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Clinical Efficacy of Different Dentin Desensitizers

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Clinical Relevance

Teethmate Desensitizer, Clinpro White Varnish, Shield Force Plus, and Gluma could be recommended for treating dentin hypersensitivity in terms of clinical efficacy.

SUMMARY

Objective: The aim of this study was to evaluate the clinical efficacy of widely used dentin-desensitizing agents (DDAs) (Teethmate Desensitizer, Clinpro White Varnish, Shield Force Plus, and Gluma) in the treatment of dentin hypersensitivity (DH) according to different evaluation parameters over a four-week follow-up period.

Methods and Materials: This study was a randomized, single-center, controlled, parallel group study involving 144 teeth in 40 subjects. The baseline DH levels of the subjects were determined using different evaluation parameters. Daily life hypersensitivity and evaporative air stimulus hypersensitivity scores were recorded using a visual analog scale (VAS), and tactile hypersensitivity scores were recorded using a Yeaple probe and measured in grams and on the VAS. Subjects who experienced evaporative air stimulus DH (30-80 mm on the VAS) and tactile hypersensitivity (10-50 g with the Yeaple probe) were included in the study. After application of the DDAs, these evaluation parameters were recorded throughout the follow-up period (immediately after application and at one day and two and four weeks post-application).

Results: All four DDAs demonstrated clinical dentin-desensitizing effects throughout the follow-up period according to evaporative air hypersensitivity, tactile sensitivity (g-VAS), and daily life hypersensitivity scores ($p<0.05$). Only Clinpro White Varnish had tactile sensitivity (g) scores that were similar at baseline and the one-day follow-up ($p>0.05$). A comparison of DH-reducing effects among the DDAs revealed that they yielded different results immediately after application and at the one-day follow-up time point, depending on which evaluation parameter was used. However, all DDAs showed similar DH-reducing effects at the two- and four-week follow-up time points.

Conclusions: Teethmate Desensitizer, Clinpro White Varnish, Shield Force Plus, and Gluma DH showed clinical efficacy for four weeks. DDAs may produce inconsistent clinical evaluation scores not only across different evaluation parameters but also between early and later follow-up time points.

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INTRODUCTION

Dentin hypersensitivity (DH) is a common dental problem that mostly affects the quality of life of the adult population. DH may occur while eating, drinking, and toothbrushing or even while breathing.[1,2] DH is defined as a short, sharp pain arising from exposed dentin that cannot be ascribed to any other dental pathologies; it typically occurs in response to external factors, such as evaporative, thermal, tactile, osmotic, or chemical stimuli.[3,4] This pain can occur at any age, but it mostly affects individuals ranging from 20 to 50 years old, and it may show a tendency to decrease with age.[5,6] The prevalence of DH ranges from 1% to 98% in the adult population. This wide range results from differences in assessment methods, clinical practice, study locations, subjectivity, and accompanying periodontal disease.[2,6,7] For example, the prevalence of DH ranges from 60% to 98% in patients with periodontitis.[4] In a recent review, it was concluded that the best estimate of the incidence of dentin hypersensitivity is approximately 11.5%, and the average across all published studies is 33.5%. The considerably high degree of heterogeneity among studies is only partially explained by the characteristics of the studies.[8]

Some studies have indicated that the prevalence of DH is higher in female than in male patients.[9,10] This could be because women have better oral hygiene awareness and generally exert greater effort in pursuing wellness.[11]

Generally, DH occurs when dentin tubules become exposed to the oral environment as a consequence of gingival recession or enamel loss caused by abrasion, erosion, and abfraction.[2,5,12] Therefore, the buccal cervical areas of teeth, especially on the canines and first premolars, are most frequently affected by DH.[6,13]

Many theories have been proposed for the mechanism of DH, but the most widely accepted contemporary theory is the hydrodynamic theory of Brännström and Aström.[5,14] According to this theory, when an external stimulus touches the exposed dentin surface, it causes dentinal tubule fluid movement and corresponding pressure changes across the entire dentin surface, which stimulates intradental nerve fibers, leading to the perception of short, sharp pain.[5]

Therefore, the treatment of DH is aimed at occluding exposed dentin in an attempt to prevent dentinal tubule fluid movement and/or block the pain response by the intradental nerve fibers.[4] Many studies have been performed to explore the nature of this pain and inhibit or at least reduce the uncomfortable sensation of DH.

A growing range of products is available for the treatment of DH on the dental market. These products are generally separated into two categories: at-home and in-office treatments. Home treatments are first-step treatment approaches, and if in-home treatment fails to reduce pain or the pain becomes a more powerful irritant, in-office treatments are appropriate to treat DH;[13] moreover, if the DH affects one or two teeth, in-office treatments could be indicated.[15]

In-office treatments can be categorized as noninvasive and invasive treatments. The first-line treatment approaches are noninvasive treatments, which are generally topically applied by a dental professional; these therapeutics are called desensitizing agents.

Desensitizing agents generally function by physically or chemically blocking or occluding exposed dentin tubules and contain ions and salts (e.g., oxalate [potassium or ferric oxalate], oxalic acid [phytocomplexes],[16-19] fluoride,[20,21] calcium phosphate,[22] and calcium phosphate derivatives [CPP-ACP][23,24]) or proteins, such as glutaraldehyde,[2,25] arginine, and calcium carbonate paste, that plug and cover dentin tubules.[26,27] If noninvasive treatments fail to reduce DH, invasive treatments (glass ionomer cement,[28,29] resin composite filling applications,[30,31] periodontal surgery,[32,33] lasers,[2,34,35] pulp removal, and root canal filling treatments) are indicated for resistant DH.

Fluoride-containing agents are among the most commonly used agents for treating DH. Topical fluoride treatments have been shown to reduce DH when used at high concentrations during in-office treatments.[6,21,36] Within the dentin tubules, fluoride may act to occlude the tubules via calcium fluoride precipitation, thus reducing dentin tubular permeability and DH.[21,37] Despite the fact that clinical studies have supported the beneficial results of fluoride, several clinical studies have suggested that fluoride has limited efficacy.[38,39]

Clinpro White Varnish (CWV; 3M ESPE, St Paul, MN, USA) is a modified formulation of fluoride with calcium phosphate. It contains sodium fluoride (5%) and tricalcium phosphate, and, according to the manufacturer, when in contact with saliva, it releases calcium and fluoride ions.[40,41] Open dentinal tubules were partially obliterated after application under *in vitro* conditions.[40,42] However, we could

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not find any data about the clinical efficacy of CWV on DH.

In addition, calcium phosphate–based desensitizers include bioactive and structural tooth materials such as tetracalcium phosphate and dicalcium phosphate anhydrous. These medicaments are popular due to their biocompatibility with and similar crystal structure to tooth tissues. For this purpose, the recently developed calcium phosphate–based desensitizer Teethmate Desensitizer (TD; Kuraray Noritake Osaka, Japan) was introduced to the market.[43] It has been reported that TD forms a calcium phosphate-rich layer and effectively integrates with the dentin surface, thereby reducing dentin permeability.[44] However, in the literature, we could find only two clinical studies about the effect of TD on reducing DH.[45,46] Hence, more studies are needed to evaluate the clinical performance of TD.

