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ORIGINAL ARTICLE

Instant dentin hypersensitivity relief of a single topical application of an in-office desensitizing paste containing 8% arginine and calcium carbonate: A split-mouth, randomized-controlled study

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Abstract

Objective. The aim of this study was to evaluate the clinical efficacy of an in-office desensitizing paste containing 8% arginine and calcium carbonate relative to calcium carbonate alone in the reduction of dentin hypersensitivity in a randomized, double-blind, split-mouth clinical trial. ***Materials and methods.*** Sixty teeth (30 subjects) with an air blast hypersensitivity score of 2 or 3 (Schiff Cold Air Sensitivity Scale) were randomly assigned to one of two treatment groups: (1) test paste containing 8% arginine and calcium carbonate (elmex sensitive professional desensitizing paste) and (2) control paste: paris white (calcium carbonate). Tactile and air blast dentin hypersensitivity examinations were performed at baseline, immediately after paste application and 4 and 12 weeks later. ***Results.*** A statistically significant difference in air blast ($p = 0.001$) and tactile ($p = 0.047$) hypersensitivity reduction over time was observed between the two therapy modes. After 12-weeks, statistically significant differences were indicated between the test and control group with respect to baseline-adjusted mean tactile (41.94%; $p = 0.038$) and air blast hypersensitivity scores (46.5%; $p = 0.017$). ***Conclusions.*** The tested in-office desensitizing paste containing 8.0% arginine and calcium carbonate provides significantly greater hypersensitivity relief compared to calcium carbonate alone.

Key Words: *dentin hypersensitivity, desensitizing agents, hyperesthesia*

Introduction

Dentin hypersensitivity (DH) has been defined as a short, sharp pain arising from exposed dentin in response to thermal, tactile, osmotic or chemical stimuli and which cannot be ascribed to any other dental defect or pathology [1,2]. Some research has placed the incidence of DH as high as 74% [1], but in most populations it appears to range between 10–30%, depending on the population studied, study setting and study design [3,4]. The condition is dependent on dentin exposure and the patency of dentinal tubules [5]. Gingival recession, resulting from abrasive tooth brushing or periodontal disease, is the primary route for which the underlying dentin becomes exposed [6] and dietary acids as well as extensive root debridement are the major reasons for loss of cementum. Therefore, among periodontal patients, the prevalence of root sensitivity has been reported to be up to 98% [7].

The theory of hydrodynamic transmission proposed by Brännström [8] is generally accepted for pain generation: an external stimulus provokes a movement in the dentin fluid, which in turn triggers nerve endings within the pulp. Products for the management of dentin hypersensitivity typically aim to control the hydrodynamic mechanisms of pain [9]. Approaches to control the condition fall into two broad categories: agents or products that reduce fluid flow within the dentin tubules by occluding the tubules themselves, thereby blocking the stimuli, and those that interrupt the neural response to stimuli [9].

A novel dentin hypersensitivity treatment technology, consisting of 8% arginine and calcium carbonate, mimics the natural process of plugging patent dentin tubules. When applied to exposed dentin, the

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open dentin tubules are sealed with a plug that contains arginine, calcium, phosphate and carbonate [10]. In contrast, no dentin occlusion was observed with calcium carbonate alone [10]. Four 8-week clinical studies have shown that the arginine-containing toothpaste provided highly significant DH reductions after 2, 4 and 8-weeks of daily product use [11–14]. Four further clinical studies have shown that a single in-office application resulted in instant relief of DH and that the relief was maintained with subsequent twice-daily at-home brushing [15–19]. Preferably, a desensitizing in-office product should result in instant relief of DH and the relief should be maintained without further interventions. Therefore, this randomized controlled, double-blind, split-mouth clinical trial evaluated the clinical efficacy of the desensitizing paste containing 8% arginine and calcium carbonate on DH relief after a single professional application without further at-home brushing, as compared to calcium carbonate alone.

Materials and methods

Ethical considerations

The Ethics Committee of Innsbruck Medical University, Austria, approved the study. The study was conducted in accordance with the Helsinki Declaration of 1975 and as revised in 2000. All subjects signed informed written consent prior to the study enrolment.

