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Comparative *In Vivo* Study on the Desensitizing Efficacy of Dentin Desensitizers and One-bottle Self-etching Adhesives

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Clinical Relevance

Dentin desensitizers and one-bottle self-etching adhesives can significantly reduce dentin hypersensitivity. Clinical desensitizing effectiveness depends on the individual dentin desensitizers/adhesives used.

SUMMARY

This *in vivo* study evaluated the desensitizing efficacy of two one-bottle self-etching adhesives, two dentin desensitizers and a placebo (water). Methods: Thirty-one volunteers with 55 hypersensitive teeth were recruited into this clinical investigation. The sensitive teeth were randomly assigned into five groups and treated with one of the following materials: iBond, Heraeus; Xeno V, Dentsply; Gluma desensitizer, Heraeus; Bifluorid 12, Voco; placebo (water). Mechanical and thermal stimuli were used to assess the tooth sensitivity response. Discomfort interval scale (DIS) scores of the sensitive teeth were recorded at three different investigation times (baseline, immediately and one month after treatment). Impressions were taken from the sensitive teeth at all three different investigation times, and replica models were made for the evaluation of the dentin surfaces by scanning electron microscopy. The Friedman test and the Mann Whitney U-test were used to analyze the data. Results: All dental materials significantly reduced the dentin hypersensitivity immediately (*p*<0.05) and one month after treatment (*p*<0.05), with the exception of Bifluorid 12 for mechanical

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tooth sensitivity. The placebo (water) only caused a short-term effect on the thermal dentin hypersensitivity (*p*<0.05). Topical application of the dentin adhesives/desensitizers on sensitive dentinal areas resulted in occlusion of the patent tubules. Conclusions: The one-bottle self-etching adhesives and dentin desensitizers involved in the current clinical investigation could significantly relieve dentin hypersensitivity immediately and over the course of a month after treatment (except for Bifluorid 12 for tooth mechanical sensitivity). The placebo (water) had an immediate effect on thermal dentin hypersensitivity.

INTRODUCTION

Dentin hypersensitivity (DH) is one of the most common problems encountered in daily dental practice. The typical short and sharp tooth pain on exposed dentin arises from a variety of exogenous stimuli, including thermal, evaporative, tactile, osmotic and chemical changes.[1-2] The prevalence of DH reported in the literature varies from 4% to 74%,[2] depending on differences in the populations studied and the various methods of investigation, such as questionnaires[2] or different clinical examinations.[3]

Brännström's hydrodynamic theory is most widely accepted as an explanation of tooth sensitivity.[4-8] Assumptions of the hydrodynamic theory conclude that exogenous stimuli applied to the exposed dentinal tubules result in the flow of dentinal tubular fluid, activating the intradental nerves to create pain.[4-5] Previous research reveals that the dentin tubules of hypersensitive teeth are approximately eight times more open and two times wider than dentin tubules in control teeth.[9]

Dentin desensitizers and adhesives are applied to the exposed dentin surfaces to occlude the patent dentinal tubules[10-11] or to depolarize the intradental nerves by dentin desensitizers.[12-13]

Recently, one-bottle self-etching adhesives have been developed to greatly simplify the multiple steps of application to one step. Self-etching adhesives might be used to desensitize the DH by reducing dentin permeability.[10,14] Many dentin desensitizers do not adhere to the dentin surface, as do self-etching adhesives, and thus, their effects are temporary.[3] However, self-etching adhesives applied to the dentin surface produce an acid-resistant hybrid layer.[15] This may result in longer-lasting clinical effectiveness. The clinical effectiveness of dentin desensitizers and self-etching adhesives in reducing the DH has not to date been clarified in detail.

The aim of the current study was: 1) to evaluate the clinical effectiveness of two dentin desensitizers, two one-bottle self-etching adhesives and a placebo for DH treatment and 2) to observe the micromorphology of the hypersensitive dentin surface treated with either self-etching adhesives, dentin desensitizers or placebo.

The null-hypothesis tested in the current study was that all the dental materials in this study would significantly reduce the DH to some degree.

METHODS AND MATERIALS

DH Treatment

This clinical investigation on the efficacy of DH treatment was carried out in the Department of Stomatology, No 1 Hospital Affiliated to Medical College, Zhejiang University, Hangzhou, China.

