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A COMPARISON OF THE EFFICACY OF DIFFERENT REMINERALIZATION AGENTS: AN *IN VITRO* STUDY

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ABSTRACT

Purpose: The objective of this study was to evaluate and compare the remineralizing efficacy of a solution containing silver diamine fluoride (SDF) with agents containing sodium fluoride (NaF) and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on artificial caries lesions using laser fluorescence (DIAGNODent) and micro-computed tomography (μ-CT).

Methods: Artificial caries lesions were created on extracted primary incisors without any lesions or defects in the enamel tissue. The teeth were randomly divided into four groups (n = 8): Group 1: SDF (Advantage Arrest, Elevate Oral Care, USA); Group 2: NaF (Clinpro, 3M ESPE, USA); Group 3: CPP-ACP (GC Tooth Mousse, Recaldent, USA); Group 4: control. After applying remineralization agents, the samples were kept in an artificial saliva solution and measured by DIAGNODent at regular intervals. When the remineralization process was complete, enamel surfaces were analyzed by μ-CT for mineral density, lesion depth, and area using the computer program. Data obtained were statistically analyzed.

Results: In the comparison of DIAGNODent values between the groups, a statistically significant difference was found between the values measured on the fourteenth day (p-value=0.003). A significant difference was found between the mineral density (g/cm3) values measured by μ-CT on the fourteenth day after remineralization according to the groups (p-value=0.001).

Conclusions: All agents used in this study provided remineralization. The DIAGNODent and μ-CT measurements demonstrated that the SDF group had a higher remineralization value than the other groups. Considering the ease of use as well as its effectiveness, it is thought that the SDF solution can be used successfully to arrest early childhood caries. SDF application positively influences enamel remineralization

Key-words: remineralization; initial caries; silver diamine fluoride; DIAGNODent; micro-computed tomography.

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INTRODUCTION

Dental caries is an important public health problem that can adversely affect body health as well as oral health. To avoid dental caries, which is also known as the most common chronic disease in the world, extensive research should be carried in societies, it is emphasized today. According to reports, educating people about dental caries as a disease that can be prevented and controlled as well as distributing preventative techniques will help lower the incidence of dental caries in communities (1, 2).

To stop the progression of early caries or prevent the development of dental caries, pit and fissure sealants, mechanical and chemical plaque control, various probiotics, and prebiotics can all be applied (3). Topical fluoride applications, one of the chemical plaque control methods, are scientifically proven methods in preventing dental caries. These applications can be applied by individuals at home, while those with high concentrations are applied by dentists in clinics (4). Recently, fluoride-containing Silver Diamine Fluoride (SDF) varnishes are being used more frequently to arrest dental caries from developing. SDF slows the progression of dental caries by raising the pH of plaque, lowering dentin demineralization, and acting as an antibacterial agent against cariogenic bacteria (5).

When all remineralization agents are examined, it is revealed that fluoride-containing compounds are widely accepted as the gold standard in many studies (6). Depending on a child's caries risk level, topical fluoride applications should be performed every three to six months, according to the reference manual of American Academy of Pediatric Dentistry (AAPD) named "Caries-risk assessment and management for infants, children, and adolescents" (4). Recent updates to the guide's remineralizing agents contain SDF, which has been shown in trials to be more effective than Sodium Fluoride (NaF) varnishes in preventing caries after only one application (7).

SDF was first investigated in Japan in 1969 and has subsequently been utilized as an anti-caries agent in nations such as Australia, Brazil, Mexico, and China. In 2014, the U.S. Food and Drug Administration (FDA) has approved the SDF as a class II medical device. To reduce dental caries in children and adults, the FDA designated SDF as a "breakthrough treatment" around the end of 2016 (8,9). AAPD released a guideline regarding the application of SDF in 2017 for the management of dental caries in children and adolescents, including those with special healthcare (10).

The usage of SDF is limited by a few contraindications. In the tooth to which GDF will be applied, clinically irreversible pulpitis symptoms, presence of abscess and fistula, presence of radiological periradicular pathology are tooth-related contraindications. In addition, the use of SDF is not recommended in individuals with silver, fluoride, or ammonia allergy, in pregnant women, in the presence of oral ulceration, gingivitis and mucositis (11, 12).

