Review

Clinical Trials of Silver Diamine Fluoride in Arresting Caries among Children: A Systematic Review

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Abstract: *This review aims to investigate the clinical effectiveness of silver diamine fluoride (SDF) in arresting dental caries among children. A systematic search of publications was conducted with the key words "silver diamine fluoride," "silver diammine fluoride," "silver fluoride," "diamine silver fluoride," or "diammine silver fluoride" as well as their translation in Chinese, Japanese, Portuguese, and Spanish in 7 databases: PubMed (English), Embase (English), Scopus (English), China National Knowledge Infrastructure (Chinese), Ichushi-web (Japanese), Biblioteca Virtual em Saude (Portuguese), and Biblioteca Virtual en Salud Espana (Spanish). Duplicated publications were deleted. The title and abstract were screened and irrelevant publications were excluded. The full text of the remaining publications was retrieved. Prospective clinical studies of SDF that reported a caries-arresting effect among children were included. Meta-analysis was performed for quantitative analysis. A total of 1,123 publications were found, including 19 publications of clinical trials. Sixteen clinical trials studied the caries-arresting effect on primary teeth, and 3 clinical trials were on permanent teeth. Fourteen studies used 38% SDF, 3 used 30% SDF, and 2 used 10% SDF. Meta-analysis was performed on extracted data from 8 studies using 38% SDF to arrest caries in primary teeth. The overall percentage of active caries that became arrested was 81% (95% confidence interval, 68% to 89%;* $P < 0.001$*). Apart from staining the arrested lesion black, no significant complication of SDF use among children was reported. SDF was commonly used at 38%. It was effective in arresting dentine caries in primary teeth among children.*

Knowledge Transfer Statement: *This systematic review found that 38% silver diamine fluoride (SDF) can effectively arrest caries among children. SDF treatment is noninvasive and easily operated. It can be a promising strategy to manage dental caries in young children or those who have special needs.*

Keywords: meta-analysis, pediatric dentistry, tooth remineralization, dental caries, fluorides, silver compounds

Introduction

Although people's dental knowledge has generally improved and dental treatment techniques have advanced in the past few decades, early childhood caries (ECC) still remains a global health problem. ECC is the presence of 1 or more decayed, missing due to caries, or filled tooth surfaces (dmfs) in any primary tooth in a child at 71 mo of age or younger (American Academy of Pediatric Dentistry 2008). While dietary sugars and poor oral hygiene are important factors causing

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ECC, poor parental education, adverse socioeconomic conditions, low family income, having a single parent, and regular medication are all related to a higher risk of ECC in preschool children (Chu 2000). Moreover, ethnic and cultural variables are also significant factors that predispose children to ECC because feeding habits, diet, and pacifier use differ between cultures. In the United States, the prevalence of dental caries was 50% among children aged 5 to 9 y (Bagramian et al. 2009). In Southeast Asia, a study reported almost half (47%) of young children aged 25 to 30 mo suffered from ECC (van Palenstein Helderman et al. 2006). Untreated ECC can cause toothache, pain, and infection. The consequences will influence not only children's oral health but also their general health, such as their growth, quality of life, and their cognitive development.

Conventional dental treatment for ECC is often either unavailable or unaffordable for many child populations (Chu and Lo 2008). Moreover, cooperation from children during dental treatment is another challenge for dentists. Hence, alternative treatments that can be easily carried out and at a low cost are required for ECC management in children (Chu et al. 2009). Some clinicians have suggested using silver diamine fluoride (SDF) for caries management (Chu et al. 2002; Llodra et al. 2005). It is a colorless ammonia solution containing silver and fluoride ions. As neutral silver fluoride is unstable, it is commonly dissolved in water containing ammonia to form a more stable complex ion (Mei, Ito, et al. 2013). Fluoride has proven to be effective in enhancing the remineralization of dental hard tissue. Silver ion acts as an antibacterial agent in SDF (Mei, Chu, Low, et al. 2013). Laboratory studies have shown that 38% SDF is effective in inhibiting dentine demineralization and preserving collagen from degradation (Mei, Ito, et al. 2013; Mei, Chu, Low, et al. 2013; Mei et al. 2014). After being treated with SDF, a highly remineralized surface zone rich in calcium and phosphate can be found on the arrested cavitated carious lesion. The dentine collagens are protected by the remineralized mineral materials (Mei et al. 2014). SDF also has antibacterial properties and inhibits the growth of cariogenic biofilms (Mei, Chu, Low, et al. 2013).