Thirty-one volunteers (22 females and 9 males) with 55 sensitive teeth were recruited into the clinical study. The volunteers' ages ranged from 18 to 78 years, with the mean age being 42.4 years. A prospective randomized, subject-blinded, placebo-controlled, split-mouth study was performed after informed written consent of the volunteers was obtained. The sensitive teeth were randomly allocated to one of five groups/treatments by drawing lots. Each individual volunteer had only one hypersensitive tooth in one quadrant. The sensitive teeth of the different quadrants were treated using different materials. All the volunteers fasted for two hours after treatment, and they were instructed to eat and drink as usual during the clinical investigation period. The clinical research was conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version, 2002 www.wma.net/e/policy/b3.htm) and the study was independently reviewed and approved by the local ethical committee. The medical and dental histories of all the volunteers were recorded. Exclusion criteria for volunteers were: 1) tooth sensitivity due to improper restorations, dental caries, tooth fractures, tooth defects, tooth cracks or pulpitis; 2) use of tooth desensitizing pastes within the past six weeks; 3) surgical or non-surgical periodontal treatment within the past three months; 4) use of medications, including antihistamines, anti-inflammatory drugs, anti-depressants or analgesics; 5) pregnancy or in lactation of the female volunteers.

The detailed treatment materials and methods used in the current study are described in Table 1.

Sensitivity Assessment

To assess a response to mechanical stimulation, the sensitive area of the tooth was tenderly scratched with a new standard dental explorer by the same investigator (Yu X). To assess a response to thermal stimulation, the sensitive tooth was isolated with cotton rolls and zero-degree water celsius (a mixture of ice and water kept in the refrigerator at 4°C) was dropped onto the tooth's sensitive area.

DIS scores of the sensitive teeth were recorded at three different investigation times (baseline, immedi-

Table 1: *The Treatment Materials and Methods Used in the Clinical Investigation*

Materials	Manufacturers Lot #s	Ingredients	Application Procedures
iBond	Heraeus Kulzer Hanau, Germany Lot #010087	4-MET, UDMA, TEGDMA, acetone, glutaraldehyde, photo initiator, stabilizer, purified water	The sensitive tooth surface was rinsed with water, gently air-dried, the adhesive was then applied three times, left undisturbed for 30 seconds, gently air dried until no movement, thoroughly air-dried and light-cured for 20 seconds.
Xeno V	Dentsply Konstanz, Germany Lot #0706000875	Bifunctional acrylic amide, acidic acrylic amide, functionalized phosphoric acid ester, acrylic acid, water, tertiary butanol	The sensitive tooth surface was rinsed with water, gently air-dried, the adhesive was applied twice and agitated for 20 seconds, thoroughly air-dried at least 5 seconds and light-cured for 20 seconds.
Gluma desensitier	Heraeus Kulzer Wehrheim, Germany Lot #075.8	HEMA, glutaraldehyde, purified water	The sensitive tooth surface was rinsed with water, gently air-dried, the desensitizer was applied once, left undisturbed for 60 seconds, carefully air-dried until the fluid film has disappeared and the surface was no longer shiny, rinsed with water again.
Bifluorid 12	Voco Cuxhaven, Germany Lot #781471	Sodium and calcium fluoride	The sensitive tooth surface was rinsed with water, thoroughly air-dried, the bottle shaken, the desensitizer applied once, left undisturbed for 20 seconds and air-dried.
Placebo		Deionized water	The sensitive tooth surface was rinsed with water, air-dried for 10 seconds. Water was applied once and left undisturbed for 10 seconds, water was applied again.

Note: ***4-MET****, 4-methacryloyloxyethyl trimellitic acid;* ***UDMA****, urethane dimethacrylate or 1,6-di(methacryloyloxyethylcarbamoyl)-3,30,5-trimethylhexaan;* ***TEGDMA****: triethylene glycol dimethacrylate;* ***HEMA****: 2-hydroxyethyl methacrylate*

ately and one month after treatment). The DIS scores ranged from 0 to 4: 0: no pain; 1: mild pain; 2: moderate pain; 3: severe pain and 4: intolerable pain.[16]

Statistical Work

All the data were analyzed using the SPSS software package (version 16.0, SPSS Inc, Chicago, IL, USA). The Friedman test procedure was used to analyze the clinical treatment efficacy of all the materials, and the Mann Whitney U-test was used to analyze the clinical efficacy of the different desensitizing materials at the different investigation times (baseline, immediately and one month after treatment). The level of significance was set at $p<0.05$.

