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HUMAN RANDOMIZED CONTROL TRIAL

Comparative efficacy of novel bioactive glass versus sodium fluoride toothpaste for dentin hypersensitivity

Hatice Hasturk[1] | **Daniel Boyd**[2] | **Kathleen MacDonald-Parsons**[3] | **Stephanie Turner-Cahill**[3] | **Joon Seong**[4] | **Nicola West**[4] | **Heather J. Doucette**[2]

[1]Center for Clinical and Translational Research, ADA Forsyth Institute, Somerville, Massachusetts, USA

[2]Faculty of Dentistry, Dalhousie University, Halifax, Nova Scotia, Canada

[3]IR Scientific Inc., Halifax, Nova Scotia, Canada

[4]Bristol Dental School, University of Bristol, Bristol, UK

Correspondence
Heather Doucette, Faculty of Dentistry, Dalhousie University, 5981 University Ave., Halifax, NS B3H 1W2, Canada.
Email: Heather.doucette@dal.ca

Scopus Author ID: 6506490350 (HH), Scopus Author ID: 8960215500 (DB), Scopus Author ID: 7201560180 (KM-P), Scopus Author ID: 7402275687 (ST-C), Scopus Author ID: 54950445200 (JS), Scopus Author ID: 7103330591 (NW), Scopus Author ID: 55058353100 (HJD)

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Abstract

Background: This first-in-human clinical study aimed to evaluate the safety and efficacy of a bioglass incorporated in a toothpaste, in reducing dentin hypersensitivity (DH) compared to a sodium fluoride (NaF) toothpaste over a 2-week period.

Methods: A double-blind, randomized, parallel-arm, proof-of-concept clinical trial was conducted with 46 participants experiencing self-reported and clinically confirmed DH. Participants were assigned to 1 of 2 groups: (1) Test toothpaste (5 wt% bioglass with 1425 ppm fluoride as NaF), or (2) NaF toothpaste (1425 ppm fluoride). Outcomes included Schiff Airblast Sensitivity Score (primary endpoint), Visual Analog Scale (VAS) for pain, and Yeaple Probe tactile sensitivity (secondary endpoints). Statistical analyses, including analysis of covariance (ANCOVA) and descriptive statistics, were performed to evaluate intergroup differences.

Results: The Test group exhibited a statistically significant reduction in Schiff Airblast Sensitivity Scores at Day 14 compared to the NaF group (ΔMean: −0.8 vs. −0.5, $p = 0.0341$). Significant improvements were also observed in VAS pain scores in as little as 2 days (ΔMean: −1.03 vs. 0.04, $p = 0.0057$). Rapid pain relief was noted within 2 days, indicating both immediate and cumulative effects. The difference in tactile scores was not statistically significant between groups although greater change was seen with Test toothpaste (ΔMean 13 vs. 3 g; $p = 0.068$). No severe adverse events were reported, and safety profiles were comparable across groups.

Conclusion: The toothpaste containing the bioglass demonstrated superior efficacy in alleviating DH symptoms at both early and later time points through its mechanism of rapid tubule occlusion. This innovative approach aligns with World Health Organization (WHO) recommendations for fluoride use and addresses unmet needs in DH management globally. Further research is

warranted to explore its long-term applications in preventive and restorative dentistry.

Clinical trials registration: U.S. National Institutes of Health Clinical Trials Registry (http://www.clinicaltrials.gov) ID NCT06166745.

KEYWORDS
bioactive glass, dentin hypersensitivity, fluoride, tubule occlusion

Plain language summary

This clinical study evaluated the safety and effectiveness of a bioglass incorporated into a toothpaste, in reducing dentin hypersensitivity (DH), or tooth sensitivity, compared to a standard toothpaste containing sodium fluoride (NaF) over 2 weeks. Forty-six adults with tooth sensitivity participated in the study. They were randomly assigned to 1 of 2 groups: test toothpaste (containing 5% bioactive glass and 1425 ppm fluoride as NaF) group, and regular fluoride toothpaste (containing only 1425 ppm fluoride) group. Tooth sensitivity was measured by the clinician as the response to airblast, while participants' response to airblast was assessed by a pain scale (Visual Analog Scale or VAS). Additionally, the tactile score, which indicates how much pressure by a probe the tooth can tolerate, was recorded. After 2 weeks, participants using the test toothpaste showed a significantly greater reduction in sensitivity when exposed to airblast compared to those using the fluoride toothpaste. Pain relief was observed as early as 2 days, with VAS pain scores improving significantly. Tactile scores were greatly improved using the test toothpaste, with no statistically significant difference compared to the control. These results suggest that the toothpaste containing the novel bioglass provides both rapid and lasting relief of tooth sensitivity generated by air. Both toothpastes were well tolerated, with no severe side effects reported. These findings support the novel bioglass as a promising option for managing tooth sensitivity, although further studies with larger groups are recommended to confirm its long-term benefits.

1 | INTRODUCTION

Dentin hypersensitivity (DH) is a common condition involving sudden, temporary pain in response to stimuli, such as thermal, osmotic, evaporative, or tactile, in the absence of underlying dental diseases.[1] This condition primarily affects adults (ages 20–50) peaking at ages of 30–40,[2] with slightly higher occurrence in women.[3] The mechanistic basis of pain is attributed to the hydrodynamic theory, which suggests that flow of fluid within exposed dentin tubules activates nociceptors, leading to discomfort.[4] Exposure of dentin commonly occurs due to the loss of enamel or recession, making the underlying dentin susceptible to external stimuli.[4] Treatments for DH generally involve two primary approaches: nerve stabilization and tubule occlusion.[5] Nerve stabilization often involves the use of potassium salts, which are believed to reduce nerve excitability by preventing depolarization. However, clinical effectiveness of these treatments remains inconclusive.[6] In contrast, tubule occlusion blocks exposed dentinal tubules, preventing fluid movement that triggers pain.[7] This can be achieved using various agents, including strontium salts, bioactive glasses, and arginine, as well as professional treatments like fluoride varnishes.[8] While these occlusive treatments can provide immediate relief, their effectiveness varies, emphasizing the need for ongoing research to refine these therapies and develop novel strategies for managing DH.

A novel inorganic soluble bioglass has demonstrated potential for managing DH through dual mechanisms: (1) immediate physical occlusion of exposed dentinal tubules via its particulate morphology and (2) hydrolytic

degradation to release calcium, sodium, and magnesium ions upon interaction with oral fluids. Release of these ions increases the pH in the local environment and promotes the precipitation of apatite-phases. When formulated into toothpaste with a soluble fluoride source, such as sodium fluoride (NaF), a synergistic interaction forms fluoridated apatites, thereby enhancing resistance to acid challenge.[9]

The aim of this study was to evaluate the clinical performance of this novel bioglass when incorporated into a NaF toothpaste in reducing DH over a two-week period.