Shield Force Plus (Tokuyama, Taitou-ku, Japan) is an advanced light-cured, resin-based desensitizer that, according to the manufacturer, delivers immediate and long-term relief for preoperative, postoperative, and other forms of dentinal sensitivity. Shield Force Plus contains phosphate monomer, bisphenol A-glycidyl methacrylate, triethylene glycol dimethacrylate, and 2-hydroxyethyl methacrylate. The manufacturer suggests that the resin tags permeate 50 μm deep to seal dentinal tubules, thus providing immediate relief.[47] Shield Force Plus has been evaluated in only a few *in vitro* studies,[48] and we found only one study about the clinical effect of this agent. However, it was written in Russian, and only the abstract was available in English.[49] There are therefore no clinical studies about the effectiveness of this agent.

A combination desensitizing agent consisting of an aqueous solution of 5% glutaraldehyde and 35% hydroxyethyl methacrylate (Gluma Desensitizer, Heraeus, Kulzer GmbH & Co, Hanau, Germany) has been used for a few decades to treat DH.[50] The mechanism involves a reaction between glutaraldehyde and serum albumin in dentinal tubules that leads to precipitation and blocking of the tubules.[25,51] Scanning electron microscopy and confocal laser scanning electron microscopy studies have shown that Gluma provides intratubular blocking via protein coagulation.[46,52] Clinical and *in vitro* studies have shown that the success rates of Gluma in reducing DH range from 5% to 27%.[46,52,53]

Despite the fact that there are a large number of products on the dental market for the treatment of DDAs, the continued release of new dentin-desensitizing agents suggests that no product has yet been proven to be ultimately successful, and information as to what products are more clinically effective than others is quite limited.[54] Only a few studies have examined and compared the clinical effectiveness of these DDAs. Hence, in the present study, we evaluated and compared the short-term clinical effectiveness of these dentin-desensitizing agents in reducing DH *in vivo* according to different measurement parameters.

We aimed to compare the clinical effectiveness of DDAs that include bioactive materials with resins. The results of this clinical study may allow clinicians to be able to choose the most effective DDA, thus preventing repeated applications as well as time loss in the treatment of DH. Therefore, the most effective and safe DDA will be preferred, and this should contribute to patient satisfaction.

The null hypothesis tested in this study was that four different DDAs (TD, Gluma, Shield Force Plus, and CWV) would significantly reduce DH during a one-month follow-up period (tests were performed immediately after application and after one day, two weeks, and four weeks of follow-up).

METHODS AND MATERIALS

The main steps of the method to be followed in this study were as follows:

1) Clinical examinations of subjects who complained of DH to establish a study group from volunteers
2) Determination of baseline DH levels
3) Application of one of the DDAs to each group
4) Measurement of DH parameters immediately after application and one day, two weeks, and four weeks later

Clinical Examination of Subjects With the Complaint of DH and Establishing the Study Group From Volunteers

This study was designed as a randomized, single-center, controlled, parallel clinical trial. First, the baseline DH levels were measured in subjects who came to the School of Dentistry of Karadeniz Technical University with the complaint of DH and met the inclusion criteria for the study.

The criteria for inclusion in the study were as follows:

- Systemically healthy subjects (in particular, patients with a condition that reduces the flow of

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saliva and those who need to use a continuous medication were excluded from the study)
- Subjects without malignant or benign pathological lesions in the mouth
- Subjects between 18 and 65 years of age
- Subjects with a minimum of one natural, caries-free canine and/or premolar and/or incisor tooth that had gingival recession and/or cervical erosion and/or cervical abrasion
- Subjects who could come to the clinic for follow-up in four weeks
- Subjects without active periodontal disease
- Subjects who signed the informed consent form

The criteria for exclusion in the study were as follows:

- Malignant or benign pathological lesions in the mouth
- Xerostomia
- Chronic diseases and diseases that cause chronic pain and require continuous analgesic medication
- Advanced mobility of teeth exhibiting DH
- DH indicating teeth with dental caries, enamel cracks, resin composite restoration, crown restoration, removable prostheses, orthodontically banded, or exposed occlusal trauma
- Periodontal surgery or orthodontic treatment within the past three months
- Nonsurgical periodontal treatment within the past month
- DH treatment within the past three months
- Bleaching treatment within the past three months
- Allergy to the test product and its contents
- Use of desensitizing toothpastes (within the past six weeks), antibiotics and anti-inflammatory drugs (within the past month), or cigarette and tobacco products
- Pregnant or nursing

The follow-up periods were explained to the subjects who volunteered for enrollment in the study, and informed consent forms were read and signed by the subjects who agreed to participate in the study. This study was carried out with four groups, each consisting of 10 subjects (for a total of 40 individuals and 122 teeth). All DH assessment exams and DDA application procedures and assessments were performed by a single dental examiner in all subjects for the duration of the study.

Determination of Baseline DH Scores

Determination of Daily Life DH Scores—The DH level experienced in daily life was determined at the baseline visit. For this purpose, the patient was asked to mark the level of pain or discomfort experienced in the past two weeks when breathing, brushing the teeth, drinking cold or hot drinks, or eating sweet and sour foods on the VAS scale (0-100 mm). All subjects were asked to score daily life DH scores at the follow-up time points (one day, two weeks, and four weeks later) but not immediately after DDA application. Then clinical DH levels (evaporative air stimulus and tactile sensitivity) were determined with two different scales.

Determination of Evaporative Air Stimulus DH Scores—Each tooth exhibiting DH was isolated from adjacent teeth with fingers or cotton pellets. Then, at a distance of approximately 1 cm, air pressure was applied perpendicular to the cervical surface of the tooth at a room temperature of 18°C-21°C for one second at a pressure of approximately 415 kPa. Subjects recorded discomfort on a 100-mm VAS scale. On this scale, the level of discomfort was rated 0-100 (0, no pain or discomfort, to 100, intense pain or discomfort). Evaporative air stimulus DH scores of 30-80 mm were included in the study. In cases in which there was more than one tooth with a complaint of DH, the scoring of each tooth was performed and recorded separately in each subject for all determinations and follow-up time points except for the daily life DH scores.

Determination of Tactile Sensitivity DH Scores—Tactile hypersensitivity was assessed using a calibrated Yeaple probe (Electronic Force-Sensing Probe, Model 200A, Serial Number 1304, Jojen Technologies LLC, XiniX Research, Pittsford, NY, USA), as previously described.[55,56] Tactile hypersensitivity was assessed 10 minutes after the evaporative air stimulus determination test. For this measurement, each tooth with a complaint of DH was isolated from the adjacent teeth with fingers or cotton pellets. Then a Yeaple probe was placed perpendicular to the cervical surface of the tooth. Starting with 10 g of pressure, pressure was increased until the subject felt discomfort or reached a maximum of 80 g. Subjects who experienced pain between 10 and 50 g during the application of the Yeaple probe were included in the study. The discomfort scores measured as grams with the Yeaple probe were recorded separately. Then each subject reported the discomfort rate caused by the Yeaple probe on the VAS scale (0, no pain or discomfort, to 100, intense pain or discomfort).

