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Suppression of root caries progression by application of Nanoseal®: A single-blind randomized clinical trial

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The aim of this single-blind, parallel and randomized controlled trial was to evaluate the effect of Nanoseal® application on root caries progression. Adult patients (n=129, mean age: 66.4±10.1 years) with root caries were randomly allocated into three groups: high-frequency (HF, n=43; intervention: Nanoseal application at baseline and 1–5 months), low-frequency (LF, n=43; intervention: Nanoseal application at baseline and 3 months), and control (n=43; intervention: no application of Nanoseal) groups. Measurements of fluorescence laser values of carious lesions using a DIAGNOdent™ Pen (D-value) were performed for each subject before intervention (baseline) and at 3 and 6 months. Significantly lower D-values for the HF (p=0.017) and LF (p=0.034) groups were observed compared with the control group at 6 months. Nanoseal application would be an effective procedure to suppress root caries progression.

Keywords: Calcium-fluoroaluminosilicate glass, caries prevention, exposed tooth root, fluorescence laser

INTRODUCTION

Root surface exposure after periodontal treatment frequently causes root caries to be a major concern of periodontal maintenance therapy[1]. In addition, tooth roots are commonly exposed in the teeth of elderly people because gingival recession naturally occurs with aging[2]. Root caries is a mildly progressive disease; however, some severe cases have required tooth extraction when caries extends to the subgingival level[3]. In general, conservative and restorative treatments, such as glass ionomer or composite resin filling, should be carried out as treatment of root caries and include local anesthesia when necessary. However, very elderly individuals and people with frequent root caries require non-invasive approaches to safely treat root caries.

A tooth surface coating product to clinically reduce dentin hypersensitivity, Nanoseal® (Nippon Shika Yakuhin, Shimonoseki, Japan) is composed of two liquids: an aqueous dispersion of nanoparticulate calcium-fluoroaluminosilicate glass and phosphoric acid solution[4]. After mixing the two liquids, calcium-fluoroaluminosilicate glass particles begin to aggregate by the acid-base reaction of glass particles and phosphoric acid to close the dentinal tubules, resembling silicate cement[5]. It is assumed that the application of the acidic mixture of the two liquids to the tooth surface causes tooth decalcification. Simultaneously, an insoluble mineral layer, which contains calcium fluoride, calcium phosphate, phosphor-silicate compounds, and calcium-fluoroaluminosilicate, forms on the tooth surface[4,6]. Previously, it was reported that Nanoseal-applied tooth substrate incorporates ions released from acidized calcium-fluoroaluminosilicate glass to reduce tooth decalcification[7]. Hence, we hypothesized that Nanoseal application to root caries would inhibit root caries progression. Here, we conducted a clinical study at Hokkaido University Hospital to determine whether Nanoseal application affects root caries progression as measured by laser fluorescence.

MATERIALS AND METHODS

This study was a 6-month single-blind, randomized controlled clinical trial with a parallel design. The study protocol was approved by the Institutional Review Board of Hokkaido University Hospital for Clinical Research (approval no. 13-285) and written informed consent was obtained from each patient.

Patients (aged≥20 years) included in the study had at least one tooth with root caries to allow the setting of the laser fluorescence device, DIAGNOdent™ Pen (wavelength 655 nm, 1 mW; KaVo, Biberach, Germany). Patients who had received recent treatment using Nanoseal were excluded from the study. In addition, root caries with fluorescence intensity values<40 as measured by the DIAGNOdent™ Pen (referred to as the D-value) was employed because the manufacturer recommends restorative treatment for caries with D-values>40. The samples of this study consisted of 129 teeth with untreated root caries (43 teeth per group) from 129 adult patients with a mean age of 66.4±10.1 years (56 males and 73 females). We selected the most anterior tooth for patients that had multiple teeth with root caries.