2 | MATERIALS AND METHODS

This research was carried out in accordance with the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (ICH E6)[10] and the Code of Federal Regulations (CFR) on the Protection of Human Participants (45 CFR Part 46). https://www.hhs.gov/ohrp/regulations-and-policy/regulations/index.html. The study adhered to the CONSORT (Consolidated Standards of Reporting Trials) guidelines to ensure comprehensive reporting of clinical trial methodology and results,[11] was approved by the ADA Forsyth Institute human subjects ethics board, and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013 (Approval date: 09-08-2022; Protocol #22-03). Approval of the protocol, study consent form, and patient instructions were obtained prior to subject enrollment. The trial was registered at clinical.trials.gov (NCT06166745).

2.1 | Products tested

NaF, a primary source of fluoride in dental products,[12] was selected as the soluble fluoride source for the two toothpastes developed for this study. Fluoride levels were set to 1425 ppm fluoride, to align with typical over-the-counter (OTC) toothpaste fluoride levels, which vary between 1000 and 1500 ppm. Two toothpastes were developed for this study: 1 containing the novel bioglass and NaF (Test)* and 1 with the exact same ingredients in the same quantities without the addition of the bioactive glass (Control); allowing for isolation of the results that could be attributable to the bioglass.

2.2 | Study design

This was a single center, prospective, randomized, double-blind, parallel-arm, proof-of-concept study, designed with the following clinical endpoints: (1) hypersensitivity by evaporative airblast stimuli (Schiff Score)[13]; (2) hypersensitivity by tactile stimuli (Yeaple Probe); (3) pain perception by visual analog scale following evaporative stimuli; and (4) safety by the occurrence of adverse events that are possibly, probably, or definitely related. Study duration was 14 days, with 3 visits (Baseline, Day 2, and Day 14) following screening. Study participants were healthy adults, ≥ 18 years, with self-reported and clinician-confirmed dentin hypersensitivity affecting at least two separate teeth. Eligible individuals were randomly assigned in a 1:1 ratio to the Test group, (5 wt% bioglass formulated with 1425 ppm NaF), or the Control group, (toothpaste containing 1425 ppm NaF). Both toothpastes contained identical inactive ingredients; carbomer, glycerin, polyethylene glycol (PEG), peppermint oil, potassium acesulfame, polyvinyl pyrrolidone (PVP), silica, sodium lauryl sulfate, (SLS), and titanium dioxide.

Clinical evaluations were performed by a single, trained dental clinician (> 30 years experience), using the detailed study parameters. Prior to study initiation, training exercises were conducted by a Gold Standard examiner (J.S.) on airblast and tactile stimuli to confirm the repeatability and proper use of air syringe, Yeaple probe, and assessment of participants' responses. Study personnel responsible for Yeaple probe calibration, chair-side recording, and Study Product administration with instructions to subjects, were specifically trained by the expert clinician/researchers (J.S. and N.W.) and the Study Investigator (H.H.).

2.3 | Study population

The first participant was enrolled on October 16, 2023, and the last participant completed on November 29, 2023. Participants were recruited from the clinical trial patient database at ADA Forsyth and through recruitment flyers placed in locations in Greater Boston and Cambridge. Individuals with self-reported DH and an interest in participating in the study were invited to be screened for inclusion. An internal review board approved written informed consent was obtained from all participants before study screening procedures, following an informed consent process that included a thorough explanation of the study and the opportunity to ask questions privately. Figure 1 illustrates the flow of participants through the study.

The inclusion criteria included being aged 18–80, willing and able to abide by terms of the consent form and sign it independently, having at least 2 nonadjacent hypersensitive teeth between second premolars in separate quadrants in both maxilla and mandible with a Schiff Airblast Sensitivity Score of ≥2, and agreeing to

* Sensi-IP, IR Scientific Inc., Halifax, Nova Scotia, Canada.