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Table 1: *Compositions, Lot Numbers, and Application Instructions of the Dentin-Desensitizing Agents*

Agent (Manufacturer)	Composition	Lot Number	Application Instructions
Teethmate Desensitizer (Kuraray Noritake Osaka, Japan)	Powder: tetracalcium phosphate, dicalcium phosphate, anhydrous Liquid: water, preservative	041127	Mix the powder and liquid (15 s) carefully, apply with the applicator, rub for 30 s, and rinse with water.
Clinpro White Varnish (3M ESPE, St Paul, MN, USA)	Sodium fluoride (5%), tricalcium phosphate (TCP), xylitol	N7550369	Mix according to the dosage guide and apply to clean and dry dentin.
Shield Force Plus (Tokuyama, Taitou-ku, Japan)	SR Monomer Matrix, bisphenol A-glycidyl methacrylate, 3G (triethylene glycol dimethacrylate), 2-hydroxyethyl methacrylate, alcohol, water, camphorquinone	130E16	Apply to dentin with a brush and wait for 10 s. Mildly air-dry for 5 s and then air-dry strongly. Next, polymerize with blue light for 10 s.
Gluma, Heraeus (Kulzer GmbH & Co, Hanau, Germany)	35% 2-hydroxyethyl methacrylate, 5% glutaraldehyde	010502	Apply to clean dentin with a cotton pellet or brush and allow it to dwell for 30-60 s. Air-dry and rinse.

Randomization and Application of One of the DDAs in Each Group

After the baseline DH scores were determined, subjects were placed into four randomized groups, one for each DDA, using a randomization table. The randomization list was produced on the Research Randomiser website (www.randomiser.org). Each DDA (TD, CWV, Shield Force Plus, and Gluma) was applied to each randomized group (n=10 per group) according to the manufacturer's instructions. Subjects did not know which DDA was applied. Only the dental examiners knew the agent name. In the presence of more than one tooth with DH, the same DDA was applied to each tooth because untreated teeth with DH may have affected the daily life DH scores. The compositions, lot numbers, and application instructions of these agents are shown in Table 1.

Measuring DH Scores Immediately After Application and One Day, Two Weeks, and Four Weeks Later

The DH scores of subjects were measured and recorded on the VAS immediately after application as well as one day, two weeks, and four weeks later to evaluate both evaporative air sensitivity and tactile sensitivity. In addition, daily life DH scores were requested from the patients and recorded on the VAS at one day, two weeks, and four weeks after application. The clinical effectiveness of the DDAs was determined by comparing the scores on the VAS.

Statistical Analyses

A statistical data entry program (SPSS 17.0) was used for statistical analysis. In the comparisons between groups, the Kruskal-Wallis test, Mann-Whitney U-test, and Bonferroni correction were used, while the Friedman and Wilcoxon tests and Bonferroni correction were used for time-dependent variables (in-group).

One-way ANOVA was used to compare the ages between the groups. Chi-square tests were used to compare the distributions of tooth numbers, sex, and the anterior-premolar distribution and smoking. A value of $\alpha = 0.05$ was used to determine statistical significance.

RESULTS

This study was performed on a total of 122 teeth in adult volunteers who suffered from DH and ranged in age from 18 to 57 years. The demographic data (mean and standard deviation) of all subjects of this study are listed in Table 2.

In this study, 33 subjects were female (87.5%), and seven were male (17.5%). Demographic data obtained in this study showed that the only statistically significant differences were for smoking ($p<0.05$). The distribution of teeth that were treated in each group of participants are listed in Table 3.

The baseline mean and standard deviation and median (min-max) values for daily life sensitivity, evaporative air stimulus sensitivity, and tactile sensitivity of the teeth treated with DDAs are shown in Table 4.

When baseline scores were evaluated across the groups, for all of the evaluation criteria (daily life sensitivity scores, evaporative air stimulus sensitivity scores, and tactile sensitivity scores), there was no statistically significant difference among the DDA groups ($p>0.05$). In addition, when tactile sensitivity (g) measurements were examined, the mean values were between 17.88 and 22.26 g, and the subjects were very sensitive to tactile stimulation at the baseline of the study ($p>0.05$). However, the base-

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Table 2: *Demographic and Baseline Characteristic Scores of the Dentin-Desensitizing Agents: Patient and Tooth-Based Scores*

	Teethmate	Clinpro WV	Shield Force Plus	Gluma
Age (years), mean (SD)	39.5 (11.5)	43.10 (10.07)	42.60 (9.52)	40.23 (12.57)
Sex, n (%)				
Male	2 (20.0)	3 (30.0)	0 (0.0)	2 (20.0)
Female	8 (80.0)	7 (70.0)	10 (10.0)	8 (80.0)
Smoker, n (%)				
No	7 (70.0)	4 (40.0)	3 (30.0)	10 (10.0)
Little	3 (30.0)	2 (20.0)	3 (30.0)	0 (0.0)
Yes	0 (0.0)	4 (20.0)	4 (40.0)	0 (0.0)
Tooth type, n (%)				
Incisor	6 (27.0)	14 (38.0)	17 (50.0)	13 (41.0)
Premolar	15 (73.0)	22 (62.0)	16 (50.0)	18 (49.0)

line VAS scores for daily life DH (53.30-58.61) and the evaporative air stimulus VAS scores (52.26-58.79) were less sensitive than was tactile sensitivity.

The DH scores are shown according to the evaporative air stimulus test (VAS) for different time points and comparisons among the DDAs in Table 5 and Figure 1.

Evaporative air stimulus test scores (VAS) were significantly lower for all DDAs at all follow-up periods than at baseline ($p<0.01$). When the evaporative air stimulus test scores (VAS) were evaluated immediately after DDA application, there was a significant difference in all the DDA groups between these scores and the baseline VAS scores ($p<0.001$). In addition, in the comparisons among the DDAs, immediately after application, CWV produced significantly lower evaporative air stimulus test scores (mean VAS score=10) than were produced by the other groups (with TD, $p<0.01$; with Shield Force Plus and Gluma, $p<0.05$). In addition, TD produced significantly lower evaporative air stimulus test scores at the four-week follow-up than at the one-day and two-week follow-ups ($p<0.05$). For TD, Shield Force Plus, and Gluma, at the end of the four-week period, the evaporative air stimulus VAS scores were similar to the scores obtained immediately after application ($p>0.05$).

