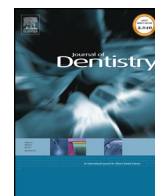




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Randomized clinical trial on arresting dental root caries through silver diammine fluoride applications in community-dwelling elders



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ABSTRACT

Objectives: To investigate the effectiveness of silver diammine fluoride (SDF) solution application in arresting dental root caries and to assess the color of arrested caries lesions.

Methods: This study was conducted in elderly centers in Hong Kong. A total of 83 elders with 157 root surfaces with active caries lesion were randomly allocated into 3 groups: Gp1 (placebo control)—annual application of soda water; Gp2—annual application of SDF solution; Gp3—annual application of SDF solution immediately followed by potassium iodide (KI) solution. Color of the arrested root caries lesion was assessed with reference to PANTONE color plates and classified into one of the followings: yellow (7401U); light brown (1245U); dark brown (4635U); and black (Black U). Status of root surfaces was assessed every 6 months by the same independent examiner.

Results: After 30 months, 100 (64%) of the included root caries lesions were reviewed. The arrest rates of root caries were 45%, 90%, and 93% in Gp1 (control), Gp2 (SDF) and Gp3 (SDF/KI), respectively (χ^2 test, $p < 0.001$). Pairwise comparisons showed elders in the control group had a lower proportion of the active root caries changed to arrested ($p < 0.001$) and the proportions of root caries being arrested in the SDF and SDF/KI groups were not significantly different ($p > 0.05$). The distributions of arrested caries lesions by color were not significantly different between the SDF and SDF/KI groups (χ^2 test, $p > 0.05$).

Conclusions: Application of SDF solution, with or without application of KI afterwards, is effective in arresting root caries among elders in a water fluoridated area. In the long term, blackening of arrested root caries is not reduced by immediate application of KI after the application of SDF.

Clinical significance: In a water fluoridated area, annual application of SDF solution or SDF/KI solution can arrest dental root caries in elders. In the long term, application of KI does not reduce the blackening of arrested caries lesions caused by SDF.

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1. Introduction

Dental root caries is a prevalent oral disease among elders world-wide and the incidence increases with age [1]. The reported prevalence of root caries in elders varies in different countries but a high proportion of the caries lesions being untreated active decay is common [2–4]. A recent oral health survey conducted in Hong Kong found that 25% of the community-dwelling adults aged 65–74 years had root caries experience and 80% of the caries lesions were untreated [5]. Poor oral health knowledge, infrequent tooth brushing and low utilization of dental care services among the

elders are some possible explanations for the high proportion of untreated caries [4,6,7]. Since advanced root caries can cause pain, tooth loss, and impact on general health, there is a need to develop affordable and effective treatment approaches to manage the untreated caries lesions on root surfaces in the elders.

Nonsurgical intervention for shallow dentin caries lesion has been advocated [8,9]. Topical application of fluoride agents is a conservative treatment and a potentially good alternative to the surgical approach. Silver diammine fluoride (SDF) has been shown to be effective in arresting dentin caries in primary teeth of young children [10–13], and recommended for preventing and arresting root caries lesions [14–16]. However, so far, only one clinical trial on using SDF to arrest dental root caries among community-dwelling elders can be found in the literature which reported that annual application of 38% SDF solution was effective and that oral health education had synergetic action with SDF application [17]. It should be noted that the final 24-month follow-up examination in

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that study was conducted after only two applications of SDF solution on the study root surfaces, i.e. at baseline and after one year. The longer term effectiveness of SDF needs further investigation.

Previous clinical studies on SDF reported that it was common to have black stain on the arrested caries lesions which may cause an aesthetic concern [10]. It has been suggested that by applying a saturated solution of potassium iodide (KI) immediately after the application of silver fluoride, staining of the dentin caries lesion can be minimized while the caries arrest effect of silver fluoride is not affected [18]. The proposed explanation is that the iodide ions from the KI solution will react with the excess silver ions from the silver fluoride solution to form a precipitate of silver iodide. It would be a win-win situation if KI can prevent the staining associated with SDF without reducing its effectiveness in arresting caries. However, evidence from clinical trial is lacking to support this claim.