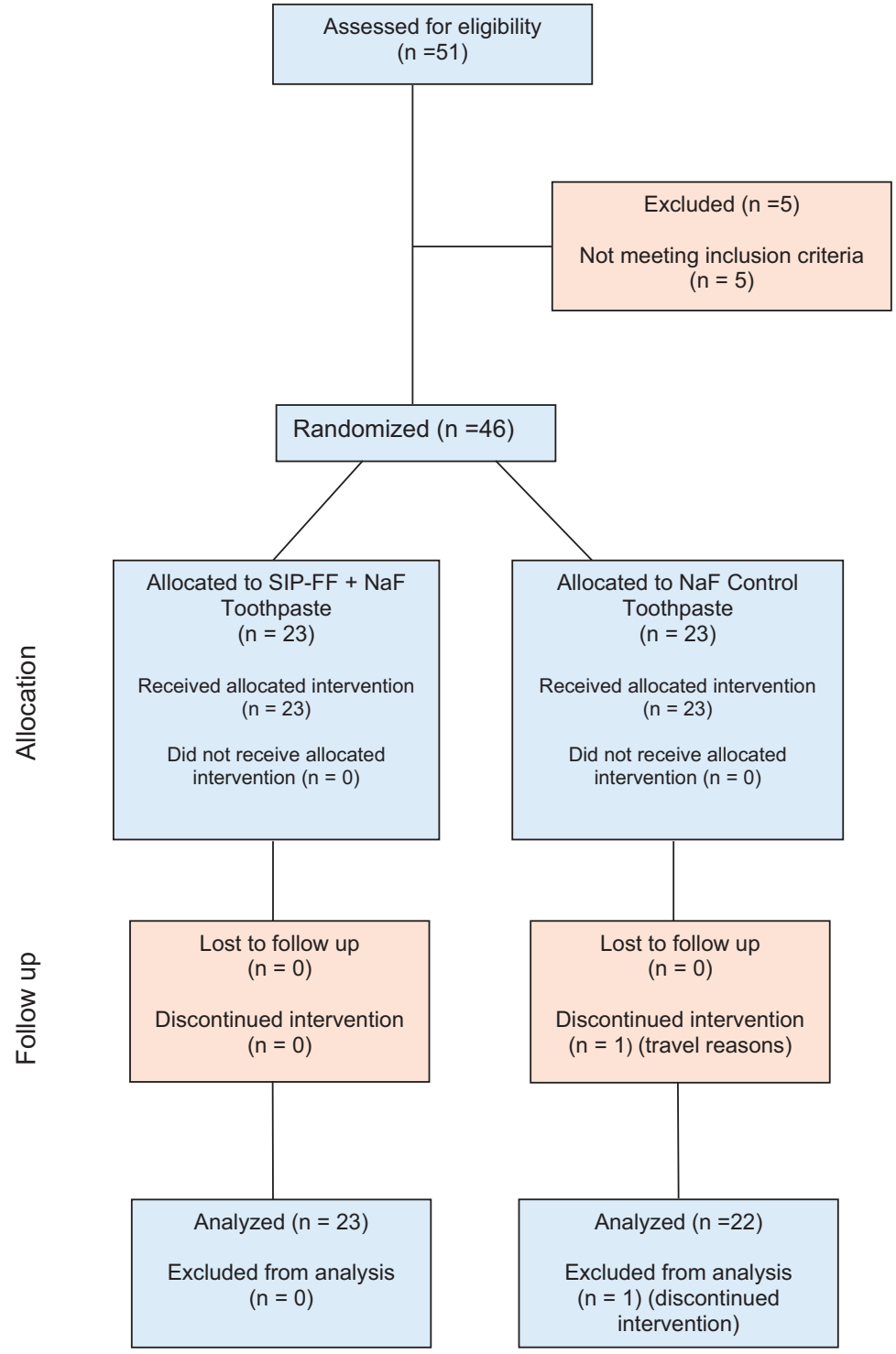

FIGURE 1 CONSORT diagram illustrating flow of participants through the clinical trial.

refrain from other desensitizing, whitening, or other dental procedures for the duration of the trial. For inclusion in the study, target teeth were required to have cervical dentin exposure, not have extensive restorations such as crowns, veneers, or bridges, fractures, gingivitis or periodontitis (probing depth > 3 mm, Gingival Index > 1 or presence of bleeding on probing), carious lesion, orthodontic brackets, endodontic treatment or pulp alterations, or serving as abutments for fixed or removable partial dentures. Participants also agreed to abstain from all oral hygiene procedures, including study products and chewing gum, for 8 h before each visit, and to refrain from eating and drinking for 4 h prior to each visit. Exclusion criteria included: pregnancy or breastfeeding, unwillingness to

remove lip or tongue piercings for the duration of the study, active oral ulcers, desensitizing treatment within 1 month, tooth bleaching within 8 weeks, scaling or polish interventions within 1 month, current orthodontic treatment, concomitant medication/therapy that may affect dentin hypersensitivity, severe bruxism, reduced salivary flow, gingival surgery within the previous 6 months, allergies to study toothpaste ingredients, active caries or conditions such as pulpitis that would precipitate pain, self-reported eating disorders, uncontrolled gastroesophageal reflux disease, excessive exposure to acids or other systemic conditions that may be predisposed to DH, participation in other clinical trials within the past 4 weeks, diagnosis of an unstable mental illness or chronic pain, and inability to comply with trial requirements.

2.4 | Sample size determination

The sample size was determined based on the following specifications: (1) Superiority study of test product (BioGlass Containing Toothpaste) to control product (NaF Toothpaste); (2) Primary Endpoint: Change from Baseline (CFB) in Schiff Airblast Sensitivity Score at Day 14 (assuming a 0.88 difference [Test group: -1.83 ± 0.55; Control group: -0.95 ± 0.46] in the reduction of Schiff Index Score compared to control group)[14]; (3) Allocation: 1:1; (4) One-sided alpha = 0.025; (5) Satterthwaite *t*-test; (6) True mean and standard deviation (SD); and (7) Power = 90%. Based on the above specifications, the required sample size was 9 subjects per treatment group. To provide more precise estimates of efficacy and a fuller evaluation of safety, the sample size was increased to 20 subjects per treatment group. To account for the potential of a 15% dropout rate, as many as 46 participants were planned to be enrolled and treated, with the goal of 20 participants per arm.

2.5 | Screening visit

Eligible individuals who provided signed informed consent were screened for study eligibility at the study site, ADA Forsyth. Medical and dental histories, full-mouth dental and periodontal examination, including pocket depth, clinical attachment level, gingival index, and bleeding on probing were recorded for eligibility determination. Women of childbearing potential were administered a pregnancy test. DH was measured by a clinician-assessed response to an evaporative airblast stimulus. Eligible participants entered a washout period of 7 ± 2 days to align with the study brushing requirements (i.e., twice daily for 1 min) and to standardize their oral hygiene status prior to initiation of the test period. All participants were provided with brushing instructions, a standard-of-care full-head medium toothbrush and OTC fluoride toothpaste to use during the washout period. Use of any other oral care products was contraindicated.

2.6 | Baseline and randomization visits

Following a 1-week wash-out period, participants returned for baseline measurements, where brushing diaries were reviewed to confirm meeting the eligibility criteria for plaque removal, oral hygiene, and brushing frequency. Evaluations of DH and safety were performed twice: before (baseline/pre-randomization) and after the first brushing with instructions and supervision (post-randomization). Individuals who fulfilled the criteria for the number of brushings required for the wash-out period (at least 90% compliance) and had at least 2 hypersensitive teeth according to both evaporative air blast stimuli ($\geq$2 Schiff score) and tactile stimuli ($\leq$20 grams, Yeaple probe) were randomly assigned a study ID and randomly assigned to the Test or Control group by the unblinded study examiner in a 1:1 allocation using permuted blocks generated by an independent biostatistician. The variable block sizes were 4 and 6, with the size of each block selected randomly with equal probability for the 2 sizes. No stratification was applied for patient characteristics. Treatment allocations were kept in a password-protected Excel file on a password-protected computer accessible only to unblinded study staff. The randomization code was concealed from the study examiner and the principal investigator until after data analysis. Participants performed brushing with instructions and supervision at each study visit. Post randomization, participants were instructed to use the assigned products daily (once in the morning and once in the evening) according to the specified brushing instructions, and to document the use of products using a diary provided.

2.7 | Study visits 3 and 4

Participants returned on Day 2 (+1 day) and Day 14 ($\pm$ 2 days) to evaluate endpoints. Clinical measurements commenced with a tactile stimulus using a Yeaple probe calibrated at the beginning of each study day. Following a 5-minute recovery period, the Schiff airblast sensitivity test[13] was conducted. Immediately after the airblast sensitivity test, participants completed a visual analogu scale to record their perception of pain experienced. Compliance was assessed during Visits 3 and 4 by reviewing the diary to determine the number and duration of brushing. Finally, at the final visit (Visit 4), unused toothpaste was returned and weighed to support compliance.