Table 3: *Tooth Distribution in Participants for Each Dentin-Desensitizing Agent*

Group	Tooth Distribution										Total
	8	7	6	5	4	9	10	11	12	13	
Teethmate	1	1	1	6	3	0	1	1	3	3	20
Clinpro	2	4	1	3	3	3	4	6	5	5	36
SFP	1	1	3	2	1	5	4	4	8	4	33
Gluma	3	2	2	4	3	3	1	3	4	6	31
Total	7	8	7	15	10	11	10	14	20	18	120

The DH scores are shown according to tactile sensitivity (g, obtained with a Yeaple probe), and time and comparisons among and within the DDA groups are shown in Table 6 and Figure 2. When the tactile sensitivity (g) test scores were evaluated, compared to baseline values, immediately after DDA application, there was a statistically significant decrease in all of the DDA groups ($p<0.001$). In addition, for all DDAs except CWV, there was a significant difference between scores obtained for tactile sensitivity (g) at all follow-up periods and scores obtained at baseline ($p<0.01$). For CWV, there was no significant difference between scores obtained at baseline and one day after application ($p>0.05$), indicating that subjects treated with CWV showed the same tactile sensitivity at baseline and one day after application. In addition, in a comparison among the DDAs, at one day after application, the tactile sensitivity (g) DH scores were significantly lower in the CWV and Shield Force Plus groups than in the TD group (for CWV $p<0.01$ and for Shield Force Plus $p<0.05$). This indicates that in the TD group, tactile hypersensitivity scores were lower than those in the CWV and Shield Force Plus groups at one day after application. At the other follow-up periods (two and four weeks), there was no statistically significant difference among the DDAs ($p>0.05$).

The tactile sensitivity (g-VAS) scores obtained with a Yeaple probe are shown according to time, and comparisons among and within the DDA groups are shown in Table 7 and Figure 3.

When the tactile sensitivity (g-VAS) test scores were evaluated in each test group immediately after DDA application, the scores were significantly lower

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Table 4: *Baseline Tooth-Based Scores Among the Dentin-Desensitizing Agents*[a]

	Teethmate	Clinpro WV	Shield Force Plus	Gluma
Daily life DH				
Mean (SD)	53.3 (10.64)	58.61 (16.75)	57.27 (13.05)	57.74 (16.87)
Median (min-max)	50.0 (40-70)	60.0 (40-80)	60.0 (40-80)	50.0 (40-90)
Evaporative air stimulus test VAS (mm)				
Mean (SD)	55.24 (16.61)	56.39 (19.94)	58.79 (16.55)	52.26 (17.83)
Median (min-max)	50.0 (40-80)	57.5 (10-80)	60.0 (20-80)	50.0 (30-100)
Tactile sensitivity (g with the Yeaple probe)				
Mean (SD)	19.57 (5.89)	18.89 (12.1)	17.88 (12.18)	22.26 (23.6)
Median (min-max)	20.0 (10-30)	10.0 (10-50)	10.0 (10-50)	10.0 (10-50)
Tactile sensitivity (g-VAS)				
Mean (SD)	28.57 (11.95)	30.83 (18.57)	40.0 (20.15)	32.26 (20.28)
Median (min-max)	30.0 (10-40)	30.0 (10-80)	30.0 (10-80)	30.0 (10-80)

Abbreviation: VAS, visual analog scale.
[a] *There was no significant difference between groups ($p<0.05$).*

Table 5: *Evaporative Air Stimulus Test Tooth-Based Scores (VAS) Among the Dentin-Desensitizing Agents*[a]

VAS Scores	Teethmate	Clinpro WV	Shield Force Plus	Gluma
Baseline (BL)				
Mean (SD)	55.24 (16.61) A	56.39 (19.91) A	58.79(16.15) A	52.26 (17.83) A
Median (min-max)	50.0 (40-80)	57.5 (10-80)	60.0 (20-80)	50.0 (30-80)
Immediately after application (IM)				
Mean (SD)	26.67 (21.05) BCa	10.0 (15.11) Bb	21.21 (22.04) Ba	18.71 (16.68) Ba
Median (min-max)	30.0 (0-80)	0.0 (0-50)	20.0 (0-80)	30.0 (0-50)
p (IM/BL)	<0.001*	<0.001*	<0.001*	<0.001*
p (with Clinpro)	0.001**; <0.01		<0.05**	<0.05**
1 d after application				
Mean (SD)	31.43 (23.7) B	31.94 (23.64) C	25.45 (20.01) B	22.26 (22.3) B
Median (min-max)	30.0 (0-80)	30.0 (0-80)	20.0 (0-80)	20.0 (0-80)
p (1D/BL)	0.002*; <0.01	<0.001*	<0.001*	<0.001*
p (G1/IM)		<0.001*		
2 wk after application (VAS)				
Mean (SD)	32.38 (22.78) B	30.56 (25.74) C	21.52 (26.35) B	20.65 (18.78) B
Median (min-max)	30.0 (0-80)	25.0 (0-80)	10.0 (0-80)	20.0 (0-80)
p (15D/BL)	0.001*; <0.01	<0.001*	<0.001*	<0.001*
p (15D/IM)		<0.001*		
4 wk after application (VAS)				
Mean (SD)	21.43 (20.0) C	32.50 (24.06) C	21.82 (10.00) B	20.65 (20.32) B
Median (min-max)	20.0 (0-80)	30.0 (0-80)	10.0 (0-80)	20.0 (0-80)
p (30D/BL)	0.001*; <0.01	<0.001*	<0.001*	<0.001*
p (other)	0.016*; <0.05 (1D/30D)	<0.001* (30D/IM)		
	0.027*; <0.05 (15D/30D)			

Abbreviation: VAS, visual analog scale.
[a] *According to the Bonferroni test, in each column (each tested product), values with different uppercase letters indicate significant differences among different follow-up periods in the same groups ($p<0.05$), and in each row, values with different lowercase letters indicate significant differences ($p<0.05$) among different test groups. The mean difference is significant at the 0.05 level.*
** Differences within the same DDA in each column.*
*** Differences among different DDAs in each row.*

