A clinical assessment of the efficacy of a Stannous - containing Sodium Fluoride Dentifrice on Dental Hypersensitivity

By Trevor N. Day, PhD; Johannes Einwag, Prof. Dr. med. dent.; Joachim S. Hermann, PD Dr. med. dent.; Tao He, DDS, PhD; Mary Kay Anastasia, BA; Matthew Barker, PhD; Yuqing Zhang, MS

Aim: To measure the desensitizing benefit of an experimental stannous-containing sodium fluoride dentifrice versus a regular sodium fluoride negative control.

Methods and Materials: This study was a randomized, double-blind, parallel group, four-week clinical trial. Subjects reporting tooth hypersensitivity were enrolled and randomized to the experimental dentifrice or the control dentifrice to use twice daily for four weeks.

Efficacy assessments (Air Blast) were performed at baseline and weeks two and four. Separate analyses were performed for the two most sensitive teeth at baseline and for all 12 teeth. Results for weeks two and four combined also were analyzed.

Results: Thirty-one subjects were included in the analyses. For the two most sensitive teeth, the experimental dentifrice showed statistically significantly less sensitivity (p < 0.05) versus the control at sodium fluoride two and four and for weeks two and four combined. The sensitivity reduction ranged from 24.9% to 28.4% over the control. For all 12 teeth, the experimental group had statistically significantly (p < 0.05) lower sensitivity scores versus the control group at week two, and weeks two and four combined.

Conclusion: The experimental dentifrice demonstrated significant desensitizing advantages versus the control.

Clinical Significance: This stannous-containing sodium fluoride dentifrice provides an effective treatment for patients with dental hypersensitivity, significantly reducing sensitivity versus a negative control in this four-week clinical trial.

Introduction
Dental hypersensitivity is a highly prevalent condition reported to affect from 4% to 57% of the population. The causes of sensitivity are well characterized as exposed dentinal tubules most commonly resulting from gingival recession followed by loss of cementum. The mechanism by which nerves are triggered to result in the pain associated with hypersensitivity is now widely accepted as that of the Brännström hydrodynamic theory. This postulates that changing physical conditions on the dentin surface such as heat, pressure, or osmotic potential give rise to fluid movement in the tubules. The consequent pressure change stimulates the nerves giving rise to the pain.

The mechanism of action of stannous ions in reducing dental hypersensitivity has been found to be the precipitation of stannous compounds occluding the dentinal tubules and thus preventing stimulation of the nerves in the pulp cavity. In vitro studies using various techniques, such as scanning electron microscopy, electron probe microanalysis, and Vickers surface microhardness, demonstrated deposition of tin and fluoride on the surface and covering of the dentinal tubules. One laboratory evaluation showed that while both zinc and tin covered or obturated tubules, zinc was largely removed by washing whereas tin remained covering the tubules. Another study showed specimens treated with stannous fluoride (Crest® Pro-Health®, The Procter & Gamble Company, Cincinnati, OH, USA) appeared to resist acid solubilization. A number of clinical studies also have been conducted to investigate the effectiveness of stannous-containing oral care products upon dentinal hypersensitivity. Most of the early studies focused on gels containing 0.14% stannous fluoride, whereas the majority of contemporary trials have evaluated stannous-containing dentifrice formulations. The collective findings demonstrate the effectiveness of numerous stannous-containing products in reducing sensitivity.

Recently, a new stannous-containing sodium fluoride dentifrice was developed. This clinical trial was conducted to evaluate the effectiveness of this formulation relative to a negative control, in the treatment of dental hypersensitivity.

Methods and Materials Study Design
This was a randomized, parallel group, double-blind, four-week clinical trial to assess changes in subject perceived tooth hypersensitivity via air blast induced examiner grade assessment among subjects using a stannous-containing sodium fluoride dentifrice compared to those using a negative control dentifrice. Measurements were conducted at baseline, week two, and week four visits.

