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Is Silver Diamine Fluoride Effective in Preventing and Arresting Caries in Elderly Adults? A Systematic Review

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Abstract

Aim:

Silver diamine fluoride (SDF) has invoked interest in recent times due to its remineralization capacity and non-invasive application procedure. The aim of this systematic review was to report the findings concerning the effectiveness of SDF in managing caries in the elderly adults.

Materials and Methods:

A systematic search of publications was conducted using four databases: PubMed, MEDLINE, Embase, and CENTRAL. The key MeSH term combinations used were (silver diamine fluoride) AND (caries) AND (elderly).

Results:

The review found only three well-conducted randomized controlled trials evaluating the effectiveness of SDF on root caries in community-dwelling elders. None of the studies addressed coronal caries. The effectiveness improved when combined with structured oral health education.

Conclusion:

The available limited evidence on SDF shows that it is effective in arresting and preventing root caries in the elderly. More high-quality studies need to be done to verify the effectiveness on coronal caries and long-term effects of SDF in the elderly with varying levels of dependency.

Keywords: *Caries*, *elderly adults*, *oral health*, *prevention*, *silver diamine fluoride*

Introduction

Dental caries is the most common pandemic on the globe,[1] which affects a large proportion of the world's population, regardless of gender, age, and ethnicity. It is estimated that around 2.5 billion (35%) people on the planet have untreated caries in their permanent dentition.[2] A variety of evidence-based approaches for caries prevention have been reported; however, these strategies demand significant financial investment and infrastructure and depend heavily on the availability of oral health workforces.[3] In the UK, 23% of the population will be aged 65 years and over compared to 18% aged 16 years or younger by the year 2023.[4] With a concomitant decrease in the edentulousness, there is an increased incidence of caries in the elderly. However, the need for improved preventive efforts and treatment strategies for this population remains sparse.[5]

Silver diamine fluoride – history and mechanism of action

Silver (Ag) has been documented to be used for medicinal purposes dating back to 1000 BC for storage of water.[6] Dental use of silver nitrate can be traced back to Japan around 1000 AD, where it was used for cosmetic blackening of teeth. Before silver diamine fluoride (SDF), silver nitrate followed by fluoride varnish was the only noninvasive option available for caries treatment.[7] Case series of carious lesions arrested by silver nitrate date to the 19th century, where 87 of 142 treated lesions were arrested.[8] SDF was formed when ammonia was added to silver nitrate to make it stable and effective as an antibacterial for application to caries lesions and infected root canals.[9] SDF has been widely used in Australia and Brazil since 1980 with *in vivo* studies done in the respective countries.[10,11]

Upon application of SDF to a decayed surface, a squamous layer of silver-protein conjugate is formed; this increases resistance of the tooth against acid dissolution and enzymatic digestion.[12] The treated lesion increases in mineral density and hardness while the lesion depth decreases.[13] Silver ions act directly against the bacteria in the caries by breaking the cell membrane, denaturing proteins, and inhibiting DNA replication.[14,15] SDF has been shown to outperform other anticaries and medicaments in killing cariogenic bacteria in dentinal tubules *in vitro*.[16] Silver and fluoride ions penetrate up to 25 μ into enamel and 50–200 μ into dentin.[17,18] Fluoride promotes remineralization, and silver is available for antimicrobial action upon release via reacidification. When bacteria killed by the silver ions are added to the living bacteria, the silver is reactivated effectively killing the live bacteria eliciting a zombie effect.[19]

Interest in SDF has resurfaced in recent times with several studies proving its effectiveness in preventing and arresting caries in the primary dentition and first permanent molar in children.[20,21,22,23,24] A review published in the USA had discussed the details about the protocol, rationale, indications, and consent for using SDF for caries arrest and prevention in children.[25] A recent update to this protocol recommends the eradication of the rinsing step following application backed by evidence of safety.[26] SDF has been suggested for difficult-to-treat lesions and patients with high risk of caries including those with medical or behavioral complications, those who require multiple treatment visits, or those without access to dental care.[25] However, the caveats to the use of SDF include black staining of the arrested carious tooth due to the precipitation of silver phosphate and its acceptance among the general population.[27]

The need for anticaries agents such as SDF is perhaps best understood in terms of the World Health Organization (WHO) Millennium Development Goals for Health and particularly oral health.[28] The proposed path to achieving these goals is the provision of a basic oral health package, consisting of emergency care, prevention, and cost-effective interventions, in that order.[29] This review aims to evaluate the scientific evidence regarding the effectiveness of SDF in preventing and arresting caries in elderly adults. If proven effective, SDF may benefit this population significantly, especially where dental care is not accessible or absent or in elders who are noncompliant for routine dental procedures.