SDF is an anti-caries fluoride agent with antibacterial and remineralizing capabilities in spite of all those contraindications above. It can stop the formation of biofilms, encourage remineralization, and prevent demineralization, prevent the collagen degradation, and clog the dentin tubules. It can be used to prevent Early Childhood Caries (ECC) and secondary caries, desensitize hypersensitive teeth, and control root caries and infected root canals. Consequently, SDF treatment is defined as a simple, painless, non-invasive, non-aerosol-generating, and reasonably priced technique to arrest dental caries (13).

The main hypothesis is this study, the solution containing silver diamine fluoride (SDF) will demonstrate a greater remineralizing efficacy on artificial caries lesions compared to agents containing sodium fluoride (NaF) and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) when evaluated using laser fluorescence (DIAGNODent) and micro-computed tomography (µ-CT).

MATERIAL AND METHODS

Tooth Selection

The number of teeth selected for use in the study was determined as n=6 per group, based on a "power analysis" conducted after reviewing relevant literature. Taking into account potential issues that may arise during the study, it was decided to use 8 teeth per group, totaling 32 teeth. The study included primary incisors with physiological mobility, expected to exfoliate soon, free from caries, and without any prior restorative procedures. Each tooth was examined for restorative procedures, enamel defects, and/or caries using a 2.5X magnification dental loupe (Keeler Ltd., Windsor, Berkshire, UK).

Sample Preparation

The selected primary teeth were cleaned with a micromotor and a polishing brush and were stored in a 0.1% thymol solution at 4°C for up to six weeks until the experiment time (14).

Following the numbering process, DIAGNODent (KaVo, Biberach, Germany) measured each tooth's fluorescence value three times from the incisor edges, and the average value was recorded. According to the user manual, the DIAGNODent device was used on dry surfaces with the proper tip, calibrated using the ceramic area on the device's edge before to each measurement, and then used.

The experiment surface has been reduced, and it is planned to cover the tissues outside the window with acid-resistant nail polish because of the demineralization process will end when the minerals in the solutions reach saturation (15). The buccal surfaces of the teeth were marked with paper tape in a 3x3 mm area for this purpose, and the exposed surfaces were covered with nail polish.

Initial measurement of samples

Using DIAGNODent, the 3x3 mm buccal surfaces were measured three times, and the average values were calculated for every sample. By subtracting each tooth's fluorescence value from the calculated average value, each tooth's initial value (T0) was formed (16). After taking the initial reading, nail polish was applied to 3x1 mm area in the middle of the 3x3 mm region.

Creation of Initial Enamel Lesions

In order to create artificial enamel caries on the teeth, a demineralization solution in accordance with the literature was prepared in Istanbul University, Faculty of Dentistry, Division of Basic Medical Sciences, and Department of Biochemistry. 2mM Ca(NO3)2, 2mM KH2PO4, 75 mM potassium acetate buffer, and 4.3 as the desired pH were adjusted in this solution (17). Each container was filled with 20 ml of the solution to begin the demineralization process. Every sample was immersed in the demineralization solution for 72 hours, and the solution was refreshed every 24 hours.

Measurement of Post-Demineralization Values of Samples

The teeth were rinsed with sterile saline and dried after the lesion development. According to the user manual, measurements were taken three times from the exposed areas on the buccal surfaces using DIAGNODent. The values after demineralization were calculated by subtracting the average value from the fluorescence values of the teeth (T1).

Preparation of Remineralization Groups

After the demineralization process, the teeth were randomly separated into 4 groups, with 8 samples each: Group1; SDF (Advantage Arrest, Elevate Oral Care, USA), Group2; NaF (Clinpro, 3M ESPE, USA), Group3; CPP-ACP (GC Tooth Mousse, Recaldent, USA), Group4; control. Another 3x1 mm sections of the exposed area on their buccal surfaces were covered with nail polish. The 3x1 mm uncovered areas was prepared for application of remineralization agents.