SDF at 38% has been used to arrest ECC in Argentina, Australia, Brazil, China, Japan, and recently the United States. Because this treatment is noninvasive and easily performed, it can be a promising strategy to manage dental caries in very young children or those who have special needs (Chu et al. 2009). One significant limitation of SDF treatment is that it will stain carious lesions black. This appearance may not be acceptable for some children and their parents. Hence, it is necessary to inform patients of this outcome of SDF treatment. Pretreatment discussion about the pros and cons of SDF treatment with the children and their parents is vital to patient satisfaction. A primary tooth with its caries arrested can act as a space maintainer and sustain chewing function until the tooth is replaced with a permanent successor tooth. SDF at 38% has high fluoride content (44,800 ppm). Some clinicians were concerned about the use of SDF in young children because of the risk of causing dental fluorosis. However, since only a very small amount of SDF solution is applied onto a carious lesion, researchers concluded that occasional application of SDF is well below the concentrations associated with toxicity (Mei et al. 2016).

Since SDF has not been commonly used in dentistry in most of the developed Western countries, the number of English publications regarding SDF use is limited. Instead, there may be more publications in Japanese, Chinese, Spanish, and Portuguese because it has been used in countries using these languages. Until now, there has been no comprehensive systematic review to evaluate the evidence about the clinical effectiveness of using SDF for arresting dental caries among children. The aim of this study was to review the prospective clinical studies that investigated the effectiveness of SDF in arresting dental caries among children.

Materials and Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, which is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses (Moher et al. 2009).