Study subjects

Thirty subjects (aged 18–80 years) from the Department of Operative Dentistry, Innsbruck Medical University were enrolled in the study. They were required to possess a minimum of two hypersensitive teeth in two different quadrants which demonstrated cervical erosion/abrasion or gingival recession and for which an air blast stimuli score of 2 or 3 (Schiff Cold Air Sensitivity Scale; SCASS) was presented at the baseline examination. Any teeth with cracked enamel, caries, mobility greater than one or extensive/defective restorations, teeth used as abutments and teeth with orthodontic appliances were excluded. Additional exclusion criteria were: subjects with gross oral pathology, chronic disease, advanced periodontal disease, periodontal or orthodontic treatment (within the last 6 months), eating disorders, excessive exposure to acids, pregnant or lactating women, current users of anti-convulsants, antihistamines, antidepressants, sedatives, tranquilizers, anti-inflammatory drugs or daily analgesics, as well as subjects who used a desensitizing dentifrice within the last 3 months or with a history of allergy to oral care/personal care consumer products or their ingredients.

Clinical interventions

Study subjects were instructed to refrain from all oral hygiene procedures and chewing gum for 8 h and from eating and drinking for 4 h prior to examinations. At baseline, one investigator (I.K.) selected two hypersensitive teeth in two different quadrants with SCASS 2 or 3. After clinical evaluation and randomization, the same investigator applied the test and control pastes to the selected teeth. Baseline and follow-up examinations were done by a blinded investigator (C.P.).

Air blast hypersensitivity. The test and control teeth were isolated from the adjacent teeth by the placement of red boxing wax. Air was delivered from a standard dental unit air syringe at maximal pressure (45 psi) and at an environmental temperature of 19–24°C. The air current was applied for 1 s at a distance of 1 cm and perpendicular to the buccal surface of the tooth. The Schiff Cold Air Sensitivity Scale (SCASS) was used to assess subject response to this stimulus. The scale is scored as follows: 0 = subject does not respond to the stimulus; 1 = subject does not respond to the stimulus, but considers stimulus to be painful; 2 = subject responds to air stimulus and moves from the stimulus; 3 = subject responds to air stimulus, moves from the stimulus and requests immediate discontinuation of the stimulus [9]. Patients were informed before testing about the different score levels.

Tactile hypersensitivity. Tactile hypersensitivity was assessed by scratching on the dentinal surface with a sharp-tipped probe and a maximum pressure of 70 g. The subjects scored pain intensity on a visual analogue scale (VAS) (0 = no pain and 10 = extreme, unbearable pain). Patients were instructed to point to the VAS.

Qualifying teeth were randomly assigned to the study treatments by tossing a coin. Control and test teeth were polished with their assigned paste for 10 s using a disposable prophylaxis angle (I.K.):

- Test paste: Desensitizing paste containing 8% arginine and calcium carbonate (elmex sensitive professional desensitizing paste, GABA Gmbh, Lörrach, Germany).
- Negative control paste: calcium carbonate (paris white).

The test and control pastes were carefully rinsed after 30 s without contamination of the contralateral tooth.

Tactile and air blast dentin hypersensitivity examinations, as well as oral soft and hard tissue assessments, were performed immediately and 4 and 12-weeks later following the same methodology

employed at the baseline examinations (blinded investigator C.P.). All subjects received a fluoride-free toothpaste (Paradontax Classic GlaxoSmithKline, Middlesex, UK) and a toothbrush (Oral-B Indicator 30 Toothbrush, Procter and Gamble, Schwalbach am Taunus, Germany) and were instructed in modified BASS-technique.