"Advantage Arrest" (Elevate Oral Care, USA) solution containing 38% SDF is the remineralization agent used on the first group. The teeth were dried in accordance with the manufacturer's recommendations. With the use of a micro brush, the solution was applied to the demineralization tooth surfaces only once, as 1-2 drops for each tooth. Following application, the solution was left to dry on its own without being rinsed. The second group had "Clinpro" (3M ESPE, USA), which contains 5% NaF as a remineralization agent. According to the manufacturer's recommendations, it was applied to each tooth with the aid of the application brush that came with the package. After a 2-minute wait, the excess was wiped off using a cotton pad. After a single application of the agent, there was no need to cleanse the teeth. The remineralization agent applied to the third group is "GC Tooth Mousse" (Recaldent, USA)

cream containing CPP-ACP. It was applied for 1-2 minutes, then left on the exposed surfaces of each tooth for 3 minutes, as directed by the manufacturer. For this group, the process was repeated every 24 hours.

The teeth's remineralization process was examined for 14 days, during which time the teeth were kept in an artificial saliva solution prepared in Istanbul University, Faculty of Dentistry, Division of Basic Medical Sciences, Department of Biochemistry. According to the sample literature, the artificial saliva is made up of 1mM CaCl2, 50mM KCl, 2mM KH2PO4, and 1M KOH. The pH was adjusted to 7 and 0.01% NaN3 was added to maintain the solution's freshness (18). Each sample was kept in separate containers containing 20 ml of artificial saliva solution, and the solutions were changed every 24 hours.

Measurement of Post-Remineralization Values of Samples

The exposed regions on the buccal surface of each sample were measured three times using DIAGNODent right after remineralization agents were applied, and average value was calculated. By subtracting the fluorescence value of every tooth from the value found, the value after remineralization was calculated (T2). This process was carried out two more times: at the end of the seventh day (T3), and on the fourteenth day (T4).

Analysis of Samples Using Micro-Computed Tomography (µ-CT)

The nail polishes were cleaned with acetone after the final DIAGNODent measurement in order to prepare them for images to be captured using micro-computed tomography system. Inonu University Scientific and Technological Research Center µ-CT laboratory received each tooth, numbered in its own container. All samples were used to create sections using µ-CT. numerical values regarding the mineral density of the sample surfaces, the depths, and the areas of the demineralized and remineralized sections were isolated from the collected images using an image processing computer program called "Image J" (Figure 1)

Statistical Analysis

IBM SPSS V23 was used to evaluate the data. The Shapiro-Wilk test was used to evaluate conformity to the normal distribution. To compare the normally distributed data according to paired time, a paired two-sample t-test was used. Binary time data that were not normally distributed were compared using the Wilcoxon test. In groups of three or more, normally distributed data were compared using the one-way test of variance, and multiple comparisons were examined the Tukey HSD test. The data that were not normally distributed into groups of three or more were compared using the Kruskall-Wallis H test, and multiple comparisons were examined using the Dunn's test. Data that were normally distributed three or more times were compared using Friedman test, and multiple comparisons were examined at using the Dunn's test. The Pearson correlation coefficient was used to analyze the relationship between the normally distributed quantitative data, considering both in-group and group discrimination. Spearman's rho correlation coefficient was used to analyze the relationship between the quantitative data that was not regularly distributed, regardless of in-group or group discrimination. For quantitative data, the analysis' findings were shown as mean ± standard deviation, and median (minimum-maximum). A significance level was set as $p<0.05$.