This study focused on promoting oral health among elders, including preventing new root caries and arresting existing active root caries. This paper reports on the effectiveness of the following three methods in arresting dental root surface caries among community-dwelling elders: (1) annual application of soda water (placebo); (2) annual application of 38% SDF solution; and (3) annual application of SDF solution immediately followed by KI solution. Another objective was to assess whether application of KI solution immediately after SDF application could affect the color of the arrested root caries lesions. The first null hypothesis to be tested was that there is no difference in the effectiveness of the three methods in arresting root caries. The second null hypothesis was that there is no difference in the distribution of arrested root caries lesions by color between the SDF group and the SDF/KI group.

2. Materials and methods

This study was a randomized clinical trial conducted in community elderly centers in Hong Kong, a city with water optimally fluoridated at 0.5 ppm, using a parallel group design. Ethical approval was obtained from the Institutional Review Board of the University of Hong Kong and the trial was registered (clinicaltrials.gov # NCT02360124).

2.1. Subject recruitment

The study population was community-dwelling elders without serious health problems. These elders lived independently in their own home and could participate in various activities organized by community centers. Notices regarding a free oral health talk were put up in 12 selected community centers for elders located in different districts of Hong Kong. Members of the elderly centers freely chose to attend the function. Details of this clinical trial were given at the end of the talk and elders who were interested were clinically examined by a dentist in the center. Subject inclusion criteria were having one or more teeth (not indicated for extraction) with active root surface caries; no cognitive problems in communication; and having self-care ability for normal daily activities. Elders whose salivary gland function had been significantly affected by disease, medication, or treatment such as radiotherapy in the head and neck region were excluded. Written informed consent was obtained before commencement of the study.

2.2. Baseline examination

The baseline examination was carried out by a trained examiner. A portable dental chair, intra-oral LED light, disposable

dental mirrors, CPI probes and graduated (in mm) periodontal probes were used in the examination. Status of the exposed root surfaces of each natural tooth was assessed. Plaque and calculus obscuring visual inspection of the root surfaces was removed using cotton buds and hand instruments. Four surfaces per tooth (mesial, distal, buccal and lingual) were examined and the status was diagnosed according to the criteria recommended by the International Caries Detection and Assessment System (ICDAS II) Coordinating Committee [19]. Root caries lesion and its activity status was detected by visual-tactile examination. Active caries was recorded when the lesion surface could be easily penetrated by a blunt (0.5 mm ball-ended) probe with light force. Inactive (arrested) caries was recorded if the lesion surface was hard and smooth [20]. Caries lesion that have an extension of at least 1 mm beyond the cementum-enamel junction was recorded as root caries lesion. A caries lesion was recorded as involving more than one root surface when it extended beyond the line angle to involve at least one-third of the adjacent tooth surface. Other clinical parameters recorded on each included root surface were: presence or absence of plaque seen visually, greatest gingival recession (in mm), and close proximity (within 3 mm) to a partial denture.

2.3. Intervention

After the baseline examination, subjects satisfying the study inclusion criteria were randomly allocated to three groups using block randomization. A list was produced with a block size of 6 which contained 90 different combinations. A dental surgery assistant carried out the subject allocation according to the combinations randomly generated by computer. Both the examiner and the subjects were blinded to group assignment. Interventions were provided by another dentist. In Group 1, placebo control, soda water with a bitter flavor (to mimic the bitter metallic taste of SDF) was painted onto root surfaces with active caries by using a disposable microbrush. In Group 2, a 38% SDF solution (Saforide, Toyo Seiyaku Kasei Co., Ltd., Osaka, Japan) was painted onto the active caries lesions. In Group 3, KI solution (2.36 mol/l) was painted onto the caries lesion immediately after the application of 38% SDF solution. The KI solution was prepared in laboratory with distilled water and KI powder (SIGMA-ALDRICH Co., St. Louis, USA). The above procedures were repeated after 12 and 24 months. In addition, individualized oral hygiene instructions, including how to properly brush the teeth with a manual toothbrush and use of interdental brush, and a tube of fluoride toothpaste (1450 ppm fluoride, Colgate, USA) were given to all study subjects at each examination.

2.4. Follow-up

Follow-up lasted for 30 months and clinical examination was carried out every 6 months after baseline by the same examiner. The same equipment and diagnostic criteria were used in all examinations. Arrested root caries was recorded when an active root caries lesion found at baseline changed into inactive at follow-up. Color of the arrested root caries lesion was classified into one of four categories according to PANTONE® color plates placed next to the lesion (Fig. 1), namely yellow (7401U), light brown (1245U), dark brown (4635U), and black (BlackU). A random sample of 10% of the subjects were re-examined at baseline and follow-up examinations to monitor examiner reproducibility.