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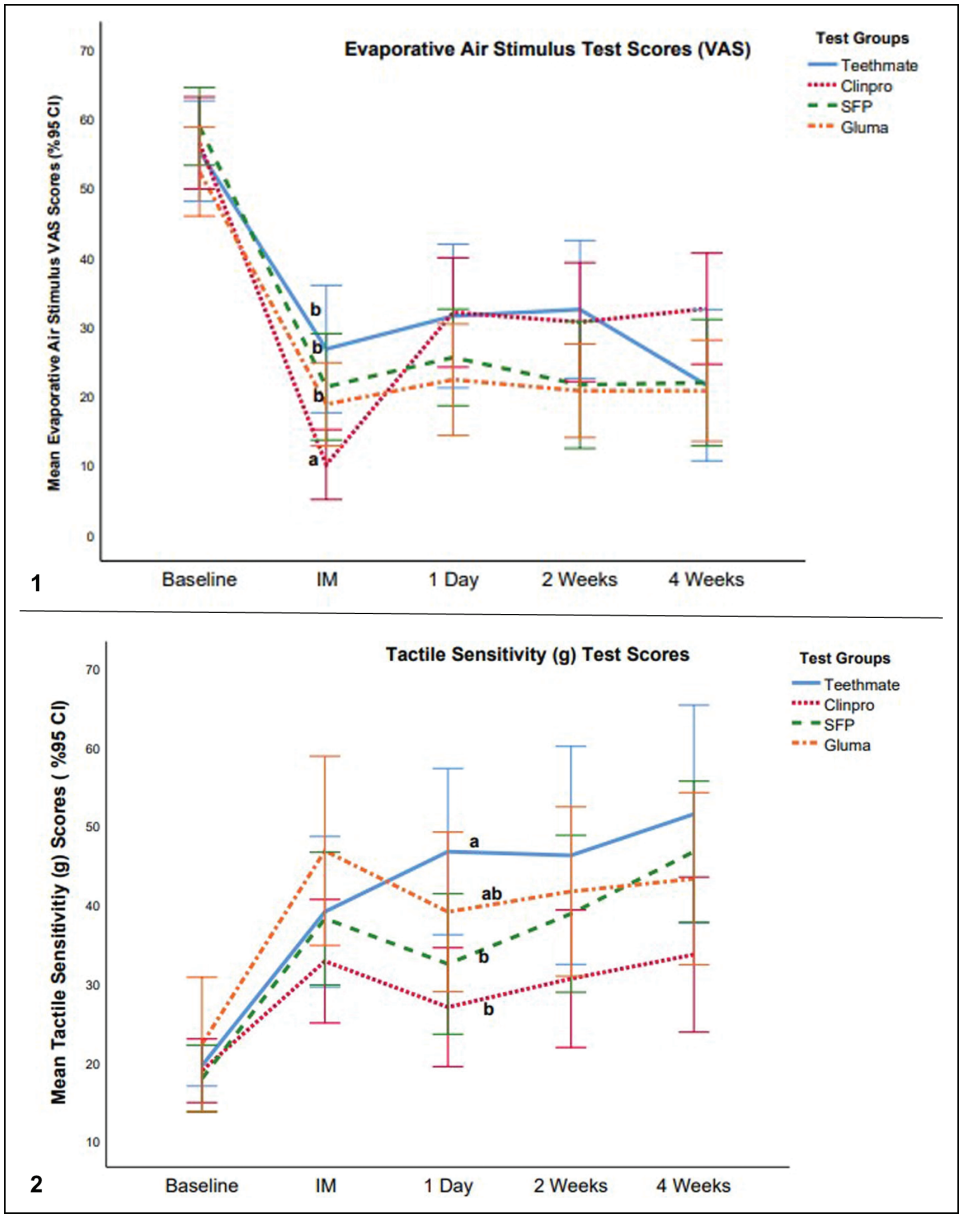


Figure 1. *According to the Bonferroni test, immediately after the application (IM) follow-up period, Clinpro WV showed significantly lower evaporative air stimulus test scores than other dentin-desensitizing agents (DDAs). Different lowercase letters show significant differences among the DDAs at IM (*p*<0.05).*

Figure 2. *According to the Bonferroni test, values with different lowercase letters indicate significant differences at one-day follow-up among different test groups. According to the Bonferroni test, tactile sensitivity (g) scores of Clinpro WV and Shield Force Plus were significantly lower than Teethmate Desensitizer (for Clinpro* p*<0.01 and for Shield Force Plus* p*<0.05).*

than those obtained at baseline in all four DDA groups ($p<0.01$). In addition, for all four DDAs, there was a significant difference in tactile sensitivity scores (g-VAS) between baseline measurements and those obtained at all follow-up time points ($p<0.05$).

In addition, in a comparison among the DDAs, at one day after application, the tactile sensitivity (g-VAS) scores were significantly lower for TD and Gluma than for CWV ($p<0.01$). This result indicates that TD and Gluma produced a greater DH-reducing effect with regard to tactile DH than was produced by CWV at the one-day follow-up time point. At the other follow-up periods (two and four weeks), there was no significant difference among the DDAs ($p>0.05$).

The daily life DH scores (VAS) are shown according to time, and the comparisons among and within the DDA groups are shown in Table 8 and Figure 4.

When daily life scores were evaluated in each test group, the VAS scores for all groups were significantly different between baseline and each follow-up time point ($p<0.05$). In addition, there was no statistically significant difference among the DDAs at each follow-up period ($p>0.05$).

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Table 6: *Tactile Sensitivity Test Tooth-Based Median Scores (g) Among the Dentin-Desensitizing Agents*[a]

Dentin Hypersensitivity Scores in Grams	Teethmate	Clinpro WV	Shield Force Plus	Gluma
Baseline (BL) (g)				
Mean (SD)	19.52 (5.89) A	18.89 (12.1) A	17.88 (12.18) A	22.26 (23.62) A
Median (min-max)	20.0 (10-30)	10.0 (10-50)	10.0 (10-50)	10.0 (10-50)
Immediately after application (IM)				
Mean (SD)	39.05 (21.88) B	32.78 (23.49) B	38.18 (24.16) B	46.77 (33.40) B
Median (min-max)	30.0 (10-80)	25.00 (10-80)	40.0 (10-80)	40.0 (10-80)
p (IM/BL)	0.001*; <0.01	<0.01*	<0.001*	<0.001*
1 d after application				
Mean (SD)	46.67 (24.15) Ba	26.94(22.65) ABb	32.42 (25.62) Bb	39.03 (28.2) Bab
Median (min-max)	40.0 (10-80)	20.0 (10-80)	20.0 (10-80)	30.0 (10-80)
p (ID/BL)	<0.001*		<0.05*	<0.01*
p (with TM)		<0.01**	<0.05**	
2 wk after application (VAS)				
Mean (SD)	46.19 (31.69) B	30.56 (26.18) B	38.79 (28.58) B	41.61 (29.89) B
Median (min-max)	30.0 (10-80)	20.0 (10-80)	30.0 (10-80)	40.0 (10-80)
p (15D/BL)	0.004*; <0.01	<0.05*	<0.001*	<0.01*
4 wk after application (VAS)				
Mean (SD)	51.43 (31.66) B	33.56 (26.18) B	46.67 (25.69) B	43.23 (30.37) B
Median (min-max)	60.0 (0-80)	20.0 (10-80)	50.0 (10-80)	30.0 (10-80)
p (30D/BL)	<0.01*	<0.05*	<0.001*	<0.001*

[a] *According to the Bonferroni test, in each column (each tested product), values with different uppercase letters indicate significant differences among different follow-up periods in the same groups (p<0.05), and in each row, values with different lowercase letters indicate significant differences (p<0.05) among different test groups. The mean difference is significant at the 0.05 level.*
** Differences within the same DDA in each column.*
*** Differences among different DDAs in each row.*

DISCUSSION

DH is a very common condition that negatively affects people's quality of life.[57,58] For this reason, a large number of DDAs with different ingredients are available on the market. However, there is no standardized treatment modality for the treatment of DH and no clear data on the clinical efficacies of these agents.[59] Hence, in this study, we aimed to clinically evaluate the short-term efficacy of DDAs (TD, CWV, Shield Force Plus, and Gluma) commonly used in clinics at four time points over a four-week follow-up period (immediately after application and one day and two and four weeks later).