Materials and Methods

This systematic review was conducted and reported as directed by the preferred reporting items for systematic reviews and meta-analysis guidelines[30] [Figure 1].

Search strategy

The relevant studies were searched in four online databases (PubMed, MEDLINE, Embase, and CENTRAL). All the records identified by the searches were screened based on the title first followed by abstract. An initial online search was performed by a single reviewer, using the search terms that were carefully identified in accordance with the stated PICO focus question. Then, the search was repeated by a second reviewer, to confirm the number of discovered articles by the employed search strategy. Hand searches and searches resulting from reference crosschecks to identify studies that were not found online were done by a third reviewer. The search terms employed were MeSH terms or key words classified under general (all fields) category. The search terms were then combined with an "OR" and PICO categories were combined using "AND" to create a final logic search query. This query was then run in the above-mentioned databases to yield results [Table 1].

Study selection

The search was conducted from January 2017 to October 2017. The study design was restricted to randomized controlled trials (RCTs) using SDF as one of the interventions on elderly adults aged 60 years and over with cavitated lesions on one or more tooth surface or having high risk of caries development. All languages were included in the search to maximize the study pool. The exclusion criteria included other study designs and studies done in population <60 years of age. The eligibility protocol was strictly applied, and the trial reports were assessed independently by the two reviewers. Each trial was scrutinized for multiple publications from the same data report. Any disputes regarding eligibility of a study were resolved by discussion among the reviewers. All identified articles underwent an abstract review and/or full article review to confirm the eligibility. Personal communication was sent to the author(s) where required.

Quality assessment

The Cochrane's Risk of Bias tool was used for assessing the methodological quality in the RCTs according to the Agency of Healthcare Research and Quality.[31]

Summary measures

Primary outcome measure The primary outcome measures of interest were the mean number of new and arrested carious surface post application of SDF. The numbers needed to treat, prevented fraction (PF), and relative risks (RRs) from the extracted data were quantified.

Caries is defined as any lesion which is detectable clinically and/or radiographically or by any validated method, involving enamel or dentin with or without cavitation. The number needed to treat (NNT) is defined as the number of patients required to treat in the intervention (s) group to prevent a carious lesion from occurring or to prevent a carious surface from progressing compared to the control group. PF is defined as the reduction in the incidence of caries surface or in the rate of preventing the carious tooth surface from progressing in the intervention arm (s) relative to the control arm (s) of the trial. RR is defined as how much likely new carious surfaces will form or existing caries surface will be prevented from the progressing in the intervention group (s) relative to the control group.

Secondary and tertiary outcome measures Clinical outcomes

- Duration and frequency of the SDF application

- Acute or chronic toxicity associated with SDF during the length of the trial
- Staining of tooth surface
- Percentage of dropouts from baseline to follow-up.

Patient-reported outcomes

- Pain and any discomfort associated during or after the procedure
- Any functional physical/psychological discomfort assessed by any valid patient-reported measure
- Patient-reported satisfaction by an appropriate index of patient satisfaction.

Results

Search results

Initial search identified 23 clinical trials done with SDF. An additional RCT was found during the rerun of the search and hand searching of the references. Only three RCTs met all the inclusion criteria and were included in this systematic review.[32,33,34]

Common characteristics of the included studies

All the three studies were conducted in community-dwelling elders in Hong Kong. The studies investigated the effects of SDF on root caries of the elderly comparing them with other interventions or a placebo. The SDF used in all three studies were the same preparation, that is, 38% SDF solution (Saforide, Toyo Seiyaku Kasei Co. Ltd., Osaka, Japan). The studies looked at the mean number of new caries lesions on the exposed root surface and/or the mean number of arrested root caries surface in the intervention and the control group. Disposable microbrushes were used for the painting of SDF on the affected or exposed root surfaces without any excavation of caries. No adverse events were noted with SDF in any of the studies. The summary of the characteristics and results of the included study are presented in Tables 2 and 3, respectively.

