

## Short-term Efficacy of Agents containing $KNO_3$ or CPP-ACP in Treatment of Dentin Hypersensitivity

Adalaiti MAHESUTI<sup>1</sup>, Yin ling DUAN<sup>2</sup>, Ge WANG<sup>2</sup>, Xiang Rong CHENG<sup>2</sup>, Bruce A MATIS<sup>3</sup>

**Objective:** To evaluate the short-term efficacy of agents containing  $KNO_3$  or casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) in the treatment of dentin hypersensitivity.

**Methods:** UltraEZ, containing  $KNO_3$  and MI Paste, containing CPP-ACP were applied in this study. The dentin hypersensitivity of 102 subjects was established by a tactile stimulus with a Yeaple pressure probe, and the degree of hypersensitivity was measured using a visual analogue scale (VAS). The patients were divided into four groups: A, B, C and D, using a random number table. UltraEZ, a placebo of UltraEZ, MI Paste, and a placebo of MI Paste were applied to group A, B, C and D respectively for 2 weeks. Dentin hypersensitivity was measured using VAS before the treatment (baseline), on day 2, 7, and 14 during the treatment, and on day 30 and 60 posttreatment.

**Results:** The efficacy of UltraEZ on dentin hypersensitivity was significantly better than that of the corresponding placebo group on day 7 during the treatment, whereas the efficacy of MI Paste exhibited better than that of the placebo group on day 14 during the treatment. However, there were no differences between the efficacy of the two agents on day 14 during the treatment, day 30 or day 60 posttreatment.

**Conclusion:** Both UltraEZ and MI Paste had a significant effect on dentin hypersensitivity. UltraEZ showed quicker effects than MI Paste, but MI Paste had a greater sustained action after treatment than UltraEZ.

**Key words:** tooth sensitivity, amorphous calcium phosphate, potassium nitrate, fluoride, desensitising agents

Dentin hypersensitivity is one of the most commonly encountered dental complaints, affecting between 8 and 30% of the adult dentate population<sup>1</sup>. Hypersensitivity is associated with the exposure of dentin and is characterised by short sharp pain that varies between people in response to thermal, evaporative, tactile, chemical or osmotic stimuli, and which cannot be ascribed to any other form of dental defect or pathology<sup>2,3</sup>.

Abrasion, attrition, erosion, gingival recession, tooth-whitening procedures and direct and indirect restorations contribute to the loss of enamel and cementum, exposing dentinal tubules to the oral environment<sup>4</sup>. When thermal, osmotic, and mechanical stimuli (such as tooth brushing, sweet and sour foods or hot and cold water) are applied to exposed dentin, the patient feels a short sharp pain, or dentin hypersensitivity.

The treatment for dentin hypersensitivity is variable. Treatment methods include laser irradiation, iontophoresis, root coverage and desensitising agents, such as strontium chloride, potassium nitrate and formalin<sup>5-7</sup>. Although the exact mechanism underlying the desensitising agents is still not fully understood, it is thought that those agents act by one of the following mechanisms: blocking the dentinal tubules through coating; altering the tubular content through coagulation, protein precipitation or the creation of insoluble calcium complexes; or direct interference of sensory nerve activity.

1 The People's Hospital of the Xinjiang Uygur Autonomous Region North Hospital, Department of Stomatology, Urumqi, P.R. China.

2 Key Lab for Oral Biomedical Engineering of Ministry of Education, School and Hospital of Stomatology, Wuhan University, Wuhan, P.R. China.

3 Department of Restorative Dentistry, Indiana University School of Dentistry, Indianapolis, USA.

**Corresponding author:** Dr Ge WANG, Key Lab for Oral Biomedical Engineering of Ministry of Education, School and Hospital of Stomatology, Wuhan University, 237 Louyu Road, Wuhan 430079, P.R. China. Tel: 86-27-87218643; Fax: 86-27-87873260; E-mail: wanggeinus@aliyun.com



The effectiveness of the desensitising strategy reported in the literature is dependent on the research methodologies used. The two most important questions with regards to the desensitising agents are “Is it effective?” and “How long will it last after treatment?”.