Entrance Criteria
Following Ethics Committee approval, at least 30 generally healthy adults (ages 18-70) reporting tooth hypersensitivity were sought. Subjects had to agree to refrain from using anti-hypersensitivity products or having elective dental procedures (including prophylaxis) performed during the study.

Subjects who were currently using an antisensitivity toothpaste or another anti-sensitivity product or who had used such a product in the previous month were excluded. Subjects with varicous teeth or with any other condition that the investigator considered may compromise the results also were excluded.

Subjects taking daily doses of antidepressants, sedatives, tranquilizers, or other mood-altering drugs were excluded as well as subjects with a history of significant adverse effects following the use of oral hygiene products such as toothpaste and mouth rinse.

Test Dentifrices, Assignment to Treatment Sequence
The two treatments used in this study were:
1. An experimental stannous-containing sodium fluoride dentifrice with 1450 ppm F- sodium fluoride and stannous chloride as a key excipient (Procter & Gamble UK, Surrey, United Kingdom)
2. Crest® Decay Protection (UK) with 1450 ppm F- sodium fluoride (Procter & Gamble UK, Surrey, United Kingdom)

Both were supplied to the subjects with (medium) Oral-B Advantage 40 toothbrushes (The Procter & Gamble Company, Cincinnati, OH, USA). The test products were supplied in kits containing the assigned toothpaste, toothbrush, and written usage instructions. The dentifrices in both kits were supplied blinded in white tubes.
hold were assigned to the same treatment group.

Treatment Regimens

Subjects used the assigned products for the first time under supervision at the clinical site. Subjects used the products at home in the morning and evening for two weeks, and week four visits. Each tooth was isolated with cotton rolls and the adjacent gingiva was covered from a distance of 1.0 centimeter for 1 second. The following scale was used to assess the level of hypersensitivity for each of the 12 teeth examined:

- 0 – Absence of pain, but perceiving stimulus
- 1 – Slight pain
- 2 – Pain during application of stimulus
- 3 – Pain during application of stimulus
- 4 – Pain immediately thereafter

Statistical Methods

For air blast-induced hypersensitivity scores, separate analyses were performed for the two treatment groups at baseline and for all 12 teeth combined. Analysis of covariance (ANCOVA) was performed with tooth and observer as a factor and the baseline score and age as the covariates. Analysis of the differences in hypersensitivity at the post-baseline visits. Also for the hypersensitivity scores, separate repeated measures models were used to investigate the overall relationship among: treatment group and the post-baseline visits (weeks two and four) with statistical testing for the interaction and overall treatment effects using a two-sided 5% significance level. In this study, the interaction between treatment and week was not statistically significant (p=0.15) for each hypersensitivity score, and the interaction was removed from the repeated measures model.

Results

Thirty-one subjects were enrolled at the baseline visit, received product, and completed the study. Of the 31 subjects, 25 (81%) completed the study. Subjects ranged in age from 25 to 65 years with an average of 42 years of age. Twenty-two of the subjects were female. The treatment groups were balanced (p=0.86) for all demographic characteristics. Mean baseline scores were not significantly different between groups (p=0.96) between groups at baseline for either the two most sensitive teeth or for all 12 teeth combined.

Efficacy Results

At week two and four combining weeks two and four, the experimental group had a mean air blast score for two most sensitive teeth that was 28.4%, 24.9%, and 27% lower, respectively, than the control group (p<0.05). The experimental group also demonstrated significantly greater reductions in the control in tooth sensitivity via air blast measurements among all 12 teeth on post-baseline measurements at week two and the combined results for weeks two and four (p<0.05). The assessment of all 12 teeth was included in this trial for comparison purposes but is not a widely used measure in sensitivity trials since the condition typically does not affect each tooth.