Statistical methods

The main focus of the statistical analysis was the difference in change rates (VAS and SCASS) between the test and the control group. Thus, power analysis was done for a group-by-time interaction in a repeated measure analysis of variance with two groups and four assessment time points. A sample of 60 teeth (30 per group) assessed at four time points is sufficient to detect a group-by-time interaction with an effect size of $F = 0.15$ in a repeated measure analysis of variance ($\alpha = 0.05$, $\beta = 0.20$, correlation between assessments $r = 0.5$, and non-sphericity correction $e = 1$). For each time-point and group, the percentage change was calculated as follows: follow-up mean (post-application, 4-weeks or 12 weeks) relative to the baseline mean. A positive value indicates an improvement in air blast/tactile hypersensitivity. The percentage difference between test and control treatment was calculated as follows: difference between test and control mean expressed as a percentage of the baseline mean for the control paste. A positive value indicates an improvement in hypersensitivity for the test paste relative to the control paste. Comparisons of the treatment groups were performed using paired *t*-test. Within-treatment comparisons of the baseline vs follow-up scores were performed using paired *t*-tests. All statistical tests of hypotheses were 2-sided and employed a level of significance of $\alpha = 0.05$.

Results

Subject characteristics and baseline data

Subjects' demographic background is presented in Table I. Thirty subjects were included at baseline, after 4-weeks one subject dropped out due to periodontal treatment during the study period. Therefore, 29 subjects (21 females, eight males) completed the study. All participants were Caucasians, aged 18–78 years, mean age (SD) was 47.13 (14.05) years.

Table I. Subjects' demographic background and smoking habit.

	Subjects ($n = 29$)
Mean age (SD), years	47.1 (14.1)
Gender	
Male, *n* (%)	8 (27.6%)
Female, *n* (%)	21 (72.4%)
Smoking	
non-smokers, *n* (%)	23 (79.3%)
smokers, *n* (%)	6 (20.7%)

Baseline data

The mean tactile and air blast hypersensitivity scores measured at the baseline examination for those subjects who completed the clinical study are shown in Table II. No statistically significant difference was indicated between the treatment groups with respect to either hypersensitivity score at baseline.

Treatment effect: Air blast hypersensitivity

Comparisons versus baseline. For the test paste, a percentage change of 50% was measured instantly after product application ($p < 0.001$) as compared to 13.3% for the control paste ($p = 0.022$). After 4 weeks, the percentage changes were 47.5% for the test teeth ($p < 0.001$) and 13.3% for the control teeth ($p = 0.085$). After 12 weeks, the percentage changes were 61.2% for the test group ($p < 0.001$) and 22.7% for the control group ($p = 0.006$) (Table II).

Comparison between treatment groups. A statistically significant difference in air blast hypersensitivity reduction over time was observed between the two therapy modes ($p = 0.001$) (Figure 1, Table II).

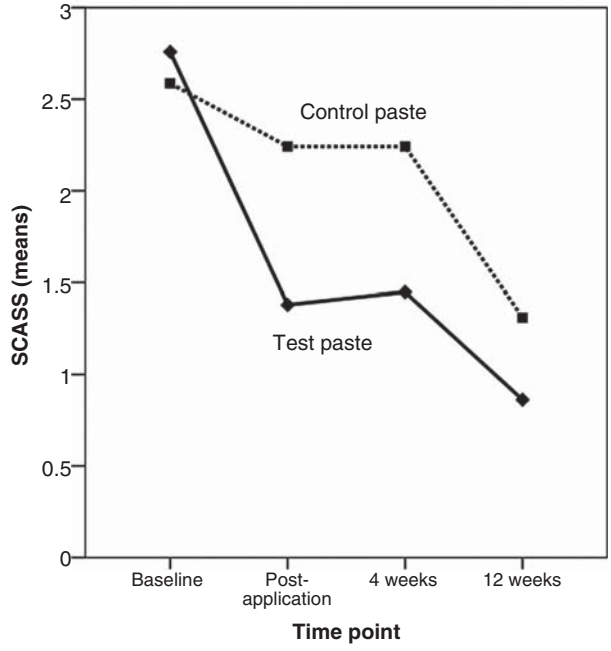

Figure 1. Relationship of time to treatment and air blast hypersensitivity. Schiff Cold Air Sensitivity Scale (SCASS) scored as follows: 0 = subject does not respond to the stimulus; 1 = subject does not respond to the stimulus, but considers stimulus to be painful; 2 = subject responds to air stimulus and moves from the stimulus; 3 = subject responds to air stimulus, moves from the stimulus and requests immediate discontinuation of the stimulus.