Sample size calculation was performed using power analysis software (G*Power3.1.7; Franz Faul, Uni Kiel, Kiel, Germany) based on the findings from a previous study carried out in Niigata city, Japan[8]. The study evaluated the reduction of the D-value of root caries after application of calcium phosphate complex paste for 6 months compared with control (no application). A sample size of 43 teeth for each group was calculated to

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achieve 90% power, 5% significance level, and anticipated effect size of 0.68, including dropout patients.

The patients were divided into three groups by simple randomization using the RANDBETWEEN function of Microsoft Excel (Microsoft, Redmond, WA, USA). Root caries was cleaned by a conventional Robinson polishing brush (Sun Dental, Osaka, Japan) in a low-speed handpiece (speed 2,000 rpm) with water. Subsequently, the reference point of the surface of root caries was decided for D-value measurement and surface color of root caries was recorded. Hardness of root caries surface was not investigated due to ethical considerations. D-value at baseline was measured using a fissure probe by directing light in the direction of the probe in accordance with the manufacturer's instructions. D-value was repeatedly measured at least three times to confirm showing the same value.

The study protocol is shown in Fig. 1. In the high-frequency (HF) group (n=43), patients received polishing and subsequent Nanoseal application at baseline and 1–5 months. The low-frequency (LF) group (n=43) received polishing every month and application of Nanoseal at baseline and 3 months. In the HF and LF groups, a Nanoseal mixture of liquid A (aqueous dispersion of nanoparticulate calcium-fluoroaluminosilicate glass) and B (phosphoric acid solution) was mildly applied (without rubbing) to root caries for at least 20 s using a micro-applicator (Nippon Shika Yakuhin) and then washed with water (Fig. 2). In the control group (n=43), patients received polishing only every month and no Nanoseal application. After baseline assessment, patients were instructed to use a toothpaste that did not include polishing material (Brosal; Nippon Shika Yakuhin) for self-care through the experimental periods. Following baseline measurement, the D-value of root caries of all groups was measured at 3 and 6 months.

At baseline, statistical differences between the three groups with regard to age and sex ratio (male/female) were analyzed by Welch's analysis of variances (ANOVA) test and the chi-squared test, respectively. For root caries color, statistical differences were analyzed by the chi-squared test. In addition, two-way repeated measures ANOVA with Bonferroni correction was performed to compare D-values. p Values<0.05 were considered statistically significant. All statistical procedures were performed using a software package (SPSS 11.0, IBM, Armonk, NY, USA).

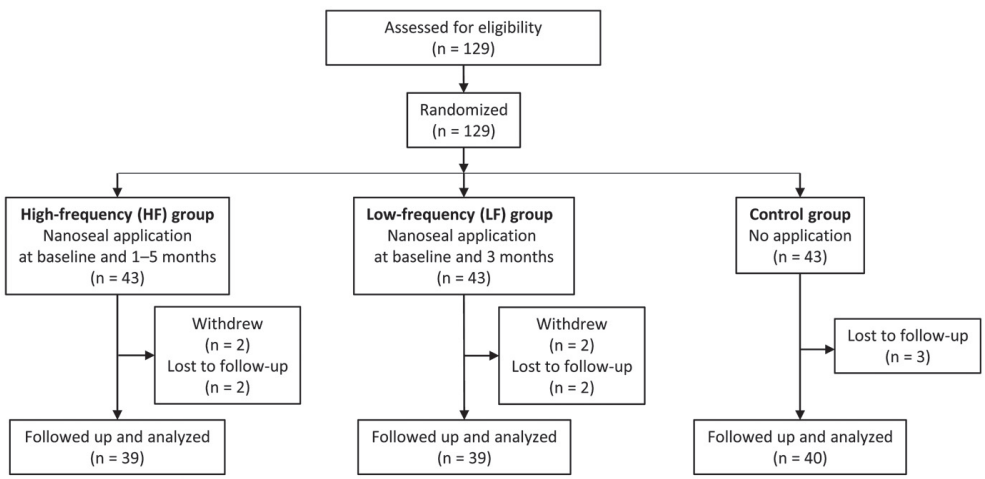


Fig. 1 Study flowchart.