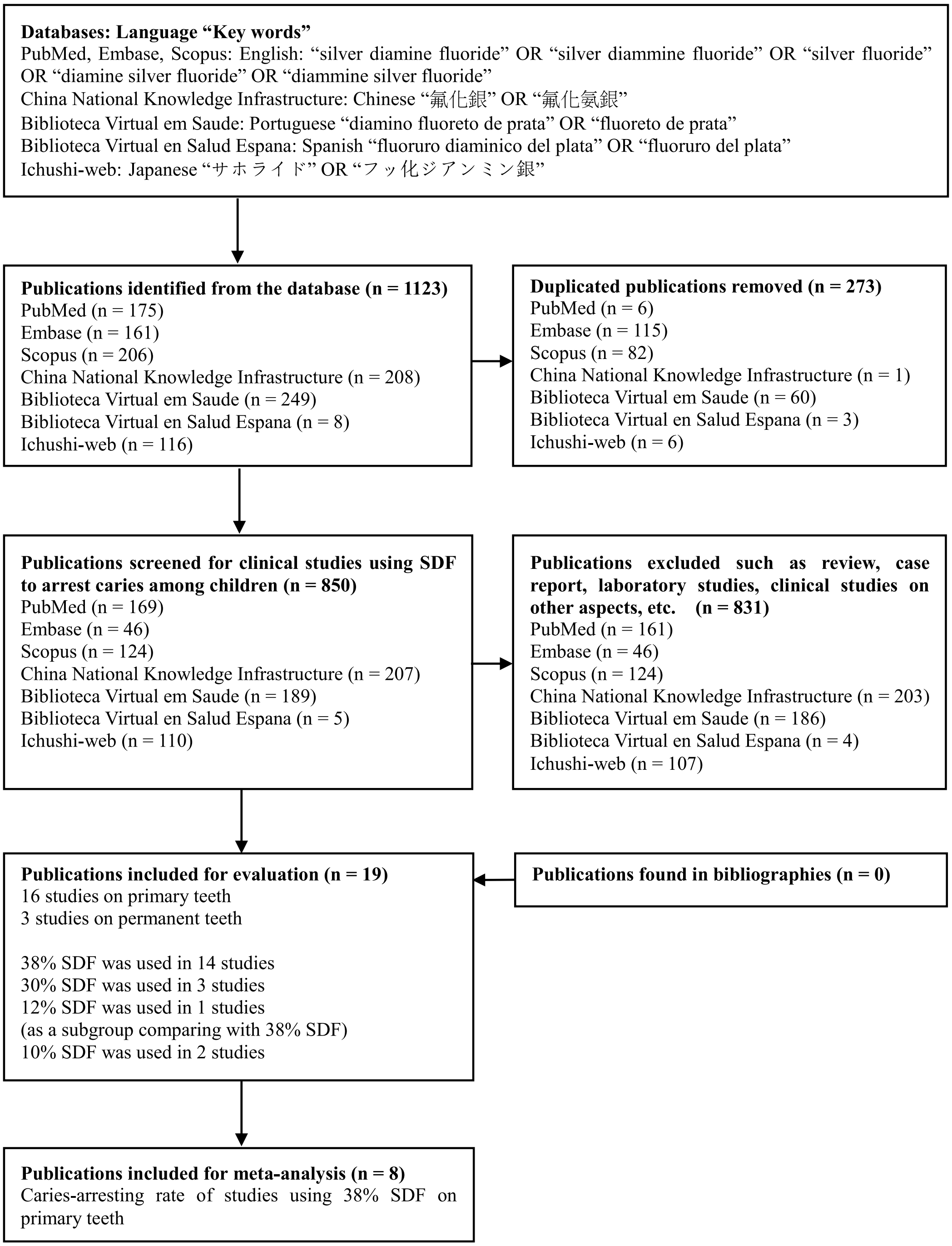
Search Strategy

A systematic search of literature was performed in 7 databases containing English, Chinese, Japanese, Portuguese, and Spanish articles. English publications were searched in PubMed, Embase, and Scopus by using the following English key words: "silver diamine fluoride," "silver diammine fluoride," "silver fluoride," "diamine silver fluoride," or "diammine silver fluoride." Chinese literature was searched using the China National Knowledge Infrastructure (CNKI) with the Chinese key words "氟化銀" or "氟化氨銀." Japanese papers were searched using Ichushi-web with the Japanese key words "サホライド" or "フッ化ジアンミン銀." The search for Spanish and Portuguese publications was conducted using Biblioteca Virtual en Salud Espana (BVSE) and Biblioteca Virtual em Saude (BVS) by using the Spanish key words "fluoruro diaminico del plata" or "fluoruro del plata" and the Portuguese key words "diamino fluoreto de prata" or "fluoreto de prata," respectively. No limit on the time of publication was set, and the last search was made at the end of March 2016. Publications that contained the key words above formed a potentially eligible list and were included for the first screening (Fig. 1).

Selection of Clinical Studies

Articles in the potentially eligible list were screened manually by title and abstract. Duplicated publications were removed. Literature reviews, case reports, laboratory studies, clinical trials in other

Figure 1. Flowchart of literature search. SDF, silver diamine fluoride.



aspects (such as not investigating caries arrest in children), clinical treatment guidelines, and other irrelevant studies were excluded. The full text of the remaining studies was retrieved. A manual screening of bibliographies was conducted to identify related articles. Prospective clinical studies investigating the caries-arresting effect of SDF treatment in children with or without control groups were selected for analysis in this systematic review. The 2 reviewers (SSG and ISZ) would discuss with another independent investigator (CHC) when they disagreed on include/exclude decisions. There was no appraisal of agreement frequencies for include/exclude decisions.

Data Collection and Analysis

Related information about the non-English studies included in the final list was translated into English for analysis. Data evaluating the caries-arresting effect were extracted and reviewed by 2 independent investigators. Information on the dentition (primary or permanent teeth), sample size, study period, and treatment and control groups (if applicable) was sought from the included publications. The percentage of dental caries that had become arrested after SDF treatment in each study was calculated if the number of teeth or tooth surfaces with active caries at baseline and the number of teeth or tooth surfaces with arrested caries at follow-up could be found in the retrieved studies. Otherwise, the original data were reported. The 2 reviewers then discussed their retrieved data and analysis after reviewing. If necessary, the result was discussed with the third investigator before making a decision. All studies included in the final list were summarized in a table for qualitative evaluation. Meta-analysis (Stata 13.1; StataCorp LP) was performed on studies in which the caries-arresting rate using 38% SDF solution on primary teeth could be obtained or calculated. The logistic-normal random-effects model was adopted to evaluate the caries-arresting proportions at different follow-up time points, which referred to the period of the baseline and follow-up examination. The overall caries-arresting proportions were pulled up from appropriate studies as well. Risk of bias was assessed for each included study from 6 aspects: 1) random sequence generation (selection bias), 2) allocation concealment (selection bias), 3) blinding of outcome assessment (detection bias), 4) incomplete outcome data (attrition bias), 5) selective reporting (reporting bias), and 6) other bias.