Discussion

In this clinical trial, the experimental group exhibited a significantly greater reduction in tooth sensitivity via air blast measurements than the control among the two most sensitive teeth (p<0.05) at both post-baseline measurements and the combined weeks two and four visits. The experimental group also demonstrated significantly greater reductions in the control in tooth sensitivity via air blast measurements among all 12 teeth on post-baseline measurements at week two and the combined results for weeks two and four (p<0.05). There were no significant differences between the two treatments at either week four or eight (p>0.54) for either measurement. One conclusion from this stannous-containing sodium fluoride dentifrice formulation relative to other desensitizing treatments is its effectiveness against other common oral conditions. A recent study by He and colleagues (2015) evaluated the plaque prevention efficacy relative to a positive control (Colgate® Total, Colgate-Palmolive, New York, NY, USA) and negative (Crest® Cavity Protection, The Procter & Gamble Company, Cincinnati, OH, USA) control dentifrices. The results indicate that there was significantly less plaque and higher fluoride uptake in the users of the experimental group compared to the control group throughout the study period (p<0.0001).

Further research is warranted on this formulation to demonstrate the full breadth, as well as magnitude, of benefits.

Conclusion

This stannous-containing sodium fluoride dentifrice provides statistically significant benefits for dentin hypersensitivity and should be considered as a home care option for patients who experience this condition.

Clinical Significance

This stannous-containing sodium fluoride dentifrice provides an effective treatment for patients with dentinal hypersensitivity.

References

9. Full list of references available from the publisher.
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By A. Rinaldi, D. Carugo, L. Capretto, M. Aspiras, M. De Jager, J. Ward and P. Stoodley

Abstract

The influence of the impact of a high-velocity water microdrop on the detachment of Streptococcus mutans UA159 biofilms from the interproximal (IP) space of teeth in a typodont model was investigated experimentally and computationally. Twelve-day-old S. mutans biofilms were exposed to a prototype AirFloss delivering 115 μL wa-
ter at a maximum exit velocity of 60 m/sec in a 50-msec burst. Using confocal microscopy and image analysis, we obtained quantitative measurements of the percentage removal of bio-
films from different locations in the IP space. The 3D geometry of the typodont and the IP spaces was obtained by micro-computed tomography (μ-CT) imaging. We performed computational fluid dynamics (CFD) simulations to calculate the wall shear stress ($\tau_w$) distribution caused by the drops on the tooth surface. A qualitative agreement and a quantitative re-
lation between experiments and simulations were achieved. The wall shear stress ($\tau_w$) gen-
erated by the prototype AirFloss and its spatial distribution on the teeth surface played a key role in dictating the efficacy of biofilm removal in the IP space. Key words: Oral Hygiene, Strept-
tococcus mutans, micro-com-
puted tomography, microscopy, interproximal cleaning, dental plaque.

Introduction

Good oral hygiene practice maintains a healthy oral cavity, biologically inert surface (free of biofilm) and predicts further complications such as gum diseases and tooth decay (Con-
terton et al., 1999; Jakobovics and Kolenderander, 2010; Bjarn-
sholt et al., 2011; Marsh et al., 2011).

The challenge of dental care products is efficiently and quickly remove plaque from the interproximal (IP) space. Mechanical removal of IP plaque by traditional dental flossing products has been accomplished with bleeding, stuck or shred-
ded floss, and prolonged flossing time (Darby, 2005). Fluid shear stress is an alternative mecha-
nical approach for controlling biofilm build-up (Stewart, 2012). Previous studies have demon-
strated that if sufficiently high fluid shear stress can be generated, this alone can stimulate biofilm detachment (Butter and Vincent, 1988; Hope et al., 2005; Sharma et al., 2005a; Panning-
ova et al., 2006). High-velocity water droplets (C ense et al., 2006) and extrabed air bubbles (Parni et al., 2005; Sharma et al., 2005b) have also been shown to be able to remove bacteria and biofilms from surfaces utilizing the additional effect of gener-
ing a “surface-tension force” through the passage of an air/water interface (Gómez-Suárez et al., 2001). An advantage of using fluid forces to remove biofilms is that me-
chanical forces can be projected beyond the device itself, by gen-
erating currents in the fluid sur-
rounding the teeth by powered brushing (Adams et al., 2002) or through the generation of wa-
ter jets by oral irrigation (Eide, 2011). However, continuous wa-
ter jets have a disadvantage of requiring large reservoirs and can be messy to use because of the large volumes of water involved. Moreover, the Sunicare™ AirFloss device has been introduced for removing IP plaque. The AirFloss shoots a high-velocity air-entrained water jet at a high velocity into the IP space in a discrete burst. These high fluid shear stress ($\tau_w$) and high-im-
pact pressure over short periods of time entrain air bubbles and water vol-
ume and cleaning times.