According to the findings of the current study, the null hypothesis was accepted in that all DDAs were effective in reducing DH at each follow-up time point over a four-week period. These DDAs have different contents and produced dentin-desensitizing effects at all follow-up time points (immediately after the first application and one day and two and four weeks later) when compared to baseline ($p<0.05$) (Tables 5 through 8).

In this study, age and tooth type were also evaluated. Although DH is seen in all age groups, it usually occurs between the ages of 20 and 50 years and reaches a peak between the ages of 30 and 39 years.[5,46] When the ages of the patients in this study were analyzed, the mean age of the participants was 39.5-42.6 years in these groups, in accordance with the literature.[60]

Similar to other studies,[46,61,62] our sample size contained more female than male subjects. Although women reported higher DH than was reported by men in these studies,[46,61-64] other studies have shown higher DH levels in the male population.[65,66]

However, when our study design was initiated, the number of participants identified during enrollment showed a strong female predominance. This might be attributable to the finding that female subjects pay much more attention than male subjects do to their oral health hygiene.[11] Thus, it is possible that the presence of more female participants influenced the results of this study.

In addition, DH is observed mostly in the buccal cervical margins of canine and premolar teeth.[60] Canine and premolar teeth are the most frequently brushed and are thus the most exposed to the abrasives in toothpastes.[6,67,68] Moreover, it has been

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Table 7: *Tactile Sensitivity Test Tooth-Based Median Scores (g-VAS) Among the Dentin-Desensitizing Agents*[a]

Dentin Hypersensitivity Scores as g-VAS	Teethmate	Clinpro WV	Shield Force Plus	Gluma
Baseline (g)				
Mean (SD)	28.57 (11.95) A	30.83 (18.57) A	40.0 (20.15) A	32.26 (20.28) A
Median (min-max)	30.0 (10-40)	30.0 (10-80)	30.0 (10-80)	30.0 (10-80)
Immediately after application (IM)				
Mean (SD)	14.76 (10.7)	14.03 (13.82)	14.20 (11.99)	11.61 (14.39)
Median (min-max)	10.0 (0-40)	10.00 (0-60)	10.0 (0-40)	10.0 (0-50)
p (IM/BL)	<0.01* B	<0.01* B	<0.001* B	<0.001* B
1 d after application				
Mean (SD)	10.95 (7.68)	21.81 (16.30)	17.42 (18.29)	10.97 (10.11)
Median (min-max)	10.0 (10-80)	20.0 (0-80)	10.0 (0-70)	10.0 (0-40)
p (1D/BL)	<0.01*Ba	<0.01* Bb	<0.001* Bab	<0.001*Ba
p (with TM)		<0.01**		
p (with Gluma)		<0.01**		
2 wk after application				
Mean (SD)	8.57 (9.10)	20.83 (19.62)	14.12 (12.92)	9.35 (7.71)
Median (min-max)	10.0 (0-30)	10.0 (0-70)	10.0 (0-50)	10.0 (0-20)
p (15D/BL)	<0.001* B	<0.05* B	<0.001* B	<0.001* B
4 wk after application				
Mean (SD)	10.48 (12.00)	16.53 (14.43)	16.06 (17.66)	8.71 (7.6)
Median (min-max)	10.0 (0-40)	10.0 (0-50)	10.0 (0-70)	10.0 (0-20)
p (30D/BL)	<0.01* B	<0.01* B	<0.001* B	<0.001* B

Abbreviation: VAS, visual analog scale.
[a] According to the Bonferroni test, in each column (each tested product), values with different uppercase letters indicate significant differences among different follow-up periods in the same groups (p<0.05), and in each row, values with different lowercase letters indicate significant differences (p<0.05) among different test groups. The mean difference is significant at the 0.05 level.
** Differences within the same DDA in each column.*
*** Differences among different DDAs in each row.*

shown in clinical trials that brushing teeth aggressively and improperly increases gingival recession.[68] Therefore, canines and premolars receive good oral hygiene but frequently exhibit dentin exposure on their cervical surfaces. For these reasons, canines and premolars are the teeth that most frequently develop DH. The incisors are the next most commonly affected after the canines and premolars.[60] In this study, subjects complained of DH in canines, premolars, and incisors (Table 3).

TD, one of the test agents used in this study, contains bioactive structural elements similar to those found in teeth; these include tetracalcium phosphate and dicalcium phosphate anhydrate. These components add to the structure of dentin to form a calcium phosphate–rich layer that decreases the permeability of dentin.[43,44] In this study, TD produced a dentin-desensitizing effect at all follow-up time points and by all evaluation criteria compared to baseline measurements ($p<0.01$) (Tables 5 through 8). A comparison of the DDAs showed that the dentin-desensitizing effect was weaker for TD than for CWV only with regard to evaporative air sensitivity scores and only immediately after application (compared to baseline, $p<0.05$). In contrast, immediately after application, TD produced dentin-desensitizing effects for tactile hypersensitivity (g and g-VAS scores) that were similar to those produced in the other groups. Then, at the one-day follow-up, the dentin-desensitizing effect was stronger for TD than for CWV with regard to tactile (both g and g-VAS scores) hypersensitivity ($p<0.05$). Moreover, at the end of the four-week follow-up period, the dentin-desensitizing effects of TD were stronger in terms of all evaluation criteria than those produced by the other agents. However, these differences were not significant ($p>0.05$)

In addition, according to the results of this study, the clinical dentin-desensitizing efficacy of TD began immediately after application and was maintained or increased throughout the four-week follow-up period. This may be due to the bioactive structural components of TD, which become incorporated into the structure of hydroxyapatite, thus strengthening the structure of the tooth.[69] In addition, in a long-term clinical study, TD produced a stronger DH-