Results

The initial search found 1,123 publications. There were 542 publications in English, 208 publications in Chinese, 249 publications in Portuguese, 8 publications in Spanish, and 116 publications in Japanese. A total of 273 duplicated publications were removed. After manually screening the remaining studies by title, abstract, and full text when necessary, 829 of the 850 remaining publications were removed because they were literature reviews, case reports, laboratory studies, or clinical studies on caries prevention, hypersensitivity, or endodontic treatment. A total of 21 clinical studies investigated the caries-arresting effect of SDF. No additional publications were found in the bibliographies. Two studies that reported on the caries-arresting effect of root caries among elders were excluded. Finally, 19 studies were reviewed in detail, including 8 studies published in English, 4 studies in Chinese, 3 studies in Portuguese, 1 study in Spanish, and 3 studies in Japanese. Details of these studies are summarized in Table 1. A summary of the risk of bias is presented in Table 2.

Among these 19 studies, 16 studies investigated the caries-arresting effect of using SDF on primary teeth (Nishino et al. 1969; Yoshida et al. 1976; Tsutsumi 1981; Wang 1984; Maciel 1988; Ye 1995; Miasato 1996; Fukumoto et al. 1997; Chu et al. 2002; Yang et al. 2002; Llodra et al. 2005; Huang et al. 2006; Yee et al. 2009; dos Santos et al. 2012; Zhi et al. 2012; Duangthip et al. 2016), while the other 3 clinical trials studied permanent teeth (Oliveira 1985; Mauro et al. 2004; Braga et al. 2009). Different concentrations of SDF solution were used in the 19 studies. Fourteen studies used 38% SDF as a caries-arresting agent (Nishino et al. 1969; Yoshida et al. 1976; Tsutsumi 1981; Wang 1984; Oliveira 1985; Ye 1995; Fukumoto et al. 1997; Chu et al. 2002; Yang et al. 2002; Mauro et al. 2004; Llodra et al. 2005; Huang et al. 2006; Yee et al. 2009; Zhi et al. 2012). Compared with a negative control (no treatment) or a placebo (treatment with water), 38% SDF solution was found to be effective in arresting dentine caries in primary teeth (Nishino et al. 1969; Yoshida et al. 1976; Tsutsumi 1981; Wang 1984; Chu et al. 2002; Llodra et al. 2005; Huang et al. 2006; Yee et al. 2009). In 3 studies conducted in Hong Kong and South America for management of dental caries, 30% SDF solution was used (Miasato 1996; dos Santos et al. 2012; Duangthip et al. 2016). The results showed that 30% SDF was more effective in arresting dentine caries in primary teeth among children than 5% sodium fluoride (NaF) varnish (Duangthip et al. 2016). A study in Nepal found that a one-off application of 12% SDF solution was ineffective in arresting caries in primary teeth (Yee et al. 2009). Two studies used 10% SDF solution to arrest caries in permanent and primary teeth. One of these studies reported that it was not effective in arresting dentine caries in permanent teeth (Braga et al. 2009), while the other study reported that it was effective in primary teeth (Maciel 1988). The 2 studies investigating the caries-arresting effect of 38% SDF in permanent teeth did not find any statistically significant results (Oliveira 1985; Mauro et al. 2004).

Meta-analysis was conducted on 8 studies, which used 38% SDF to arrest dentine caries in primary teeth in children and had properly reported data (Chu et al. 2002; Fukumoto et al. 1997; Llodra et al. 2005; Wang 1984; Yang et al. 2002; Ye 1995; Yee et al. 2009; Zhi et al. 2012). The results showed that the caries-arresting rate of SDF treatment was 86% (95% confidence interval [CI], 47% to 98%; $P = 0.06$) at 6 mo, 81% (95% CI, 59% to 93%; $P = 0.01$) at 12 mo, 78% (95% CI, 70% to 85%; $P < 0.001$) at 18 mo, 65% (95% CI, 35% to 86%; $P = 0.32$) at 24 mo, and 71% (95% CI, 56% to 83%; $P = 0.01$) at or beyond 30 mo (Fig. 2). The overall proportion of arrested dental caries after SDF treatment was 81% (95% CI, 68% to 89%; $P < 0.001$). It is noteworthy that the application frequency of SDF varied in different studies. Apart from staining the arrested caries lesion black, the 19 clinical trials did not report any significant complication of SDF use among children.

Discussion

Two reviews on the use of SDF searched studies published in English on the caries-arresting effects (Chu and Lo 2008; Gao et al. 2016). Another review

Table 1.
Summary of SDF Studies on Children.