SEM (Scanning Electron Microscopy)

Impressions were taken of the sensitive teeth with an extremely low-viscosity hydrophilic vinyl polysiloxane (Imprint II Garant, 3M ESPE, Seefeld, Germany, Lot #20070809) plus putty rubber (Express STD, 3M ESPE, Lot #20061128) using a two-step impression method at the three different investigation times. The replica models were then made with epoxy resin (EpoFix Lot #6120-7535, Struers A/S, Ballerup, Denmark) for evaluation of the dentin surfaces by SEM (Scanning Electrical Microscopy) (Stereoscan 260, Cambridge, UK). Epoxy resin replicas were gold-sputtered (ion sputter, E-1020, HITACHAI, Tokyo, Japan), and the same locations of interest on the replicas were analyzed with SEM.

RESULTS

Discomfort Internal Scale (DIS)

DIS scores of the hypersensitive teeth are summarized in Tables 2 and 3. Regardless of the type of stimulus, all dental materials significantly reduced tooth sensitivity immediately after treatment ($p<0.05$). All the

Table 2: *Frequency Distributions of Tooth Sensitivity Scores in the Treatment Groups (Mechanical stimuli evaluation, Analysis with Friedman-test)*

Groups	# of Teeth	Discomfort Internal Scale															*p*-values*
		Baseline					Immediately					One Month After					
		0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	
i Bond	11	2	5	1	2	1	8	2	1	0	0	8	2	1	0	0	<0.01
Xeno V	12	2	5	4	1	0	9	3	0	0	0	6	5	1	0	0	<0.01
Gluma	12	1	8	1	2	0	4	6	2	0	0	10	2	0	0	0	<0.001
Bifluorid 12	10	1	7	0	1	1	8	2	0	0	0	5	3	1	1	0	<0.01
Placebo	10	1	8	1	0	0	5	5	0	0	0	6	3	1	0	0	ns

*$p<0.05$ was accepted as statistically significant. ns: no significance.

Table 3: *Frequency Distributions of Tooth Sensitivity Scores in the Treatment Groups (Thermal Stimuli Evaluation, Analysis with Friedman-test)*

Groups	# of Teeth	Discomfort Internal Scale															*p*-values
		Baseline					Immediately					One Month					
		0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	
i Bond	11	0	7	4	0	0	3	8	0	0	0	5	6	0	0	0	<0.01
Xeno V	12	0	6	6	0	0	2	9	1	0	0	2	8	2	0	0	<0.05
Gluma	12	0	6	5	1	0	4	6	2	0	0	4	8	0	0	0	<0.01
Bifluorid 12	10	0	4	3	2	1	5	5	0	0	0	3	4	2	1	0	<0.01
Placebo	10	1	5	3	1	0	4	6	0	0	0	3	4	2	1	0	<0.05

p*<0.05 was accepted as statistically significant. ns: no significance.*

Table 4: *Statistcal Comparison of DIS Scores Immediately and One Month After DH Treatment, Respectively, with Baseline DIS Scores Using the Mann Whitney U-test (*p*-values)*

Groups	Thermal Stimuli		Mechanical Stimuli	
	Immediately	One Month After	Immediately	One Month After
i Bond	<0.05	<0.05	<0.01	<0.01
Xeno V	<0.01	<0.05	<0.01	<0.05
Gluma	<0.01	<0.01	<0.05	<0.01
Bifluorid 12	<0.05	<0.05	<0.01	ns
Placebo	<0.05	ns	ns	ns

p*<0.05 was accepted as statistically significant. ns: no significance.*

dental materials significantly relieved the thermal sensitivity of the teeth over a month ($p<0.05$). All the dental materials, with the exception of Bifluorid 12, also significantly decrease mechanical sensitivity of the teeth over a month ($p<0.05$). The placebo (water) only significantly relieve the tooth thermal sensitivity immediately after treatment ($p<0.05$). Changes in the thermal/mechanical DIS scores over time by the different treatment materials are presented graphically in Figures 1 and 2.

SEM

There were a large variety of patent dentinal tubules on the sensitive areas of the investigated teeth (Figures 3-7). The application of water (placebo) on the sensitive areas did not close the open dentin tubules (Figure 7). In contrast, topical application of the dentin adhesives/desensitizers on the sensitive dentinal areas resulted in occlusion of the patent tubules (Figures 3-6). Some occluded dentin tubules were partly reopened one month after treatment (Figures 3-6).