2.8 | Assessments

2.8.1 | Primary and secondary endpoints

The Schiff Airblast Sensitivity Scale[13] (Primary endpoint measure)

In a response-based approach, the level of pain was evaluated after applying a consistent, reproducible, and standardized stimulus (timed air blast). The air was directed for one second, from approximately 1 cm, at the exposed buccal surface of the sensitive tooth, after isolating it from neighboring teeth. The Schiff cold airblast sensitivity scale,[13] a well-established tool for assessing a subject's response to a stimulus, was utilized by a single, previously trained clinician.

Visual Analog Scale[15] (Secondary endpoint measure)

The VAS,[15] employed as a secondary endpoint measure, comprised a line of 10 cm in length, anchored at both ends with descriptors that represented the absolute minimum and maximum levels of pain a patient can experience due to an external stimulus. Participants were requested to evaluate their reaction to evaporative stimuli and rate their pain from zero to ten by marking the line that corresponded to the intensity of the perceived pain. The VAS score was determined by measuring the distance in millimeters from the left-hand end of the line to the point marked by the patient.[15]

The Yeaple Probe Tactile Stimulus[16] (Secondary endpoint measure)

DH in response to tactile stimuli was determined using the Yeaple probe[16] calibrated at the start of each study day. Starting at a force of 10 g and increasing by 10 g increments, the tip of the Yeaple probe was passed over the exposed dentin on the buccal surface of the target teeth, apical to the cement-enamel junction. Participants indicated the presence of discomfort by providing a "yes" response. The force setting that elicited the "yes" response was repeated, and if a second "yes" was not obtained, the force setting was increased by 10 g. Sensitivity was assessed until a force that elicited two consecutive "yes" responses with 2 consecutive stimuli.

2.8.2 | Compliance

Protocol and product use compliance were evaluated at every visit. Participant diaries were reviewed, and participants with at least 80% compliance were able to continue in the trial. Plaque index was not recorded as the subjects were asked to refrain from brushing for 8 h prior to study visits; however, brushing instructions and overall oral hygiene status were evaluated every visit.

3 | Safety assessments

Participants underwent a comprehensive medical and dental history review prior to treatment with either Study product. Participants were instructed to record any adverse effects experienced on their brushing diaries. The Principal Investigator closely monitored participant safety at each Study visit and assessed it based on participant-reported adverse effects and oral exam findings. A urine pregnancy test was conducted at screening for females of childbearing potential, using commercially available pregnancy tests. A general extraoral assessment was conducted at each visit to identify allergic and potential toxic reactions to study products as well as examination of oral hard and soft tissues, including the lips, buccal mucosa, tongue, soft and hard palate, tonsillar and pharyngeal area, teeth, gingiva, and overall oral mucosa.

4 | Data analysis

The primary study endpoint, the Change in Schiff Airblast scores[13] at Day 14, was analyzed using descriptive statistics, including the number of observations, mean, median, standard deviation, minimum, and maximum. Additionally, the change from the baseline (pre-randomization score) value was summarized using descriptive statistics for each treatment group. For each participant, two teeth were designated as the study teeth prior to randomization, and the analysis was based on the mean score of the two study teeth. Analysis of covariance (ANCOVA) was employed to evaluate the effect of treatment. The dependent variable was the change from baseline at Day 14, and the model included a term for treatment and the baseline pre-randomization value of the endpoint as a covariate. The least squares mean was presented for the treatment group difference (Test Toothpaste — Control Toothpaste), along with a 95% confidence interval for the true difference. The *p*-value for the effect of treatment was also presented. The two secondary study endpoints were analyzed in an analogous manner. Moreover, the number of designated teeth (0, 1, or 2) that remained sensitive were analyzed by treatment group at each time point. The estimated true proportion and the corresponding 95% confidence interval were presented, together with the relative risk reduction for the Test Toothpaste compared to the Control Toothpaste and the corresponding 95% confidence interval for the true relative risk reduction.

5 | RESULTS

A total of 51 adults were assessed for inclusion. Of these, 46 were deemed eligible and enrolled in the study. The clinical and demographic characteristics of the study population are shown in Table 1. Groups were balanced with respect to sex (two-tailed chi-squared p-value = 0.4894), race, and other characteristics as well as periodontal status. Twenty-three participants were randomized into Test group, while 23 participants were randomly assigned to Control group. All 46 randomized participants received at least one study treatment. A total of 45 participants completed the Day 14 visit (23 participants in the Test group and 22 participants in the Control group). One participant (2.17% of randomized participants) discontinued the study early due to their inability to attend the last study visit for travel reasons, resulting in a 4.3% dropout rate in the Control group compared to 0% in the Test group. The product compliance was 100% for all except one participant in the Test group who did not miss any brushing time but came 1 day earlier than the visit window; thus, 1 day was counted as missed (83.3%).

5.1 | The Schiff Airblast Sensitivity Scale (Primary endpoint measure)

The primary efficacy goal was to measure the average change in airblast sensitivity score from baseline at Day 14. Both treatment groups showed a significant decrease in the mean airblast score at Day 14 compared to their baseline values (Table 2; $p_{test} \leq 0.0001$ and $p_{control} = 0.0192$), the reduction being statistically significant in the Test group compared to the Control group ($p = 0.0341$). At Day 14, the least squares (LS) mean change in airblast score from the baseline was −0.8 in the Test group and −0.5 in the Control group (Table 3). The secondary efficacy analysis also compared the change in airblast sensitivity score from baseline at post-randomization and Day 2. Intra-group analysis showed significant decreases only in the Test group compared to its baseline values (Table 2, $p = 0.0081$ and $p = 0.0012$, respectively). However, there was no significant difference between the groups at these earlier time points, post-randomization, and Day 2, with respect to the change in airblast sensitivity score (Table 3).

5.2 | VAS (Secondary endpoint measure)

The secondary efficacy endpoint was the alteration from baseline in response to airblast stimulus assessed by VAS at Day 14. Tabular representation of descriptive statistics for all time points is illustrated in Table 4. Both treatment groups exhibited statistically significant diminutions in mean response measured by VAS at Day 14 from their respective baselines (Table 2; $p_{test} \leq 0.0001$ and $p_{control} = 0.0007$); however, the reduction was more pronounced and statistically significant in the Test group compared to the Control group ($p = 0.0220$). At Day 14, the LS mean change in VAS score was −2.46 mm in the Test group and -1.37 mm in the Control group (Table 4). In summary, the Test group manifested greater improvement in VAS response to evaporative air blast stimulus at all time points (Table 2; $p = 0.0025$, $p = 0.0054$ and $p < 0.0001$, compared to baseline), with statistically significant differences observed at Day 2 and Day 14 as opposed to the Control group (Table 4; ($p = 0.0057$ and $p = 0.0220$, respectively).