Ultra EZ, as a desensitising agent, is claimed to be effective in treating dentin hypersensitivity. MI Paste, as a protective agent, is applied after tooth bleaching, preparation or orthodontic treatment to prevent enamel opaque spot or dentin hypersensitivity through remineralisation. Previous studies about the two agents on their desensitising effects are mostly laboratory investigations<sup>8-11</sup>. However, there may be inconformity between laboratory and clinical results because of biocomplexity. Thus, clinical trials are believed to be golden standard to evaluate effects of desensitising agents. The objective of the present study was to determine the clinical performance of the two agents in treating dentin hypersensitivity.

## Materials and methods

This study was a single-centre, placebo-controlled, randomised, and double-blinded, parallel-group design, with 102 subjects involved. No subjects dropped out over the course of the study. The study was designed according to the Guidelines for Good Clinical Practice (GCP)<sup>12</sup>, the World Medical Association Declaration of Helsinki and approved by the Institutional Review Board of Wuhan University. Each of the subjects was given verbal and written information regarding the study and signed an informed consent statement.

### Inclusion criteria

Subjects with the following criteria were recruited:

- Between the ages of 18 and 70 years.
- Presenting with at least two hypersensitive teeth that had a painful response, which could be elicited by a dental probe.
- A visual analogue scale (VAS) score at baseline of at least 3 for the sensitive tooth.

### Exclusion criteria

Subjects with any of the following conditions were excluded from the study:

- A history of allergy to any of the chemicals used in the study, such as potassium nitrate, calcium phosphate, milk protein, etc.
- The use of antibiotic, antimicrobial, analgesic medications, mouthwash or desensitising gel over the previous 2 months.

- A history of dentin hypersensitivity treatment within the past 2 years.
- Orthodontic treatment with a fixed appliance.
- The presence of any removable device, such as a removable partial denture or orthodontic retainer.
- The presence of any fixed appliance, large or defective restorations, cracked enamel or caries on the hypersensitive teeth. Smoking within the past 30 days.
- Pregnancy or lactating.

### Diagnosis and recruitment criteria

Dentin hypersensitivity was diagnosed by initially asking patients to rate their perception of sensitivity to hot and cold food and drink, sweet and sour food, tooth brushing, etc. Sensitive teeth were identified by the response to a tactile stimulus, which was performed with a Yeaple pressure probe (Yeaple Research) set at 50 g weight, drawn across the hypersensitive area.

The stimulus was applied to the teeth where the patients complained of sensitivity. The subjects were asked to record their perceived sensitivity on a 10 cm VAS, anchored at each end by the phrases “no pain” and “extreme pain”. The time that lapsed between any of the tests was no less than 5 min<sup>13</sup>. Only the teeth with a VAS score higher than 3 were diagnosed as dentin hypersensitivity. For each patient, the tooth with the highest VAS score was chosen as the test tooth.

### Fabrication of custom trays

The desensitising agents were delivered in trays. When a patient was accepted for the study, impressions were taken of their dental arch in which the test teeth were located. Approximately 0.5 to 1.0 mm of light-curing resin (Block-Out, Ultradent Products) was applied to the arch casts of each subject on the areas in which they experienced sensitivity. The resin was cured for about 1 min using a light-curing unit. A custom tray was made (Sof-Tray 0.035, Ultradent Products) according to the manufacturer’s instructions.

### Agent distribution

One hundred and two subjects were included and asked to return to the study centre within 4 weeks of the initial evaluation. The subjects were randomly divided into groups A, B, C or D, using a random number table. The random number of each subject was divided by 4. The subject with a remainder of 1 were placed into group A (n = 28), with a remainder of 2 into group B (n = 25), with a remainder of 3 into group C (n = 28) and 0 into group D

**Table 1** VAS Scores (mean ± SD) of dentin hypersensitivity

Group	Treatment (day)			Posttreatment (day)		
	Baseline	2	7	14	30	60
A	5.32 (1.91)	4.07 (2.31)	3.04 (1.75)	2.00 (1.68)	1.79 (1.60)	1.14 (1.11)
B	5.16 (1.70)	4.60 (2.38)	4.72 (2.15)	4.04 (2.01)	5.00 (0.28)	5.28 (1.75)
C	5.00 (1.33)	4.36 (1.76)	3.25 (1.83)	2.14 (1.63)	1.68 (1.52)	0.79 (1.07)
D	4.71 (1.52)	4.24 (1.87)	3.52 (1.50)	3.33 (1.32)	5.10 (1.08)	5.00 (1.27)