DISCUSSION

The placebo response involves conscious and non-cognitive expectancies. The placebo achieved its effects on the DH.[17-19] The placebo (water) used in the current study had only an immediate effect on the thermal DH

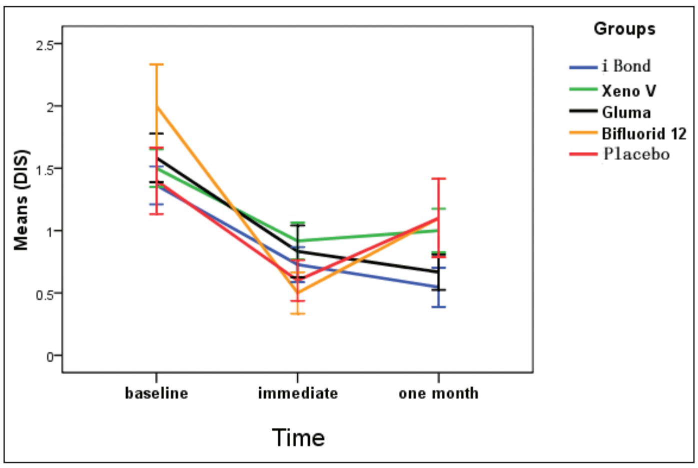

Figure 1: *Changes in DIS scores induced by thermal stimuli over time (means ± SE). The different colors represent the different materials (blue: i Bond; green: Xeno V; black: Gluma; yellow: Bifluorid 12; red: placebo).*

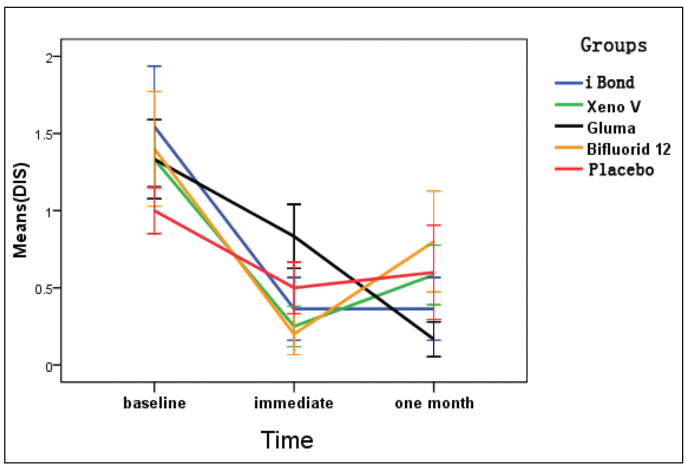

Figure 2: *Changes in DIS scores induced by mechanical stimuli over time (means ± SE). The different colors represent the different materials (blue: i Bond; green: Xeno V; black: Gluma; yellow: Bifluorid 12; red: placebo).*

Figure 3: *SEM micrographs of dentin surface areas before and after treatment with i Bond.*

