps this happened because this material has polyalkenoic acid, a compound based on glass ionomers Vitremer and Vitrebond. The presence of this copolymer is believed to form complexes within the dentinal tubules, playing a stress-relaxing effect. In addition, the monomer 10-methacryloyloxydecyl dihydrogen phosphate was included in its formulation (10-MDP), that in contact with the dental substrate initiates a chemical interaction in the form of nano-layers with calcium ions, forming a salt of MDP-Ca. It is assumed that this chemical adhesion is responsible for the good results of the material, in addition to greater stability in aqueous media [25]. Burke et al. [26], observed that the use of Scotchbond, it was also possible to observe a significant reduction in DH in the period of one week.

In contrast, after 1 year of application, the Single Bond Universal was the one that showed a difference between its baseline and final value. Based on its chemical formulation, similar or superior behavior was expected to be similar to the other evaluated agents, but this did not happen. The presence of the polyalkenoic acid copolymer in the composition of the Universal Single Bond may have competed with 10-MDP for the calcium binding of hydroxyapatite. In addition to impairing the binding of MDP to dentin, the polyalkenoic acid copolymer could have prevented monomers from approaching during polymerization, due to its high molecular weight [27]. Consequently, a reduction in the quality of the hybrid layer formed may have occurred, making it more susceptible to the action of the oral environment over time.

Patil *et al.* [28] compared the Single Bond Universal adhesive and the Gluma desensitizing in the treatment of dentin hypersensitivity for 6 weeks and demonstrated better performance in reducing pain levels in the Gluma group. One of the problems with most products that use a tubular occlusion strategy is that the precipitate cannot withstand the continuous impact of the acid challenge on the oral environment [29]. Because of this, hypersensitivity's causative factors must be eliminated to achieve the long-term resolution of this condition [30].

Canali *et al.* [31] evaluated different self-etching adhesive systems in the treatment of HD over six months and found no differences between the materials tested. In this research, the period was one year, enough to abrasion the adhesive layer formed by the Single bond adhesive system.

Gluma is used as a control group in several studies because it performs well as a desensitizing agent. This product comprises HEMA and glutaraldehyde, responsible for killing bacteria and coagulating plasma proteins within dentinal fluids, forming a coagulation buffer [32]. The mechanism of action of this product is based on the formation of precipitations resulting from

the reaction of glutaraldehyde with proteins present in dentinal tubules, leading to a reduction in its diameter. In addition, these precipitations can also lead to HEMA polymerization, obliterating or occluding dentinal tubules, using tags capable of reaching a depth of 200 μm [33]. Lopes *et al.* [33] consider Gluma a non-invasive treatment of DH since the pain levels were reduced and remained the same until the evaluation at 18 months after treatment. Yu *et al.* [12] revealed that this desensitizing relieved DH immediately and one month after the application. Ozen *et al.* [32] demonstrated that this agent caused a statistically significant reduction in dentin hypersensitivity for one week after treatment. In the study of Pion *et al.* [21], the group treated with Gluma showed promising results, suggesting complete obliteration of the dentinal tubules and reduced pain levels. However, some authors consider glutaraldehyde irritating to soft tissues, indicating its use in moderation [34]. In the present study, the Gluma desensitizing agent was shown to be effective in reducing cervical dentin hypersensitivity for 1 year.

Garofalo *et al.* [14] did not observe significant dentinal tubule occlusion when using Clinpro White Varnish. The authors suggest a lack of protection against erosive wear or a low amount of TCP (modified tricalcium phosphate) added to the varnish. On the other hand, the study of Tosun *et al.* [35] showed that, at the end of a PH cycle, the material remained on the dentin surface and significantly reduced the diameter of the dentinal tubules, obtaining a favorable result. In the present study, the decrease in DH with the application of Clinpro White Varnish matched the self-etching AdheSe adhesive tested and the desensitizing Gluma in reducing hypersensitivity for the period evaluated.

The two-step self-etching adhesive AdheSE is composed of a primer that contains acidic functional monomers. It modifies the dentin surface's smear layer and incorporates it into the hybrid layer [36]. Some authors believe it is common to obliterate the orifices of the dentinal tubules after an adhesive procedure. There may be a decrease in postoperative sensitivity, since the residual layer exposes fewer tubules, minimizing the flow of dentinal fluid [36]. The application of the AdheSE on non-carious cervical lesions decreased DH in the patients in this study. However, similar research using AdheSE to treat hypersensitivity is scarce in the literature, and further clinical investigations are needed to compare this therapeutic method.

The materials Gluma Dessensitizer, Climpro White Varnish, and AdheSE adhesive, tested in this study, achieved satisfactory results in reducing pain caused by hypersensitivity to dentin over 1 year. In contrast, after 1 year of application, the Single Bond Universal adhesive proved inferior to the other materials tested in this study since the sensitivity levels approached the initial pre-treatment values. In this period, for the intergroup comparison, the statistical test could not detect these differences because it was underpowered in the function of the high variances. In future research, it would be suitable to increase the number of teeth evaluated to obtain enough power and possibly thus detect the differences between the SB group and the others in the 1-year evaluation.

5. Conclusion

Desensitizing agents Gluma Desensitizer, Clinpro White Varnish, and the AdheSE adhesive, tested in this study, were effective in decreasing cervical dentin hypersensitivity immediately after application and remaining over 1 year.

Single Bond adhesive significantly reduced pain until the 7-day follow-up; however, after the 30-day follow-up, the sensitivity progressively increased again until the 1-year follow-up.

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