Characteristics of individual studies included

Tan *et al*. investigated the effect of SDF in the prevention of the root caries in the community-dwelling elders across 21 community centers. In this study, the root caries index was calculated, and visual plaque index was measured.[35,36] The participants were followed up for 3 years. They reported that SDF was more effective in preventing new caries than the other three groups. The PF for the root caries for SDF was calculated as 71% which was better than chlorhexidine (CHX) (57%) and sodium fluoride varnish (64%) ($P < 0.001$). The NNT for SDF was calculated to be 2.5 as opposed to 3.2 and 3.1 for CHX and sodium fluoride, respectively.

Zhang *et al*. investigated the effect of SDF on the prevention and arresting of root caries in community-dwelling elders. In this study, the elders from 11 community centers were randomly allocated to three groups. The oral health education (OHE) program was directed at controlling the snacking habit, teaching the correct grasp of the toothbrush, and use of additional tooth-cleaning aids. This was administered by a trained dental hygienist and each session lasted for 30 min. Traditional visual tactile diagnosis for root caries was used for the diagnosis.[37] The participants were examined annually for 2 years. Statistical significance was found for the difference of mean numbers of root surfaces for the three groups ($P < 0.05$). It was noted to be 1.33, 1.00, and 0.70 for the control, SDF, and SDF + OHE groups, respectively. The prevention fraction was extrapolated keeping the control group as reference and was calculated as 25% and 47% for the SDF + oral hygiene instructions (OHI) and SDF + OHI + OHE groups, respectively. The NNT for preventing one new caries root surface was calculated to be 3 and 1.6 for the SDF + OHI and SDF +

OHI + OHE groups, respectively. The mean number of arrested root caries surface were also significant ($P < 0.01$) and were calculated as 0.04 (control), 0.28 (SDF + OHI), and 0.33 (SDF + OHE). The NNT to arrest one root caries lesion was calculated as 4.2 for the SDF group and 3.5 for the SDF + OHE group.

Li *et al*. investigated the effectiveness of SDF on the root caries of the elderly and the effect of potassium iodide (KI) for reducing the stained tooth surface of the arrested lesion. SDF was found to be effective in arresting the caries; however, there was no effect of KI on the color of the arrested caries lesion. In this study, elders living across 12 community centers were randomly allocated to three groups. All the participants received OHI at baseline and 6 months later. The OHI had a focus on manual brushing techniques and a tube of fluoridated toothpaste was provided at each examination. The caries diagnosis was carried out based on the recommendations by the International Caries Detection and Assessment System 11 Coordinating Committee.[38] The follow-up examination was 30 months with a duration of 6 months between each examination. The percentage of arrest caries lesions was calculated to be 45%, 90%, and 93% for the control, SDF, and SDF + KI group, respectively ($P < 0.001$). The difference in caries arrest rates between the SDF and SDF + KI group was not statistically significant.

Discussion

This review reveals that limited published literature exists assessing the effectiveness of SDF on arresting and preventing caries in the elderly adults. However, with the available evidence, the potential of SDF was seen to be effective in arresting and preventing root caries of the elders with basic self-care ability. The review identified three well-conducted double-blinded RCTs in community-dwelling elders using 38% SDF applied on an annual basis. All the studies were of high quality and had a low degree of bias. The studies were assessed against the six domains from the Risk of Bias Tool which are summarized in Table 4 .