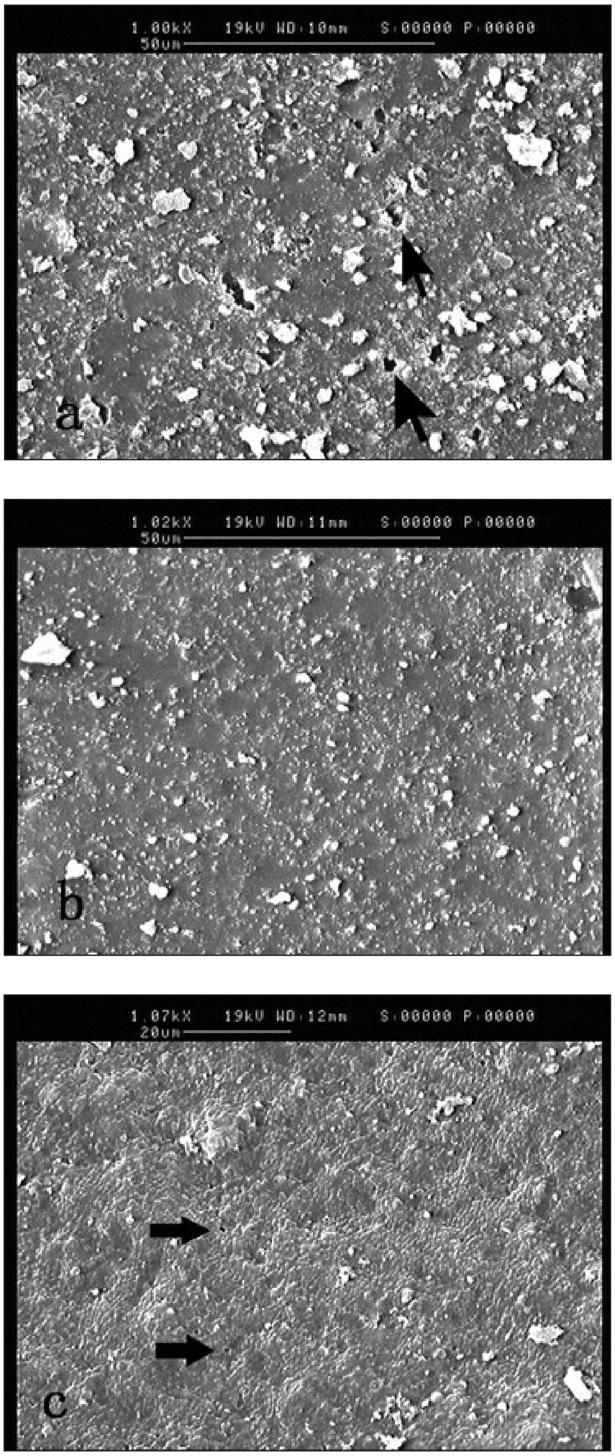

Figure 3a: There are several open dentin tubules on the sensitive dentin (marked with arrows) before the treatment (1,000x, bar=50 μm). Figure 3b: Most dentin tubules are occluded immediately after the application of iBond (1,020x, bar=50 μm). Figure 3c: Some dentinal tubules are re-opened one month after iBond treatment (tiny holes marked with arrows) (1,070x, bar=50 μm).

Figure 4: *SEM micrographs of dentin surface areas before and after treatment with Xeno V.*

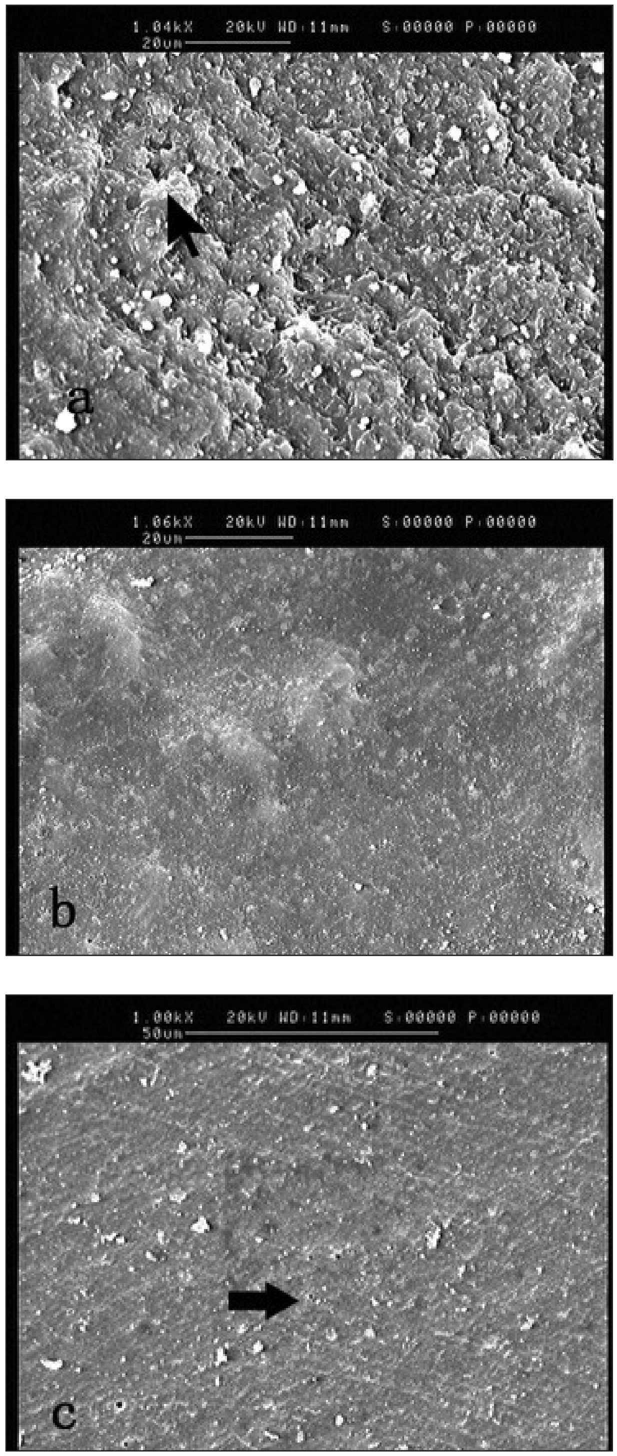

Figure 4a: There are several open dentin tubules on the sensitive dentin (marked with arrows) before the treatment (1,040x, bar=20 μm). Figure 4b: Most dentin tubules are occluded immediately after the application of Xeno V (1,060x, bar=20 μm). Figure 4c: Some dentinal tubules are re-opened one month after Xeno V treatment (tiny holes marked with arrows) (1,000x, bar=50 μm).