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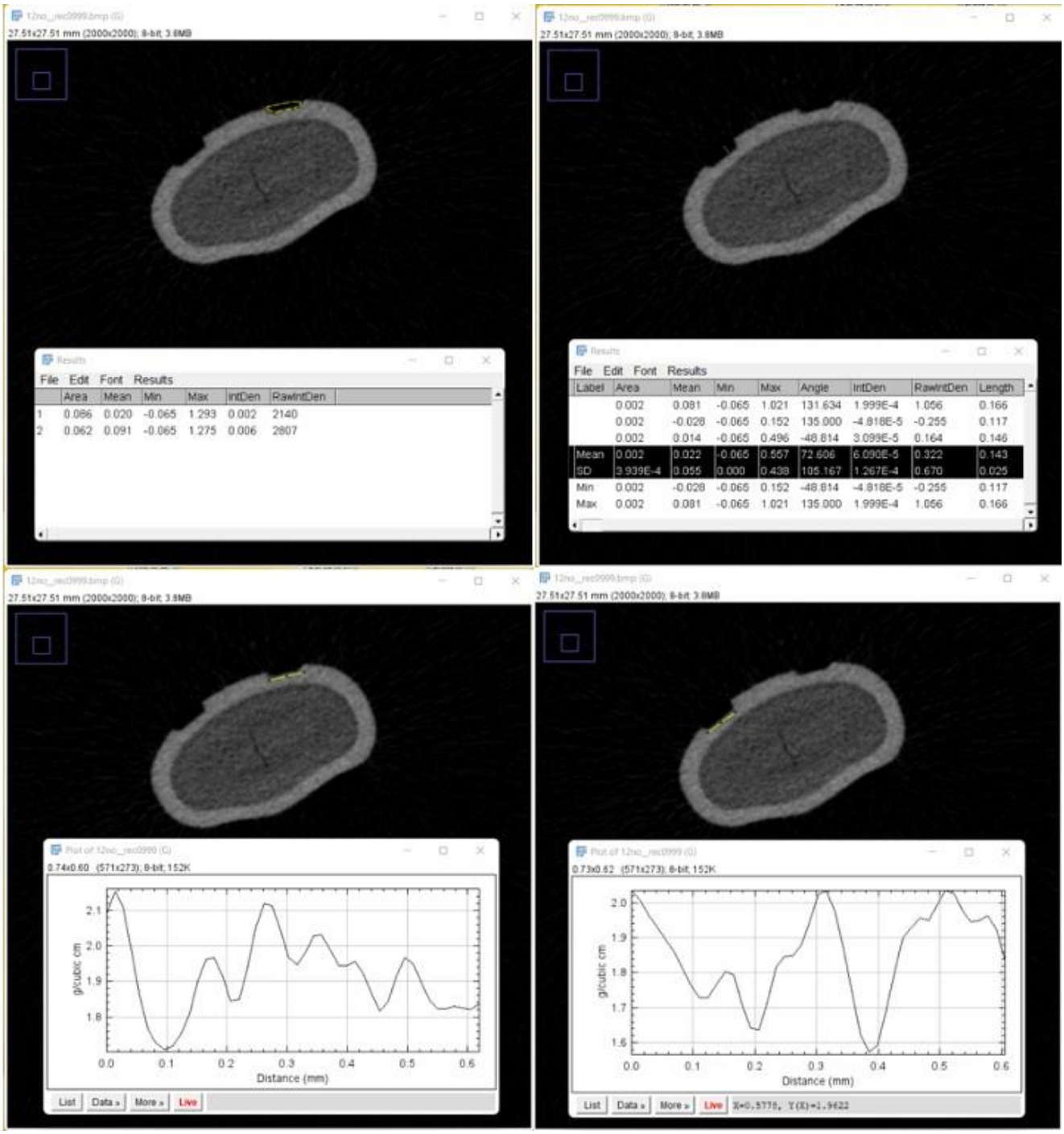

Figure 1: Analysis of Micro Computed Tomography images with a computer program

RESULTS

In this study, four groups were compared in primary incisor teeth for their effects on caries remineralization, using the DIAGNODent and µ-CT devices. The groups included:

1. Advantage Arrest (Elevate Oralcare, USA) with 38% silver diamine fluoride (SDF)

2. Clinpro (3M ESPE, USA) with 5% sodium fluoride (NaF)

3. GC Tooth Mousse (Recaldent, USA) containing casein phosphopeptide-amorphous calcium phosphate (CPP-ACP)

4. Control group kept in artificial saliva

The findings were as follows:

DIAGNODent Median Values:

- Median DIAGNODent values showed no statistically significant differences from baseline (p-value=0.236), after demineralization (p-value=0.738), immediately after remineralization (p-value=0.119), or on the seventh day after remineralization (p-value=0.052).

- By the 14th day following remineralization, a statistically significant difference was observed between the DIAGNODent median values across groups (p-value=0.003), specifically between Groups 1, 2, and 4.

- Time-dependent analysis within each group indicated:

o Group 1: Significant difference in DIAGNODent values over time (p-value=0.001), specifically between T0 and T4 with T1.

o Group 2: Significant difference over time (p-value<0.001), specifically between T0 and all other time points (T1, T2, T3, and T4).

o Group 3: Significant difference over time (p-value=0.002), particularly between T0 and other time points (T1, T2, T3, and T4).

o Group 4: Significant difference over time (p-value=0.006), specifically between T0 and T4 with T1 (Table 1).