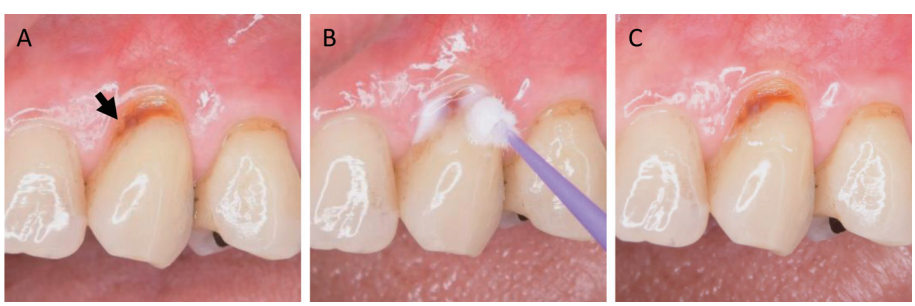


Fig. 2 Representative image of a canine with root caries.
(A) Pre-application. The black arrow indicates root caries. (B) Nanoseal application to root caries. (C) After washing with water.

RESULTS

At baseline, there were no significant differences between the three groups with regard to age (p=0.287), sex (p=0.969), and root caries color (p=0.2) (Tables 1 and 2). Root caries discoloration was not observed in any group over the 6-month study period. After the start of the trial, 11 patients (HF group: n=4; LF group: n=4; control group: n=3) were excluded from the study because they were lost to follow-up. Hence, a total of 118 patients (HF group: n=39; LF group: n=39; control group: n=40) completed the 6-month trial and were included in subsequent analyses (Fig. 1).

Mean D-values of all groups are shown in Table 3. Two-way ANOVA showed that there were significant differences in D-value related to application frequency (F=7.237, p<0.001) and observation periods (F=5.062, p=0.008). In addition, there was a significant interaction between frequency and periods (F=9.648, p<0.001). In sub-effect tests, D-value data collected at baseline and 3 months were not significantly different between groups (p>0.05). However, at 6 months, the mean D-value of the control group was significantly increased compared with those of the HF (p=0.017) and LF (p=0.034) groups.

Table 1 Demographics of study groups

	High-frequency	Low-frequency	Control
Age (y; mean±SD)	66.2±12.6	68.2±11.0	64.8±9.0
Sex ratio (male/female)	0.79	0.72	0.79

SD, standard deviation

Table 2 Surface color of root caries (%)

	High-frequency	Low-frequency	Control
Light brown	35.9	17.9	30.0
Dark brown	64.1	82.1	70.0

Table 3 DIAGNOdent™ values (mean±SD)

	High-frequency	Low-frequency	Control
Baseline	26.4±6.9	22.4±8.3	25.2±8.3
3 months	21.6±6.2	21.9±10.5	26.8±10.9
6 months	20.9±7.8*	21.6±11.8*	28.9±16.5

*p<0.05, compared with control group (two-way repeated measures ANOVA with Bonferroni correction). SD, standard deviation

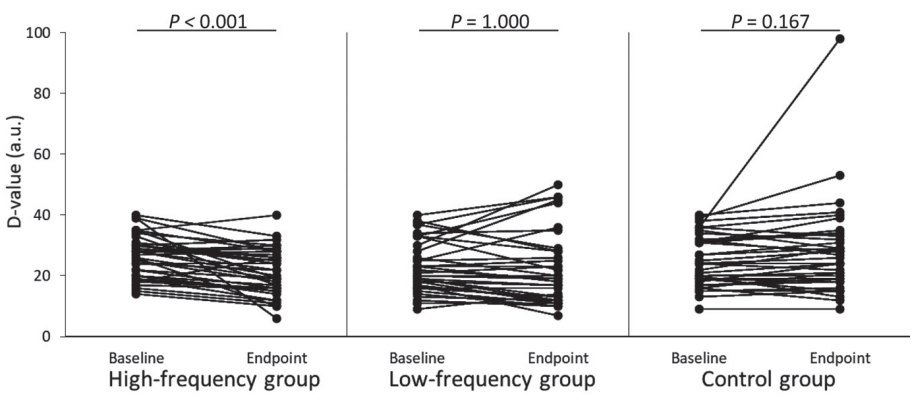


Fig. 3 Comparison of individual changes in D-value of each group between the study baseline and endpoint (6 months).
Significant differences were assessed using two-way repeated measures ANOVA with Bonferroni correction.

