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Full Length Article

Exploratory randomised controlled clinical study to evaluate the comparative efficacy of two occluding toothpastes – a 5% calcium sodium phosphosilicate toothpaste and an 8% arginine/calcium carbonate toothpaste – for the longer-term relief of dentine hypersensitivity

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ABSTRACT

Objective: To compare the longer-term clinical efficacy of two occlusion-technology toothpastes — a 5% calcium sodium phosphosilicate (CSPS) toothpaste and a commercially available 8% arginine/calcium carbonate toothpaste — in relieving dentine hypersensitivity (DH). Efficacy was also compared with that of a regular fluoride toothpaste control.

Methods: This was an exploratory, randomised, examiner-blind, parallel-group, 11-week, controlled study in healthy adults with self-reported and clinically diagnosed DH. After an acclimatisation period, subjects were randomised to one of three study treatments with which they brushed their teeth twice daily. Sensitivity was assessed at baseline and after 1, 2, 4, 6 and 11 weeks treatment in response to evaporative (air) and tactile stimuli (measured by the Schiff Sensitivity Scale/visual analogue scale and tactile threshold, respectively).

Results: A total of 135 subjects were randomised to treatment. The two occlusion-technology toothpastes performed similarly over the 11-week treatment period. All study treatments showed statistically significant reductions from baseline in DH at all timepoints for all measures ($p < 0.05$). Statistically significant and clinically relevant sensitivity relief was observed for both occluding formulations compared with the regular fluoride toothpaste: for evaporative (air) sensitivity within 1 week and for tactile sensitivity at Week 11. No significant differences were detected between the two occluding formulations at any timepoint, for any endpoint. Study treatments were generally well tolerated.

Conclusions: In this exploratory study, a 5% CSPS occluding toothpaste was effective in relieving DH compared with a regular fluoride toothpaste; an 8% arginine/calcium carbonate anti-sensitivity toothpaste provided similar benefits. Improvements in DH continued throughout the 11-week study.

Clinical significance: Dentine hypersensitivity (DH) is a common and painful condition. Twice-daily use of a 5% calcium sodium phosphosilicate toothpaste reduces DH within 1–2 weeks of initiating use. Ongoing, twice daily use of the sensitivity toothpastes evaluated in this study was associated with continued, clinically significant improvements in DH.

1. Introduction

Gingival recession, or the gradual loss of enamel by tooth wear, can lead to exposed dentine and dentine hypersensitivity (DH) [1]. DH typically presents as a short, sharp pain in response to an external chemical, thermal, tactile or osmotic stimulus that cannot be ascribed to any other dental defect or disease [2–4]. According to the widely accepted hydrodynamic theory [5], DH arises when such a stimulus comes into contact with exposed dentine, causing movement of fluid within patent dentinal tubules. This movement is believed to stimulate nerve terminals at the pulpal end of the tubule, resulting in pain [6].

Based on this hypothesis, there are currently two accepted treatment approaches for DH: (i) direct diffusion of depolarising agents, such as potassium ions, to reduce intra-dental nerve

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activity [7,8]; and (ii) physical blockage of the open dentinal tubules with occluding agents. Agents employed in the latter approach include stannous, strontium or oxalate salts; arginine; silicas and bioactive glasses, all of which act by forming precipitates over the dentine surface and within the tubules, thereby reducing dentinal fluid movement and nerve activation in response to external stimuli [1,7–12].

Calcium sodium phosphosilicate (CSPS) is a particulate bioactive glass incorporated into oral care products for the treatment of DH [13]. Laboratory and clinical *in situ* studies have shown that CSPS binds preferentially to exposed dentine thereby physically occluding the tubules [14–18]. On exposure to the aqueous oral environment, CSPS undergoes a series of reactions that promote the formation of a hydroxycarbonate apatite-like layer on the dentine surface and within the tubules [10,15,19]. At least thirteen published clinical studies have shown that toothpaste formulations containing CSPS are effective for the treatment of DH [13,20–31], the majority of which used similar longitudinal clinical trial designs [3].

Toothpastes formulated with 8% arginine (an amino acid) and calcium carbonate (a source of calcium ions) have also been shown to provide relief from the pain of DH in similarly designed clinical studies [32–38]. *In vitro* studies report occlusion of dentinal tubules following treatment; the association of arginine and calcium carbonate is described as creating the alkaline conditions that encourage calcium and phosphate ions from saliva to deposit onto dentine [39–41].

As recommended by consensus guidelines [3], the clinical study design for testing dentifrice efficacy in the relief of DH assesses product performance after a period of use, typically after weeks, to allow sufficient time for product effectiveness to become apparent. Since these consensus guidelines were established in 1997, very few DH dentifrice studies that utilise longer treatment periods beyond 8 weeks have been published. For example, a recent systematic review and meta-analysis of clinical studies of desensitizing toothpaste versus placebo included only three studies of 12 weeks duration in its selected data set of 31 studies [42]. The remaining 28 studies were of 8 weeks duration or less. Of the three 12 week studies selected, two were published in the 1990s [43,44] and one in 2005 [45] and all evaluated dentifrice containing a nerve depolarisation technology, 5% potassium nitrate, not occlusion based dentifrice technologies.

