Evaluation of fluoride effects on incipient caries lesion using the Q-Ray™ system

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Evaluation of fluoride effects on incipient caries lesion using the Q-Ray™ system

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또한 이 연구가 잘 될 수 있도록 도와준 열린마음치과 원장님들과 직원들에게 감사를 드립니다.

마지막으로 이 모든 과정을 이끄시고 변함없이 사랑해주시는 주님께 감사의 기도 올려드립니다.

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ABSTRACT

Evaluation of fluoride effects on incipient caries lesion

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(Directed by Professor Baek-Il Kim)

As the global frequency of cavitated dental caries has decreased, more interest has been paid to the early detection of incipient non-cavitated dental caries. The Quantitative Light-Induced Fluorescence-Digital (QLF-D, Q-Ray™) device introduced recently is one of the computer-based incipient caries lesion detection devices that can subtly spot and quantify minimal changes in tooth minerals. The machine is capable of taking intra-oral cavity images, and has been utilized clinically as well. Meanwhile, the remineralization effect of fluoride has been sufficiently proven by multiple preceding studies. Still more studies are necessary to qualitatively show the degree and developments of short-time changes treated with fluoride application in an oral environment with a high risk of incipient caries becoming mature.

Therefore, the present research sought to assess the remineralization recovery of incipient caries lesions after fluoride application by studying, first, pediatric patients with lesions among those with non-cavitated incipient caries lesions by utilizing the Q-Ray™ system. Second, the study aimed to discover the factors that affect remineralization recovery through fluoride application by a specialist. Third, based on the clinical database created during this process, the researcher aimed to identify the critical fluorescence loss amount (ΔF) to which the lesion could recover one or four weeks after fluoride treatment.

The research was performed under the approval of the research review committee (IRB No. 2-2013-0043) at the Yonsei University College of Dentistry. At the start of this research, the research subjects underwent oral cavity examination, stimulated salivary flow examination, plaque measurements, oral hygiene state examination and oral prophylaxis. Incipient caries lesions found during the oral cavity examination were photographed with the Q-Ray™ system before and after the oral prophylaxis. After the image taking process, a 1.23% acidulated phosphate fluoride (APF) gel-based fluoride application was conducted for one minute. The subjects re-visited the hospital to take Q-Ray™ images again one week and four weeks after the fluoride application. Based on the Q-Ray™ images taken, the detected fluorescence loss of the incipient caries lesion was analyzed.

One week after the fluoride application (31 subjects; 101 lesions), the recovered lesion group (N=68) improved in ΔF, ΔF_{max}, Area, and ΔQ compared to their pre-fluoride application state ($p<0.0001$). On the other hand, the unrecovered lesion group (N=33) showed worse ΔF and ΔF_{max} compared to their pre-fluoride application status ($p<0.0001$). Four weeks after the fluoride application (27 subjects; 90 lesions), the recovered group (N=53) improved in ΔF, ΔF_{max}, Area, and ΔQ ($p<0.0001$) compared to their pre-fluoride application status. The unrecovered lesion group (N=37) was found to show the opposite of the recovered group in every aspect (p<0.05).

The logistic regression analysis found that $\Delta F_{(0)}$ affected lesion recovery. Accordingly, we analyzed the degree of recovery in the three groups of lesions divided by the $\Delta F_{(0)}$. No change was observed in group 1 ($\Delta F_{(0)} \geq -10\%$) one week after fluoride application. However, group 2 ($-20\% \leq \Delta F_{(0)} < -10\%$) and group 3 ($\Delta F_{(0)} < -20$) were recovered about 12.01% and 29.05% one week after fluoride application (p<0.05).

A receiver operating characteristic (ROC) curve analysis was conducted to identify the amount of critical fluorescence loss ($\Delta F_{(0)}$) up to which lesions can recover. The result of this analysis found that the lesions with fluorescence loss ($\Delta F_{(0)}$) of less than -11.8% and -13.0% could be recovered one week and 4 weeks after fluoride application, respectively.

This clinical research has discovered the effect of fluoride on incipient caries lesion recovery and its extent, and that the severity of incipient caries lesions discovered in the first examination affected post-fluoride application remineralization recovery. In addition, by studying the cutoff point of fluorescence loss according to incipient caries lesion recovery, the researcher could more effectively investigate changes in the lesions of incipient caries patients by using the Q-Ray™ system within a shorter period of time. In this sense, the present research is expected to lay a cornerstone for the more proactive management of incipient caries lesions that will receive continued attention in the field of dentistry in the future.

Key words: Diagnostic tools, fluoride, incipient caries, quantitative light-induced fluorescence-digital (QLF-D, Q-Ray™), remineralization

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1. INTRODUCTION

In modern society, where people's average life expectancy is continuously increasing, people want a healthy life span more than anything else. In other words, they want to delay their period of physical deterioration prone to diseases as much as possible and have a healthy status as long as possible so that they can function efficiently throughout their lives. In line with this rising interest in a healthy life, the health management paradigm has changed. Today, people go beyond the conventional approach where medical treatment began only after a disease had already developed to some extent by visiting hospitals on a regular basis before a disease develops and receiving a variety of examinations, such as blood tests, endoscopic examinations, and cancer examinations, even though they do not feel any discomfort. That is, health management's target has gone beyond treating just patients to include normal people seeking to maintain their health. Such a health care paradigm shift required changes not only in the medical sector, but also across all of the related industries. With the remarkable development of information technology and advanced diagnosis and treatment accuracy, early diagnosis has become possible in the initial stage of a disease, thus treatment effectiveness has improved, resulting in higher patient satisfaction.

This paradigm change has also been seen in the dental treatment area, stressing early disease detection and diagnosis as well as building efficient treatment plans accordingly. In the case of South Korea, a national oral cavity health status investigation found that the DMFT index of 12-year-old children decreased to 1.8 in 2012 from 3.3 in 2000 (Ministry of Health and Welfare, 2001, 2013). This figure indicates a 50% drop over 12 years in the number of teeth with caries among the total teeth in the oral cavity. Given the Organization for Economic Co-operation and Development (OECD) national averages, this decrease is similar to the OECD average DMFT index fall from 4.7 in 1980 to 1.5 in 2006. From this observation, we can see that prevalence of dental caries has decreased considerably in South Korea and beyond (Social Policy Department O, 2010). Such a dynamic shift implies that normal people’s interest in oral cavity health related to dental caries has shifted from invasive treatment to management. Thus, just as in the medical sector, the dental sector needs to put more effort into effective oral cavity health management.

As caries decreases in the visible cavity formation process, more attention is being paid to its preceding states. In the early stage, caries is caused as minerals are lost on the enamel subsurface, in terms of microstructure. From a visual inspection, the tooth surface is distinguished from normal teeth by looking whiter and opaque or brown. The pH level in the intra-oral cavity environment continuously changes due to various factors such as food intake, saliva, etc. Along with such a series of reactions, the tooth surface maintains a dynamic equilibrium through demineralization and remineralization. If the oral cavity pH level is not appropriately restored and stays under the critical pH continuously, the porosity of enamel was increased due to mineral loss, and if such a process continues, it ends up with cavity formation, requiring restorative treatment. Therefore, it is a significant variable to accurately detect such white spots early, a surrogate indicator of caries development caused by tooth demineralization. Doing so before caries cavity formation on the tooth surface, allows the patient to keep teeth healthy while also avoiding the restorative treatment that often accompanies irreversible tooth damage. Monitoring the dental caries using this surrogate indicator needs the objective criteria that can accurately diagnose the progression of a disease at the early stage. However, one of the largest problems faced clinically is that the lesion status, which can remineralize incipient caries, is not precisely diagnosable.

Clinical practitioners have traditionally used explorers for palpation along with visual inspection by distinguishing dental caries. However, according to the previous studies, more frequent occlusal early caries is hard to detect at the early stage, thus, even though visual inspection and palpation are utilized simultaneously, it was found that the actual sensitivity for the diagnosis of early occlusal surface caries was less than 20% (Bader et al., 2001). As such, the diagnostic accuracy is lower, largely because of the absence of an objective and a consistent standard for the diagnosis of dental caries lesion. In the case of a non-cavited lesion especially, lesion detection based on conventional methods is more limited. To overcome this problem, several methodologies have been developed to minimize subjective judgment and improve sensitivity (Ekstrand et al., 1997). Of these, the recently developed International Caries Detection and Assessment System (ICDAS) further categorized dental caries progress into six phases and verified them histologically for successful settlement. Nevertheless, to get accustomed to this classification system, one should undergo a certain amount of training. For this reason, it has yet to be fully utilized in clinical practices. Following visual inspection and palpation, the third most commonly utilized diagnostic method in clinical practices is radiation image examination. It also, however, has a diagnostic sensitivity of a mere 30% regarding incipient caries (Bader et al., 2001; Pretty, 2006). Such preceding research findings, after all, indicate that conventional examination methods are limited in diagnosing incipient caries.

As the medical area has seen diverse diagnostic equipment development along with science technology advancement, the dental sector has also developed equipment capable of diagnosing and detecting dental caries more accurately. Good examples of useful equipment include quantitative light-induced fluorescence (QLF), electrical conductance measurements (ECM), infrared (IR) laser fluorescence, direct digital radiography and digital imaging fiber-optic transillumination (DIFOTI). Of these, the QLF system can detect subtle changes in teeth minerals, so it has been recognized as a very useful device to detect incipient caries and assess its progress. The QLF system shines a visible ray on the tooth surface and digitizes the auto-fluorescence manifestation reaction of the tooth enamel (Bjelkhagen et al., 1982). The QLF system uses a blue visible ray with a peak intensity of 405nm as its light source (de Josselin de Jong et al., 1995). The light shed on a tooth is scattered in the parts of the incipient caries lesion that have reduced minerals and the fluorescence amount is naturally lost in a sound tooth surface. This makes such areas look darker in the QLF system compared with that are taken of healthy teeth. This QLF system caries detection mechanism can quantify the amount of minerals lost from the tooth surface according to the dental caries progress phases, thus presenting the status of caries progress whenever necessary (Stookey, 2005). Indeed, the QLF system has been known to be effective in discovering incipient caries not detectable by ocular inspection (Heinrich-Weltzien et al., 2005). Recently, instead of older cameras, digital cameras were adopted for the second version of the Quantitative Light-Induced Fluorescence Digital Biluminator™ (hereinafter, Q-Ray™). The Q-Ray™ system can produce normal images and fluorescent images at the same time with just one shooting session.