Analysis of data from the studies reveals that the annual application of 38% SDF can significantly arrest caries and reduce the incidence of new caries. Tan *et al*. reported a prevention fraction of 71% for the SDF group. Zhang *et al*. observed a PF of 47% and 25% in the SDF + OHI + OHE and SDF + OHI groups, respectively. Li *et al*. reported an arrest rate of 93% and 90% for the SDF and SDF + KI groups, respectively. All the participants of the study were given individualized OHI with a focus on manual tooth brushing. In addition to providing OHI, the Li *et al*.'s study participants received a tube of fluoridated toothpaste at each examination. This may have attributed to the differences in the arrest rates between the studies. In the Zhang *et al*.'s study, in addition to the OHI, a structured OHE was given to one group which had an emphasis on controlling the snacking habits and the proper use of oral health aids. This was proved to be more effective in preventing new caries in this group than the SDF + OHI group.

Li *et al*. used SDF along with saturated solution of KI to reduce stains. The KI is considered to have an antimicrobial action by inhibition of the biofilm formation and reduce further demineralization to resist caries progression.[34,39] The precipitation of silver iodide is thought to reduce the black staining of the teeth by SDF. However, it was established that application of KI had no effect on the esthetic problems caused by the black staining of the tooth though KI can improve the antimicrobial activity.

None of the studies reported any adverse events by the application of SDF or during the follow-up examination. The studies reported the black staining of the teeth, but it was deemed acceptable by the participants.[32] This correlates with the findings of another study done on the parental perceptions of the staining caused by SDF in children seeing the color changes as positive indication that treatment was effective.[40] Two studies in children reported adverse events of black staining and oral lesions using 30% and 38% SDF.[22,41] Although these studies suggest that lower concentration might reduce the onset of the adverse events, these concentrations are less effective in arresting caries.[42] Silver allergy is considered as a contraindication for SDF application. However, silver has been used for centuries as an antimicrobial agents and toxicity or adverse events associated with silver are very rare.[43] Fluoride use is

associated with fluorosis, but none of the studies reported any participant developing fluorosis. In a pharmacokinetic study of SDF application, the teeth of six, 48–82-year-old adults showed no ulceration or significant increase in the serum fluoride.[44] Furthermore, a study carried out by the Health Department of Western Australia found no evidence of fluorosis resulting from long-term use of SDF.[45] The studies included in this review were conducted in Hong Kong where the water is fluoridated at 0.5 ppm. These evidences suggest that long-term usage of SDF may be safe for adults.

The search strategy did not yield any trials on coronal caries in elderly adults. However, studies done in children provide evidence in the effectiveness of SDF in the prevention and arrest of the coronal caries compared to other caries preventing agents such as sodium fluoride, CHX fissure sealants, and glass ionomer cement.[27,46,47,48,49] Evidence also suggests that SDF is effective in reducing dentinal hypersensitivity in adult dentition.[50] Ongoing trials are examining the efficiency of SDF on interproximal caries, and these results will be of interest.[51] SDF may also be effective in the prevention and arresting of coronal caries in adults; however, more studies are required to substantiate this claim.

Conclusion and Recommendations

The main advantages of SDF are it is inexpensive and easy to apply. Unlike conventional restorative treatment, SDF does not require costly equipment or support infrastructure.[52] SDF application can be done by nondental professionals with adequate training. This makes SDF an ideal candidate for public health measure to control caries in the elderly where there is limited or no access to dental services with its low-cost, simple, and noninvasive application procedure.[53] The WHO has estimated oral diseases as the fourth most expensive disease to treat in most industrialized countries where 5%–10% of the health spending is on treating dental caries.[54,55,56] SDF can fill the void of the need for a cost-effective and potential caries management option. However, the cost implications of wider use of SDF need to be understood.

The studies identified were carried out on community-dwelling elders with basic self-care ability and no cognitive decline. However, in countries such as the United Kingdom, this is not often the case where the Alzheimer's Society[57] estimates that 80% of care home residents have dementia or severe memory problems. Research with adults in care homes with moderate-to-severe dementia had reported poor oral health.[58] Further research into the use of SDF in this patient group is required. NICE guidelines are published in the UK to inform decisions in medicine, public health, and social care by evidence-based recommendations. A recent guideline (NG48) for oral health for adults in the care homes was published in 2016.[59] This highlights the importance of addressing the untreated dental caries which can have an impact on the general health and well-being in elders living in care homes, especially those who cannot express their distress or pain and ask for help. This includes the elders with dementia and cognitive disabilities. There is a lack of good-quality data on the effectiveness of oral health interventions and the costs of delivering them to residents in care homes in England.[59] There are also no robust data on the differential effects on subpopulations in care homes. This includes people with dementia, people in poor physical health, and those with a short life expectancy. These data are needed for evaluation purposes, to inform future guidance and commissioning decisions, and are vital for informing efficient and fair use of increasingly limited resources as identified by the guideline.