2.5. Sample size

While this paper reports on the effects of SDF solution on arresting active root caries, this clinical trial also studied prevention of new root caries in the elders and the findings will

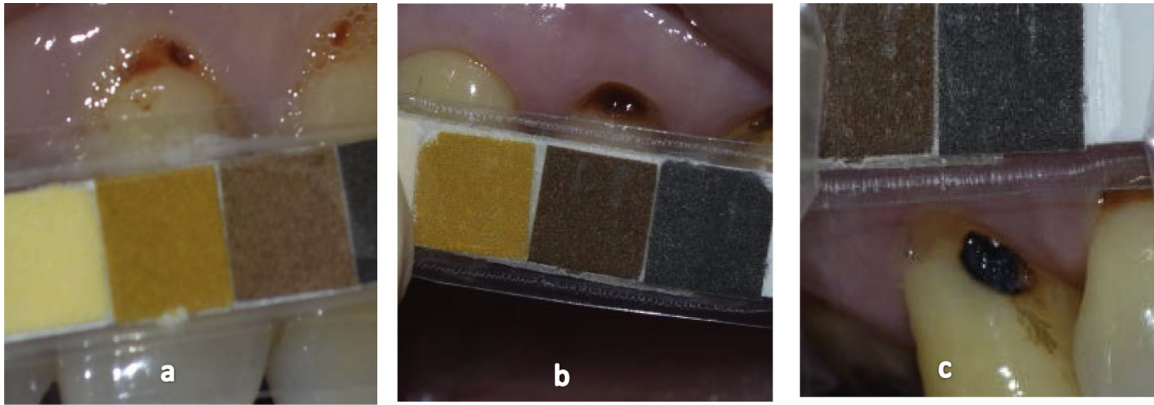


Fig. 1. Assessment of the color of arrested caries lesion using color plates: a) the lesion was light brown; b) the lesion was dark brown; and c) the lesion was black.

be reported in another paper. The study sample size calculation was based on the primary outcome which was development of new root caries over 30 months. An annual increment of 0.8 carious tooth root surface was found in the control group elders in a previous clinical trial in Hong Kong [21]. In order to show that a 50% difference between the highest and the lowest mean caries increments in the three study groups was statistically significant at a 5% significance level and at a 80% power, a sample size of 80 subjects in each group was required. Allowing for a drop-out rate of around 25% over 30 months, an initial sample size of slightly over 100 subjects in each group was used.

2.6. Data analysis

All collected data were input into computer and analyzed using the statistical software SPSS for Windows version 20. The intention-to-treat approach for data analysis was adopted. One way analysis of variance (ANOVA) was used to assess the differences among the three study groups regarding the mean number of exposed sound root surfaces, root caries experience and active decayed root caries lesions at baseline. Chi-square test was used to find out if there were statistically significant differences among the three groups in the distribution of active root caries lesion which became arrested after intervention. Chi-square test was also used to assess the distribution of the arrested caries lesion according to color in the SDF group and the SDF/KI group. The statistical significance level for all tests was set at 5%.

In addition, multilevel survival analysis was conducted using the grouped proportional hazards (PH) model in WinBUGS (version 14) to assess factors that affected the time for an active root caries lesion to change into arrested (the arrest time).[22] In the 2-level model adopted in this analysis (root surface as level-1 and subject as level-2), the arrest times of active root caries lesion in the three study groups were compared. Education level, frequency of sweet snack intake, tooth brushing frequency, visible plaque index (VPI) score at baseline, close proximity to a denture, and presence of plaque on lesion surface at baseline were included in the model as covariates. Survival functions were used to estimate the caries arrest rates.

3. Result

Study subject recruitment and baseline clinical examination were conducted in April to October 2012. At baseline among the 323 recruited subjects, there were 157 active root caries lesions in the teeth of 83 elders. Twenty (24.1%) of them were men and 63

(75.9%) were women. Their mean age was 72.2 (± 5.8) years. A total of 67 subjects (80.7%) and 100 root caries lesions (63.7%) were followed for 30 months (Fig. 2). The drop-out rates of subjects and caries lesions in the three groups were not significantly different (χ^2 test, $p > 0.05$). The Kappa statistic values for duplicated examination of root caries at surface level were between 0.85 and 0.89 in the baseline and follow-up examinations.