Figure 5: *SEM micrographs of dentin surface areas before and after treatment with Gluma desensitizer*.

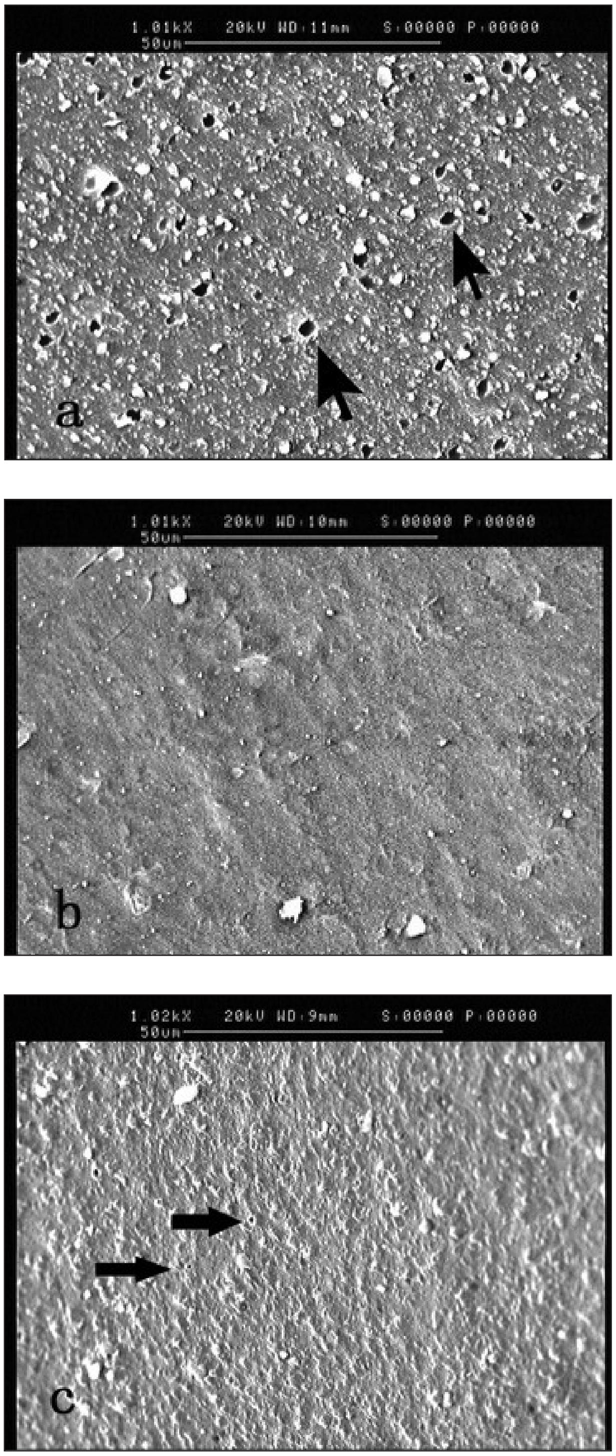

Figure 5a: There are several open dentin tubules on the sensitive dentin (marked with arrows) before treatment (1,010x, bar=50 µm). Figure 5b: Most dentin tubules are occluded immediately after application of Gluma desensitizer (1,010x, bar=50 µm). Figure 5c: Some dentinal tubules are re-opened one month after Gluma desensitizer treatment (tiny holes marked with arrows) (1,020x, bar=50 µm).

Figure 6: *SEM micrographs of dentin surface areas before and after treatment with Bifluorid 12*.