Among the various incipient caries lesion detectors, the Q-Ray™ system was reported to have a correlation of at least 0.82 with transverse microradiography (TMR), a gold standard analysis device that measures tooth mineral changes (Pretty, 2006). In particular, in baby teeth caries at an early stage, QLF (fluorescence loss) and TMR (mineral loss) were found to have a correlation of 0.88, indicating the usefulness of using QLF in dental clinical cases instead of TMR, which is impossible to use clinically (Ando et al., 2001).

It has already been widely known that the use of fluoride can reduce the progress of early caries remarkably (Angmar-Mansson et al., 1998; Hume, 1993). Fluoride changes tooth surface hydroxyapatite into fluorapatite, which gives stronger resistance against the dental caries formation and causes remineralization on the demineralized surface to delay caries progress. Today, thanks to the use of fluoride-containing toothpastes, dental caries has been significantly reduced from being widely known. Experts have seen that fluoride-containing toothpastes are a significant reason for the huge dental caries reduction in adults in their 20s in Europe for the past 30 years (Bratthall et al., 1996). It is no longer controversial that fluoride is the main material that prevents dental caries effectively, but its remineralization effectiveness and prognosis according to the severity of incipient caries lesions need to be considered further (Lynch and Ten Cate, 2006). A relevant *in vitro* study (Kim et al., 2013) conducted fluoride treatment for artificial incipient caries lesions with different levels of severity and analyzed the extent of these tooth specimens' recovery according to their severity with the Q-Ray™ system. As a result, the study found differences in the remineralization recovery status according to the caries lesion severity. It also presented critical points at which to recognize recovery status for each fluorescence loss amount measured by the Q-Ray™ system, indicating the need to treat the patients having different severity of lesions. However, since the research lab experiment was performed under a thoroughly controlled condition while excluding several host elements, such as the dental plaque management of the dental caries recovery requirements, plaque control, saliva flow rate, saliva buffering capacity, etc., the findings need to be applied to diverse actual cases of the incipient caries lesion found during clinical processes and the cases need to be traced and properly assessed to see how much they can recover.

With this recognition, the present research sought to, first, assess any lesion change in terms of the remineralization recovery status of incipient caries lesions in pediatric patients with non-cavitated early caries with the Q-Ray™ system after professional fluoride application treatment. Second, the researcher aimed to analyze the external factors affecting the remineralization recovery status as a result of the professional fluoride application and check for any lesion changes according to these factors. Third, based on this research's experimental findings, the researcher aimed to identify the critical fluorescence loss amount (ΔF) to which the lesion could recover the status against further demineralization one or four weeks after fluoride treatment.

2. MATERIALS AND METHODS

2.1. Study subjects

The research was performed with the approval of the research review committee of the Yonsei University College of Dentistry (IRB No. 2-2013-0043).

Subjects were invited from August 2013 to May 2014, and included children between ages 2 and 12 who had at least one non-cavitated incipient caries lesion without tooth damage found during ocular inspection. The research subjects, on their first hospital visit, underwent a caries risk assessment survey examination, tooth examination, microorganism examination, saliva flow rate examination and oral biofilm examination, and their labial and buccal incipient caries lesions were photographed with the Q-Ray™. One week after the fluoride application, 31 subjects (lesion=101) completed the follow-up, and between one week and four weeks, 27 subjects (lesion=90) completed the follow-up. People excluded from this research experiment were those with no periodontal disease or oral cavity disease, who had a tooth with no crown due to a serious dental caries, who were taking antibiotics or other drugs for systemic diseases and who had an uncontrollably serious systemic disease or weakened immune system (AIDS, uncontrollable diabetes, radiation-intensive investigation, heart disease, homeostasis/blood-related disease).

2.2. Study design

2.2.1. Clinical research introduction and subject consent

Before this research experiment, the researcher reported its purposes and processes to the subjects and their parents, and informed consent was provided. This study included only those who agreed to participate in the experiment. The explanation of the research and consent to participate were given to the parents (adults) and the research subjects (children) (Appendix Figures 1 and 2).

2.2.2. Caries risk assessment

Before taking the Q-Ray™-based images of incipient caries lesions, the researcher examined the subjects' characteristics on their first hospital visit to evaluate caries risk assessment as follows:

2.2.2.1. Survey investigation

With an arranged paper survey, the researcher investigated the subjects for their basic personal information (age, sex, experience of living in a region without fluorinated water), experience of decayed tooth treatment for the past three years, fluoride application experience (fluoride varnish, professional fluoride gel application and 0.05% NaF mouth rinse use), hexamedine experience, xylitol gum chewing experience, previous usage of remineralization products (Tooth mousse or 3M Clinpro®), fluoride toothpaste usage and oral cavity care products usage (dental floss and interdental brush usage).

2.2.2.2. Tooth examination

To examine the research subjects' dental caries and filling status, the researcher performed visual inspection and recorded any dentin caries, interproximal enamel caries, deep fossa and fissure, exposed dental roots, orthodontic appliance use, existence of incipient caries lesions and filled teeth.

2.2.2.3. Microorganism examination

The commercially available Cariview® kit (Huneth, Seoul, Korea) was used to measure the acidogenicity of the bacteria in plaque across the tooth surface of the research subjects. To this end, dental plaque on the buccal surfaces of the subjects' teeth was taken with sterilized swabs and immediately put into a culture medium for 48-hour cultivation at 37℃. Then, an indicator was added to show different colors from red to blue according to the pH levels of culture medium. This color analysis was converted into digital images with scores from 0 to 100, and the acid-producing capacity of dental plaque was measured. The Cariview® score was used to divide subjects into three caries risk groups as following: score 0 – 40; low risk group, score 41-70; moderate risk group, and score 71-100; high risk group.

2.2.2.4. Saliva flow rate examination

To examine the stimulated salivary flow, the subjects were instructed to masticate paraffin wax for three minutes and collect saliva in a tube. The collected saliva was quantified and converted into the unit of ml per one minute. Those with a saliva amount of more than 0.7 ml/min were viewed as normal and those under 0.7 ml/min were viewed as having an insufficient saliva rate.

2.2.2.5. Plaque measurements

The whole tooth surface inside the oral cavity was dyed with one-tone disclosing solution (Chrom-O-Red, Germiphene Corporation, Canada). Then dental plaque of subject status and management status were assessed with the O'Leary index.

2.2.3. Using the Q-Ray™ system to take images of incipient caries lesions

In the tooth examination of the research subjects, if an incipient caries lesion was found in at least one tooth surface, the lesion severity was quantified. To continuously monitor the post-fluoride application progress of remineralization, the Q-Ray™ system (quantitative light-induced fluorescence—digital; QLF-D Biluminator™, Inspektor Research Systems BV, Amsterdam, The Netherlands) was employed to take images of the lesion. Images were taken after the overall oral prophylaxis process. Lesion images were also taken when the subjects re-visited the hospital at one week and four weeks after the fluoride application, which was done after the prophylaxis of the teeth.

In taking lesion images, the Q-Ray™ system image taking conditions were set as those described in Table 1, and the white- and blue-light fluorescence images were taken. All of the images were saved as bitmap images.

Table 1. Photographing conditions of the Q-Ray™ system used in this study

	White light	Blue light
Shutter speed	1/60s	1/30s
Aperture value	10.0	5.6
ISO speed	1600	1600
Pixel size	2592 × 1728	2592 × 1728

2.2.4. Fluoride application

After oral prophylaxis, the tooth surface was dried and then fluoride was applied for one minute, using 1.23% APF gel (60 SECOND GEL, Germiphene, Branford, Canada). After the fluoride application, the subjects and their parents were told not to rinse with water for 30 minutes and not to eat food or drink water for 30~60 minutes. At the first hospital visit, all subjects' parents received identical 990 ppm fluoride-added toothpaste for their kids to use. They were also instructed to guide their kids not to swallow the toothpaste during use.