Table 1: Comparison of DIAGNODent values within and between groups

	Group 1	Group 2	Group 3	Group 4	**p****
Initial (T0)	0 (0 - 3)^{A}	1 (0 - 2)^{B}	2 (0 - 3)^{B}	1 (0 - 1)^{A}	0.236
After demin. (T1)	5 (3 - 6)^{B}	5 (4 - 7)^{A}	5 (2 - 7)^{A}	5 (2 - 8)^{B}	0.738
After remin. Day 1 (T2)	3 (2 - 6)^{AB}	5 (3 - 7)^{A}	5 (3 - 7)^{A}	8 (1 - 10)^{AB}	0.119
After remin. Day 7 (T3)	3 (2 - 6)^{AB}	5 (3 - 7)^{A}	5 (2 - 7)^{A}	7 (1 - 10)^{AB}	0.052
After remin. Day 14 (T4)	2 (0 - 2)^{Ab}	4 (3 - 6)^{ABab}	3 (2 - 6)^{ABab}	5 (1 - 9)^{Aa}	**0.003**
p**	**0,001**	**<0,001**	**0,002**	**0,006**	

*Kruskall Wallis H test, **Friedman test, median (min-max), a-b: there is no difference between groups with the same letter. A-B: there is no difference between times with the same letter

µ-CT Mineral Density (g/cm³):

- No statistically significant differences in µ-CT mineral density median values were noted between groups at baseline (p-value=0.463) and after demineralization (p-value=0.329).

- At T4, however, the groups showed a significant difference (p-value=0.001), particularly between Groups 1 and 2.
- Time-dependent analysis within each group revealed:

o Group 1: Significant difference over time (p-value=0.005), particularly between T0 with T1 and T4.

o Group 2: Significant difference over time (p-value=0.001), especially between T0 and T1.

o Group 3: Significant difference over time (p-value=0.005), specifically between T0 with T1 and T4.

o Group 4: Significant difference over time (p-value=0.001), specifically between T0 and T4 (Table 2).

Table 2: Comparison of µ-CT mineral density (g/cm^3), depth (mm), and area (mm^2) values within and between groups

		Group 1	Group 2	Group 3	Group 4	**p***
Mineral density (g/cm^3)	Initial (T0)	2,14 (2 - 2)^{B}	2,18 (2 - 2)^{B}	2,23 (2 - 2)^{B}	2,07 (2 - 2)^{B}	0,463
	After demin. (T1)	1,81 (2 - 2)^{B}	1,76 (2 - 2)^{A}	1,87 (2 - 2)^{A}	1,91 (2 - 2)^{AB}	0,329
	After remin. Day 14 (T4)	2,09 (2 - 2)^{Aa}	2,02 (2 - 2)^{ABb}	1,97 (2 - 2)^{Aab}	1,83 (2 - 2)^{Aab}	**0,001**
	p**	**0,001**	**0,005**	**0,005**	**0,001**	
						p*
Depth (mm)	After demin. (T1)	0,13 (0 - 0)	0,14 (0 - 0)	0,1 (0 - 0)	0,1 (0 - 0)	0,051
	After remin. Day 14 (T4)	0,11 (0 - 0)	0,13 (0 - 0)	0,08 (0 - 0)	0,13 (0 - 0)	0,113
	p***	**0,018**	1,000	**0,018**	**0,018**	
						p^{+}
Area (mm^2)	After demin. (T1)	0,09 ± 0,029^{cd}	0,12 ± 0,021^{d}	0,06 ± 0,031^{c}	0,08 ± 0,032^{c}	**0,003**
	After remin. Day 14 (T4)	0,08 ± 0,025^{cd}	0,09 ± 0,034^{cd}	0,06 ± 0,038^{d}	0,12 ± 0,046^{c}	**0,021**
	p^{++}	**0,009**	0,922	0,075	**0,010**	

*Kruskall Wallis H test, **Friedman test, ***Wilcoxon test, median (min-max), +One-way test of variance, ++Paired two-sample t-test, mean ± standad deviation, a-b-c-d: there is no difference between groups with the same letter. A-B: there is no difference between times with the same letter

µ-CT Depth (mm):

- Median values of µ-CT depth did not significantly differ between groups at T1 (p-value=0.051) or T4 (p-value=0.113).