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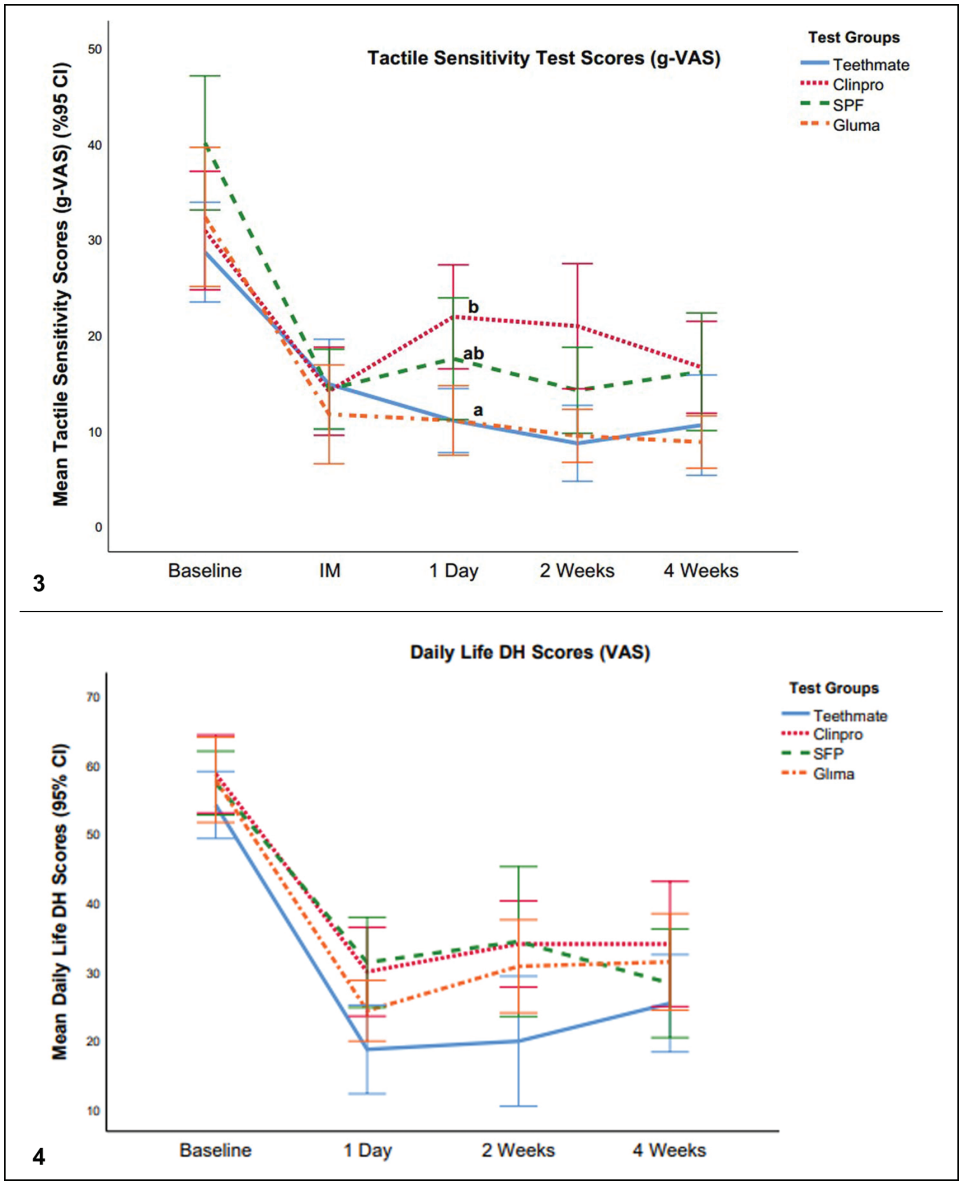


Figure 3. *According to the Bonferroni test, values with different lowercase letters indicate significant differences at the one-day follow-up among different test groups. According to the Bonferroni test, at the one-day follow-up period, Teethmate Desensitizer and Gluma showed significantly lower tactile hypersensitivity (g-VAS) scores than Clinpro WV (*p*<0.01).*

Figure 4. *According to the Bonferroni test, there was no statistically significant difference among the dentin-desensitizing agents (DDAs) at each follow-up period (*p*>0.05).*

reducing effect than was found for any other hydroxyapatite-forming desensitizing agent. According to the results of that study, the better performance of TD was attributed to its formulation, which may have allowed faster formation of hydroxyapatite crystallites and the highest rate of resistance to tubular occlusions.[45] In addition, according to a previous randomized clinical trial, TD produced a desensitizing effect similar to that of Gluma over a long-term evaluation period.[46] In another clinical study published in the literature, applying TD before bleaching reduced the sensitivity of dentin after the procedure.[70]

Fluoride-containing DDAs are the most commonly used agents in the treatment of DH. Fluoride has been reported to plug and possibly form calcium fluoride precipitates within dentin tubules.[15,38,39] While some studies have supported the clinical effectiveness of fluoride, several studies have reported that fluoride exerts limited effects.[71,72] CWV contains 5% sodium fluoride and tricalcium phosphate and releases calcium and fluoride ions. It has been reported that CWV obstructs open dentin tubules under *in vitro* conditions.[40,73] However, there are not enough data about its clinical efficacy in the literature. In this study, CWV produced dentin-desensitizing effects compared to baseline measurements at all time points throughout the four-week follow-up period. The hypersensitivity scores for CWV were statistically similar between

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Table 8: *Daily Life Dentin Hypersensitivity (DH) Tooth-Based Median Scores (VAS) Among the Dentin-Desensitizing Agents*[a]

Daily Life DH scores	Teethmate	Clinpro WV	Shield Force Plus	Gluma
Baseline (VAS)				
Mean (SD)	53.3 (10.64) A	58.61 (16.75) A	57.27 (13.05) A	57.74 (16.87) A
Median (min-max)	50.0 (40-70)	60.0 (40-80)	60.0 (40-80)	50.0 (40-80)
1 d after application				
Mean (SD)	18.57 (20.0)	29.86 (19.10)	31.21 (18.50)	24.19 (12.04)
Median (min-max)	20.0 (0-60)	30.0 (0-60)	20.0 (10-70)	20.0 (0-80)
p (1D/BL)	<0.001 B	<0.001 B	<0.001 B	<0.001 B
2 wk after application				
Mean (SD)	19.76 (20.76)	33.89 (18.55)	34.24 (30.69)	30.65 (18.42)
Median (min-max)	10.0 (0-70)	45.0 (0-50)	30.0 (0-80)	30.0 (0-80)
p (15D/BL)	<0.001 B	<0.001 B	<0.001 B	<0.001 B
4 wk after application				
Mean (SD)	18.57 (22.86)	33.89 (26.86)	28.18 (22.28)	31.29 (20.36)
Median (min-max)	10.0 (0-80)	30.0 (0-80)	30.0 (0-70)	30.0 (0-80)
p (30D/BL)	<0.001 B	<0.001 B	<0.001 B	<0.001 B

Abbreviation: VAS, visual analog scale.
[a] *According to the Bonferroni test, in each column (each tested product), values with different letters indicate significant differences among different follow-up periods in the same groups* ($p<0.05$).

baseline and the one-day follow-up when based on tactile (g) stimulus scores ($p>0.01$). In addition, compared to the other DDAs, CWV produced the lowest VAS scores (mean 10.0) in terms of evaporative air application immediately after application ($p<0.05$). In contrast, at the one-day follow-up, the CWV group reported higher tactile hypersensitivity (g and VAS) than was found in the TD group, but there was no difference in evaporative air application measurements ($p<0.05$). At the other follow-up time points (after two and four weeks), there was no significant difference among the groups ($p>0.05$). In an *in vitro* study, it was reported that the dentin tubule–plugging efficiency of CWV was good, but its adhesion to the dentin surface was not satisfactory immediately after application.[73] However, it has also been reported that calcium release by CWV is not good enough for the first 24 hours but increases significantly after 48 hours.[74] This may explain why the tubule-plugging activity of CWV may not be good enough after 24 hours.