Author, Site, Year (Language)	Methods	Main Findings
Duangthip et al., Hong Kong, 2016 (English)	Primary teeth, 18 mo Gp1: 30% SDF, annually (*n* = 458) Gp2: 30% SDF, one-off (*n* = 426) Gp3: 5% sodium fluoride, one-off (*n* = 523)	Caries-arresting rate: Gp1 (40%) > Gp2 (35%) > Gp3 (27%)
dos Santos et al., Brazil, 2012 (English)	Primary teeth, 12 mo Gp1: 30% SDF, one-off (*n* = 183) Gp2: glass ionomer, one-off (*n* = 162)	Caries-arresting rate: Gp1 (67%) > Gp2 (39%)
Zhi et al., China, 2012 (English)	Primary teeth, 24 mo Gp1: 38% SDF, annually (*n* = 218) Gp2: 38% SDF, semiannually (*n* = 239) GP3: glass ionomer, annually (*n* = 262)	Caries-arresting rate: Gp2 (91%) > Gp1 (79%), Gp3 (82%)
Yee et al., Nepal, 2009 (English)	Primary teeth, 24 mo Gp1: 38% SDF, one-off (*n* = 3,396) Gp2: 12% SDF, one-off (*n* = 1,652) Gp3: no treatment (*n* = 1,590)	Caries-arresting rate: Gp1 (31%) > Gp2 (22%), Gp3 (15%)
Braga et al., Brazil, 2009 (English)	Permanent teeth, 30 mo Gp1: CTT, one-off (*n* = 18) Gp2: 10% SDF, one-off (*n* = 20) Gp3: glass ionomer, one-off (*n* = 20)	Carious scores: no difference among groups
Huang et al., China, 2006 (Chinese)	Primary teeth, 18 mo Gp1: 38% SDF biannually, anterior teeth (*n* = 226) Gp2: no treatment, anterior teeth (*n* = 223) Gp3: 38% SDF biannually, posterior teeth (*n* = 144) Gp4: no treatment, posterior teeth (*n* = 145)	Caries-arresting effect: Gp1 > Gp2 (no data provided) Gp3 > Gp4 (no data provided)
Llodra et al., Cuba, 2005 (English)	Primary teeth, 36 mo Gp1: 38% SDF, semiannually (*n* = 675) Gp2: no treatment (*n* = 658)	Caries-arresting rate: Gp1 (85%) > Gp2 (62%)
Mauro et al., Argentina, 2004 (Spanish)	Permanent teeth, 12 mo Gp1: ammonium fluoride, one-off (*n* = 48) Gp2: 38% SDF, one-off (*n* = 49) Gp3: 5% sodium fluoride, one-off (*n* = 44)	Caries-arresting rate: Gp1 (56%), Gp2 (57%), Gp3 (47%) No difference among groups
Chu et al., Hong Kong, 2002 (English)	Primary teeth, 30 mo Gp1: 38% SDF, annually (*n* = 641) Gp2: 5% sodium fluoride, every 3 mo (*n* = 576) Gp3: no treatment (*n* = 273)	Caries-arresting rate: Gp1 (65%) > Gp2 (41%), Gp3 (34%)
Yang et al., China, 2002 (Chinese)	Primary teeth, 6 mo 38% SDF, one-off (*n* = 158)	Caries-arresting rate: 94.4%
Fukumoto et al., Japan, 1997 (Japanese)	Primary teeth, 48 mo 38% SDF, one-off (*n* = 130)	Caries-arresting rate: 54%
Miasato, Brazil, 1996 (Portuguese)	Primary teeth, 6 mo 30% SDF, every 3 mo (*n* = 88)	Caries-arresting rate: 83%
Ye, China, 1995 (Chinese)	Primary teeth, 12 mo 38% SDF, one-off (*n* = 300)	Caries-arresting rate: 92%
Maciel, Brazil, 1988 (Portuguese)	Primary teeth, 6 mo Gp1: 10% SDF, one-off (*n* = 104) Gp2: no treatment (*n* = 80)	Caries-arresting rate: Gp1 (90%) > Gp2 (74%)

(continued)

Table 1.
(continued)