Comparisons of individual changes in D-value between the study baseline and endpoint are shown in Fig. 3. A significant difference was found between baseline and endpoint D-values in only the HF group ($p<0.001$). Some patients in the control group exhibited remarkably increased D-values during the experimental period in contrast to patients in groups that received Nanoseal application.

DISCUSSION

This study showed that Nanoseal application to root caries significantly inhibited the increase in D-values in the HF and LF groups. In addition, the HF group had significantly decreased D-values at the study endpoint (6 months). The laser fluorescence system of the DIAGNOdent™ pen calculates the absorbance of a low-power laser to determine the stage of caries progression. DIAGNOdent™ has been validated as a caries detection tool in several studies[9-12]. Wicht *et al.*[9] showed that the D-value of root caries was reproducibly measured by different operators. Zhang *et al.*[11] found a significant difference between D-values obtained from normal and carious roots. They revealed that surfaces with root caries had higher D-values than sound root surfaces. Hence, D-value evidence obtained in this study suggested the suppression of root caries progression through Nanoseal application.

Nanoseal consists of an aqueous dispersion of nanoparticulate calcium-fluoroaluminosilicate glass and phosphoric acid solution. After mixing the two liquids to acidize the glass, glass nanoparticles aggregate through the acid-base reaction. In addition, some ions associated with tooth minerals are released from the decalcified tooth surface. It is anticipated that some precipitates and insoluble mixtures form on the tooth surface to protect the tooth. From the evidence of this study, we speculate that these reaction products stably bind to the tooth surface to exert a suppressive effect. In addition, frequent application of Nanoseal should augment this effect. Previous *in vitro* assessments showed that the tooth surface layer including glass nanoparticles and precipitates enhanced resistance to demineralization. Han and Okiji[4] revealed that the tooth surface was covered with a nanoparticle layer incorporating calcium and silicon after Nanoseal application. Lodha *et al.*[6] examined mineral loss in bovine dentin placed into an acetic acid solution. Nanoseal application consequently suppressed mineral loss in the dentin compared with control (no application), fluoride varnish, and a conventional desensitizer agent. Taken together, we consider that the region of root caries was covered with a layer of calcium-fluoroaluminosilicate glass and other precipitates to supply ions to improve the carious tooth substrate. Furthermore, the layer may act as a physical barrier against oral bacteria and acidic food to reduce tooth demineralization.

In the clinical setting, fluoride application has been attempted to prevent root caries. A caries-preventive effect was exhibited by supplying fluoride toothpaste, varnish, and mouthwash[13-16]. Fluorapatite, which is created in human teeth exposed to fluoride ions, possesses great acid resistance[17]. A previous study reported that fluoride-releasing dental material increased the acid resistance of tooth surfaces around the material[18]. In addition, Nathanael *et al.*[19] reported that fluoride-incorporated hydroxyapatite exhibits antibacterial activity and reduces *Streptococcus mutans* growth, and additionally exhibits acid-resistant activity. Accordingly, long-term application of Nanoseal may strengthen the tooth through fluoride ion release from calcium-fluoroaluminosilicate glass and subsequent incorporation into the root surface. Further study is needed to elucidate the behavior of ions released from Nanoseal.

CONCLUSION

The root caries suppressive effect of Nanoseal was assessed as measured by the D-value. Nanoseal application groups exhibited significantly lower D-values of root caries compared with the control (no application) group at 6 months. In addition, the HF group showed significantly reduced D-values at 6 months. Nanoseal would be beneficial to suppress root caries progression.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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