The mean numbers of exposed sound (ESS_{root}), decayed and filled (DFS_{root}), and active decayed (ADS_{root}) root surfaces of the three study groups are shown in Table 1. For all the parameters, the differences between the elders who attended the baseline examination and those who remained after 30-month were not statistically significant (t-test, $p > 0.05$). There were no significant differences in these parameters among the three study groups (ANOVA, $p > 0.05$).

The arrest rates of root caries at the 30-month follow-up were 45% in the placebo control group, 90% in the SDF group, and 93% in the SDF/KI group (χ^2 test, $p < 0.001$) (Table 2). Pairwise comparisons showed that elders in the control group had a lower proportion of their active root caries changed to arrested ($p < 0.001$), and the caries arrest rates in the SDF and SDF/KI groups were not statistically significantly different ($p > 0.05$).

Most of the active root caries lesions that became arrested at the 30-month examination in the SDF group were either black or dark brown in color, 69% and 25% respectively. The color distribution of the arrested lesions in the SDF/KI group was similar, 62% being black and 32% being dark brown. The difference between the two groups was not statistically significant (χ^2 test, $p \geq 0.05$). No adverse effects on the teeth and soft tissues were found in the follow-up examinations.

Parameter estimates of the grouped proportional hazards (PH) model revealed that education level, frequency of sweet snack intake, tooth brushing frequency, close proximity to a denture, baseline VPI score, and presence of plaque on lesion surface at baseline had no statistically significant effects on the root caries arrest time (95% credible interval included 0) (Table 3). In contrast, annual application of SDF or SDF/KI shortened the arrest time significantly compared to control (95% credible interval not including 0). The caries arrest times of the SDF group and the SDF/KI group were not significantly different (95% credible interval included 0).

4. Discussion

Previous clinical studies on SDF mainly focused on its effectiveness in arresting dentin caries and the black stain caused was usually accepted as an unavoidable side effect. This study is the

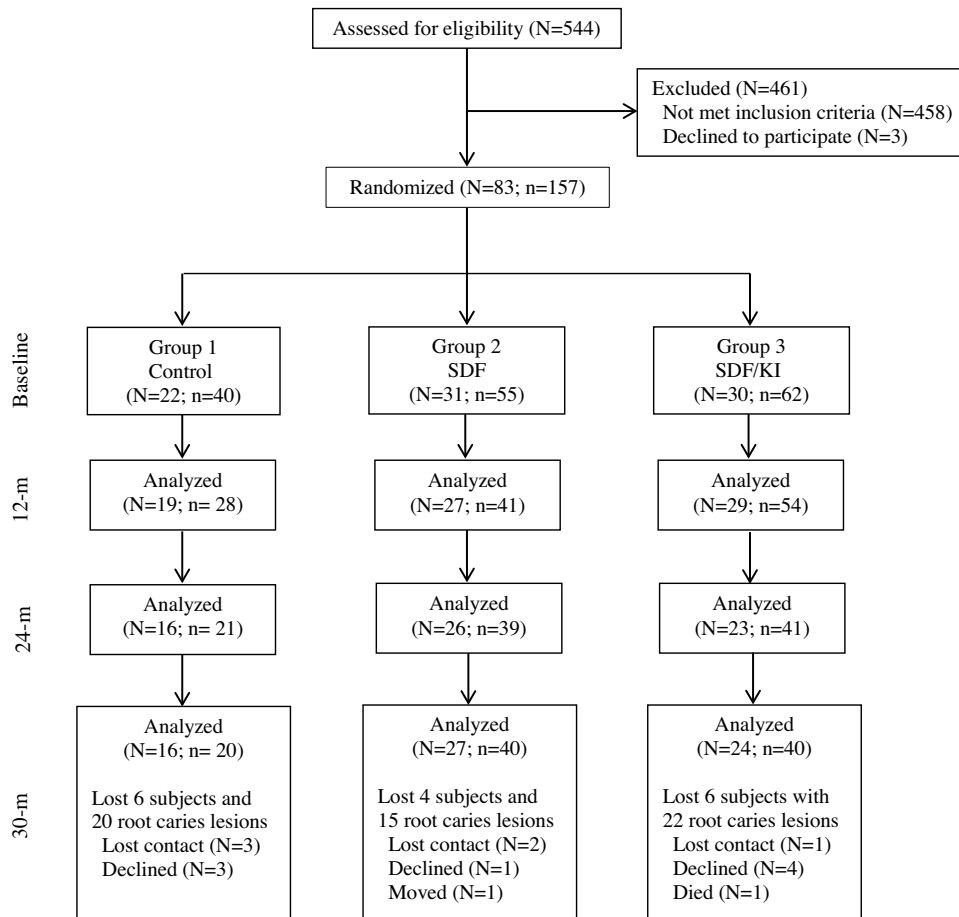


Fig. 2. Flow of subjects and root caries lesions in this clinical trial. N = the number of subjects with root caries. n = the number of root caries lesions.