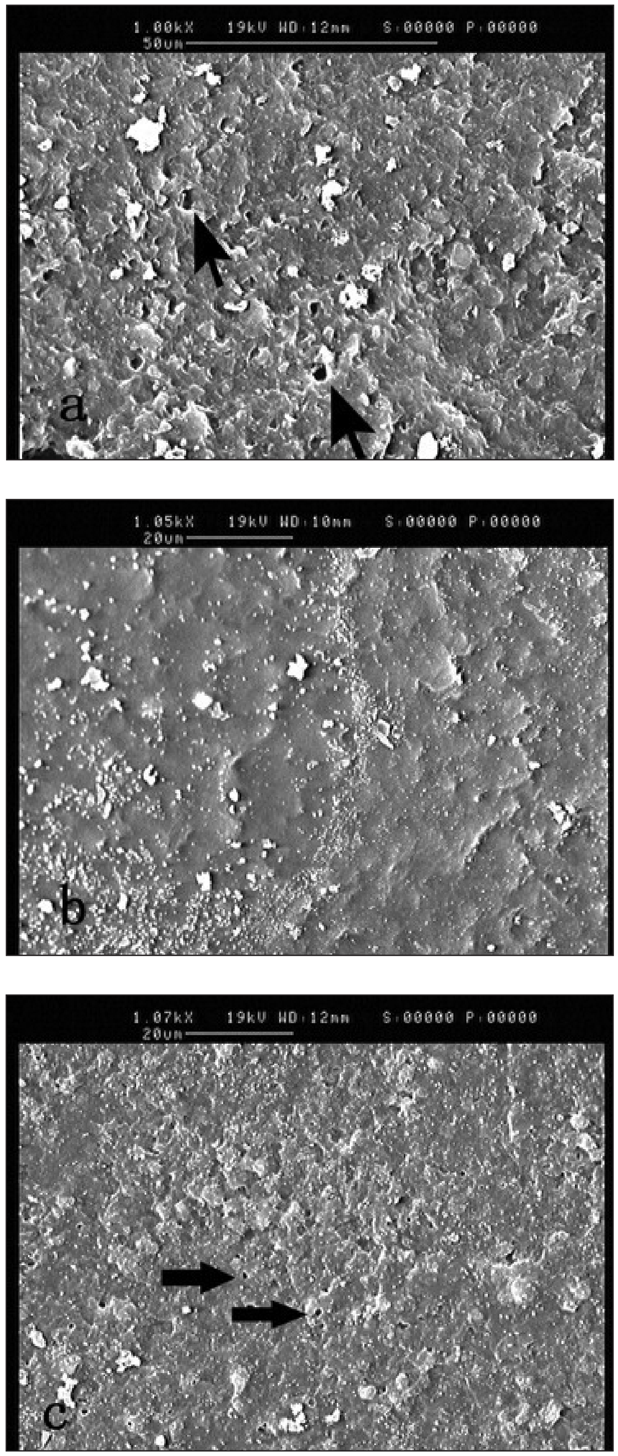

Figure 6a: There are several open dentin tubules on the sensitive dentin (marked with arrows) before the treatment (1,000x, bar=50 µm). Figure 6b: Most dentin tubules are occluded immediately after the application of Bifluorid 12 (1,050x, bar=50 µm). Figure 6c: Some dentinal tubules are re-opened one month after Bifluorid 12 treatment (tiny holes marked with arrows) (1,070x, bar=20 µm).

Figure 7: *SEM micrographs of dentin surface areas before and after treatment with Placebo.*