Table II. Summary of the tactile hypersensitivity and air blast hypersensitivity mean scores for subjects who completed the 12-week clinical trial (n = 29).

	Baseline	Post-application	4-weeks	12-weeks	p-value[d]
Air blast hypersensitivity (SCASS)					$p = 0.001$
Test paste[a]					
mean ± SD	2.8 ± 0.4	1.4 ± 0.8	1.4 ± 0.8	0.9 ± 1.0	
percentage change[b], %	—	50.0	47.5	68.9	
Control paste[c]					
mean ± SD	2.6 ± 0.7	2.2 ± 0.7	2.2 ± 0.8	1.3 ± 1.2	
percentage change[b], %	—	13.3	13.3	51.7	
Tactile hypersensitivity (VAS)					$p = 0.047$
Test paste[a]					
mean ± SD	2.9 ± 2.8	1.7 ± 2.0	1.5 ± 1.9	1.2 ± 1.3	
percentage change[b], %	—	43.5	49.4	56.1	
Control paste[c]					
mean ± SD	2.3 ± 2.2	1.8 ± 1.8	2.4 ± 2.6	2.2 ± 1.9	
percentage change[b], %	—	23.5	4.4	5.6	

n, number; VAS, visual analogue scale; SD, standard deviation.
[a] Desensitizing paste containing 8% arginine and calcium carbonate.
[b] Percentage change: follow-up mean (post application, 4-weeks, 12-weeks) relative to the baseline mean. A positive value indicates an improvement in air blast/tactile hypersensitivity.
[c] Calcium carbonate (paris white).
[d] Interaction between time and treatment: repeated measures ANOVA (Huynh-Feldt correction).

Instant post-application, the comparison of treatment groups revealed a 38.5% difference between test and control teeth ($p < 0.001$). After 4 weeks, the test teeth exhibited a 61.8% improvement ($p = 0.002$) and after 12 weeks a 46.5% improvement in air blast hypersensitivity scores when compared with the control teeth ($p = 0.017$).

Treatment effect: Tactile hypersensitivity

Comparisons versus baseline. For the test paste, a percentage change of 43.5% was measured instantly after product application ($p < 0.001$) as compared to 23.5% for the control paste ($p = 0.069$). After 4 weeks, the percentage changes were 49.4% for the test teeth ($p < 0.001$) and 4.4% for the control teeth ($p = 0.085$). After 12-weeks, there was a 56.1% improvement compared to baseline for the test group ($p = 0.004$) and a 5.6% improvement for the control group ($p = 0.692$) (Table II).

Comparison between treatment groups. A statistically significant difference in tactile hypersensitivity reduction over time was observed between the two therapy modes ($p = 0.047$) (Figure 2, Table II). Instant post-application, the comparison of treatment groups revealed a 39.4% difference between test and control teeth ($p = 0.774$). After 4 weeks, the test group exhibited a 39.4% improvement ($p = 0.112$) and after 12 weeks a 41.9% improvement in tactile hypersensitivity scores when compared with the control group ($p = 0.038$).

Discussion

DH is a problem that plagues many patients. In the majority of cases DH is chronic and recurring due to a given action, e.g. drinking cold beverages, eating hot