5.3 | The Yeaple probe tactile stimulus (Secondary endpoint measure)

The results of the secondary efficacy analysis for the group comparison of change in response to tactile stimulus for all timepoints are presented in Table 5. Both treatment groups exhibited increases in mean response, measured by pressure (in grams), at which participants reported pain compared to baseline values at Day 14; however, only the Test group's effect was statistically significant compared to baseline ($p_{test} = 0.0041$, $p_{control} = 0.3345$). At Day 14, the LS mean change in pressure that elicited a response was 13 grams in the Test group versus 3 grams in the Control group, although the difference between groups was not statistically significant ($p = 0.0677$). The change in response to tactile stimulus over time (post-randomization, Day 2, and Day 14) from baseline (pre-randomization) was also compared between groups (Table 5). Overall, the Test group demonstrated greater improvement in response to tactile stimulus at all time points, however, apart from a close-to-statistically significant difference at Day 14 ($p = 0.0677$), there was no statistically significant difference in response to tactile stimulus between groups.

5.4 | Comparison of teeth sensitivity proportion

The proportion of teeth that remained sensitive was assessed and compared between the groups at 3 time points: post-randomization, Day 2, and Day 14. The Test group demonstrated more improvement in tooth sensitivity than the Control group, but the differences were not statistically significant ($p = 0.164$, $p = 0.164$, $p = 0.079$) at each respective time point (Table 6).

TABLE 1 Participant demographics and dentin sensitivity level at baseline

Variable	Statistic	Test toothpaste ($N = 23$)	Control toothpaste ($N = 23$)
Age (years)			
	n	23	23
	Mean	33.0	31.7
	Median	32.0	23.0
	SD	12.2	14.6
	Min—max	18–58	18–68
Sex			
Male	n (%)	7 (30.4)	4 (17.4)
Female	n (%)	16 (69.6)	19 (82.6)
Ethnicity			
Hispanic or Latino	n (%)	7 (30.4)	5 (21.7)
Not Hispanic or Latino	n (%)	16 (69.6)	18 (78.3)
Unknown	n (%)	0 (0.0)	0 (0.0)
Race			
American Indian/Alaska Native	n (%)	0 (0.0)	0 (0.0)
Hawaiian Native/Pacific Islander	n (%)	0 (0.0)	0 (0.0)
White	n (%)	9 (39.1)	9 (39.1)
Black	n (%)	4 (17.4)	5 (21.7)
Asian	n (%)	5 (21.7)	5 (21.7)
Other	n (%)	0 (0.0)	0 (0.0)
Mixed	n (%)	5 (21.7)	4 (17.4)
Female reproductive status: Childbearing potential			
Yes	n (%)	14 (87.5)	16 (84.2)
No	n (%)	2 (12.5)	3 (15.8)
N/A (if male)	n	7	4
Nicotine use			
Current	n (%)	0 (0.0)	0 (0.0)
Former	n (%)	0 (0.0)	2 (8.7)
Never	n (%)	23 (100.0)	21 (91.3)
If "Current" or "Former" in #1, specify	n (%)		
Type			
Cigarettes	n (%)	0 (0.0)	2 (8.7)
E-cigarettes	n (%)	0 (0.0)	0 (0.0)
Cigars	n (%)	0 (0.0)	0 (0.0)
Pipe	n (%)	0 (0.0)	0 (0.0)
Chewing tobacco	n (%)	0 (0.0)	0 (0.0)
Snuff	n (%)	0 (0.0)	0 (0.0)
Periodontal measures of selected teeth (mean ± SD)			
Pocket depth (mm)	1.8 ± 0.30	1.7 ± 0.36	
Recession (mm)	0.5 ± 0.68	0.5 ± 0.56	
Gingival Index[22]	0.3 ± 0.28	0.2 ± 0.25	
Bleeding on probing	0 ± 0.11	0 ± 0.05	
Dentin hypersensitivity level of selected teeth			
Schiff Score; sensitive tooth #1	n	23	23
	Mean	2.3	2.3
	SD	2.0	2.0

(Continues)

TABLE 1 (Continued)

Variable	Statistic	Test toothpaste ($N = 23$)	Control toothpaste ($N = 23$)
	Median	0.4	0.5
	Min	2	2
	Max	3	3
	p-value	*0.7500*	
Schiff Score; sensitive tooth #2	n	23	23
	Mean	2.2	2.3
	SD	2.0	2.0
	Median	0.4	0.5
	Min	2	2
	Max	3	3
	p-value	*0.5127*	
Yeaple Probe; sensitive tooth #1	n	23	23
	Mean	11.3	11.3
	SD	10.0	10.0
	Median	3.4	3.4
	Min	10	10
	Max	20	20
	p-value	*1.0000*	
Yeaple Probe; sensitive tooth #2	n	23	23
	Mean	10.4	11.3
	SD	10.0	10.0
	Median	2.1	3.4
	Min	10	10
	Max	20	20
	p-value	*0.3059*	
VAS Score; sensitive tooth #1	n	23	23
	Mean	6.09	6.06
	SD	5.90	6.40
	Median	1.57	2.1
	Min	2.7	1.5
	Max	8.9	9.5
	p-value	*0.8867*	
VAS Score; sensitive tooth #2	n	23	23
	Mean	6.12	6.12
	SD	6.10	6.20
	Median	2.22	1.72
	Min	1.9	2.2
	Max	9.2	9.2
	p-value	*0.7975*	

Abbreviation: VAS, Visual Analog Scale.

5.5 | Safety assessment

No serious adverse events, including those leading to discontinuation or death, were reported during the trial. A total of 6 adverse events were reported by 5 participants: two from the Test group and 3 from the Control group. Most of these events (tissue inflammation around partially impacted third molar, sore throat, cold, nasal congestion, and increased tooth sensitivity) were mild and resolved during the study. Only 1 participant in the Con-

TABLE 2 Primary and secondary endpoints - change from baseline over time by treatment group.