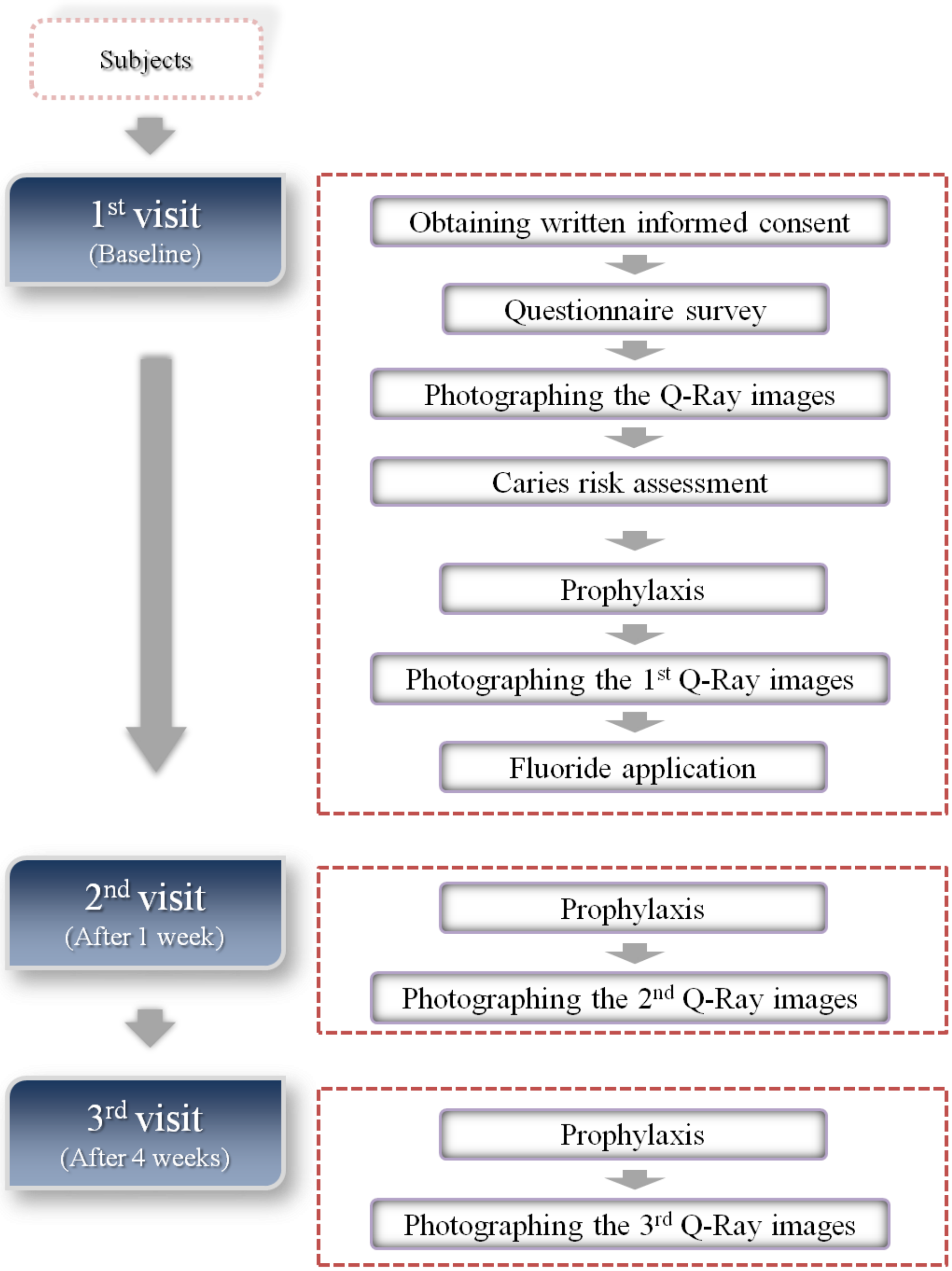

Figure 1. Study procedure

2.2.5. Assessment of caries risk using Cariogram model

A Cariogram is a tool for estimating comprehensive caries risk in consideration of nine elements, including a caries, caries-related systemic disease status, fermentative carbohydrate intake, snacking frequency, dental plaque management level, microorganism level (Mutans streptococci), saliva flow rate, saliva buffering capacity, and clinical judgment (Bratthall and Hansel-Petersson, 2005). As the actual program can produce a caries risk result even without some of the elements (Campus G et al., 2012), this research used the caries experience teeth (dft), dental plaque management level (O'Leary plaque control index), microorganism level (Cariview® score), saliva flow rate, fluoride program (fluoride toothpaste usage), and clinical judgment to produce a chance to avoid new caries (%) with the Cariogram program. Each subject's caries risk was assessed based on the Cariogram outcome. According to the results, subjects were divided into three groups; $0\% \le$ score $\le 25\%$ for high-risk group, $25\% <$ score $\le 75\%$ for mid-risk group, and $75\% <$ score for low-risk group.

2.2.6. Analysis on fluoride-based remineralization recovery of incipient caries lesions

To observe the mineral amount change in incipient caries lesions with fluorescence loss (ΔF_{Tx}), the Q-Ray™ system's exclusive analysis program (C3 v1.23, Inspektor Research Systems BV, Amsterdam, The Netherlands) was employed to calculate pre-fluoride application ($\Delta F_{(0)}$), and one week after the fluoride application ($\Delta F_{(1)}$) and four weeks after the fluoride application ($\Delta F_{(4)}$) to measure any changes in lesion fluorescence loss. To identify the amount of minerals in the incipient caries lesions that were restored after each fluoride application, the following equation was used to find out ΔF recovery ($R_{\Delta F}$):

$$\text{Recovery rate of } \Delta\Delta F\ (\%, R_{\Delta F}) = [(\Delta F_{(0)}-\Delta F_{(1)\ or\ (4)})/\Delta F_{(0)}] \times 100$$

Together with this, the corresponding lesion's average fluorescence loss, ΔQ ($\Delta F \times$ Area), was also calculated by considering the lesion size and average fluorescence loss, the ΔF(%) and maximum fluorescence loss, ΔF_{max}(%) and the lesion Area (pixel). The recovery rates of these variables were calculated using above formula.

2.2.7. Statistical analysis method

The research examined by dividing lesions separately as one unit. Accordingly, this research analysis is based on the data of 31 subjects (lesion=101) who participated until one week after the fluoride application and 27 subjects (lesion=90) who participated until four weeks after the fluoride application.

First of all, the lesions were divided into the recovered group ($R_{\Delta F} \geq 0$) and unrecovered group ($R_{\Delta F} < 0$) according to their remineralization recovery status. They were tested to see how much their lesions (N=101 or 90) changed one and four weeks after the fluoride application through a paired t-test. Here, an independent t-test was performed at each point to see any differences in the lesion variables (ΔF, ΔF_{max}, Area and ΔQ) between the recovered group and unrecovered group. A logistic regression analysis was also conducted to find out which risky characteristics affected the subjects' lesion remineralization restoration. In this analysis, before the fluoride application, early fluorescence loss ($\Delta F_{(0)}$) was found to affect lesion remineralization recovery. Therefore, according to early fluorescence loss ($\Delta F_{(0)}$), changes in the pre- and post-fluoride application (one week and four weeks) fluorescence loss amount (ΔF) were examined by a repeated measures analysis of variance (ANOVA). Lastly, a ROC curve analysis was followed to find the critical points of baseline fluorescence loss ($\Delta F_{(0)}$) in the lesions, which showed effects of remineralization or inhibition of further demineralization after one week and four weeks from fluoride application. The statistical analysis in this research was done with a significance level of 0.05, and IBM SPSS software (IBM® SPSS® Statistics ver. 20, IBM Corp., Armonk, NY, U.S.A.) and Medcalc software (MedCalc® Version 13.2.2.0, Medcalc Software bvba, Ostend, Belgium)were employed.

Table 2. Inspection and analysis item in this study

Examination	Inspection and analysis item
Questionnaire	• Age and sex • Residency in water fluoridated area • Restorative treatment for decayed teeth in last 3 years • Every day mouth rinsing with a 0.05% NaF solution • Fluoride varnish application in last 6 months • Professional Fluoride application in last 6 months • Chewing xylitol gum more than 4 times a day in last 6 months • Use of Tooth mousse and 3M Clinpro® products in last 6 months • Use of Fluoride toothpaste • Use of dental floss and interdental brush
Tooth	Decayed, filling primary teeth, and incipient caries lesions
Microbiology	Cariview®
Saliva	Saliva flow rate
Plaque	Plaque index (O'leary index)
Caries risk Classification	Cariogram
Incipient caries severity by Q-ray	ΔF, ΔF_{max}, Area, and ΔQ

3. RESULTS

3.1. Subject population

Of the subjects, a total of 31 subjects (16 male subjects, 15 female subjects) completed re-examination after one week, and from them, 101 teeth with incipient caries in total were analyzed (Table 3). The average age of the subjects was 5.74±1.61 with age distribution between 3 and 10. They received basic oral examinations on their first hospital visit. The average of the stimulated salivary flow was 1.12±0.61 ㎖/min. Of the subjects, 20 showed flow rates higher than 0.7 ml/min and included within the normal range. A Cariview® kit, an oral hygiene state examination based on the acid-producing capability of bacteria in the dental plaque, was used to check the subjects' caries activity. As a result, the average outcome of the subjects as a whole was 42.27±22.70, indicating a moderate risk of caries development. Of the total, 18 were included in the low-risk group, scoring at 31.32±2.51; 7 in the moderate-risk group with 61.69±10.85; and 6 in the high-risk group with 85.65±9.53. A Cariogram, an assessment tool for caries risk anticipation, was used for the analysis and the subjects' chances of avoiding new caries were 18.65±15.38. Their caries development risks were mostly in the moderate-risk and high-risk group. The moderate-risk group had 4 subjects with 52.75±11.38% chance of avoiding new caries; and the high-risk group of 27 subjects had 13.59±7.24% chance. The participating subjects' dental plaque management scores (Plaque index, O'Leary index) were 81.41±15.94. The subjects were found to have at least 1 to a maximum of 17 decayed and filling primary teeth (dft), averaging 6.48±3.87 dft index (Table 3).

Four subjects dropped out during the experiment. Therefore, a total of 27 subjects (13 male subjects, 14 female subjects) completed re-examination four weeks after the treatment, and from them, 90 teeth with incipient caries were analyzed (Table 3). The subjects' average age was 5.89±1.60 with age distribution between 4 and 10. They received basic examinations on their first visit to the hospital. The average of the stimulated salivary flow was 1.12±0.59ml/min. Eighteen of the subjects showed higher flow rates than 0.7ml/min, falling below the normal range. A Cariview® kit was used to check the subjects' caries activity. The subjects' average score was 49.17±23.45, exhibiting a mid-risk level of caries activity. Of the total, 16 were in the low-risk group with 32.39±2.66; 5 in the moderate risk group with 59.12±11.23; and 6 in the high-risk group with85.65±9.53. A Cariogram was used for analysis and the subjects' average chance of avoiding new caries was 17.52±13.94%. Their caries development risks were mostly in the moderate risk and high-risk group. The moderate risk group had 3 subjects with an average chance of avoiding new caries at 49.67±11.72% and the high-risk group had 24 subjects with a chance of 13.50±7.49%. The participating subjects' average dental plaque management score (Plaque index, O'Leary index) was80.95±16.72. The subjects were found to have at least 1 to a maximum of 17 decayed and filling primary teeth (dft), averaging 6.74 ±3.82 dft index (Table 3).