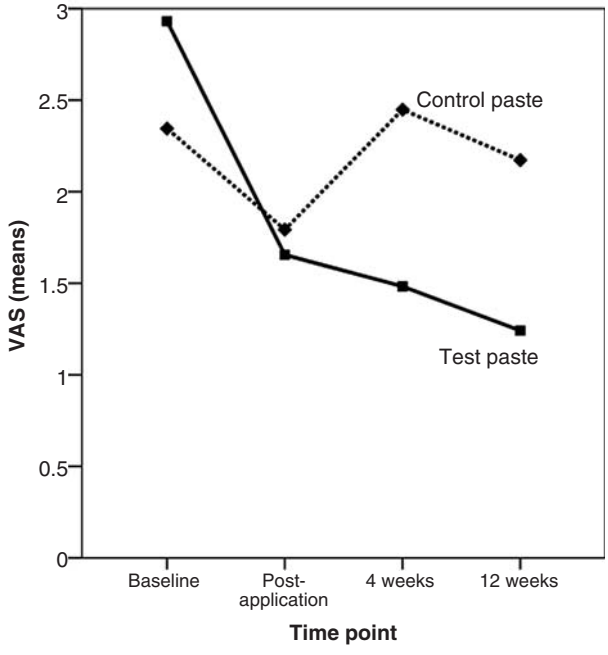

Figure 2. Relationship of time to treatment and tactile hypersensitivity. Visual analogue scale scored as follows: 0 = no pain and 10 = extreme, unbearable pain.

foods, breathing in and out. Products and techniques used for treatment of DH are diverse, suggesting uncertainty among dentists about the best way to treat patients, as well as dissatisfaction with outcomes of available treatments [4]. The development of a therapy that can provide both immediate relief following professional application and a lasting desensitizing effect for a significant time period after use would be of great assistance to clinicians in dealing with DH [9].

Thirty subjects with a history of DH were enrolled in this split-mouth, randomized-controlled study. Before paste application, tactile and air blast hypersensitivity scores were recorded through the patient's verbal report for all teeth included in the trial. DH was re-evaluated immediately after paste application and after 4- and 12-weeks. Verbal reports are known to be shaped by a variety of psychosocial variables. Additionally, pain is not a simple sensory state but is influenced by cultural learning, the meaning of the situation, attention and other psychological variables [21]. Therefore, to overcome inter-individual differences between test and control patients, we investigated the in-office paste in a split-mouth clinical trial. We followed the guidelines for design and conduct of clinical trials on DH [5].

The essential components of the tested in-office desensitizing paste are arginine (an amino acid), bicarbonate (a pH buffer) and calcium carbonate (a source of calcium) [6]. This technology has been shown to physically plug and seal exposed dentin tubules *in vitro* [10]. The significant reduction in DH after a single topical application in the present study confirms the results of previous clinical studies [11–19]. When applying the air blast stimulus with a standard dental unit air syringe at maximal pressure to the test teeth before paste-application, all participants moved away from the stimulus or requested immediate discontinuation (SCASS 2 or 3). Immediately after paste-application, 21 participants did not respond the stimulus anymore (SCASS 0 or 1) ($p < 0.001$). In previous studies, the relief was maintained with subsequent twice-daily at-home brushing [15–18]. In the present study, the relief was maintained without further application of arginine for 12 weeks (Figure 1). In the present study, the reduction of tactile stimulated hypersensitivity was much lower than previously reported [11–19]. These differences are caused by low baseline scores for tactile hypersensitivity in the present study. Many participants did not respond to tactile hypersensitivity stimulation, even if air blast stimulation reached the highest score.

Single application of the control paste (calcium carbonate) also resulted in improvement of DH and this improvement was also maintained over 12 weeks in the present study. This is amazing, as, *in vitro*, no occlusion of dentin tubules was observed when calcium carbonate was applied to the dentin surface [10]. *In vivo*, saliva of caries-free adults contains 8.98–42.7 nM/mL arginine [20], which might play a critical role in reducing DH when calcium carbonate is applied. Additionally, abrasives like calcium carbonate have been reported to cause obliteration of the tubules by the abrasive or by the formation of a smear layer during brushing/polishing 22. Nevertheless, statistically significant differences in tactile and air blast hypersensitivity reduction were observed between the two therapy modes ($p < 0.05$). After 4 weeks, there was an additional reduction in DH in test and control teeth. All participants were provided a fluoride-free toothpaste at baseline. After 4 weeks, 12 participants complained about the flavour of the toothpaste and six participants reported a burning mouth after tooth brushing. Therefore, the fluoride-free toothpaste was substituted by a fluoride-containing toothpaste, which might explain the further reduction in DH.

The in-office desensitizing paste containing 8% arginine and calcium carbonate provides a statistically significant reduction in dentin hypersensitivity instantly after a single professional application of the product and this reduction is maintained for 12 weeks without further application of arginine.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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