Even though the review has found no mention of adverse effects associated with the SDF use in the elderly, there are no data on the long-term effect of SDF. Black staining is an inevitable consequence of SDF application. Furthermore, to be noted is that all the studies were conducted in communities with water fluoridation. However, water fluoridation is either not uniform or absent in many countries. Hence, it is important to take this factor into account when recommending SDF for caries prevention. It will be interesting to see the effectiveness of SDF when it is not used in conjunction with OHI or OHE.

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Conflicts of interest

There are no conflicts of interest.

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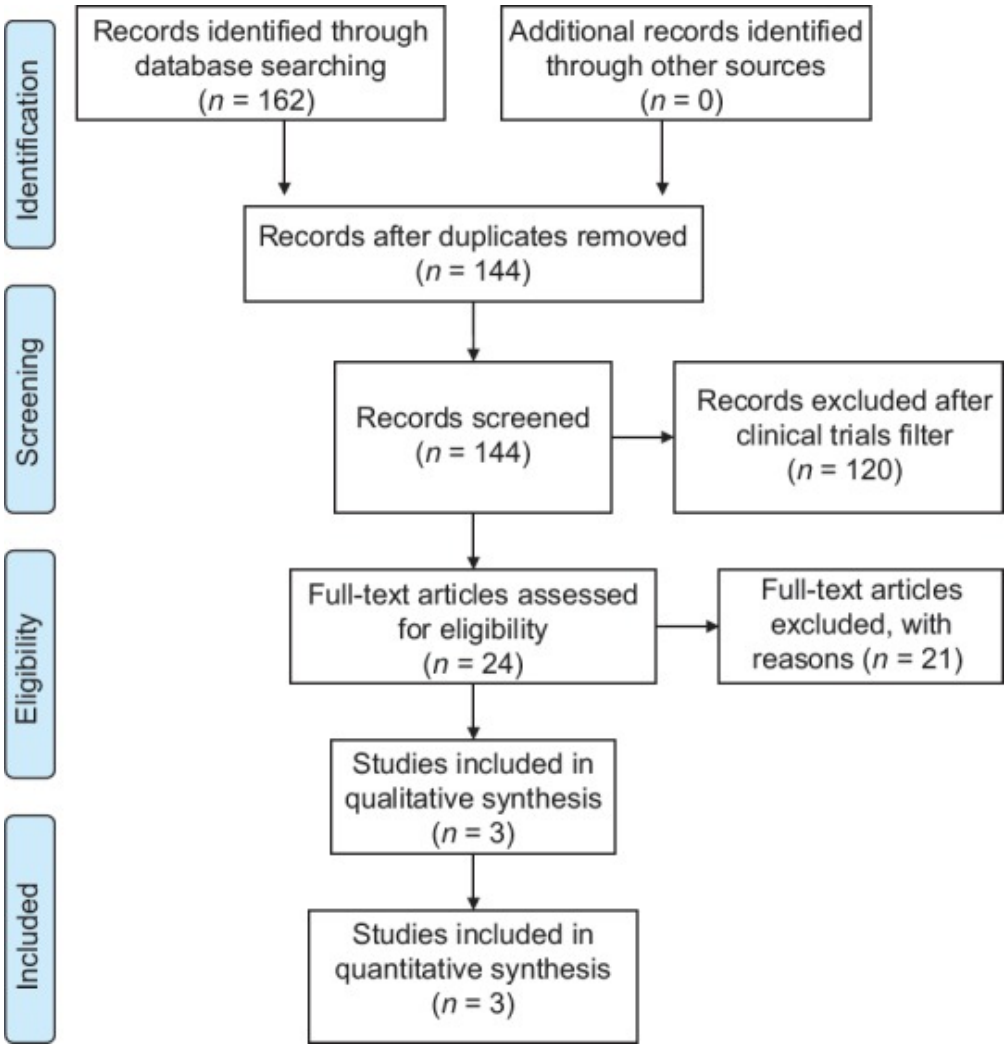
Figures and Tables