Table 3. Distribution of demographic and investigated factors of subjects included in this study

	1 week follow-up			4 weeks follow-up		
Variables	Mean (SD)	N	%	Mean (SD)	N	%
Subjects		31	100.00		27	100.00
Sex						
Male		16	51.61		13	48.15
Female		15	48.39		14	51.85
Total		31	100.00		27	100.00
Incipient caries lesions monitored		101	100.00		90	100.00
Range of lesions per subject	1 – 8			1 – 8		
Age	5.74 (1.61)	31	100.00	5.89 (1.60)	27	100.00
Minimum - maximum	3 – 10			4 – 10		
Saliva flow rate						
Low	0.53 (0.20)	11	35.48	0.50 (0.21)	9	33.33
Normal	1.45 (0.50)	20	64.52	1.43 (0.46)	18	66.67
Total	1.12 (0.61)	31	100.00	1.12 (0.59)	27	100.00
Cariview score						
Low	31.32 (2.51)	18	58.06	32.39 (2.66)	16	59.26
Moderate	61.69 (10.85)	7	22.58	59.12 (11.23)	5	18.52
High	85.65 (9.53)	6	19.35	85.65 (9.53)	6	22.22
Total	42.27 (22.70)	31	100.00	49.17 (23.45)	27	100.00
Cariogram score						
Low	0	0	0	0	0	0
Moderate	52.75 (11.38)	4	12.90	49.67 (11.72)	3	11.11
High	13.59 (7.24)	27	48.39	13.50 (7.49)	24	88.89
Total	18.65 (15.38)	31	100.00	17.52 (13.94)	27	100.00
Plaque index (O'Leary)	81.41 (15.94)	31	100.00	80.95 (16.72)	27	100.00
Decayed and filling Teeth	6.48 (3.87)	31	100.00	6.74 (3.82)	27	100.00
Minimum - maximum	1 – 17			1 – 17		

In addition, as a result of the survey investigation of the subjects in the first week of their re-examination, they were found to have never lived in areas with fluorinated water projects, and 96.77% (30 subjects) said they had received decayed tooth treatment for the past three years. In general, the subjects tended to have less experience with remineralization treatment including fluoride application (0.05% NaF solution 6.45%, F varnish 25.81%, professional fluoride application 35.48%, hexamedine usage 0%, xylitol gum 0% and remineralization products 0%), and normally used oral cavity management tools less frequently (interdental brush 6.45%, dental floss 32.26%). But 79.97% were found to have used fluoride toothpaste as they brushed their teeth (Table 4).

The fourth week of subject re-examination found that they had never lived in areas with fluorinated water and 96.30% (26 subjects) said they had received decayed tooth treatment for the past three years. They tended to have received remineralization treatment including fluoride application less frequently (0.05% NaF solution 3.70%, F varnish 22.22%, professional fluoride application 29.63%, hexamedine usage 0%, xylitol gum 0% and remineralization products 0%), and normally used oral cavity management tools less frequently (interdental brush 7.41%, dental floss 33.33%). But 70.37% were found to have used fluoride toothpaste as they brushed their teeth (Table 4).

Table 4. The response to the questions of dental treatment experience and use of oral care products

Question	1 week follow-up				4 weeks follow-up			
	Yes		No		Yes		No	
	N	%	N	%	N	%	N	%
Residency in water fluoridated area	0	0.00	31	100.00	0	0.00	27	100.00
Restorative treatment for decayed teeth in last 3 years	30	96.77	1	3.23	26	96.30	1	3.70
Every day mouth rinsing with a 0.05% NaF solution	2	6.45	29	93.55	1	3.70	26	96.30
Fluoride varnish application in last 6 months	8	25.81	23	74.19	6	22.22	21	77.78
Professional Fluoride application in last 6 months	11	35.48	20	64.52	8	29.63	19	70.37
Mouth rinsing with Hexamedine® for 1 week in last 6 months	0	0.00	31	100.00	0	0.00	27	100.00
Chewing xylitol gum more than 4 times a day in last 6 months	0	0.00	31	100.00	0	0.00	27	100.00
Use of Tooth mousse and 3M Clinpro® products in last 6 months	0	0.00	31	100.00	0	0.00	27	100.00
Use of Fluoride toothpaste *	22	70.97	4	12.90	19	70.37	3	11.11
Use of interdental brush	2	6.45	29	93.55	2	7.41	25	92.59
Use of dental floss	10	32.26	21	67.74	9	33.33	18	66.67

* Unknown responses were excluded in this table.

3.2. Post-fluoride application lesion change according to recovery status

3.2.1. Change after one week of fluoride application

The 31 subjects who participated until one week after the fluoride application had their 101 lesions in total investigated to assess their fluorescence loss ($\Delta F_{(1)}$, %) after the first week. As a result, it was found that the recovered lesion group ($R_{\Delta F(1)} \geq 0$, N=68) showed approximately 21.20% recovery $\Delta F_{(1)}$ from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p<0.0001$, Table 5). On the other hand, the unrecovered group ($R_{\Delta F(1)} < 0$, N=33) showed about 22.80% deterioration $\Delta F_{(1)}$ than the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p<0.0001$, Table 5). $\Delta F_{(0)}$ of the two groups were compared and it was found that $\Delta F_{(0)}$ of the recovered group (-14.89±6.81) was statistically significantly lower than $\Delta F_{(0)}$ of the unrecovered group (-10.32±3.70) ($p<0.0001$, Table 5), showing a change in recovered pattern according to the fluorescence loss amount in the pre-fluoride application lesion status.

Maximum fluorescence loss ($\Delta F_{max(1)}$, %) was measured one week after the fluoride application and the recovered group was found to have about 26.42% recovery in the $\Delta F_{max(1)}$ value from the pre-fluoride application ΔF value ($\Delta F_{max(0)}$) ($p<0.0001$, Table 5). On the other hand, the unrecovered group was found to show about 37.33% deterioration in the $\Delta F_{max(1)}$ value from the pre-fluoride application ΔF_{max} value ($\Delta F_{max(0)}$) ($p<0.0001$, Table 5). $\Delta F_{max(0)}$ of two groups were compared with each other and the $\Delta F_{max(0)}$ of the recovered group(-36.63±19.57) was statistically significantly lower than the $\Delta F_{max(0)}$ of the unrecovered group (-23.79±13.55) ($p<0.0001$, Table 5).

The lesion area of subjects and ΔQ were also measured one week after the fluoride application. The recovered group exhibited a 24.73% reduction in the $Area_{(1)}$ value from the pre-fluoride application $Area_{(0)}$ and $\Delta Q_{(0)}$ (p=0.001), and the $\Delta Q_{(1)}$ value was recovered by 35.19% (p<0.0001, Table 5). On the other hand, the unrecovered group demonstrated no significant difference in Area and ΔQ value from the pre-fluoride application status. $Area_{(0)}$ and $\Delta Q_{(0)}$ of two groups were compared and no statistically significant differences were found between the groups (Table 5).

Table 5. Changes in ΔF, ΔF_{max}, Area, and ΔQ according to the recovery of the lesions after 1 week of fluoride application (Unit: lesion)

Groups	Range of $R_{\Delta F1}$	N	ΔF		P*	ΔF_{max}		P*	Area		P*	ΔQ		P*
			Baseline	After 1 week		Baseline	After 1 week		Baseline	After 1 week		Baseline	After 1 week	
Recovery	≥0	68	-14.89 (6.81)	-11.51 (5.70)	< 0.0001	-36.63 (19.57)	-27.09 (17.65)	< 0.0001	646.38 (634.04)	506.47 (556.23)	0.001	-10832.59 (12804.40)	-7123.99 (9358.43)	< 0.0001
Recovery rate			21.21 (19.91)			26.42 (27.04)			24.73 (60.69)			35.19 (58.64)		
Non recovery	<0	33	-10.32 (3.70)	-12.34 (4.22)	< 0.0001	-23.79 (13.55)	-29.03 (12.95)	< 0.0001	522.42 (641.33)	552.00 (519.27)	.542	-7147.00 (10917.06)	-8030.85 (9661.71)	.156
Recovery rate			-22.80 (32.99)			-37.33 (58.37)			-229.51 (872.19)			-370.37 (1215.17)		
Total		101	-13.40 (6.33)	-11.78 (5.25)		-32.44 (18.76)	-27.72 (16.23)		605.88 (635.90)	521.35 (542.26)		-9628.39 (12288.39)	-7480.88 (9417.99)	
P			<.0001	.463		<.0001	.534		.361	.694		.158	.685	

All values are means (standard deviations).
*P-values were obtained by paired t-test.
P -value were obtained by two sample t-test.

3.2.2. Change after four weeks of fluoride application

The 27 subjects who participated four weeks after the fluoride application were investigated for their 90 lesions in total to assess their fluorescence loss ($\Delta F_{(4)}$, %) four weeks after the fluoride application. As a result, it was found that the recovered lesion group ($R_{\Delta F(4)} \geq 0$, N=53) showed approximately 23.57% recovery in $\Delta F_{(4)}$ from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p<0.0001$, Table 6). On the other hand, the unrecovered group ($R_{\Delta F(4)} < 0$, N=37) showed about a 30.17% deterioration in $\Delta F_{(4)}$ value from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p<0.0001$, Table 6). The two groups' $\Delta F_{(0)}$ were compared and it was found that the recovered group's $\Delta F_{(0)}$ (-16.53±6.78) was statistically significantly lower than the unrecovered group's $\Delta F_{(0)}$ (-10.04±3.53) ($p<0.0001$, Table 6), showing a change in recovered pattern according to the fluorescence loss amount in the pre-fluoride application lesion status.