A: UltraEZ; B: placebo of UltraEZ; C: MI Paste; D: placebo of MI Paste

(n = 21). Subjects of different groups were asked to load different gels in the trays. UltraEZ (Ultradent Products) was applied in group A, placebo of UltraEZ in group B, MI Paste (GC America) in group C, and placebo of MI Paste in group D. The placebo of each agent was the same gel without the active agent. The operator who distributed the products instructed the subject and gave them a form, indicating what product was to be placed in the various areas of their trays and how to insert the trays intraorally. Neither the subjects nor the operator who performed the sensitivity exam were allowed to know the nature of their desensitising agent before the statistical results were tabulated. VAS scores were recorded and the subjects were taught how to use the materials and trays.

#### Experimental instructions

Before the study, three pilot cases were performed to optimise the amount of the gels and the time for sensitivity measurements.

The subjects were asked to follow these instructions for 14 days:

- Brush teeth thoroughly using non-desensitising toothpaste.
- Load gel in the custom tray, insert tray into mouth and remove excess gel that overflowed the tray.
- Leave the custom tray undisturbed in the mouth for 10 minutes.
- Remove the tray.
- Rinse any gel remaining in the mouth. No eating or drinking for 30 minutes following application. Clean the custom tray with a soft brush and cool tap water.

- Repeat twice a day, with one of the applications immediately before bedtime.

The subjects were informed to return to the clinic on day 2, 7, and 14 during the treatment, and on day 30 and 60 posttreatment.

To ensure objectivity, the database was “locked” to ensure evaluator blindness with regards to the desensitising agents, with the lock broken when the statistical analyses were performed. In order to avoid a possible influencing effect, the subjects were instructed not to change their usual oral hygiene habits, except for the use of the desensitising agents, during the study period. A questionnaire was used to check the patients’ compliance.

#### Statistical methods

A general linear model repeated measures analysis of variation (ANOVA), utilising SPSS 11.5 statistical software (SPSS base 11.5 for Windows, 2002, SPSS Inc), was performed. The confidence level was set at 95%. Post hoc analyses were undertaken to compare VAS scores between groups, as well as between times in each group.

#### Results

The mean VAS scores of the four groups at different times are displayed in Table 1. A two-factor mixed analysis was performed to investigate VAS scores as a function of time and group. The analysis revealed a significant main effect for the variable “group”

( $P = 0.000$ ), revealing that the VAS scores were significantly different for the four groups. The interaction of time and group was significant ( $P = 0.000$ ), too. When comparing between groups at different times, it showed that, on day 7 during the treatment, group A (UltraEZ) presented superiority to group B (Placebo of UltraEZ), whereas group C (MI Paste) presented superiority to group D (Placebo of MI Paste) on day 14 during the treatment.

With respect to the changes of VAS scores during the treatment, the Multivariate analysis showed that, a significant decrease of VAS scores happened as early as on day 2 in group A (UltraEZ); then the VAS score further decreased at each subsequent evaluation, except on day 30 post-treatment. As to Group C (MI Pastes), the significant decrease of VAS score presented on day 7, and lasted until the end of the study. As to group B (Placebo of UltraEZ), a significant decrease of VSA score was only observed on day 14 during the treatment. The VAS score of group D (Placebo of MI Paste) was reduced significantly on day 7 and 14.

On day 30 posttreatment, the VAS score of group A was still significantly lower than baseline, but not significantly different when compared with that of day 14 during treatment. The VAS score of group C on day 30 posttreatment was still significantly lower than that on day 14 during treatment. On day 30 and 60 post-treatment, the VSA scores of group A and C were still lower significantly than their baselines, the VAS scores of group B and D rebounded to their baseline.