We previously reported the in-
hfluence of high-velocity water microdrop impact on the de-
tachment of artificial plaque from the IP spaces, to demon-
strate how a real biofilm might detach (Rinaldi et al., 2015). Here, we go on to use the same in vitro model to look at bacterial biofilm removal and apply com-
pustational fluid dynamics (CFD) numerical techniques to model and predict the spatial distribu-
tion of fluid wall shear stress ($\tau_w$) required to remove the biofilm. This paper reports the results of an experimental and numerical study on the influence of a high-
velocity water microdrop impact on the detachment of Strepto-
coccus mutans biofilms from the IP spaces of a typodont model.

Materials & Methods

Bacteria and Growth Media

Biofilms were grown from S. mutans UA159 (ATCC 700610). Stock cultures of S. mutans were stored at -80°C in 10% glycerol in physiological buffered saline (PBS). Biofilms were cultured with sucrose (2% w/v) supple-
mented brain heart infusion (BHI)-
media (Sigma-Ald-
rich, Dorset, UK) and incubated at 37°C and 5% CO2.

Figure 2. Representative CLSM images of S. mutans biofilm of 3 different lo-
cations (A, B, C). D: Exposure of the prototype AirFloss tip from the proximal labial side of a maxillary central incisor (the 3 locations are identified clearly in Fig. 3). A1, B1, C1, D1, and E1 are the images of the biofilm before the burst at the untreated incisors and A2, B2, C2, D2, and E2 are the corresponding images after threshold-
ning with ImageJ (the biofilm is in black in these images, while the white areas are biofilm-free regions). Meanwhile, A3, B3, C3, D3, and E3 are the images of the same location after the burst, and A4, B4, C4, D4, and E4 are the corresponding thresholded images. The untreated samples (samples 1 and 2) and treated samples (samples 3 and 4) are not from the same specimens. We calculated the % removed by subtracting the amount of biofilm that remained from the original amount of biofilm.

Figure 1. Digitization process of the training typodont. (A) Photograph showing the typodont (maxillary dental arch). (B) CAD-based 3D rendering of the IP space used in the study. (C) The 3D meshwork showing the geometry of the tooth sur-
face that was used for the computational simulations. The sketch (right) shows the mental view of a maxillary central incisor, and the dashed square shows the region of interest used in the study.

Removal of interproximal dental biofilms by high-velocity Water Microdrops

With confocal microscopy, S. mutans biofilms grown in the IP space showed bacterial cells ag-
gregating and forming complex cell cluster colonies consisting of ‘tower’, ‘mushroom’, and ‘mound’-shaped structures. The thickness of the resulting bio-
film on each tooth surface was approximately 200 to 500 μm. After the microburst, the images taken for the proximal surface of the teeth showed almost no bio-
film close to the nozzle tip of the prototype AirFloss. Image analy-
sis showed 95% removal close to the tip, 62% removal at approxi-
mately 50 to 100 μm from the tip, 39% removal at approximately 100 μm from the tip (Fig. 3). The percentage removal values were plotted vs. the distance from the nozzle tip to the midpoint of the palatal surface of the teeth (Fig. 5). The distance between the biofilm and the ‘mound’-shaped structure was compared with values from the numerical simulations for r (at the same locations) (Figs. 5C, 3D).