Endpoint	Time point	Statistic	Schiff Airblast Sensitivity Score	*p-Value*	VAS Pain Score	*p*-Value	Tactile Score	*p*-Value[a]
Test toothpaste (N = 23)	Pre-randomization	Mean	2.239		6.104		10.87	
		SD[b]	0.3951		1.549		2.455	
		SEM[c]	0.08239		0.3231		0.5119	
	Post-randomization	Mean	2.065	*0.0081*	5.291	*0.0025*	15	***0.054***
		SD	0.4074		1.611		9.17	
		SEM	0.08496		0.3359		1.912	
	Day 2	Mean	1.957	*0.0012*	5.074	*0.0054*	13.48	***0.1855***
		SD	0.4747		1.94		8.717	
		SEM	0.09897		0.4046		1.818	
	Day 14	Mean	1.478	*<0.0001*	3.641	*<0.0001*	23.91	***0.0041***
		SD	0.5535		1.947		19.19	
		SEM	0.1154		0.406		4	
Control toothpaste (*N* = 23)	Pre- randomization	Mean	2.196		6.089		11.3	
		SD	0.4705		1.623		2.704	
		SEM	0.0981		0.3384		0.5638	
	Post- randomization	Mean	2.152	*0.1619*	5.739	*0.1013*	12.17	***0.3282***
		SD	0.4631		1.794		4.217	
		SEM	0.09656		0.3741		0.8794	
	Day 2	Mean	2.065	*0.0557*	6.126	*0.8411*	12.39	***0.2603***
		SD	0.4839		1.437		4.736	
		SEM	0.1009		0.2996		0.9875	
	Day 14	Mean	1.886	*0.0192*	4.736	*0.0007*	14.32	***0.3345***
		SD	0.6349		1.769		14	
		SEM	0.1354		0.3772		2.984	

Note: Repeated measures, 1-way ANOVA, and mixed-effect analysis of data. Analysis is based on the mean score for the 2 study teeth at each timepoint.

[a] *p*-Values show statistical significance (< 0.05) for the treatment effect over time compared to baseline.

[b] SD, standard deviation.

[c] SEM, standard error of mean.

trol group experienced a moderate event (cough), which was managed successfully with medication. Additionally, only 1 event was considered probably related to the study product or assessments; a participant in the Test group reported mild and transient increased tooth sensitivity to cold, which resolved without treatment (Appendix1 in the online *Journal of Periodontology*).

6 | DISCUSSION

This study represents the first clinical investigation into the safety and efficacy of a novel bioglass toothpaste developed for the management of DH. The findings indicate that the Test group experienced statistically significant reductions in DH symptoms compared to the Control group, as measured by both the Schiff airblast sensitivity scale[13] and the VAS[15] for pain. These results suggest a therapeutic benefit in the short-term management of DH.

The observed reduction in Schiff scores at Day 14, a widely accepted and validated clinical measure of DH severity,[13] supports the effectiveness of the intervention. Furthermore, a statistically significant decrease in VAS scores was observed after only 2 days of product use. The VAS is a subjective measure that captures the patient's perception of pain and can offer meaningful insights into patient-centered outcomes.[15] Early changes in VAS scores may reflect a rapid onset of symptomatic relief, which is clinically relevant in DH management.

TABLE 3 Change in Schiff Sensitivity Score from baseline compared to Control: all timepoints.

Endpoint	Visit	Statistic	Test toothpaste ($N = 23$)	Control toothpaste ($N = 23$)	[a]LSM for difference (Test toothpaste—sodium fluoride toothpaste)[b]	*p*-Value[c]
Change from baseline in the Schiff Airblast Sensitivity Score	Baseline—post-randomization	n	23	23		
		Mean	−0.2	−0.1	−0.1	0.4117
		95% CI for mean	(−0.3, −0.1)	(−0.2, −0.0)	(−0.2, 0.1)	
		Median	0.0	0.0		
		SD[d]	0.3	0.3		
		Min[e]—Max[f]	−1 – 0	−1 – 0		
	Day 2	n	23	23		
		Mean	−0.3	−0.3	−0.0	0.7645
		95% CI for mean[b]	(−0.4, −0.1)	(−0.5, −0.1)	(−0.2, 0.2)	
		Median	0.0	0.0		
		SD	0.4	0.4		
		Min—Max	−1 – 0	−1 – 0		
	Day 14	n	23	22		
		Mean	−0.8	−0.5	−0.3	0.0341
		95% CI for mean[b]	(−1.0, −0.5)	(−0.7, −0.2)	(−0.7, −0.0)	
		Median	−1.0	−0.5		
		SD	0.6	0.6		
		Min—Max	−2 – 0	−3 – 0		

[a]LSM, least squares mean. Analysis is based on the mean score for the 2 study teeth at each timepoint.
[b]CI based on the t-distribution.
[c]*p*-Value for the effect of treatment from an ANCOVA model with a term for treatment and the baseline pre-randomization value of the endpoint as a covariate.
[d]SD, standard deviation.
[e]Min, minimum.
[f]Max, maximum.

TABLE 4 Change in subject response to airblast stimulus (VAS) over time compared to Control.

Endpoint	Visit	Statistic	Test toothpaste ($N = 23$)	Control toothpaste ($N = 23$)	[a]LSM for difference (Test toothpaste—sodium fluoride toothpaste)[b]	*p*-Value[c]
Change from baseline in the VAS for Pain	Baseline—Post-randomization	n	23	23		
		Mean	−0.81	−0.35	−0.46	0.1440
		95% CI for mean[b]	(−1.31, -0.32)	(−0.77, 0.07)	(−1.09, 0.16)	
		Median	−0.90	−0.20		
		SD[d]	1.14	0.98		
		Min[e]—max[f]	−3.3 – 1.2	−3.3 – 1.1		
	Day 2	n	23	23		
		Mean	−1.03	0.04	−1.06	0.0057
		95% CI for mean[b]	(−1.72, −0.34)	(−0.34, 0.41)	(−1.80, −0.33)	
		Median	−0.85	0.10		
		SD	1.60	0.87		
		Min—max	−4.9 – 2.4	−1.7 – 1.5		
	Day 14	n	23	22		
		Mean	−2.46	−1.37	−1.09	0.0220
		95% CI for mean[b]	(−3.16, −1.77)	(−2.09, -0.65)	(−2.02, −0.17)	
		Median	−2.50	−1.15		
		SD	1.61	1.62		
		Min—max	−5.9 – 0.5	−4.8 – 1.3		

Abbreviation: VAS, Visual Analog Scale.

[a]LSM, least squares mean. Analysis is based on the mean score for the two study teeth at each timepoint.

[b]CI based on the t-distribution.

[c]*p*-Value for the effect of treatment from an ANCOVA model with a term for treatment and the baseline pre-randomization value of the endpoint as a covariate.

[d]SD, standard deviation.

[e]Min, minimum.

[f]Max, maximum.