Maximum fluorescence loss ($\Delta F_{max(4)}$, %) was measured four weeks after the fluoride application and the recovered group was found to have about 30.11% recovery in their $\Delta F_{max(4)}$ value from the pre-fluoride application ΔF value ($\Delta F_{max(0)}$) ($p<0.0001$, Table 6). On the other hand, the unrecovered group was found to show about 60.85% deterioration in their $\Delta F_{max(4)}$ value from the pre-fluoride application ΔF_{max} value ($\Delta F_{max(0)}$) ($p<0.0001$, Table 6). The two groups' $\Delta F_{max(0)}$ were compared to each other and the recovered group's $\Delta F_{max(0)}$ (-41.60±19.03) was statistically significantly lower than the unrecovered group's $\Delta F_{max(0)}$ (-22.95±12.48) ($p=0.0001$, Table 6).

The subjects' lesion Area and ΔQ were also measured four weeks after the fluoride application. The recovered group exhibited a 31.38% reduction in their $Area_{(4)}$ value from the pre-fluoride application $Area_{(0)}$ and $\Delta Q_{(0)}$ ($p<0.0001$), and their $\Delta Q_{(4)}$ value was recovered by 41.07% ($p<0.0001$, Table 6). On the other hand, the unrecovered group demonstrated a significant increase in their $Area_{(4)}$ value (p=0.001), showing the smaller lesion area, and a significant decrease in their $\Delta Q_{(4)}$ value from the pre-fluoride application $Area_{(0)}$ and $\Delta Q_{(0)}$ status (p<0.05, Table 6). The two groups' $Area_{(0)}$ and $\Delta Q_{(0)}$ were compared and the recovered group's Area was larger than that of the unrecovered group, while ΔQ was significantly lower in the recovered group than in the unrecovered group (p<0.05, Table 6).

Table 6. Changes in ΔF, ΔF_{max}, Area, and ΔQ according to the recovery of the lesions after 4 week of the fluoride application (Unit: lesion)

Groups	Range of $R_{\Delta F4}$	N	ΔF		P*	ΔF_{max}		P*	Area		P*	ΔQ		P*
			Baseline	After 4 weeks		Baseline	After 4 weeks		Baseline	After 4 weeks		Baseline	After 4 Weeks	
Recovery	≥0	53	-16.53 (6.78)	-12.55 (5.81)	< 0.0001	-41.60 (19.03)	-29.32 (15.91)	< 0.0001	793.36 (744.64)	621.00 (738.05)	< 0.0001	-14100.98 (14811.30)	-9134.28 (11846.59)	< 0.0001
Recovery rate			23.57 (23.97)			30.11 (26.58)			31.38 (43.63)			41.07 (40.66)		
Non recovery	<0	37	-10.04 (3.53)	-12.64 (3.95)	< 0.0001	-22.95 (12.48)	-30.08 (10.82)	< 0.0001	361.76 (378.29)	576.59 (482.75)	0.001	-4360.19 (5113.79)	-7680.00 (6793.02)	< 0.0001
Recovery rate			-30.17 (31.41)			-60.85 (101.25)			-842.28 (2954.23)			-1387.35 (4816.44)		
Total		90	-13.86 (6.50)	-12.59 (5.11)		-33.93 (18.97)	-29.63 (13.98)		615.92 (653.81)	602.74 (642.66)		-10096.43 (12727.18)	-8536.41 (10058.85)	
P			<.0001	.937		<.0001	.788		.001	.749		<.0001	.463	

All values are means (standard deviations).
**P*-values were obtained by paired t-test.
P -value were obtained by two sample t-test.

3.3. Subjects' characteristics affecting post-fluoride application lesion fluorescence loss recovery

As a results of logistic regression analysis of this research, it is found that early lesion fluorescence loss ($\Delta F_{(0)}$) was found to be a factor significantly affecting lesion fluorescence restoration one week after the fluoride application loss ($\Delta F_{(1)}$) from the pre-fluoride application status (p=0.001, Table 7). Also, early lesion fluorescence loss ($\Delta F_{(0)}$) was found to be a factor significantly affecting lesion fluorescence loss restoration four weeks after the fluoride application ($\Delta F_{(4)}$) from the pre-fluoride application status (p<0.0001, Table 8).

Table 7. Logistic regression model of early caries recovery after 1 week of the fluoride application

Variable	Odds Ratio	95% Confidence interval		*P*-value
		Lower	Upper	
Age	1.322	0.845	2.069	0.222
Gender	1.472	0.543	3.984	0.447
Saliva flow rate	0.466	0.161	1.346	0.158
Plaque index	1.015	0.987	1.043	0.289
Cariogram	0.999	0.961	1.039	0.960
$\Delta F_{(0)}$	0.834	0.745	0.933	0.001

Plaque index means O'leary index examined at baseline..
$\Delta F_{(0)}$ means the ΔF value obtained before fluoride application,
All values were measured before fluoride application.

Table 8. Logistic regression model of early caries recovery after 4 weeks of the fluoride application

Variable	Odds Ratio	95% Confidence interval		*P*-value
		Lower	Upper	
Age	0.688	0.432	1.094	0.114
Gender	1.151	0.382	3.471	0.802
Saliva flow rate	1.646	0.431	6.286	0.466
Plaque index	0.991	0.961	1.022	0.572
Cariogram	0.970	0.920	1.023	0.259
$\Delta F_{(0)}$	0.765	0.671	0.874	<0.0001

Plaque index means O'leary index.
$\Delta F_{(0)}$ means the ΔF value obtained before fluoride application.
All values were measured before fluoride application.

3.4. Post-fluoride application lesion change according to early fluorescence loss amount

As a result of the logistic regression analysis, pre-fluoride application early fluorescence loss ($\Delta F_{(0)}$) was found to be a common factor significantly affecting lesion fluorescence loss recovery one and four weeks after the fluoride application (Tables 7 and 8), and the lesions were divided into three groups by the unit of -10% of early fluorescence loss (Table 9). In the three randomly divided groups with the criteria of $\Delta F_{(0)} \geq -10\%$ (group 1), $-20\% \leq \Delta F_{(0)} < -10\%$ (group 2), and $\Delta F_{(0)} < -20\%$ (group 3), their pre-/post-fluoride application fluorescence loss changes and recovery status were analyzed. The differences in fluorescence loss between groups were also analyzed at pre-/post-fluoride application points.

The research analysis has found that group 1 exhibited no fluorescence loss amount difference between pre- and post-fluoride application (p=0.076, Table 9). However, group 2 showed 12.01±21.00% $\Delta F_{(1)}$ restoration one week after the fluoride application from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) (p=0.001). However, $\Delta F_{(1)}$ of group 2 showed no differences when compared to that of four weeks after fluoride application ($\Delta F_{(4)}$). Also, group 3 exhibited 29.05±20.84% $\Delta F_{(1)}$ restoration one week after and 29.50±19.99% $\Delta F_{(4)}$ recovery four weeks after the fluoride application from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) (p<0.0001). Given all of these lesions comprehensively, it was found that fluorescence loss ($\Delta F_{(1)}$ and $\Delta F_{(4)}$) was recovered one and four weeks after the fluoride application (p<0.0001).

To compare pre- and post-fluoride application restoration status after one week and four weeks, a one-way ANOVA analysis was performed. In the results, all three groups showed differences in $\Delta F_{(0)}$ and in $\Delta F_{(1)}$ values (p<0.0001, Table 9) before the fluoride application and after 1 week of fluoride application. However, there were no significant differences between group 2 and group 3 after four weeks ($\Delta F_{(4)}$) (Table 9).

Table 9. Changes in the fluorescence loss from the lesions over time

Groups	Ranges of F_0 (%)	N	ΔF (%)			P*
			Baseline	1 week	4 weeks	
1	≥-10	34	-7.97^{a} (1.23)	-8.44^{a} (3.02)	-9.21^{a} (3.48)	.076
2	-10> F_0 ≥-20	41	$-14.62^{b,A}$ (2.50)	$-12.79^{b,B}$ (3.73)	$-13.52^{b,A,B}$ (3.78)	.003
3	-20 >	15	$-25.16^{c,A}$ (4.94)	$-18.11^{c,B}$ (7.02)	$-17.69^{b,B}$ (6.20)	<.0001
Total		90	-13.86^{A} (6.50)	-12.03^{B} (5.37)	-12.59^{B} (5.11)	<.0001
P			<.0001	<.0001	<.0001	

All values are means (standard deviations).
P-values were obtained by one-way ANOVA.
^{a,b,c}In the same column, statistically significant differences between groups were obtained by Games-Howell post hoc and were expressed as different lower case letters.
**P*-value was obtained by repeated measures ANOVA and ^{A,B,C}statistically significant differences in baseline, 1 week after, and 4 weeks after fluoride application were analyzed by paired t-test with Bonferroni correction and were expressed as different upper case letters within row.

3.5. Analysis of the cutoff point of a lesion recovered after the fluoride application

As previously observed, $\Delta F_{(0)}$ values of recovered group and non-recovered group after fluoride application showed significant differences (Table 7 and 8). It also found that $\Delta F_{(0)}$ was a significant variable which affected maintenance and recovery of fluorescence loss of lesions, and the $\Delta F_{(0)}$ was recovered in different patterns according to the lesions severity divided by $\Delta F_{(0)}$ of -10% units. Accordingly, a ROC analysis was conducted to find the cutoff point of $\Delta F_{(0)}$, capable of recovering after fluoride application, by using Q-Ray™ system.

The ROC analysis found that if an incipient caries lesion $\Delta F_{(0)}$ value was less than -11.80%, then the $\Delta F_{(1)}$ value could be recovered ($P<0.0001$, Table 10) one week after the fluoride application. Here, area under the ROC curve (AUC) was 0.71, showing the sensitivity of 64.71% and specificity of 75.76%. Also, it was found that the $\Delta F_{(0)}$ value of less than -13.00% could be recovered 4 weeks after fluoride application ($P<0.0001$, Table 10). Here, the area under the AUC was 0.81, showing a sensitivity of 67.92% and a specificity of 81.08%.