## Discussion

The results of the present study showed that both UltraEZ, containing  $KNO_3$  and MI Paste containing CPP-ACP were effective in treating dentin hypersensitivity in our short-term observation. The current results agree with studies by Borges<sup>14</sup> and Touyz<sup>15</sup>, who demonstrated that both CPP-ACP and  $KNO_3$  reduce dentinal hypersensitivity, and by Browning<sup>16</sup>, who claimed that even a small percentage (0.5%) of potassium nitrate can significantly reduce dentin hypersensitivity. Many other studies also support the efficacy of the two agents<sup>17-22</sup>, except for studies by Prabhakar et al, who claimed that their preliminary data did not support the efficacy of MI Paste in reducing sensitivity<sup>23</sup>.

The unexpected efficacy of the placebos may result from two presumable causes. First, psychotherapy is efficient to dentin hypersensitivity. In the study of Pamir<sup>24</sup>, even distilled water as a placebo can be efficient. Second, there may be some special ingredient in the placebo gel that is efficient in treating dentin

hypersensitivity; or the gel itself can block the open dentin tubule temporarily, thus relieving sensitivity. In the study of Schiff<sup>25</sup>, sodium monofluorophosphate contributes to the prominent performance of the placebo.

There were no differences between the two agents in the present study with regards to treating dentin hypersensitivity. UltraEZ showed quicker results during treatment than MI Paste, whereas the latter performed better after treatment than the former. This difference may result from the different reactive mechanisms of the two agents. Potassium nitrate has an apparent analgesic or anaesthetic effect on nerve fibres by not allowing them to re-polarise after the initial depolarisation of the pain signal<sup>26</sup>. CPP-ACP, a water soluble extract of milk, can release Ca and P ions in the presence of acid. Normally, adding calcium and phosphate together will result in the formation of insoluble calcium phosphate crystals. But CPP can make the calcium and phosphate stay in a form that can actually penetrate into the tooth hard tissue, increasing the degree of saturation with respect to hydroxyapatite and preventing tooth hard tissue demineralisation while promoting remineralisation. The hydrodynamic theory, the most popular theory about dentin hypersensitivity, postulates that most pain-evoking stimuli increase the outward flow of fluid in the tubules. Some researchers found that dentin tubules are blocked because of remineralisation and hypersensitivity is decreased. The anesthetic effect on nerve fibers by  $KNO_3$  may happen earlier but CPP-ACP is effective as  $KNO_3$  after it blocks dentin tubules.

In view of the significant decline of the VAS score during the 2 weeks' treatment, it is deduced that the performance of the desensitising agents might become more prominent if the observation period was longer. As to MI Paste, it is supposed that the short-term efficacy is due to the colloidal particles blocking the dentin tubules, while remineralisation contributes to the long-term efficacy. There are no clear manufacturer's instructions regarding the duration of treatment for patients with dentin hypersensitivity with either MI Paste or UltraEZ. The instruction of MI Paste advises patients to apply the gel for 14 days after the bleaching treatment. A 14-day treatment period for both of the agents was chosen in the present study so as to be able to compare their efficacy. As evidenced by the data, the efficacy continued to increase throughout the 14 days of active treatment for both products. Therefore, patients can try to use the desensitising agents for a longer period of time, regardless of which agent they use. Further study on the course of treatment to achieve the best efficacy is necessary.

## Conclusions

The data from this study supports a significant short-term effect of KNO<sub>3</sub> and CPP-ACP in decreasing dentin hypersensitivity. UltraEZ showed quicker effects than MI Paste, but MI Paste had a greater sustained action after treatment than UltraEZ.