Figure 1



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PRISMA 2009 Flow diagram

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Table 1

Focus Question, Criteria, Information Sources and Search Terms

Focus question	Is SDF effective in preventing and arresting caries in elderly adults?	
Criteria	Inclusion criteria	
	Primary research article	
	Randomized controlled trials done in adults aged 60 years and over without or without dental caries	
	Randomized controlled trails done using SDF as one of the interventions for caries prevention or arrest	
	Exclusion criteria	
	Other study deigns, *in vitro* studies, reviews, and case reports	
	Studies done on children or adults <60 years of age	
Information sources	Electronic databases	
	PubMed, Embase, MEDLINE, and the Cochrane Central Register of Controlled Trials	
	Journals	
	All peer-reviewed dental and related journals available online in databases	
	Others	
	Popular online internet search engines (e.g., Google, Yahoo, etc.), Online internet research community websites (https://www.researchgate.net/), reference crosschecks, personal communications, hand searches, gray literature, etc.,	
Search terms	#1: MeSH - "silver diamine fluoride" OR "silver diaamine fluoride" OR "SDF" OR "Topical fluoride" OR "Dental fluoride" OR "AgFH6N2" OR "Diammine silver fluoride" OR "Ammonical silver fluoride" OR Silver ammonia fluoride" OR "Silver fluoride" OR "Quaternary ammonium compounds"	
	#2: MeSH - dental caries OR caries OR cavity OR white spot OR dentinal caries OR dental decay OR dentinal lesion	
	#3: MeSH - Aged OR elderly OR older adult OR frail OR institutionalised	
Filters	Language	Not applied
	Species	Humans (MeSH)
	Ages	Aged (MeSH)
Search dates	Final confirmatory online search was performed on October 31st, 2017	

SDF=Silver diamine fluoride

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Table 2

Characteristics of included studies

Study (year)	Description
Tan *et al*., (2010)[32]	Study area: Hong Kong
	Study design: 36 months; RCT; double blind
	Site: 21 residential and nursing homes
	Visits: Baseline and follow-up (12, 24, and 36 months)
	Sample: *n*=306 (80% power, α=0.05)
	Randomization: Individual random basis
	Inclusion criteria: Elders with at least 5 exposed roots
	Diagnostic criteria: DMFS; exposed root surface, caries activity and hardness
	Treatment group: 38% SDF application every 12 months
	Control: CHX and NaF every 3 months, water every 12 months
	SDF application technique: All exposed root surfaces
	SDF adverse events: None reported
Zhang *et al*., (2013)[33]	Study area : Hong Kong
	Design: 24 months; RCT; double blind
	Sites: 11 community elderly centers
	Visits: Baseline and follow-up (12 and 24 months)
	Sample: *n*=266 (80% power, α=0.05)
	Randomization: Computer-generated list
	Inclusion criteria: Elders with at least five exposed root surfaces
	Diagnostic criteria: DMFS; gingival recession and caries activity (changes in dentin hardness and color)
	TX groups: 38% SDF + OHI, 38% SDF + OHI + OHE (SDF application every 12 months, OHE every 6 months)
	Control: OHI + water (placebo) every 12 months
	SDF application technique: All exposed root surfaces no caries removal
	SDF adverse events: None reported
Li *et al*., (2016)[34]	Study area: Hong Kong
	Design: 30 months; RCT; Double blind
	Site: 12 elderly community centers
	Visits: Baseline and follow-up (6, 12, 18, 24, and 30 months)
	Sample: *n*=157 root surfaces with active caries (83 elders)
	Randomization: Assignment to groups using block randomization (block size 6)
	Inclusion criteria: Elders with one or more teeth with active root surface caries
	Diagnostic criteria: DMFS; exposed root surface, caries activity and hardness
	TX groups: 38% SDF, 38% SDF + KI every 12 months
	Control: Soda water (placebo) every 12 months
	SDF application technique: Applied on active caries lesions
	SDF adverse events: None reported