The aim of this program of studies was therefore to evaluate and compare the efficacy of a toothpaste containing 5% CSPS and a commercially available anti-sensitivity toothpaste containing 8% arginine/calcium carbonate bushed twice daily over an extended treatment period and with frequent clinical assessments (1, 2, 4, 6 and 11 weeks).

A regular fluoride toothpaste with no known anti-sensitivity properties was included as a control. To the best of the authors' knowledge, no studies directly comparing the clinical DH efficacy of these two technologies (when administered as a daily use toothpaste) had been reported in the scientific literature at the time of conducting this study.

This study (Study 1) was exploratory in nature and was not formally powered to detect between-treatment differences, its main purpose being to inform the design of a second, formally powered pivotal study (Study 2, to be reported separately).

2. Materials and methods

2.1. Study design

This was an 11-week, single-centre, randomised, controlled, examiner-blind, three-treatment, parallel-group, exploratory study in healthy adult volunteers with self-reported and clinically diagnosed DH. The study was conducted at the School and Hospital of Stomatology, Wuhan University, Wuhan, PR China. It was approved by the university's independent ethics committee (IRB number ECB201107) before initiation and conducted in accordance with the Declaration of Helsinki.

Eligible subjects were required to attend the study site on seven occasions: screening, baseline, and 1, 2, 4, 6 and 11 weeks after the baseline visit. At the screening visit, each subject provided written informed consent to participate in the study. Demographic characteristics, medical history and use of concomitant medications were recorded and an oral soft tissue (OST) examination was completed. To determine eligibility, each subject's dentition was evaluated sequentially for evidence of erosion, abrasion or facial/cervical gingival recession (EAR); gingival health; tooth mobility; and sensitivity to an air-blast stimulus (as indicated by a 'yes' response when the subject was questioned about discomfort following stimulation [46]). Subjects with at least two eligible sensitive teeth were supplied with a regular fluoride toothpaste (Colgate® Strengthen Fresh containing 1400 ppm fluoride as sodium monofluorophosphate [SMFP]; Colgate-Palmolive [China] Co. Ltd, Guangzhou, China) to use twice daily (morning and evening) for a minimum of 4 weeks between the screening and baseline visits. The purpose of this acclimatisation period was to standardise oral hygiene habits in the study population.

At the baseline visit, subjects were assessed for continuing eligibility. Each was instructed in use of a visual analogue scale (VAS) and asked to complete a VAS training exercise. Following an OST examination, the sensitivity of all clinically eligible teeth identified at the screening visit was evaluated, first by the subject's response to a tactile stimulus (administered by a constant-pressure force-sensing Yeaple probe [47]), and then to an evaporative (air) stimulus (assessed by examiner-based Schiff sensitivity score [46] and a subject-completed VAS). There was a minimum of 5 min delay between the end of the tactile assessment and the start of the evaporative (air) assessment to allow the tooth to recover. From those teeth that met a qualifying tactile threshold of $\leq$20 g and had a Schiff sensitivity score $\geq$2, the investigator selected two 'test teeth' for each eligible subject to be assessed for the remainder of the study.

Eligible subjects were randomly assigned (1:1:1) to receive one of the three study toothpastes: (i) a toothpaste containing 5% (w/w) CSPS and 1450 ppm fluoride as SMFP (an experimental formulation at the time of the study, but later commercially available as Sensodyne® Repair & Protect, GSKCH); (ii) a commercially available anti-sensitivity toothpaste containing 8% (w/w) arginine, calcium carbonate and 1450 ppm fluoride as SMFP (UK Colgate® Sensitive Pro-Relief; Colgate-Palmolive Company, Guildford, Surrey, UK) or (iii) a regular fluoride toothpaste containing 1400 ppm fluoride as SMFP (Colgate Triple Protection; Colgate-Palmolive [China] Co. Ltd, Guangzhou, China) as a negative control. Details of all toothpaste ingredients are in Table 1.

Randomisation was stratified, based on the maximum baseline Schiff score (either 2 or 3) of the two selected test teeth. The randomisation schedule was computer generated by the Biostatistics Department of GSKCH; randomisation numbers within each stratum were allocated sequentially by site staff. Individuals who performed the efficacy assessments or who could have influenced the study outcomes were blinded to study treatment. The toothpastes evaluated in this study were completely over-wrapped to mask their identity, but it was not possible to fully blind study treatments. It is rarely possible to ensure identical appearance, taste and packaging for the products evaluated in oral care studies to achieve true double blinding. Maintenance of the blind was confirmed by inspection of product supplies returned by the subjects and by checking that the emergency-use randomisation list with individually masked treatment-allocation details had not been accessed.