Author, Site, Year (Language)	Methods	Main Findings
Oliveira, Brazil, 1985 (Portuguese)	Permanent teeth, 12 mo Gp1: 38% SDF, one-off (n = 7) Gp2: 38% SDF, twice in 1 wk (n = 9) Gp3: 38% SDF, biannually (n = 21) Gp4: 38% SDF, twice in 1 wk, then biannually (n = 17)	Caries-arresting effect: Caries arrested in all groups No difference among groups
Wang, China, 1984 (Chinese)	Primary teeth, 18 mo Gp1: 38% SDF, every 3 to 4 mo (n = 110) Gp2: no treatment (n = 104)	Caries-arresting rate: Gp1 (86%) > Gp2 (31%)
Tsutsumi et al., Japan, 1981 (Japanese)	Primary teeth, 18 mo Gp1: 38% SDF, every 3 mo (n = 33) Gp2: no treatment (n = 33)	Caries-arresting effect: Gp1 > Gp2 (no data provided)
Yoshida et al., Japan, 1976 (Japanese)	Primary teeth, 12 mo Gp1: 38% SDF, every 3 mo (n = 26) Gp2: no treatment (n = 26)	Caries-arresting effect: SDF was effective (no data provided)
Nishino et al., Japan, 1969 (English)	Primary teeth, 6 mo Gp1: 38% SDF, one-off (n = 106) Gp2: no treatment (n = 82)	Caries without progression: Laterally: Gp1 (69%) > Gp2 (52%) Pulpally: Gp1 (76%) > Gp2 (65%)

CTT, cross tooth-brushing technique; GP, group; SDF, silver diamine fluoride.

searched studies published in English, Portuguese, and Spanish (Rosenblatt et al. 2009). There are limitations of these reviews, as SDF has been used for clinical care in Japan and reported in Japanese since the 1970s (Yoshida et al. 1976; Tsutsumi 1981). There are also articles in Chinese reporting caries arrest after SDF application in China since the 1980s (Wang 1984; Ye 1995). More than half of the articles found in the literature search are non-English articles, with one-third of the publications in Chinese or Japanese. The results suggest that SDF is effective in arresting caries among children.

Meta-analysis combines the findings of independent clinical trials for statistical analysis (Wong et al. 2014). It provides improved precision and accuracy of estimates, and the statistical power is increased to detect the effects of the studies' variables. Nevertheless, meta-analysis requires a high consistency for outcome measurement and data presentation of the selected clinical trials. Some trials cannot be included because of their variations in the outcome measure. In this review, studies that defined the rate of caries arrest as the proportion of caries became hardened after SDF application were used for meta-analysis. A few old studies with no data provided were excluded for meta-analysis (Yoshida et al. 1976; Tsutsumi 1981; Oliveira 1985; Huang et al. 2006). A study measured the proportion of lateral caries progression and pulpal caries progression after SDF treatment (Nishino et al. 1969). It was also not included in meta-analysis because the number of arrested carious lesions (i.e., without both lateral and pulpal progression) was unknown. In practice, clinical trials are often not standardized, and the influence of between-study heterogeneity is usually uncertain (Thompson and Pocock 1991). There are also certain inconsistencies regarding the study design for the selected trials because the studies were conducted using SDF at different concentrations, application frequencies, and follow-up periods. In this review, clinical trials using the most common concentration of SDF (i.e., 38%) were chosen for meta-analysis. Meta-analysis was not performed on studies using SDF at other concentrations because the number of the studies is very small.

A logistic-normal random-effects model within subgroup analysis was fitted in the meta-analysis. There are three advantages of using this model. First, this model uses the exact method. There is no problem if the caries-arresting proportions of some studies were close to 1 (Nyaga et al. 2014). Second, the sample size of each study had less influence on the overall result when using the random-effects model over the fixed-effects model (Borenstein et al. 2007). Third, subgroups were identified according to different follow-up durations. A meta-analysis was conducted in each subgroup and then among all subgroups. As a result, caries-arresting rates were calculated separately for different follow-up periods. Some studies included in this review had no control group, whereas others used different control groups. Since the aim of this review was to investigate the caries-arresting effectiveness of using SDF, the