first clinical trial to evaluate the effectiveness of applying KI immediately after application of SDF in lightening the dark color of arrested root caries lesion. Random allocation was carried out in this study and the subjects were evenly distributed in the three study groups.

In this study, around 20% of the elders and one third of the active root caries lesions found at baseline could not be followed for 30 months. The retention rate of elders who had more root caries lesions was lower. These elders were less willing to attend the follow-up examinations in which no dental filling was provided. Probably, the elders who had more dental caries at baseline attached a lower value to their oral health and were less interested in long-term participation in a dental research project.

Table 1

Mean number (SE in parenthesis) of exposed sound root surfaces (ESS_{root}), root surfaces with caries experience (DFS_{root}), and active decayed root surfaces (ADS_{root}) of the study subjects included at baseline and followed for 30 months.

Groups	All subjects				Subjects followed for 30-month			
	N	ESS_{root}	DFS_{root}	ADS_{root}	N	ESS_{root}	DFS_{root}	ADS_{root}
Control	22	33.0 (3.3)	2.4 (0.4)	1.8 (0.3)	16	36.9 (4.0)	2.3 (0.3)	1.6 (0.2)
SDF	31	43.4 (3.2)	2.7 (0.4)	1.8 (0.3)	27	41.7 (3.2)	2.6 (0.5)	1.8 (0.3)
SDF/KI	30	41.7 (3.2)	3.4 (0.5)	2.1 (0.3)	24	42.3 (3.6)	3.7 (0.5)	2.2 (0.3)
Significance		n.s.	n.s.	n.s.		n.s.	n.s.	n.s.

Thus, the study results might be biased towards the elders who were more concerned about their oral health.

The 30-month results showed the elders in the control group had the lowest caries arrest rate which was around one third of that of the elders who received annual applications of SDF or SDF/KI solution. This indicates that topical application of 38% SDF solution is effective in arresting active dental root caries among community-dwelling elders in a water fluoridated area. This finding agrees with that of a previous study on the effectiveness of SDF solution in arresting root caries [17]. Thus, there is now more clinical evidence to support the use of annual topical application of 38% SDF solution to arrest active root caries among community-dwelling elders. The similar caries arrest rates among the elders in the SDF group and the SDF/KI group in this study indicate that KI does not significantly affect the effectiveness of SDF in arresting

Table 2

Arrest rate of baseline active caries at the 12-month, 24-month and 30-month examination.

Study groups	12-month	24-month	30-month
	N = 75, n = 123	N = 65, n = 101	N = 67, n = 100
1) Control	32.1%	28.6%	45.0%
2) SDF	61.0%	82.1%	90.0%
3) SDF/KI	75.9%	85.4%	92.5%
Significance	p = 0.001	p < 0.001	p < 0.001
Pairwise comparisons	Gp1 < Gp2, Gp3	Gp1 < Gp2, Gp3	Gp1 < Gp2, Gp3

Table 3

Parameter estimates for grouped PH model in the multilevel survival analysis of root caries arrest time.

	Grouped PH model	
	Log hazard ratio	
	Median	95% C.I.
Study group		
<i>Contrast relative to control</i>		
SDF vs. Control	1.4	(0.3, 2.7)
SDF/KI vs. Control	1.6	(0.6, 2.9)
<i>Contrast for other pairwise comparison</i>		
SDF/KI vs. SDF	0.3	(−0.7, 1.2)
Frequency of snack intake ($\geq 1/\text{day}$ vs. $< 1/\text{day}$)	−0.2	(−1.1, 0.9)
Education (middle school vs. no education)	0.1	(−1.0, 1.3)
Education (primary school vs. no education)	−0.1	(−1.1, 0.9)
Daily tooth brushing ($\geq 2/\text{day}$ vs. $\leq 1/\text{day}$)	−0.4	(−1.7, 0.9)
Close proximity to a denture (yes vs.no)	−0.2	(−0.9, 0.5)
Visible plaque index score at baseline	−0.2	(−1.8, 1.3)
Plaque present on the root surface at baseline (yes vs. no)	0.3	(−0.4, 1.0)
γ_1 (baseline ~ 6m)	−2.8	(−5.0, −1.4)
γ_2 (6–12m)	−1.1	(−3.0, 0.5)
γ_3 (12–18m)	−1.1	(−2.7, 0.8)
γ_4 (18–24m)	−1.9	(−3.8, 0.2)
γ_5 (24–30m)	0.1	(−1.7, 2.1)
CORR _{subject}	0.4	(0.1, 0.7)