Shield Force Plus is a light-curing DDA that plugs dentin tubules with different resin monomers when used according to the manufacturer's instructions. In this study, Shield Force Plus efficiently reduced DH at all follow-up time points compared to baseline data. Immediately after application, compared to the other DDAs, Shield Force Plus produced weaker DH-reducing effects than CWV did with regard to evaporative air hypersensitivity ($p<0.05$). However, Shield Force Plus produced a dentin-desensitizing effect similar to that of CWV in terms of tactile sensitivity (g and g-VAS). In contrast, at the one-day follow-up, the Shield Force Plus group reported more tactile sensitivity (g) than the TD group reported ($p<0.05$) (Table 6), but this difference was not reflected in the g-VAS scores. At the other evaluation time points (two and four weeks), there was no difference among the test groups ($p>0.05$).

In an *in vitro* study, Shield Force Plus was applied to the dentin surface, and the subjects were then treated with citric acid daily. Increased calcium release from the dentin structure was reported after three days and was attributed to deterioration of the structure due to water absorption over time caused by 2-hydroxyethyl methacrylate content. The finding that Shield Force Plus was resistant to citric acid for two days is important to its dentin-desensitizing efficiency. In that study, a comparison was made between Shield Force Plus and adhesive agents that can bind to tooth tissues more strongly.[75] We found only one study in the literature on the clinical effectiveness of Shield Force Plus. In that clinical study, it was reported that there was no difference among Shield Force Plus, Gluma, Colgate Sensitive Pro-Relief, and Biorepair Oral Care in terms of dentin-desensitizing effectiveness.[76]

Gluma Desensitizer has been shown to have dentin tubule–plugging activity in *in vitro* studies and a successful dentin-desensitizing effect in clinical studies.[46,52,53] In the present study, Gluma produced dentin-desensitizing effects at all follow-

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up time points compared to baseline. A comparison with other agents showed that Gluma had lower DH-removal efficacy than CWV did only in terms of evaporative air application and only immediately after application ($p<0.05$). Gluma and the other DDAs showed similar efficacy with regard to tactile sensitivity (g and g-VAS) immediately after application.

In this study, we evaluated the dentin-desensitizing effects of four different DDAs using different DH stimuli (evaporative air stimulus and tactile hypersensitivity). It has been recommended that at least two hydrodynamic stimuli should be used to evaluate DH and that DH can be changed in different ways by different stimuli.[3,4,77] Tactile, cold, and evaporative air stimuli are physiological and easy controllable, and they reliably provoke the pain associated with dentin hypersensitivity.[3,77] Therefore, these stimuli are used most frequently and are widely recommended.[27,54,78] The combined use of evaporative and tactile stimuli provides a more accurate result, and these combinations are therefore recommended for DH evaluation.[54] An evaporative air stimulus is applied directly toward the exposed dentin surface with an air syringe that delivers a stream of air and is one of the most often used stimuli.[27,54,79,80]

In addition, it has been recommended that daily life hypersensitivity should be evaluated after DDA application.[3,81] Therefore, we evaluated alterations in daily life hypersensitivity without any stimulant and found that all DDAs reduced daily life hypersensitivity throughout the study.

In this study, the VAS was used to measure evaporative air stimuli, daily life hypersensitivity, and tactile hypersensitivity. To perform the VAS, a mark is traced on a 10-cm line labeled from "no pain" to "intolerable pain," and this makes it easy to statistically evaluate and compare data[39,82] because the VAS can be modified to quantify the pain response, allowing objective and quantitative analyses.[54]

In addition to the VAS, the Yeaple probe was used for the measurement of tactile sensitivity because it can be used to apply a known force to the dentin surface, with pressure beginning at 10 g and increasing in 10 g increments. The tactile threshold (g) is the maximum force that can be applied without the subject reporting pain or discomfort (a greater tactile threshold indicates a less hypersensitive the tooth).[83] Tactile sensitivity tests performed with a Yeaple probe produce more quantitative data when diagnosing and evaluating the efficiency of DDAs. Therefore, we evaluated Yeaple probe scores in g and VAS scores to digitize and objectivize tactile hypersensitivity.

According to the results of this study, recording different parameters produced different DH scores. For example, according to the evaporative air stimulus test, immediately after application, CWV had the lowest VAS scores among the groups; however, the tactile hypersensitivity scores for CWV were similar to those of the other groups. Moreover, one day after application, the TD group exhibited the lowest tactile sensitivity, but there was no significant difference among the groups according to the evaporative air stimulus. Similar results were found at other time points, including the two- and four-week follow-ups. Therefore, short-term follow-up, such as immediately after and one day after application, may not be very suitable for obtaining consistent results within limitations such as those of this study. Hence, longer follow-up periods could produce more consistent results.

In this study, we evaluated the effects of DDAs for four weeks. While this period is not a long follow-up period, it is also not too short. In our opinion, a DH-reducing effect that occurs or is maintained over four weeks could be an acceptable time frame with regard to creating a relieving effect in a patient who is experiencing DH. Performing DDA reapplication at four-week intervals would not be very burdensome when compared to enduring pain at any given moment every day. However, in clinical practice, long-term follow-up studies will be needed to show the long-term DH-reducing effects of these agents.

DH is also associated with psychological and emotional effects that may affect patient pain levels. However, evaluating DH levels over time is a difficult task because natural desensitization and placebo effects may confound or overlap, affecting clinical findings due to the apposition of peritubular and tertiary dentin.[46,84] In the protocol used in this study, placebo control could not be used due to a lack of ethical approval. Gluma was used instead of placebo and compared with DDAs.[46]

During the process of treating DH, exposure to predisposing factors may also affect the DH level. It is therefore important to evaluate and eliminate predisposing factors to achieve effective and long-term results in DH treatment.[54]

DDAs are minimally invasive and highly tolerable treatment options for DH patients. Since the nature of DH is multivariable and subjective, new studies

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that are more homogeneous and that consider predisposing factors are recommended and may achieve more consistent and reliable results. In addition, in the future, new studies with longer follow-up periods and larger sample sizes will be useful for determining the long-term clinical effectiveness of these agents.

CONCLUSIONS

Compared to baseline, at follow-ups performed immediately after application and two and four weeks later, TD, CWV, Shield Force Plus, and Gluma produced a DH-reducing effect according to all the evaluation criteria (evaporative air hypersensitivity, tactile sensitivity, and daily life hypersensitivity). Only CWV had tactile sensitivity (g) scores that were similar at baseline and the one-day follow-up. However, CWV produced efficient results according to the other evaluation criteria (evaporative air hypersensitivity, daily life hypersensitivity, and tactile sensitivity [g-VAS]).

A comparison of DH-reducing effects among the DDAs evaluated in this study revealed that these agents yielded different results immediately after application and at the one-day follow-up period according to different evaluation parameters. However, all four DDAs produced similar DH-reducing efficacy at the two- and four-week follow-ups. The DDA groups had different scores according to which evaluation parameter was used. In addition, there were inconsistencies in the scores for the DDAs between early and later periods. Finally, in the future, new studies with larger sample sizes and longer follow-up periods would be useful for determining the long-term clinical effectiveness of these agents.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the Karadeniz Technical University, School of Medicine. The approval code issued for this study is 2014/150.

Conflict of Interest

The authors of this article certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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