## References

1. Addy M. Etiology and clinical implications of dentine hypersensitivity. *Dent Clin North Am* 1990;34:503–514.
2. Addy M, Urquhart F. Dentine Hypersensitivity: its prevalence, aetiology and clinical management. *Dent Update* 1992;19:407–408.
3. Watlers PA. Dentine hypersensitivity: a review. *J Contemp Dent Pract* 2005;6:107–117.
4. Swift EJ Jr. Causes, prevention, and treatment of dentine hypersensitivity. *Compend Contin Educ Dent* 2004;25:95–106,109–110.
5. Graham L. Identifying, diagnosis, and treating dentine hypersensitivity. *Dent Today* 2005;24:72–73.
6. Pamir T, Özyazici M, Baloglu E, Onal B. The efficacy of three desensitising agents in treatment of dentin hypersensitivity. *J Clin Pharm Ther* 2005;30:73–76.
7. An J. The clinical effectiveness researches of four kinds of desensitising agents. *Int J Oral Sci* 2005;18:393–394.
8. Zorba YO, Erdemir A, Ercan E, et al. The effects of three different desensitising agents on the shear bond strength of composite resin bonding agents. *J Mech Behav Biomed Mater* 2010;3:399–404.
9. Wang X, Megert B, Hellwig E, Neuhaus KW, Lussi A. Preventing erosion with novel agents. *J Dent* 2011;39:163–170.
10. Comar LP, Souza BM, Gracindo LF, et al. Impact of experimental nano-hap pastes on bovine enamel and dentin submitted to a pH cycling model. *Braz Dent J* 2013;24:273–278.
11. Somasundaram P, Vimala N, Mandke LG. Protective potential of casein phosphopeptide amorphous calcium phosphate containing paste on enamel surface. *J Conserv Dent* 2013;16:152–156.
12. Zavras AI, Gypson B. High-quality research and patient care: an overview of clinical trials. *J Am Dent Assoc* 2000;31:1147–1155.
13. Haywood VB, Caughman WF, Frazier KB, et al. Tray delivery of potassium nitrate-fluoride to reduce bleaching sensitivity. *Quintessence Int* 2001;32:105–109.
14. Borges BC, de Vasconcelos AA, Cunha AG, et al. Preliminary clinical reports of a novel night-guard tooth bleaching technique modified by casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). *Eur J Esthet Dent* 2011;6:446–453.
15. Touyz LZ, Stern J. Hypersensitive dentinal pain attenuation with potassium nitrate. *Gen Dent* 1999;47:42–45.
16. Browning WD, Chan DC, Myers ML, et al. Comparison of traditional and low sensitivity whiteners. *Oper Dent* 2008;33:379–385.
17. Sowinski J, Ayad F, Petrone M, et al. Comparative investigations of the desensitising efficacy of a new dentifrice. *J Clin Periodontol* 2001;28:1032–1036.
18. Giniger M, Macdonald J, Ziemba S, et al. The clinical performance of professionally dispensed bleaching gel with added amorphous calcium phosphate. *J Am Dent Assoc* 2005;136:383–392.
19. Liu H, Hu D. Efficacy of a commercial dentifrice containing 2% strontium chloride and 5% potassium nitrate for dentin hypersensitivity: a 3-day clinical study in adults in China. *Clin Ther* 2012;34:614–622.
20. Ayad F, Berta R, De Vizio W, et al. Comparative efficacy of two dentifrices containing 5% potassium nitrate on dentinal sensitivity: a twelve-week clinical study. *J Clin Dent* 1994;5:97–101.
21. Leonard RH Jr, Smith LR, Garland GE, et al. Desensitizing agent efficacy during whitening in an at-risk population. *J Esthet Restor Dent* 2004;16:49–56.
22. Touyz LZ, Stern J. Hypersensitive dentinal pain attenuation with potassium nitrate. *Gen Dent* 1999;47:42–45.
23. Prabhakar AR, Manojkumar AJ, Basappa N. In vitro remineralization of enamel subsurface lesions and assessment of dentine tubule occlusion from NaF dentifrices with and without calcium. *J Indian Soc Pedod Prev Dent* 2013;31:29–35.
24. Pamir T, Dalgat H, Onal B. Clinical evaluation of three desensitizing agents in relieving dentin hypersensitivity. *Oper Dent* 2007;32:544–548.
25. Schiff T, Dos Santos M, Laffi S, et al. Efficacy of a dentifrice containing 5% potassium nitrate and 1500 PPM sodium monofluorophosphate in a precipitated calcium carbonate base on dentinal hypersensitivity. *J Clin Dent* 1998;9:22–25.
26. Peacock JM, Orchardson R. Action potential conduction block of nerves in vitro by potassium citrate, potassium tartrate and potassium oxalate. *J Clin Periodontol* 1999;26:33–37.