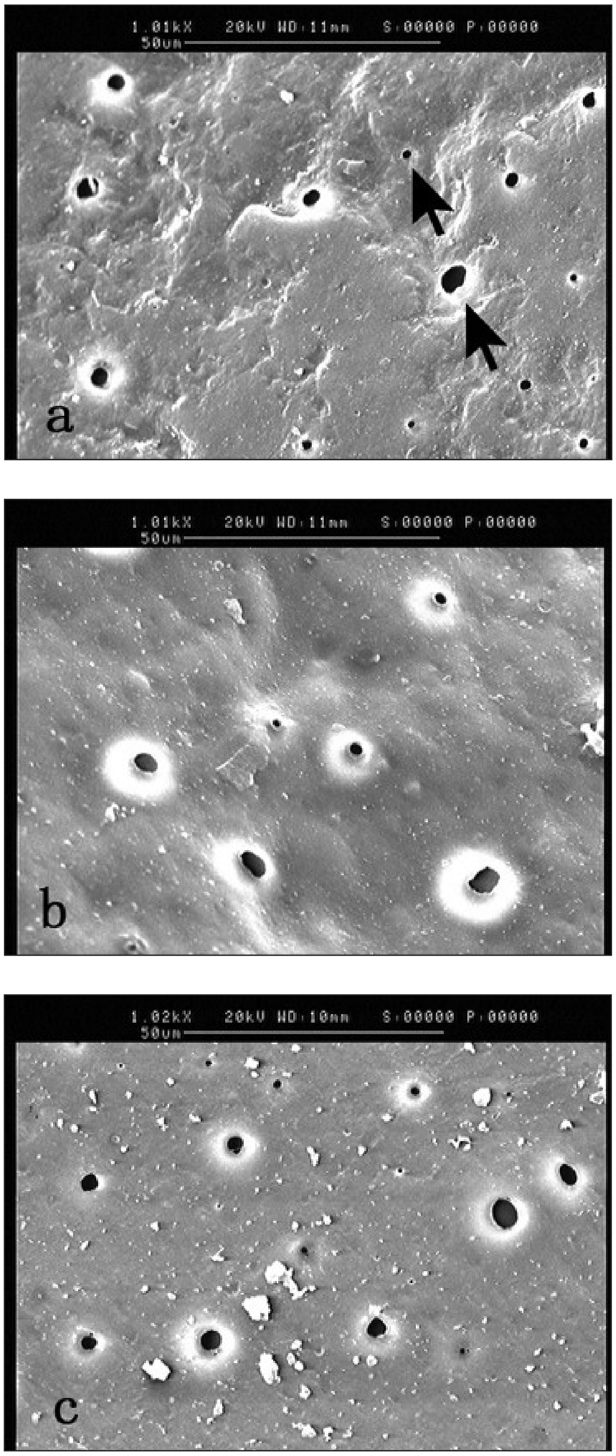

Figure 7a: There are several open dentin tubules on the sensitive dentin (marked with arrows) before the treatment (1,010x, bar=50 μm). Figure 7b: The application of placebo (water) did not close the patent dentin tubules, immediately after application of the placebo (1,010x, bar=50 μm) and Figure 7c: One month after application (1,020x, bar=50 μm).

($p<0.05$). These findings suggest that the placebo provides an immediate psychological effect on the thermal DH and does not possess a long-lasting clinical effectiveness.

Bifluorid 12 is a fluoride varnish consisting of sodium and calcium fluoride. In the current study, Bifluorid 12 significantly reduced the thermal DH immediately and over a month. However, it significantly relieved the mechanical DH immediately but did not maintain the effect over a month. It created a barrier by precipitating calcium fluoride (CaF_2) on the tooth surface and within the tubules' orifices,[3,20] as well as by occluding the dentin tubules through the crystallization of sodium fluoride.[21] However, most of the fluoride is released within two weeks of the topical application of fluoride,[22] due to the lack of bonding between the dentin and the varnish.[23] Furthermore, the varnish was easily peeled off the dentin surfaces during the impression procedure during the mechanical stimulus at the clinical investigation. This might be due to the fact that Bifluorid 12 reduced the thermal DH for a longer time, but it could not lessen the mechanical DH throughout the duration of one month. The Gluma desensitizer did not fully mechanically block dentin permeability, but it still possessed some sealing ability to reduce dentin permeability as evidenced in previous research by the authors of this study.[10] This is consistent with the current study, revealing that the desensitizer relieved the DH immediately and over one month. The desensitizer achieves its desensitizing effects by the precipitation of dentinal fluid proteins, such as serum albumin, and by reduction of the intratubular fluid flow directed to the exposed dentin surfaces.[8,13]

The topical application of dental adhesives is one well-established method to manage the DH.[3,10] Single-bottle self-etching adhesives (all-in-one adhesives) have been developed in order to simplify the multiple steps of application into one step. The single-bottle self-etching adhesives (Xeno V and i Bond) could produce an acid-resistant hybrid layer on the dentin surface for DH relief. However, the all-in-one adhesives tested in the current study did not perform better than the dentin desensitizers, with the exception of Bifluorid 12, regarding the decrease of mechanical DH. The reason for this observation might be the fact that single-bottle self-etching adhesives contain mixtures of hydrophilic and less hydrophobic monomers and, thus, are permeable to water after application to the dentinal surface.[10,25] Nevertheless, they can reduce the dentin permeability to some degree.

Based on the current data, the null-hypothesis that all the dental materials in this study can significantly reduce the DH to a certain degree is accepted. The clinical desensitizing effectiveness depends on the individual dentin desensitizers/adhesives used.

CONCLUSIONS

The one-bottle self-etching adhesives and dentin desensitizers (except Bifluorid 12) involved in the current clinical investigation significantly relieved dentin hypersensitivity immediately and over a period of one month. The fluoride containing varnish Bifluorid 12 reduced the thermal and mechanical sensitivity of dentin immediately and thermal sensitivity over one month, but it failed to relieve the mechanical sensitivity over the course of a month. Water had an immediate effect on thermal dentin hypersensitivity.

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