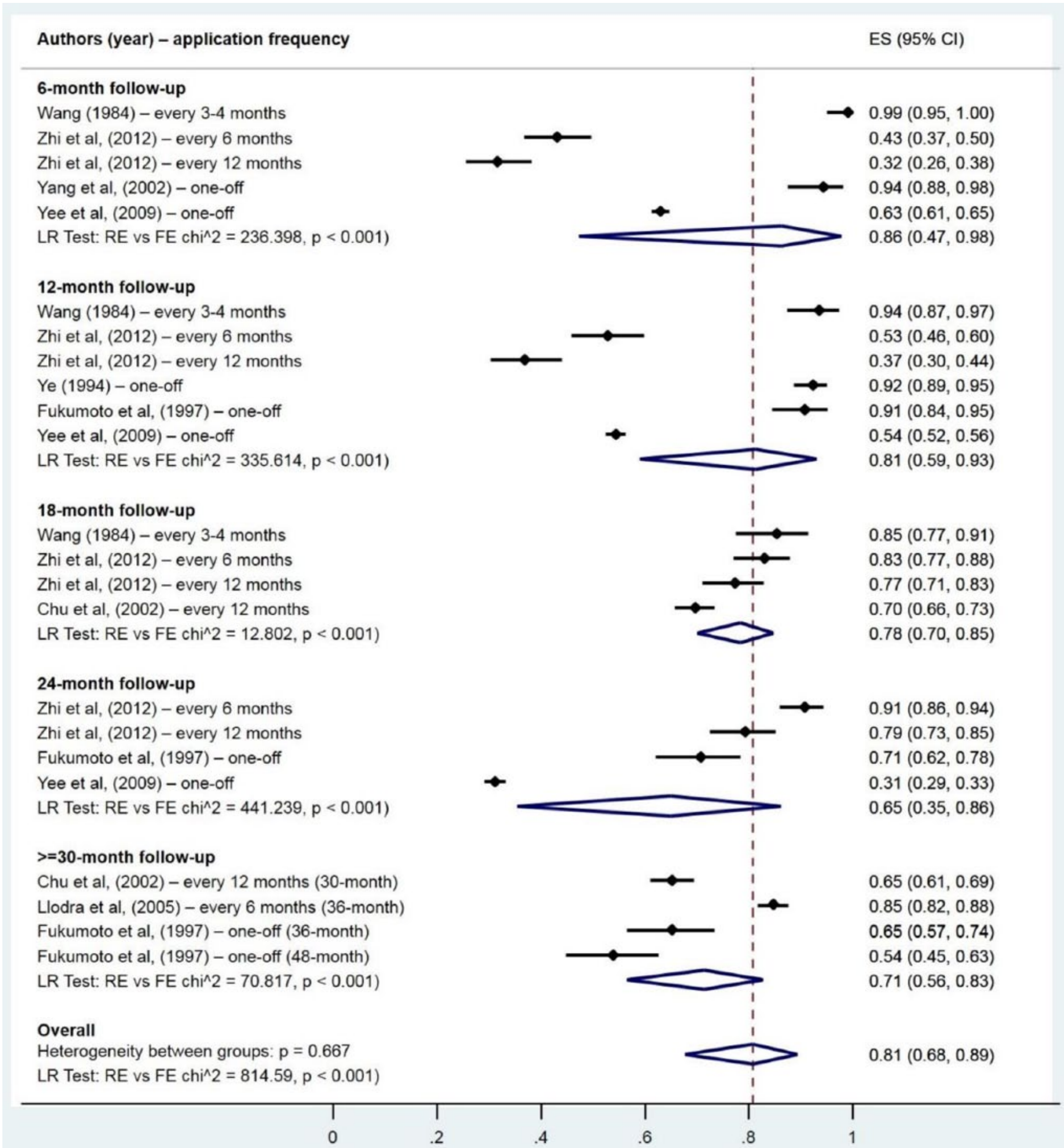
Table 2.
Risk of Bias Assessment on the Clinical Studies.

Authors, Year of Publication	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Other Bias
Duangthip et al., 2016	⊕	○	⊕	⊕	⊕	⊕
dos Santos et al., 2012	○	○	⊖	⊕	⊕	⊕
Zhi et al., 2012	⊕	○	⊕	⊕	⊕	⊕
Yee et al., 2009	⊕	○	⊕	⊕	⊕	⊕
Braga et al., 2009	⊕	○	○	⊖	⊕	⊖
Huang et al., 2005	○	○	○	⊕	⊖	⊕
Llodra et al., 2005	○	○	⊕	⊕	○	⊕
Mauro et al., 2004	○	○	○	○	○	⊖
Chu et al., 2002	⊖	○	⊕	⊕	⊕	⊕
Yang et al., 2002	⊖	⊖	⊖	⊖	○	○
Fukumoto et al., 1997	⊖	⊖	⊖	○	○	○
Miasato et al., 1996	⊖	⊖	⊖	○	○	○
Ye, 1994	⊖	⊖	⊖	⊖	○	○
Maciel, 1988	⊖	⊖	⊖	○	○	○
Oliveira, 1985	⊖	⊖	⊖	○	○	⊖
Wang, 1984	⊖	⊖	⊖	⊕	⊕	○
Tsutsumi et al., 1981	⊖	⊖	⊖	⊖	○	⊖
Yoshida et al., 1976	⊖	⊖	⊖	⊖	○	⊖
Nishino et al., 1969	⊖	⊖	⊖	○	⊖	○