Critical Shear Stress for Biofilm Aggregates

The morphology of the biofilms in the vicinity of the nozzle tip of the prototype AirFloss by confocal mi-
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other, and also within the same channel. Structural heterogeneity is a common feature of biofilms. Nevertheless, common features could be noted, as seen by the microscopic images (Appendix Fig. 2): (i) the presence of individual bacteria and (ii) the presence of biofilm clusters of different sizes.

When \( \tau_w \) was increased from 0 to 2 Pa, the smaller biofilm clusters still appeared to be firmly attached to the substrate, and remained attached even after the shear stress was increased to 3 Pa.

**Numerical Simulations**

**Mesh Independence Study**

A mesh independence study was performed, and a cell size of 0.155 mm was selected for all the numerical simulations (Appendix V).

**Quantification of Wall Shear Stress Distribution**

A representative contour plot of the fluid shear stress \( \tau_w \) on the tooth surface is shown in Fig. 5B. This simulation corresponded to \( z/H = 0.5 \), with the nozzle positioned on the line connecting the upper middle incisors. These simulations showed that \( \tau_w \) values of 1.05 Pa were observed along the inciso-gingival height (\( z/H = 0.5 \)), while the contours of \( \tau_w \) were significantly reduced at the inciso-ledge and cervico-ledge positions, namely, \( z/H = 0.15 \) (close to the incisal edge) or \( z/H = 0.85 \) (close to the cervical edge).

**Effect of the Nozzle z-position on Wall Shear Stress Distribution**

Contours of fluid \( \tau \) on the tooth surface were obtained to investigate the effect of tip positioning on the device's hydrodynamic performance. Figure 4 shows the tooth surface area where \( \tau \) is lower than the critical value of 1.7 Pa. Computational results predicted that the maximum \( \tau \) of biofilm removal would take place when the nozzle tip is placed at \( z/H = 0.15 \) or \( 0.5 \) or \( 0.66 \), while the effect of these conditions was found to be significantly reduced at extreme \( z/H \) positions, namely, \( z/H = 0.15 \) or \( z/H = 0.85 \) (close to the incisal or cervical edge).

**Discussion**

In the flow cell experiments, \( \tau \) on the tooth surface was successfully grown inside microchannel- ered ion flow cells. This agrees with the computational simulations (Eq. 1). This relationship could translate into prevention of biofilm and automatically be used to predict the efficacy of oral healthcare devices that use shear forces to remove plaque.

The computational model de- scribed the impact of the edge of the channel on the vicinity of the nozzle tip on the z-direction (inciso-gingivally) on biofilm removal efficacy. The numerical simulations predicted that when the nozzle is placed in or close to the middle of the inciso-gingival height (\( z/H = 0.5 \)), the smaller biofilm removal, in comparison with placing the tip closer to either the incisal edge or the cervical line (Fig. 4). To understand our knowledge, this is the first time that CFD has been used to calculate the wall shear stress distribution, caused by water drops ejected from the device, on the tooth surface.

In this study, an experimental set-up was built and a methodology was developed to characterize the efficacy of biofilm detachment by high-velocity water droplets, thus providing a better under- stand of biofilm and automatically translates into prevention of dental caries formation at these sites.

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**About the Authors**

A. Reu interleukin-10 (IL-10), C. Caruso, L. Capretti Specific Pathogen-Free (SPF) mice, from Jackson, M. Apel (Microbiology, and J. Wagner, P. Stoodley*). The 

*ACG, Faculty of Engineering and the Environment (FEE), University of Southampton, UK; Bioengineering Group, Faculty of Engineering and the Environment (FEE), University of Southampton, UK; Philips Oral Healthcare Limited (POH), Bothell, WA, USA; Philips Oral Healthcare, Philips Research, Eindhoven, The Netherlands; and Center for Computational Biological Science, Department of Micro- biology, Orthopaedics, The Ohio State Uni- versity, Columbus, OH, USA, are corresponding author, aaru00@soton.ac.uk.