Table 10. Results of the statistical analysis of the performance of the Q-Ray™ to determine the $\Delta F_{(0)}$ value for $\Delta F_{(1)}$ and $\Delta F_{(4)}$ values after one and four weeks of the fluoride treatment

$\Delta\Delta F$ (%)	Duration (weeks)	$\Delta F_{(0)}$ by Q-Ray™ measurements					
		ROC			SE	SP	cutoff point of $\Delta F_{(0)}$ (%)
		AUC	95% CI	*P*			
≥0	1	0.714	0.62 – 0.80	0.0001	64.71	75.76	-11.80
	4	0.814	0.72 – 0.89	<0.0001	67.92	81.08	-13.00

The areas under the receiver operating characteristic (ROC) curves (AUC) with the 95% confidence interval (CI) and the significance of difference to the diagonals (*P*) are given. Further, the sensitivity (SE) and specificity (SP) for the suggested $\Delta F_{(0)}$ cutoff point values are noted.

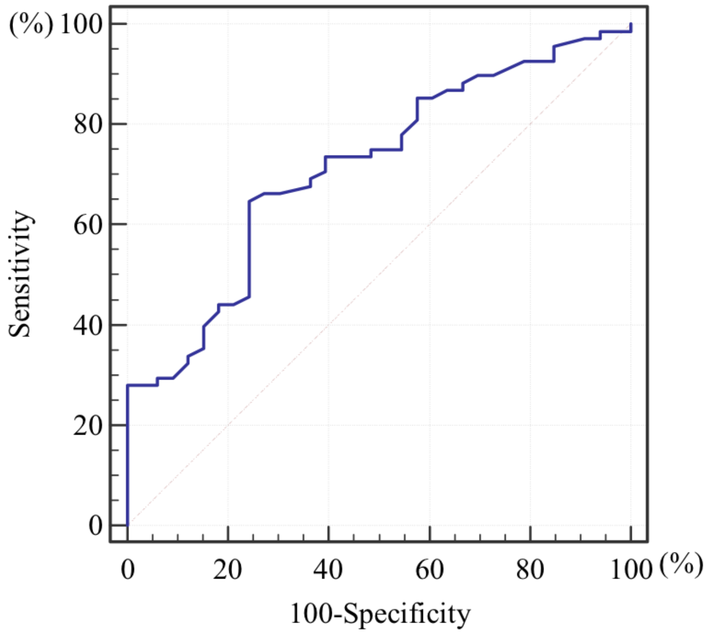

Figure 2. ROC curve for lesions recovered the $\Delta F_{(1)}$ value after one week

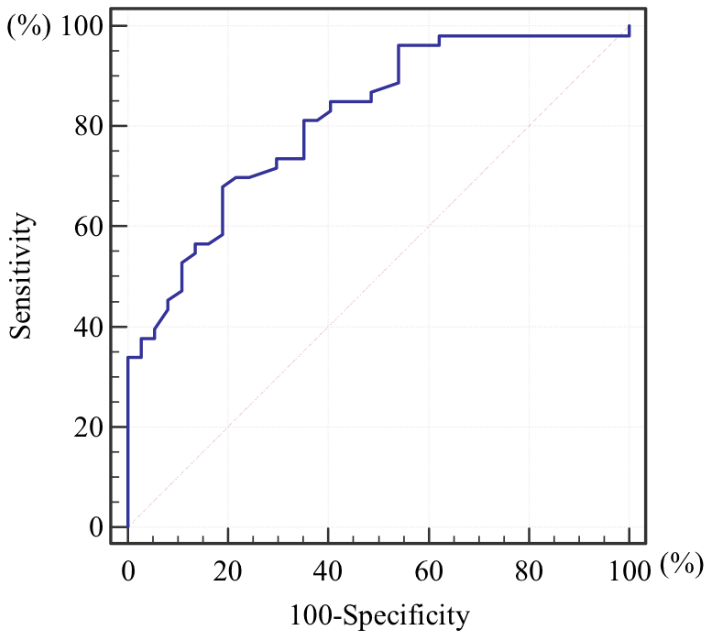

Figure 3. ROC curve for lesions recovered the $\Delta F_{(4)}$ value after four weeks

4. DISCUSSION

The significance of properly managing non-cavitated dental caries lesions has been recognized since the 1990s. Nevertheless, most clinical treatment has still focused on restoring dental caries lesions after cavities have already formed. This is because of the fact that, in the conventional dental treatment paradigm, only a clear cavity formation is defined as caries. However, a cavitated dental caries lesion is the final stage of a process. Prior to this, the more difficult to detect stage of non-cavitated caries lesions occurs. In this sense, it becomes necessary to broaden the conventional horizon of defining dental caries based on just enamel or clear dentinal cavity formation to include caries lesions in early phases (Pitts and Stamm, 2004).

It is more important to accurately diagnose symptoms appearing in an early stage of disease emergence, since an early stage caries lesion can be fully recovered to a healthy tooth depending upon the management methods. Therefore, this research examined pediatric patients with actual non-cavitated incipient caries with the Q-Ray™ system to find out the status of post-fluoride application remineralization of incipient caries lesions and identify characteristic factors of the subjects affecting lesion recovery. Based on the clinical database from this research experiment, the researcher tried to define the clinically acceptable level of lesion remineralization recovery treated with fluoride as well as the critical fluorescence loss ($\Delta F_{(0)}$) of a lesion to which the lesion could recover up to the clinically acceptable level.

The average age of the research participants was 5.74 and the average number of baby teeth with caries was 6.48 (Table 3). Given that the average number of baby teeth with caries of 5-year-olds was 2.8 in the 2012 national oral cavity health status statistics of South Korea, this finding indicates that the subjects were in a high-risk group with a 2.3 times higher number. Also, 96.77% of the research subjects said they had received dental caries treatment for the past three years, signaling that almost every research subject belonged to a higher risk group that had received caries treatment recently. An extant study has reported that one of the strongest indicators for future dental caries development in a patient is his or her past caries experience and current active caries lesions (Tinanoff and Reisine, 2009). According to this, it can be estimated that these research subjects have an oral cavity environment prone to early stage non-cavitated caries. The research subjects' dental plaque management score averaged at 81.41, meaning that their normal oral cavity management was insufficient and the existence of dental caries-activating elements. The fact that they have visited a dentist before but received fewer fluoride-based preventive treatments also supports the assertion that they are prone to caries. Reflecting on the above discussions, the research subjects with incipient caries were found to have experienced multiple caries before and even with their accompanying dental treatment experiences, they have a stronger chance of early caries turning into cavity caries.

The research subjects were applied 1.23% APF gel on tooth incipient caries lesion and visited the hospital one week and four weeks after the treatment. The mineral recovery status of their lesions was investigated with the Q-Ray™ system to be analyzed as fluorescence loss change. Consequentially, some lesions showed no remineralization; rather, they showed worse fluorescence loss due to mineral loss (Tables 5 and 6). This change was analyzed in units of lesion, and it was found that one week after the fluoride application, approximately 67.3% and four weeks after, only about 58.9% showed corresponding lesion recovery (Tables 5 and 6). Depending upon recovery status, early fluorescence loss ($\Delta F_{(0)}$) amounts were compared and it was found that lesions with pre-fluoride application fluorescence loss $\Delta F_{(0)}$ value of -10% tended not to show post-fluoride application recovery. But lesions with $\Delta F_{(0)}$ value of around -15% showed post-fluoride application recovery, signaling that lesions with higher severity can be restored when treated with fluoride. Such a tendency can also be inferred from the finding that pre-fluoride application early fluorescence loss ($\Delta F_{(0)}$) could affect $\Delta F_{(1)}$ and $\Delta F_{(4)}$ value recovery one and four weeks after the fluoride application (Tables 7 and 8). This finding of the present research is similar to the finding of another research lab experiment which reported that the more the early mineral loss in an incipient caries lesion, the more the mineral gains in a remineralization environment (Lynch and Ten Cate, 2006). More porous lesions have fewer tooth minerals that are soluble in an acidic environment, thus their remaining tooth solubility is much reduced. Therefore, porous teeth can react more sensitively to remineralization where minerals are gained than less porous lesions to demineralization. According to this logic, of the lesions observed in this research, those with early fluorescence loss of about -15% are viewed as more porous lesions with relatively more obvious fluoride remineralization in a high caries risk environment.

In a logistic regression analysis of this research, None of the subjects' characteristic factors affecting lesion recovery, such as saliva flow rate, dental plaque index (Plaque index), caries activity (Cariview®), Cariogram, etc., were found to have any significant effect. It seems that this is because dental caries is a disease based on multiple factors that function in a complicated manner, and as risk factors also include each patient's individual biological, environmental and behavioral elements as well, any one single factor can hardly have a major effect.