⊕, low risk; ⊖, high risk; ○, unclear risk.

odds ratio of treatment effectiveness between treatment and control groups was not adopted in the meta-analysis. The absolute values, or delta changes, of the number of teeth or tooth surfaces with arrested caries were not used for analysis because the number of teeth or tooth surfaces with active caries at baseline varied among the studies.

Figure 2. Forrest plot of studies using 38% SDF to arrest caries in primary teeth. CI, confidence interval; ES, estimate; FE, fixed effects; LR, likelihood ratio; RE, random effects.



Instead, the proportion of teeth or tooth surfaces with active caries that had become arrested after SDF treatment was used in the meta-analysis.

Most clinical studies on SDF solution used a concentration of 38% to manage dental caries among children while a few studies used SDF at concentrations of 30%, 12%, and 10% (Mei, Chu, Lo, et al. 2013). All studies using SDF with high concentration (38%) reported a statistically significant caries-arresting effect on children. Although the fluoride concentration was high (44,800 ppm in 38% SDF), no significant complication was reported in these studies.

Two studies used SDF with a low concentration (11,800 ppm in 10% SDF), and their results were conflicting (Maciel 1988; Braga et al. 2009). Another clinical trial found that one-off application of 12% SDF (14,100 ppm) was not effective in arresting caries among children (Yee et al. 2009). The effectiveness of using SDF at a low concentration in caries arrest is yet to be confirmed.

Studies of SDF used not only different concentrations but also different application frequencies. The application frequency could be one-off or repeated applications every 3, 6, or 12 mo. One study reported that increasing the application frequency increased the caries arrest rate of SDF application (Zhi et al. 2012). This review found that the guidelines on the prevalence of SDF application use to arrest caries have little evidence. More clinical trials are necessary to formulate the optimal treatment strategy to arrest caries among children.

Studies also reported that using SDF was better than glass ionomer cement or fluoride varnish in arresting caries in primary teeth (Chu et al. 2002; dos Santos et al. 2012; Zhi et al. 2012; Duangthip et al. 2016). Caries removal was not necessary before SDF application (Chu et al. 2002). SDF is low cost and does not require sophisticated instruments or techniques for application. It is a cost-effective agent to manage dental caries. The risk of cross infection is low. The application is painless and simple and can be used for young children or patients with special needs.

In some of the studies included in this review, details about the methodology, such as sample size calculation, randomized allocation, allocation concealment, and blinding, were not reported. Without detailed planning, selection bias, detection bias, and attrition bias may occur. In addition, publications may experience reporting bias when investigators perform elective reporting. To alleviate the problems arising from inadequate reporting of randomized controlled trials, researchers have developed a standard known as the Consolidated Standards of Reporting Trials (CONSORT) (Schulz et al. 2010). CONSORT is an evidence-based, minimum set of recommendations for reporting randomized trials. It offers a standard protocol for researchers to present their studies, facilitates complete and transparent reporting, and aids critical appraisal and interpretation. Moreover, it is part of a broader effort to improve the reporting of different types of health research and to improve the quality of research. It is noteworthy that the reliability of some studies included in this review was relatively low because most of the clinical studies on SDF were conducted before the CONSORT statement was developed. Hence, more clinical trials following the CONSORT statement are warranted to better investigate the caries-arresting effect of SDF solution among children.

Conclusion

SDF was commonly used at a high concentration (38%, 44,800 ppm fluoride) and is effective in arresting caries among children. There is no consensus on its number and frequency of application to arrest caries. Further studies are necessary to develop evidence-based guidelines on its use in children.

Author Contributions

S.S. Gao, contributed to data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; I.S. Zhao, N. Hiraishi, and D. Duangthip, contributed to acquisition and analysis, drafted and critically revised the manuscript; M.L. Mei and E.C.M. Lo, contributed to conception and design, critically revised the manuscript; C.H. Chu, contributed to conception and design, drafted and critically revised the manuscript.

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