TABLE 5 Change in response to tactile stimulus (Yeaple probe) over time compared to Control.

Endpoint	Visit	Statistic	Test toothpaste ($N = 23$)	Control toothpaste ($N = 23$)	[a]LSM for difference (Test toothpaste – sodium fluoride toothpaste)[b]	*p*-Value[c]
Change from baseline in the Yeaple probe assessment	Baseline – post-randomization	n	23	23		
		Mean	4.1	0.9	2.9	0.1847
		95% CI for mean[b]	(−0.1, 8.3)	(−0.9, 2.7)	(−1.4, 7.2)	
		Median	0.0	0.0		
		SD[d]	9.7	4.2		
		Min[e] – max[f]	−10 – 35	−5 – 15		
	Day 2	n	23	23		
		Mean	2.6	1.1	1.2	0.5651
		95% CI for mean[b]	(−1.3, 6.6)	(−0.9, 3.0)	(−3.0, 5.4)	
		Median	0.0	0.0		
		SD	9.2	4.5		
		Min – max	−5 – 30	−5 – 20		
	Day 14	n	23	22		
		Mean	13.0	3.0	9.6	0.0677
		95% CI for mean[b]	(4.6, 21.5)	(−3.3, 9.2)	(−0.7, 19.9)	
		Median	5.0	0.0		
		SD	19.5	14.0		
		Min – max	−5 – 70	−5 – 65		

[a]LSM, least squares mean. Analysis is based on the mean score for the 2 study teeth at each timepoint.
[b]CI based on the t-distribution.
[c]*p*-Value for the effect of treatment from an ANCOVA model with a term for treatment and the baseline pre-randomization value of the endpoint as a covariate.
[d]SD, standard deviation.
[e]Min, minimum.
[f]Max, maximum.

TABLE 6 Proportion of teeth remaining sensitive.

Variable	Visit	Statistic	Test toothpaste ($N = 23$)	Control toothpaste ($N = 23$)
Proportion of designated teeth that remain sensitive	Baseline—post-randomization	n	23	23
		Mean	0.91	0.98
		95% CI for true proportion[a]	(0.83, 1.00)	(0.93, 1.00)
		Median	1.00	1.00
		SD[c]	0.19	0.10
		Min[d]—max[e]	0.5 – 1.0	0.5 – 1.0
		p-Value[b]	0.1644	
	Day 2	n	23	23
		Mean	0.83	0.93
		95% CI for true proportion[a]	(0.69, 0.97)	(0.86, 1.00)
		Median	1.00	1.00
		SD	0.32	0.17
		Min—max	0.0 – 1.0	0.5 – 1.0
		p-Value[b]	0.1643	
	Day 14	n	23	23
		Mean	0.54	0.76
		95% CI for true proportion[a]	(0.36, 0.73)	(0.59, 0.93)
		Median	0.50	1.00
		SD	0.42	0.40
		Min—max	0.0 – 1.0	0.0 – 1.0
		p-Value[b]	0.0789	

[a]CI based on the t-distribution.
[b]*p*-Value from a two-sample *t*-test with a two-sided 0.05 significance level.
[c]SD, standard deviation.
[d]Min, minimum.
[e]Max, maximum.

The Yeaple probe did not detect statistically significant changes between groups. This result may be influenced by the methodological limitations of the Yeaple test, which delivers a mechanical stimulus that may elicit variable responses.[17] The inconsistencies among assessment methods underscore the complexity of DH, a condition known to be influenced by both physiological and psychosocial factors. Variability in individual pain thresholds, environmental conditions, and psychological states could have contributed to these differences in measured outcomes.

The placebo effect must also be considered when interpreting these findings. Prior studies have reported substantial placebo responses in DH trials, with up to 40% of participants experiencing symptomatic improvement even in the absence of active treatment.[18] This effect may be amplified by the Hawthorne effect,[19] wherein participants modify their behavior due to awareness of being observed. While placebo responses likely contributed to improvements in both study arms, the significant differences observed between the test and control groups suggest an effect attributable to the active intervention.

The dual-action mechanism proposed for the novel bioglass—involving both physical occlusion of dentin tubules and the release of calcium and phosphate ions—may explain the observed improvements. The continued reduction in sensitivity between early and later time points suggests a cumulative effect with repeated use. This is consistent with in vitro data indicating enhanced dentin tubule occlusion over time and improved enamel surface microhardness in the presence of fluoride.[9] Together, these findings imply both immediate and longer-term contributions to the mitigation of DH symptoms.

Differences in dissolution behavior compared to silicate-based bioglasses may also be relevant. The material tested in this study is formulated to undergo complete hydrolytic dissolution, which may reduce the risk of residue accumulation and allow for more consistent clinical performance. In contrast, silicate-based systems have been reported to dissolve more slowly and leave particulate remnants, which can influence the extent and durability of dentin occlusion.[20,21]

The test material evaluated in this study is a fluoride-free bioglass designed to be compatible with commonly used fluoride sources such as NaF, stannous fluoride, and sodium monofluorophosphate. This approach may enable its inclusion in various formulations without altering fluoride content, which is particularly relevant in contexts where fluoride exposure is already adequate or where fluoride concentrations in consumer products are regulated.

This trial provides a foundation for further research on the clinical performance of this bioglass in DH management. Future studies should include longer follow-up periods to assess the persistence of efficacy and monitor long-term safety as well as comparing its efficacy to commercially available and clinically proven products for DH such as calcium carbonate and arginine-containing toothpaste. Additional investigations examining the interaction of the active material with other oral care products, as well as performance under diverse dietary and hygiene conditions, would help clarify its role in the broader context of DH treatment.

6.1 | Strengths and limitations

The study was a well-designed, double-blind randomized controlled trial where participants completed a wash-out period, and one examiner provided consistent assessments with training. However, the small sample size, single-centre population, placebo and Hawthorne effects are limitations. Another limitation could be using a non-commercially available placebo as the control without including a commercially available NaF toothpaste, which prevented comparison of results to a currently available product. Moreover, although a detailed oral exam was conducted which evaluated the oral hygiene status including plaque levels at all visits by the same blinded clinician with > 30 years of clinical experience, a plaque index was not used to objectively assess the amount of plaque. This may influence the sensitivity levels of the teeth and limit the ability to account for the potential confounders.