In this research, the lesions were grouped according to their early severity ($\Delta F_{(0)}$), a factor affecting post-fluoride application incipient caries lesion recovery status. One week after Group 1 ($\Delta F_{(0)} \geq -10\%$) showed no statistically significant difference from their pre-fluoride application status. Group 2 ($-10\% > \Delta F_{(0)} \geq -20\%$), on the other hand, showed 12.01% and group 3 ($-20\% > \Delta F_{(0)}$) showed 29.05% recovery, a significant difference compared with their pre-fluoride application status ($p<0.05$, Table 9). This tendency was also seen four weeks after the fluoride application. However, this finding of the present research is inconsistent with a precedence study's outcome (Kim et al., 2013). In that study, similar to this research, pre-fluoride application early lesion fluorescence loss ($\Delta F_{(0)}$) was divided into 10% units to apply pH-cycling after the fluoride application. As a result, it was found that the more serious the lesion severity, the less recovery of fluorescence loss. Similarly, another research finding shows an inconsistent remineralization outcome, where about 50 ㎛-thin lesions performed better remineralization than 200 ㎛-deep lesions after fluoride application (ten Cate et al., 2006). Such gaps can be explained by the difference in mineral distribution status between a naturally formed incipient caries lesion and an artificial incipient caries lesion. The pre-fluoride remineralization mineral distribution in a lesion could affect the post-treatment remineralization effect (Lippert et al., 2011), and the effective factors of lesion recovery when treated with fluoride are lesion depth, lesion surface zone thickness, pore size, etc. The incipient caries in this research experiment were naturally formed, thus, their biochemical aspects need to be considered because they are wet by saliva all the time. The incipient caries lesions may have far thicker surface zones or far more mineral content than the artificially formed samples of the previous research. As for such artificial caries lesions, their surface is protected but no surface zone may be formed, which has more minerals than natural lesions, and their mineral content is lower than naturally formed lesions, so fluoride can adhere to the surface easier. Given that the general data standard deviation in this research was larger, it seems that each subject’s own internal caries risk factor-related biochemical potential was considerably reflected in the remineralization process.

This study founded that $\Delta F_{(0)}$ is the factor that affects lesion recovery. Therefore, this study performed ROC analysis in order to find out the cutoff point of initial fluorescence loss ($\Delta F_{(0)}$) which could be remained or recovered after fluoride application. As results, the lesions below -11.80% of $\Delta F_{(0)}$ showed that they were recovered after one week from fluoride application. In addition, the lesions below -13.00% of $\Delta F_{(0)}$ showed that they were recovered after four weeks from fluoride application. It could be thought that these results reflect the recovery trend which was observed in the lesion group having $\Delta F_{(0)}$ below -10% (group 2 and 3, $\Delta F_{(0)}$<-10%).

This research found a relatively smaller recovery than that of the preceding study (Kim et al., 2013) by analyzing the cutoff point of fluorescence loss in fluoride recovery where post-fluoride application caries was reported to restore up to 50% if the $\Delta F_{(0)}$ value was -14.60%. There may be some excessive numbers, as the previous in vitro study utilized artificial caries with mineral distribution analyzed by clinical studies and completely excluded clinically considered individual oral cavity environments, as in this study’s subjects who were in the high-risk group.

In this study, it was found that the lesions with $\Delta F_{(0)}$ of higher than -10% was not even recovered at all after fluoride application. This result is different with that of a previous study (Kim et al., 2013). These changes of the present study are meaningful statistically. However, as there was only 2% difference of fluorescence loss, the status of a focus clinically is considered to be stable without significant changes if you consider all these various circumstances in the filming of Q-Ray™ system.

This research is limited in its relatively short time period of four weeks. To make up for this, a future study is necessary to continue the fluoride treatment and monitor how much lesions can be recovered and to what extent they can be recovered. According to the previous literature, among the patients who were treated with fluoride three times a year and who used fluoride toothpaste, the patients vulnerable to dental caries lesions in their primary teeth controlled their permanent teeth over 80% without dental caries (Iijima et al., 2008). The present research is expected to be helpful to establish a long-term treatment plan. The present study showed, in a quantitative method, how much lesions are able to recover within the short period of a month among high-risk group subjects with a changeable and poorer oral cavity environment relative to caries development.

The other limitation of this research is that it performed fluoride treatment only once as a preventive intervention method for relatively shallow incipient caries, while not controlling diet and fluoride toothpaste usage frequency. Thus, it did not study additional proper preventive treatment for children with a high caries risk. If incipient caries is managed by including a more customized preventive treatment protocol for each patient's individual characteristics, such a preventive management program could be settled stably.

The research experiment could monitor lesion mineral change only one week after fluoride treatment because it utilized the Q-Ray™ system and could anticipate the further prognosis of the patients within the shorter period of four weeks. After at least one and a half years or two years from the demineralization of incipient caries lesions, any lesion change detection becomes possible (Berkey et al., 1988; Mejare and Stenlund, 2000; Shwartz et al., 1984), and ocular inspection and palpation can be conducted only for lesions progressing 300-500 um outside the enamel. However, once a caries lesion has invaded 500 ㎛ or more of the enamel, a remineralization treatment can hardly recover the lesion (Stookey, 2005). Therefore, adopting the Q-Ray™ system for dental caries monitoring, which is very sensitive to mineral changes and quantifies the amount objectively, could enable earlier incipient caries detection and more proactive remineralization, as well as follow-up management (Ellwood et al., 2012).

Regarding incipient caries lesions, more clinical studies are still necessary that enable the anticipation of lesion progress based on quantitative numbers of how much fluoride is effective. The research, in this sense, used the Q-Ray™ detection device to measure early lesion mineral loss and identified objectively how far an incipient caries lesion induced remineralization by applying fluoride to the corresponding lesions. This finding clearly shows that timely treatment of early caries could delay further caries progress as well as restorative treatment. But, as the research period was limited to one month, a following study would be helpful for clinical diagnosis of incipient caries lesion and treatment plans if the research period was longer and fluoride treatment was repeated more than once to look at the range of early caries recovery.

5. CONCLUSION

The present research, first, examined high-risk caries pediatric patients with non-cavitated early caries lesions with the Q-Ray™ system to assess their lesion changes after professional fluoride application according to incipient caries lesions' remineralization recovery status. Second, it analyzed the factors affecting remineralization recovery through professional fluoride application to identify their accompanying lesion changes. Third, based on the clinical data from this research experiment, the researcher identified the critical fluorescence loss amount (ΔF) to which the lesion could recover the status.

The research findings are as follows:

1. A total of 101 lesions of the 31 subjects who attended one week after the fluoride application were measured for their fluorescence loss ($\Delta F_{(1)}$, %). As a result, the recovered group ($R_{\Delta F(1)}>0$, N=68) showed about 21.21% recovery in the $\Delta F_{(1)}$ value from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p<0.0001$). But the unrecovered group ($R_{\Delta F(1)}\leq 0$, N=33) showed about 22.80% deterioration in the $\Delta F_{(1)}$ value from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p=0.001$).
2. A total of 90 lesions of the 27 subjects who attended four weeks after the fluoride application were measured for their fluorescence loss ($\Delta F_{(4)}$, %). As a result, the recovered group ($R_{\Delta F(4)}\geq 0$, N=53) showed about 23.57% recovery in the $\Delta F_{(4)}$ value from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p < 0.0001$). But the unrecovered group($R_{\Delta F(4)}<0$, N=37) showed about 30.17% deterioration in the $\Delta F_{(4)}$ value from the pre-fluoride application ΔF value ($\Delta F_{(0)}$) ($p<0.0001$).

3. The logistic regression analysis found that one and four weeks after the fluoride application, pre-fluoride application lesion early fluorescence loss ($\Delta F_{(0)}$) was a factor significantly affecting lesion fluorescence loss ($\Delta F_{(1)}$) recovery from the pre-fluoride application status (*p*<0.05).
4. The recovery status was analyzed according to incipient caries lesion severity and it was found that compared to the pre-fluoride application $\Delta F_{(0)}$ value, one week after the fluoride application, the $\Delta F_{(1)}$ value showed no statistical significant change in group 1 ($\Delta F_{(0)} \geq -10\%$). But group 2($-20\% \leq \Delta F_{(0)} < -10\%$) showed about 12.01% recovery. Also group 3($\Delta F_{(0)} < -20\%$) showed about 29.05% recovery (*p*<0.05). and the effect persisted up to four weeks after fluoride application. $\Delta F_{(0)}$ of group 3 had significant differences (*p*<0.0001).
5. As a results of ROC analysis, it can be seen that the lesions with $\Delta F_{(0)}$ value of less than -11.80% could recover fluorescence one week after fluoride application ($\Delta F_{(1)}$). It was also shown that the $\Delta F_{(0)}$ value of early enamel lesion, which could recovered its fluorescence four weeks after fluoride application, was less than -13.00%

In comprehensive consideration of all of the research findings above, the clinical research herein has identified the progress and status of incipient caries lesion recovery assisted by fluoride while finding out that the incipient caries severity observed in the initial diagnosis affected the post-fluoride application remineralization of the lesion. In addition, by identifying the critical point of fluorescence loss amount according to incipient caries lesions recovery status based on the Q-Ray™ system, the research could efficiently examine the lesion changes of patients with incipient caries lesions within a short period of time. In this sense, the present research is expected to lay a cornerstone for a more proactive management of incipient caries lesions that will receive increasing attention in the field of dentistry.

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APPENDICES

연세대학교 치과대학병원 임상시험심사위원회

※ 별첨 2.1. 피험자 동의서

피험자 동의서

나는 **'QLF-D를 활용한 초기우식증 진단 및 치료계획(부제: 초기충치 치료를 위한 충치 탐지 장비의 활용)'**이라는 주제의 임상시험에 관한 연구 목적, 방법, 기대효과, 가능한 위험성, 대체 치료방법의 유무 및 내용 등에 대하여 충분한 설명을 듣고 이해하였으며, 모든 궁금한 사항에 대하여 충분한 답변을 들었습니다. 충분한 시간을 갖고 생각한 이후에 연구에 참여하기를 자유로운 의사에 따라 동의합니다. 본 연구에 동의한 경우라도 언제든지 그만둘 수 있음과 이에 따른 다른 적절한 치료를 계속 받을 수 있음을 확인하였습니다.

또한 피험자 설명문 및 동의서 사본 1부를 받을 것을 이해하고 있습니다.

피험자	성 명	(서명)
	생년월일	년 월 일
	날 짜	년 월 일
법정대리인	성 명	(서명)
	날 짜	년 월 일
설명 의사	성 명	(서명)
	날 짜	년 월 일
입회인	성 명	(서명)
	날 짜	년 월 일

Appendix Figure 1.1. Written consent (for parents)

※ 별첨 2.2. 피험자 동의서(어린이용)

피험자 동의서 (어린이용)

나는 **'내 입속의 충치가 얼마나 다시 튼튼해 지는지 알아보기'** 에 대해 의사선생님에게 들었습니다. 나는 스스로 이 검사를 하고 싶습니다. 하고 싶지 않으면 의사선생님이나 엄마, 아빠에게 이야기하겠습니다.