CHX=Chlorhexidine, SDF=Silver diamine fluoride, RCT=Randomized controlled trials, OHE=Oral health education, OHI=Oral hygiene instructions, NaF=Sodium fluoride, DMFS=Decayed, Missing and Filled Surfaces

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Table 3

Summary of the results of included participants

Study (years)	Objective	Statistical analysis	Results
Tan *et al*., (2010)[32]	Assess the effectiveness of annual application of SDF and other three interventions in preventing new root caries surfaces	ANOVA Scheffe's multiple comparison Student *t*-test	*n*=306 Dropout: *n*=103 SDF was more effective for root caries prevention (71%) The three interventions group had significantly lower mean number of new root caries surface ($P<0.01$) than the control
Zhang *et al*., (2013)[33]	To investigate the effectiveness of SDF and oral health education in preventing and arresting root caries	ANOVA Chi-squared test ANCOVA	*n*=266 Dropout: *n*=39 Mean number of new arrested caries OHI + Placebo 1.33/0.04 OHI + SDF 1.00/0.28 OHI + SDF + OHE 0.70/0.33 OHI + SDF had significantly better effect on prevention ($P<0.05$) and arrest ($P<0.05$) of root caries than OHI alone Additional improvement in prevention and arrest with adding OHE to OHI + SDF ($P<0.05$)
Li *et al*., (2009)[34]	To investigate the effectiveness of SDF solution application in arresting dental root caries and to assess the color of the arrested caries lesion	ANOVA Proportional Hazards Chi-squared test	*n*=83 Dropout: *n*=16 Arrest rate at 12/24/30 months OHI + Placebo 32.1%/28.6%/45% OHI + SDF 61%/82.1%/90% OHI + SDF + KI 75.9%/85.4%/92.5% The arrest rate in SDF and SDF+KI groups was statistically significant compared to placebo ($P<0.001$), while there was no statistically significant difference in arrest rates between SDF and SDF + KI groups ($P>0.05$) There was no statistically significant difference between color distribution of arrested lesions in SDF and SDF + KI groups ($P>0.05$)

SDF=Silver diamine fluoride, OHE=Oral health education, OHI=Oral hygiene instructions

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Table 4

Assessment of risk of bias of included studies

Study	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective Outcome reporting	Other sources of bias
Tan *et al.*, (2010)	Yes "A research assistant conducted the random assignment of participants by drawing numbers from a bag"	Yes "Assignment was concealed until the time for treatment by the clinician"	Yes "Follow-up examinations were carried out annually by the same independent examiner, who did not know the participant's group assignment"	Yes "Two-thirds (203/306) of the study elders were followed up for 3 years. The participants' drop-out rates in the four groups were similar (χ^2 test, P>0.05)" Reasons provided for exclusion	No All the prespecified primary outcomes were reported	None apparent
Zhang *et al.*, (2013)	Yes "After the baseline examination, participants were randomly assigned to one of the following 3 groups according to a random list generated by a computer"	Yes "Only the data collection sheet of the specific time period was allocated to the examiner at the time of assessment"	Yes The examiner and participants were blinded. Blinding procedure adequately explained	Yes "Teeth that were lost between the baseline and follow-up examinations were not included in the assessment of treatment outcomes" reasons not provided. drop out percentage nonsignificant	No All the prespecified primary outcomes were reported	None apparent
Li *et al.*, (2016)	Yes "A dental surgery assistant carried out the subject allocation according to the combinations randomly generated by computer"	Yes Allocation examination and intervention were carried out by different persons	Yes "Both the examiner and the subjects were blinded to group assignment"	Yes "The retention rate of elders who had more root caries lesions was lower" Reasons provided	Yes Only reported arresting of new root caries. The prevention effect not yet published	Possibility of participant bias declared