- Within-group time-dependent differences were statistically significant in Groups 1, 2, and 4 (p-value=0.018) but not in Group 3 (p-value=1.000).

µ-CT Area (mm^2):

- At T1, median values of µ-CT area differed significantly between groups (p-value=0.003), specifically between Groups 2, 3, and 4.

Correlation between DIAGNODent and µ-CT Mineral Density:

- At T0, there was no significant correlation between DIAGNODent values and µ-CT mineral density in any group: Group 1 (p-value=0.933), Group 2 (p-value=0.354), Group 3 (p-value=0.434), or Group 4 (p-value=0.175), with no overall correlation across all groups (p-value=0.556).

- At T1, Group 2 showed a statistically significant positive correlation between DIAGNODent values and µ-CT mineral density (r=0.851; p=0.015). No significant correlation was found between DIAGNODent values and µ-CT depth or area values for Groups 1, 3, or 4 at T1.

- By T4, significant differences were observed between Groups 3 and 4 (p-value=0.021).

- Time-dependent analysis revealed:

o Group 1: No significant differences over time (p-value=0.075).

o Group 2: Significant difference over time (p-value=0.009).

o Group 3: No significant differences over time (p-value=0.922).

o Group 4: Significant difference over time (p-value=0.010) (Table 2).

- At T4, there was no statistically significant correlation between DIAGNODent and µ-CT values in any individual group.

- Across all groups at T4, a statistically significant positive correlation was observed between DIAGNODent values and µ-CT depth (r=0.423; p=0.025), although no significant correlation was found between DIAGNODent values and µ-CT mineral density (p-value=0.063) or area (p-value=0.077) (Table 3).

Table 3: The relationship between DIAGNODent and µ-CT mineral density (g/cm^3), depth (mm), and area (mm^2) values within and between groups at different times

			r*	p*
Mineral density vs. DIAGNODent	Initial (T0)	Group 1	-0,039	0,933
		Group 2	0,416	0,354
		Group 3	0,356	0,434
		Group 4	-0,577	0,175
		General	0,116	0,556
			r**	p*
	After demin. (T1)	Group 1	-0,227	0,625
		Group 2	0,851	**0,015**
		Group 3	-0,224	0,629
		Group 4	-0,269	0,560
		General	-0,102	0,605
			r*	p*
	After remin. Day 14 (T4)	Group 1	0,359	0,430
		Group 2	0,487	0,268
		Group 3	0,187	0,688
		Group 4	-0,218	0,638
		General	-0,357	0,063
			r**	p*
Depth vs. DIAGNODent	After demin. (T1)	Group 1	0,023	0,961
		Group 2	-0,050	0,915
		Group 3	0,213	0,646
		Group 4	-0,708	0,075
		General	0,008	0,968
			r*	p*
	After remin. Day 14 (T4)	Group 1	0,179	0,701
		Group 2	0,543	0,208
		Group 3	0,524	0,227
		Group 4	0,346	0,448
		General	0,423	**0,025**
			r**	p*
Area vs. DIAGNODent	After demin. (T1)	Group 1	0,196	0,673
		Group 2	0,444	0,319
		Group 3	-0,012	0,980
		Group 4	-0,375	0,407
		General	0,087	0,658
			r*	p*
	After remin. Day 14 (T4)	Group 1	0,179	0,701
		Group 2	0,580	0,172
		Group 3	0,505	0,247
		Group 4	-0,273	0,554
		General	0,339	0,077

r*:Spearman's rho correlation coefficient, r**:Pearson correlation coefficient

The DIAGNODent fluorescence values for each group were recorded at initial, post-demineralization, and post-remineralization intervals (day 1, day 7, and day 14), with time-dependent changes shown in Figure 2.