피험자	성 명	(서명)
	생년월일	년 월 일
	날 짜	년 월 일
법정 대리인	성 명	(서명)
	날 짜	년 월 일
설명 의사 선생님	성 명	(서명)
	날 짜	년 월 일
입회인	성 명	(서명)
	날 짜	년 월 일

Appendix Figure 1.2. Written consent (for children)

※ 별첨 3. 설문지

설 문 지

검 사 일 자	피험자 번호	피험자 이니셜	연 령	성 별
2013 년 월 일			만 세	남 / 여

본 설문에 참여해 주셔서 감사합니다. 본 설문은 충치 발생 위험도에 따라 불소도포 시 초기 충치의 회복률을 평가 하기 위해 실시하고자 합니다.
아래의 설문 항목을 잘 읽어보시고 자녀분에게 해당되는 응답에 체크해주시기 바랍니다.

1. 일반사항

1	연락처:	
2	1) 주소 2) 이사여부: 네 / 아니오 ▶ 이사 시기 : ▶ 이사 이전의 주거 지역 :	① 수불지역 아님 ② 수불지역

2. 치과적 고려사항

1	치과방문 유형에 대하여 표시 하십시오.	① 정기적으로 치과에 감(검진) ② 아플 때나 문제가 있을 때만 치과에 감 ③ 치과 치료를 받은 적이 없음
2	가장 최근의 치과 방문 시기는 언제입니까?	( )년 ( )개월 전
3	지난 3년 동안 충치 치료를 받은 적이 있습니까?	① 없다 ② 있다
4	현재 자녀분이 특별한 약을 복용하거나 장기적으로 복용하고 있는 약이 있습니까?	① 없다 ② 있다 (복용 약:)
5	침 분비와 관련된 전신적인 문제가 있습니까? (예: 방사선치료, 쉐그렌 증후군 등)	① 없다 ② 있다 (원인:)

Appendix Figure 2. Questionnaire for subjects

3. 자녀분의 치과예방진료 경험에 대해 묻고 체크해 주십시오.

1	매일 0.05% 불화나트륨 용액으로 양치를 합니까? (*불화나트륨 용액: 치과나, 보건소에서 불화나트륨으로 직접 제조한 불소 양치액)	① 없다 ② 있다
2	지난 6개월 동안 치과에서 불소바니쉬를 사용한 경험이 있습니까? (*불소바니쉬: 충치의 진행을 억제하기 위하여 치과에서 치아에 발라주는 고농도의 불소가 포함된 제품. 끈적끈적하거나 투명한 막으로 치아에 장시간 붙어 있게 됨)	① 없다 ② 있다
3	지난 6개월 동안 치과에서 불소도포한 경험이 있습니까?	① 없다 ② 있다
4	지난 6개월 동안 1주일간 헥사메딘을 사용한 적이 있습니까? (*헥사메딘: 입 안에 존재하는 세균의 수를 줄이기 위해 치과에서 처방 받아 사용하는 분홍색의 항균성 양치액)	① 없다 ② 있다
5	지난 6개월 동안 자일리톨이 들어간 껌을 하루 4회 이상 섭취한 적이 있습니까?	① 없다 ② 있다
6	지난 6개월 동안 toothmousse, 3M clinpro 제품을 사용한 적 있습니까?	① 없다 ② 있다

4. 현재 구강위생관리 실태에 대해 살펴보고 체크하십시오.

1	칫솔질 회수	하루 회
2	칫솔질 시간	분
3	칫솔질 방법	① 횡마법 ② 회전법 ③ 횡마+회전법 ④ 바스법 ⑤ 차터스법 (칫솔질 방법:)
4	사용하는 치약의 종류	① 일반 불소치약 ② NaF 함유 치약 ③ 시린이 전용치약 ④ 미백 전용 치약 (치약 제품명:)
5	사용하는 칫솔	① 일반모 ② 미세모 ③ 전동칫솔
6	치간칫솔 사용 여부	① 사용 ② 사용 안 함
7	치실 사용 여부	① 사용 ② 사용 안 함

설문에 참여해 주셔서 감사합니다.

Appendix Figure 2. Questionnaire for subjects (cont.)

ABSTRCT (IN KOREAN)

Q-ray™ 시스템을 이용한 불소 도포 후 초기우식 병소의 재광화 평가

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최근 와동형 치아우식증 발생이 전 세계적으로 감소하면서 비와동형 초기 치아우식증의 조기 탐지에 대한 관심이 부각되고 있다. 최근에 소개된 Quantitative Light induced Fluorescence-Digital (QLF-D, Q-Ray™) device는 컴퓨터 기반의 초기우식병소 탐지 장비 중 하나로써 치아 무기질의 미세한 변화를 민감하게 탐지하고 정량화하며 구내 촬영이 가능하여 임상적으로도 활용이 가능한 것으로 알려져 있다. 한편, 불소의 재광화 효과는 많은 선행연구에 의해 충분히 증명되었다. 그러나 초기우식병소가 우식 발생 위험이 높은 구강환경에서 불소처치로 인하여 단기간 내에 변화하는 정도와 양상을 정량적으로 보여주는 연구는 아직 부족한 실정이다.

따라서 본 연구는 첫째, 비와동형 초기우식병소가 있는 소아 환자를 대상으로 Q-Ray™ 시스템을 이용하여 전문가 불소도포 후 초기우식병소의 재광화 회복 여부를 평가하고자 하였다. 둘째, 전문가 불소도포를 통해서 재광화 회복 여부에 영향을 미치는 요인을 알아보고자 하였다. 셋째, 본 연구에서 얻어진 임상자료를 토대로 불소도포에 의하여 병소가 회복될 수 있는 초기형광소실량($\Delta F_{(0)}$)의 임계점을 파악하고자 하였다.

본 연구는 연세대학교 치과대학병원 연구심의위원회(IRB No. 2-2013-0043)의 승인을 받아 진행되었다. 연구 시작 시점에 연구 대상자의 구강검사, 자극성 타액 분비율 검사, 치면세균막 검사, 우식활성검사 및 치면세마를 시행하였다. 구강 검사 시 발견된 초기우식병소는 Q-Ray™ 시스템을 사용하여 치면세마 전과 후에 사진을 촬영하였고, 모든 촬영을 마친 후에 1.23% APF gel으로 1분 간 불소도포를 시행하였다. 대상자는 불소도포 1주 후 및 4주 후에 재내원하여 Q-Ray™ 사진을 재촬영 하였고, 탐지된 병소의 형광소실량을 분석하였다.

불소도포 1주 후(31명; 101개 병소) 병소가 회복된 그룹(N=68)은 불소도포 전에 비하여 불소도포 후 ΔF, ΔF_{max}, Area 및 ΔQ가 회복되었다($p<0.0001$). 반면, 병소가 회복되지 않은 그룹(N=33)은 불소도포 전에 비하여 ΔF와 ΔF_{max}가 유의하게 악화되었다($p<0.0001$). 한편 불소도포 4주 후(27명; 90개 병소) 병소가 회복된 그룹(N=53)은 불소도포 전에 비

하여 불소도포 후 ΔF, ΔF_{max}, Area 및 ΔQ가 회복되었다($p<0.0001$). 반면, 병소가 회복되지 않은 그룹(N=37)은 회복된 그룹과 모두 반대되는 양상을 나타냈다($p<0.05$).

로지스틱 회귀분석을 통하여 $\Delta F_{(0)}$ 값이 병소의 회복에 영향을 주는 요인으로 확인되었다. 이에 초기우식병소의 심도에 따라 회복 정도를 분석한 결과, 불소도포 전 $\Delta F_{(0)}$값에 비하여 불소도포 1주 후 $\Delta F_{(1)}$ 값이 1군($\Delta F_{(0)} \geq -10\%$)에서는 통계적으로 유의한 변화가 없었으나, 2군($-20\% \leq \Delta F_{(0)} < -10\%$)에서는 약 12.01%, 3군에서는 29.05%만큼 각각 회복되었다($p<0.05$). 이러한 결과를 토대로, 불소도포 후 병소의 형광소실량이 유지 또는 회복될 수 있는 초기 형광소실량의 임계점을 산출하기 위한 ROC 분석을 한 결과, 초기우식병소의 $\Delta F_{(0)}$값이 -11.80% 이하인 경우 불소도포 1주 후에 $\Delta F_{(1)}$값이 회복될 수 있는 것으로 분석되었고, 불소도포 4주 후에 $\Delta F_{(4)}$값이 회복될 수 있는 초기우식병소의 $\Delta F_{(0)}$값은 -13.00% 이하인 것으로 분석되었다($P<0.0001$)

본 임상연구를 통해 불소를 이용한 초기우식병소의 회복 유무와 회복률을 파악할 수 있었으며, 초진 시의 초기우식병소의 심도가 불소도포 후 병소의 재광화 회복 여부에 영향을 미친다는 것을 알 수 있었다. 뿐만 아니라 초기우식병소의 회복 여부에 따른 형광소실량의 임계점을 파악함으로써, Q-Ray™ 시스템을 활용하여 초기우식병소를 가진 환자의

병소의 변화를 비교적 단기간 내에 효과적으로 파악할 수 있었다. 따라서 향후 우리 치과계에서 지속적으로 관심을 가지게 될 초기우식병소를 좀 더 적극적으로 관리할 수 있는 초석을 마련할 수 있을 것으로 사료된다.

핵심되는 말: 탐지 장비, 초기 치아우식증, 초기 치아우식증 탐지, 불소, quantitative light-induced fluorescence-digital (QLF-D, Q-Ray™), 재광화