Median = median of the estimates drawn from the posterior distributions, Median > 0 corresponds to a higher chance of arrest of active dentin caries and then a shorter arrest time.

95% C.I. = 95% credible interval.

γ_1 – γ_5 = time interval.

CORR_{subject} = clustering effect among the arrest times of the active root caries lesions from the same elder.

root caries. Previous in-vitro studies have found that both silver fluoride (AgF) solution and AgF/KI solution can reduce the permeability of micro-organisms through demineralized dentin disc [23], and application of AgF/KI on dentin can prevent biofilm formation and reduce further demineralization to resist caries progression [24,25]. Besides, it was reported that silver and iodine ions were present in the dentin treated with AgF/KI [18], and iodine can inhibit oral bacteria [26].

Silver ions in the SDF solution can cause black stain. In one of the groups in this study KI was applied immediately after SDF which was an attempt to minimize the unwanted esthetic outcome. The chemical reaction between SDF and KI is: $\text{Ag}(\text{NH}_3)_2\text{F} + \text{KI} \rightarrow \text{AgI} + \text{KF} + 2\text{NH}_3$.

According to the above formula and the concentration of SDF solution used in this study (380 mg/ml), the concentration of KI solution needed to precipitate all the silver ions is 391.8 mg/ml (2.36 mol/l). At this concentration, the chemical reaction between SDF and KI should be complete and a bright yellow solid compound (silver iodide, AgI) would precipitate on the root surface. At the 30-month follow-up of this study, it was found that there was no significant difference between the distribution of the arrested caries lesions by color in the SDF group and that in the SDF/KI group. Although a bright yellow precipitate was seen after applying KI on the lesions treated with SDF solution, the application of KI had no long-term effect on improving the aesthetic problem caused by the black stains on the arrested root surface caries. Probably, in this study there were still silver ions or metallic silver on the carious root surfaces after application of KI solution. There are two possible explanations. First, the amount of SDF solution and KI solution delivered onto the root surfaces was not exactly in the ratio of 1:1 and some excess SDF solution was left. Second, as silver iodide is highly photosensitive and can be dissociated into iodine and metallic silver by exposure to light, formation of black silver compound still occurred on the lesion surface ultimately.

Results of the multilevel survival analysis show that application of either SDF or SDF/KI can shorten the arrest time of active caries

compared to control. The proportion of active root caries lesions in the SDF or SDF/KI group which had become arrested after 30 months was around 1.5 times that in the control group. In contrast, the effects of other factors such as the elder's education level, oral health behaviors, and oral hygiene status on root caries arrest time were not statistically significant. It seems that the effectiveness of SDF in arresting root caries in this group of community-dwelling elders is high and not significantly affected by these factors. These results show that SDF application is not just more effective in arresting root caries but also works faster than applying the placebo, and that KI will not affect the speed of SDF in arresting root caries.

The frequency of application of SDF solution used in this study was once a year which was commonly used in clinical trials on arresting dentin caries in young children [27], and in two previous clinical trials on arresting root surface caries [17,21]. A clinical trial on arresting dentin caries in primary teeth of preschool children found that the caries arrest rate of 6-monthly application of SDF was higher than that of 12-monthly application [12]. More clinical trials need to be conducted to find out if the rate of arresting active root caries in elders will increase with more frequent applications of SDF solution.

It should be noted that the water in Hong Kong is fluoridated at an optimal concentration of 0.5 ppm. Whether topical application of SDF solution is similarly effective in arresting root caries among elders living in non-fluoridated areas needs to be investigated in future clinical studies.

5. Conclusion

Based on the result of this study, it is concluded that applications of SDF solution or SDF/KI solution are effective in arresting active root caries. Application of KI does not affect the effectiveness of SDF in arresting root caries and also does not reduce the black staining.

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