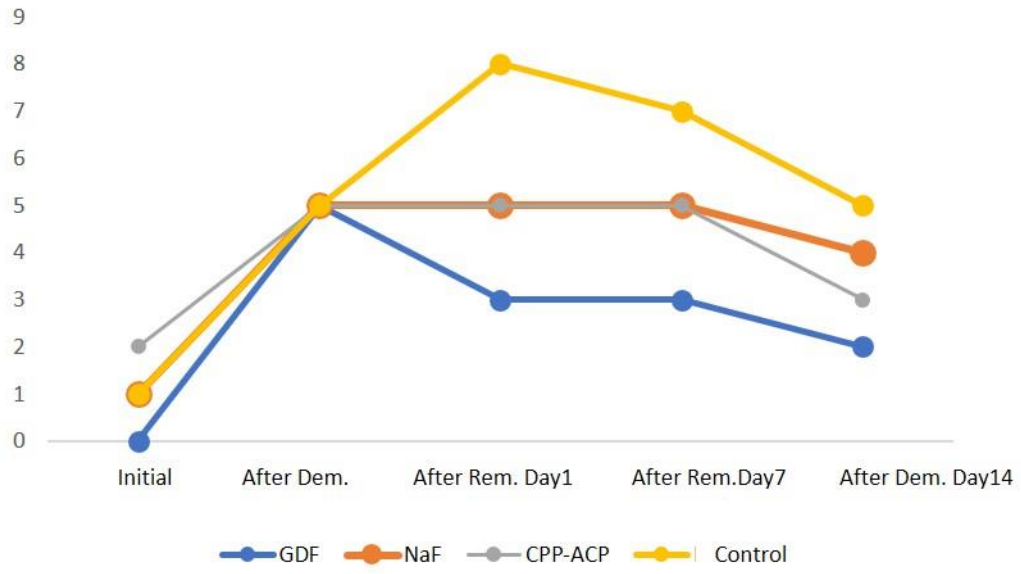

Figure 2: Comparison graph of the change of DIAGNODent values over time for all groups

DISCUSSION

Although though the DIAGNODent device and the µ-CT values used as a caries diagnosis method in this study, showed similar results, an examination of the raw data revealed no statistically significant relationship between the two methods except for two parameters. The DIAGNODent device is less sensitive and specific in detecting enamel lesions than in diagnosing dentin lesions, which may explain why there is no significant correlation between DIAGNODent and µ-CT values (19). The DIAGNODent device has been suggested to be particularly effective in identifying dentin caries in primary teeth but less successful in detecting early caries in enamel lesions (20). Additionally, it has been noted that the DIAGNODent device may not effectively detect minor caries changes, as it is more sensitive to lesion volume than to lesion depth (21). In clinical settings, combining the DIAGNODent device with visual and radiographic techniques can yield more reliable results for diagnosing early enamel caries.

A systematic review and meta-analysis examining the caries-preventive effect of SDF on primary teeth, it found that SDF not only prevented caries in treated primary teeth but also reduced the incidence of caries in other teeth. It was reported that the development of new caries was 77% lower in children treated with 38% SDF compared to untreated children (22). The caries-preventive effect was even greater when 38% SDF. was applied every six months for three years, showing better results than studies comparing fluoride varnish applications with control groups (23, 24). Another study found that 38% SDF, containing 44.800 ppm fluoride, w and applied annually, was more effective in preventing caries in primary teeth than varnish applied every three months, which contained 22,600 ppm sodium fluoride (7). A study involving children under three years of age with at least one active caries lesion compared 38% SDF to 5% NaF varnish; children treated with SDF every six months had a statistically higher caries-stopping effect after one year compared to the NaF group (25). It is suggested that the high concentration of fluoride ions in SDF, along with the formation of silver chloride and silver phosphate compounds on tooth surfaces, prevents calcium and

phosphorus loss from the tooth structure, contributing to SDF's enhanced ability to prevent caries (26).

Only 7% of parents reported being concerned by SDF's primary adverse effect, black staining, and there was no statistically significant difference in this concern between the fluoride varnish and control groups (7). Additionally, most parents prefer the aesthetic compromise of black staining of the anterior teeth over more advanced behavioral treatments, such as sedation and general anesthesia for the treatment of their children (27).

Studies suggest that using 38% SDF once or twice annually on active caries lesions in primary teeth produces effective results, even with follow-ups longer than 12 months. The frequency of

SDF application is directly correlated with caries-stopping efficacy, showing better results compared to both the ART technique and sodium fluoride varnishes (28, 29).