7 | CONCLUSIONS

The novel bioglass addresses DH pain quickly and offers long-term protection. Clinical data show potential in reducing DH symptoms, as evidenced by statistically significant improvements in Schiff airblast sensitivity and VAS pain scores. Future research should focus on long-term studies to understand its durability and explore additional applications. Considering its innovative formulation that facilitates rapid ion release and complete dissolution, the findings of this study regarding prompt symptom relief are promising. Further, the dual-action mechanism, combining tubule occlusion with active remineralization, suggests that more durable relief is possible compared to treatments relying solely on neural desensitization or temporary occlusion. Integration into broader dental care applications is also possible, as it synergizes with fluoride, enhancing enamel surface microhardness in vitro. This opens possibilities for comprehensive oral care regimens protecting against caries and enamel wear.

AUTHOR CONTRIBUTIONS

All authors have made substantial contributions to conception and design of the study. Heather J. Doucette and Hatice Hasturk have been involved in data collection and data analysis. Heather J. Doucette, Hatice Hasturk, Nicola West, Daniel Boyd, Stephanie Turner-Cahill, and Kathleen MacDonald-Parsons have been involved in data interpretation, drafting the manuscript and revising it critically, and have given final approval of the version to be published.

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CONFLICT OF INTEREST STATEMENT

H. Doucette is a consultant for IR Scientific; D. Boyd is a Founder/Inventor of IR Scientific; K. MacDonald-Parsons was the Glass Innovation Lead at IR Scientific; S. Turner-Cahill is the Quality Manager for IR Scientific; and N. West and J. Seong were each paid an honorarium by IR Scientific to advise on dentin hypersensitivity trial design and train the study site staff. H. Hasturk has no conflicts of interest.

DATA AVAILABILITY STATEMENT

The full trial protocol and raw data can be obtained from the authors upon request.

REFERENCES

1. Gillam D. *Dentine Hypersensitivity: Advances in Diagnosis, Management, and Treatment*. Springer International; 2015. doi:10.1007/978-3-319-14577-8
2. Shiau HJ. Dentin hypersensitivity. *J Evid Based Dent Pract*. 2012;12(suppl 3):220-228. doi:10.1016/S1532-3382(12)70043-X
3. West NX, Davies M, Sculean A, et al. Prevalence of dentine hypersensitivity, erosive tooth wear, gingival recession and periodontal health in seven European countries. *J Dent*. 2024;150:105364. doi:10.1016/j.jdent.2024.105364
4. Davari A, Ataei E, Assarzadeh H. Dentin hypersensitivity: etiology, diagnosis and treatment; A literature review. *J Dent (Shiraz)*. 2013;14(3):136-145. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3927677/
5. Addy M, West NX. The role of toothpaste in the aetiology and treatment of dentine hypersensitivity. *Monogr Oral Sci*. 2013;23:75-87. doi:10.1159/000350477
6. Poulsen S, Errboe M, Hovgaard O, Worthington HW. Potassium nitrate toothpaste for dentine hypersensitivity. *Cochrane Database Syst Rev*. 2001(2):CD001476. doi:10.1002/14651858.CD001476
7. Mantzourani M, Sharma D. Dentine sensitivity: past, present and future. *J Dent*. 2013;41(suppl 4):S3-S17. doi:10.1016/S0300-5712(13)70002-2
8. Dionysopoulos D, Gerasimidou O, Beltes C. Dentin hypersensitivity: etiology, diagnosis and contemporary therapeutic approaches—A review in literature. *Appl Sci*. 2023;13(21):11632. doi:10.3390/app132111632
9. MacDonald K, Boudreau E, Thomas GV, et al. In vitro evaluation of Sensi-IP®: a soluble and mineralizing sensitivity solution. *Heliyon*. 2022;8(1):e08672. doi:10.1016/j.heliyon.2021.e08672
10. *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Guideline for Good Clinical Practice*. ICH; 2016. Published online 2016. https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf
11. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *J Clin Epidemiol*. 2010;63(8):834-840. doi:10.1016/j.jclinepi.2010.02.005
12. Nassar Y, Brizuela M. The Role of Fluoride on Caries Prevention. In: *StatPearls*. StatPearls Publishing; 2024. Accessed December 9, 2024. http://www.ncbi.nlm.nih.gov/books/NBK587342/
13. Schiff T, Dotson M, Cohen S, De Vizio W, McCool J, Volpe A. Efficacy of a dentifrice containing potassium nitrate, soluble pyrophosphate, PVM/MA copolymer, and sodium fluoride on dentinal hypersensitivity: a twelve-week clinical study. *J Clin Dent*. 1994;5:87-92.
14. Seong J, Newcombe RG, Foskett HL, Davies M, West NX. A randomised controlled trial to compare the efficacy of an aluminium lactate/potassium nitrate/hydroxylapatite toothpaste with a control toothpaste for the prevention of dentine hypersensitivity. *J Dent*. 2021;108:103619. doi:10.1016/j.jdent.2021.103619
15. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs*. 2005;14(7):798-804. doi:10.1111/j.1365-2702.2005.01121.x
16. Polson AM, Caton JG, Yeaple RN, Zander HA. Histological determination of probe tip penetration into gingival sulcus of humans using an electronic pressure-sensitive probe. *J Clin Periodontol*. 1980;7(6):479-488. doi:10.1111/j.1600-051x.1980.tb02154.x
17. Pollard AJ, Khan I, Davies M, Claydon N, West NX. Comparative efficacy of self-administered dentifrices for the management of dentine hypersensitivity – A systematic review and network meta-analysis. *J Dent*. 2023;130:104433. doi:10.1016/j.jdent.2023.104433
18. Curro F, Friedman M, Leight S, Addy G, Embery W, Edgar R. Design and conduct of clinical trials on dentine hypersensitivity. In: *Tooth Wear and Sensitivity*. Martin Dunitz; 2000:299-315.
19. McCarney R, Warner J, Iliffe S, van Haselen R, Griffin M, Fisher P. The Hawthorne Effect: a randomised, controlled trial. *BMC Med Res Methodol*. 2007;7(1):30. doi:10.1186/1471-2288-7-30
20. Athanasiadou D, Eymael D, Hajhamid B, Carneiro KMM, Prakki A. Chemical and ultrastructural characterization of dentin treated with remineralizing dentifrices. *J Funct Biomater*. 2024;15(1):25. doi:10.3390/jfb15010025
21. Balasubramanian P, Büttner T, Miguez Pacheco V, Boccaccini AR. Boron-containing bioactive glasses in bone and soft tissue engineering. *J Eur Ceram Society*. 2018;38(3):855-869. doi:10.1016/j.jeurceramsoc.2017.11.001
22. Loe H, Silness J. Periodontal disease in pregnancy. I. prevalence and severity. *Acta Odontol Scand*. 1963;21:533-551. doi:10.3109/00016356309011240

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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