In a study from India by Sai et al., after inducing demineralization in primary incisors, samples were divided into three groups for remineralization treatment. The first group received 38% SDF, the second used calcium phosphate toothpaste, and the third used a cream containing CPP-ACP. The results showed that SDF had the highest remineralization capacity, with a statistically significant difference from the other groups (30). In another study from India on premolar teeth, Vinod et al. compared a remineralization agent containing SDF, CPP-ACP, and casein sucrose phosphate. The results showed significantly higher remineralization in the SDF group than in the other groups based on DIAGNODent readings taken on the seventh and fourteenth days (31). Yadav et al. studied permanent molars and compared remineralization agents containing SDF, CPP-ACP, and CPP-amorphous calcium fluoride phosphate (CPP-ACPF). SEM-EDX results showed that SDF had a statistically significant higher remineralization efficiency than all other groups (32).

A clinical study involving 1670 caries surfaces in children aged 3 to 4 with at least one active cavity divided children randomly into three groups treated with SDF solution and NaF varnish.. Caries arrest rates for the SDF groups were statistically higher than NaF varnish at both 12 and 18-months. Furthermore, treatment time was significantly shorter in the SDF groups (33). In the same study, 30-month follow-up data revealed that SDF maintained a statistically higher caries arrest rate than NaF varnish (33,34).). Consistent with these findings, our study determined that SDF was the remineralization agent with the highest caries-stopping capacity among all groups.

In a clinical trial, 38% SDF solution was compared with 5% NaF varnish in children aged 1-3 with at least one active cavity. At the end of the 12-month follow-up, caries arrest rates were reported to be 35.7% and 20.9%, respectively, for he two remineralization agents. SDF showed a statistically higher rate of caries arrest and was considered a more practical treatment than 5% NaF varnish, especially in high-caries-risk children (25). In line with this study, our research found that the SDF group's caries prevention rate was significantly higher than that of the other groups for both DIAGNODent and micro-CT values.

Topical applications of SDF are simple, safe, and cost-effective andthey have significant potential to reduce the burden of untreated dental disease in children due to their dual action in stopping and preventing dental caries in primary teeth (22).

CONCLUSIONS

This study compared the remineralization effects of different agents, specifically 38% silver diamine fluoride (SDF), 5% sodium fluoride (NaF), and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), against a control group in primary incisor teeth. Key findings indicated that while DIAGNODent and µ-CT devices both provided valuable measurements, distinct time-dependent and group-specific variations were observed across these metrics.

At the 14-day mark, DIAGNODent median values showed significant differentiation between groups, specifically highlighting the enhanced remineralization potential of SDF and NaF compared to the control. Similarly, µ-CT mineral density values at T4 further emphasized the efficacy of SDF, with notable increases in mineral density and area over time in SDF-treated groups. SDF demonstrated superior performance in halting demineralization and promoting mineral density gains, likely due to the combined impact of its high fluoride content and antimicrobial properties. NaF also showed significant remineralization over time but was less consistent compared to SDF, aligning with its established use in caries management.

The observed correlation between DIAGNODent values and µ-CT depth values at T4 suggests that these measurements, while generally consistent, may

capture slightly different aspects of caries remineralization, with µ-CT depth and density measurements offering a more comprehensive view of the mineralization changes.

In conclusion, this study supports the application of SDF as a potent agent for remineralization in primary teeth, particularly for high-risk cases of early childhood caries, where both caries arrest and mineralization are essential. Its effectiveness surpasses NaF and CPP-ACP, making it an advantageous choice in clinical settings aiming to reduce caries progression. Regular application of SDF could significantly contribute to managing early carious lesions, ultimately reducing the burden of untreated dental caries in pediatric patients.

The main limitations of this study, uncertainty of the duration of complete remineralization. Also, the procedure of remineralization in vitro is not alike in vivo within the mouth. Therefore, straightforward assumptions to clinical conditions must be bestowed with caution due to glaring constraints of in vitro studies. For future studies, it is recommended to investigate longer-term remineralization. Additionally, in vivo studies are needed to determine the efficacy of different remineralization agents.

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