

Original Research Article

Silver Diamine Fluoride Versus Sodium Fluoride for Arresting Dentin Caries in Children: A Systematic Review

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Introduction: Sodium fluoride varnish and other topical fluorides are commonly recommended as preventive treatment reagents for caries because of their antimicrobial properties and demineralization ability. Silver ions contribute to the antibacterial properties of the silver diamine fluoride solution, which is a colorless liquid consisting of ammonia with silver and fluoride ions in it. **Materials and Methods:** A systematic literature review from 2010 to 2020 was performed using databases such as PubMed, Google Scholar, and Cochrane. The key words used were “sodium fluoride”, “silver diamine fluoride”, “children caries”, “dentin caries”, “caries arrest”, and “fluorides”. PRISMA guidelines were used and presented in the form of a flowchart. **Results:** Five articles met inclusion criteria for this systematic review. All of them were randomized controlled trials, one of which was a 30 month follow-up of another included study. **Conclusion:** The studies included in this systematic review demonstrate that silver diamine fluoride solution is more effective in dentine caries arrest than sodium fluoride varnish. However, these results need to be evaluated and used with caution as further research is required to consolidate the findings.

Keywords: Silver Diamine Fluoride, Sodium fluoride, Dentin caries.

INTRODUCTION

Dental caries is a chronic sugar-dependent non-communicable disease that is common in people of all age groups worldwide. In 2015-2016, approximately 4 out of 10 examined children have presented with one or multiple dental caries sites in the United States (Slayton et al., 2018). The mechanism of caries development is believed to be linked to the human microbiota. Oral microorganisms produce acids as a result of their metabolism of carbohydrates which come from consumed food. Acid challenge increases over time, eventually destroying the tooth enamel barrier. These changes are microscopic, thus the patients usually approach the specialists later, when the carious lesion extends into underlying hard dental tissue, thus creating a macroscopic cavity named dentine caries (Lager, 2014, p. 10). There is a big variety of approaches to caries treatment and prevention. Multiple studies proved fluorides to be a successful caries prevention measure as well as a therapeutic agent in non-restorative caries treatment (Toumba et al., 2019).

Sodium fluoride varnish and other topical fluorides are commonly recommended as preventive treatment reagents for caries because of their antimicrobial properties and demineralization ability (Trieu et al., 2019). Silver ions contribute to the antibacterial properties of the silver diamine fluoride solution, which is a colorless liquid consisting of ammonia with silver and fluoride ions in it. Both popular fluoride treatments possess advantages and disadvantages in their usage. For instance, the main side effect of silver diamine solution is the temporary intense black staining of carious tooth tissue in the spot where it was used. Besides, many patients report the appearance of bitter metallic taste right after the silver diamine application procedure, which may have an unpleasant impression on pediatric patients (Gao, S et al., 2016). On the contrary, according to the previous studies, sodium fluoride is believed to have weaker antimicrobial properties compared to silver diamine fluoride solution (Trieu et al., 2019).

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Research Question

PICO model was used to write the research question, which includes patient, intervention, comparison, and outcome. Which material among silver diamine fluoride and sodium fluoride is effective against dentin caries among children?

Aim of the study

The purpose of the following systematic review is to determine and compare the effectiveness of silver diamine fluoride versus sodium fluoride for arresting dentin caries in children up to 14 years of age.

Justifications and target audience

The results of this systematic review will help clinicians to decide which type of intervention is the best fit for treating dentin carious lesions in children. The target audience of this systematic review includes pediatric dental practitioners and hygienists.

METHODOLOGY

A systematic literature review from 2010 to 2020 was performed using databases such as PubMed, Google Scholar, and Cochrane. We have searched for all relevant publications where the researchers compared the use of silver diamine fluoride versus sodium fluoride for arresting dentin caries in children. The key words used were "sodium fluoride", "silver diamine fluoride", "children caries", "dentin caries", "caries arrest", and "fluorides". The last search was conducted on the 1st of September, 2020.

The following search in databases resulted in a total of 98 citations found. After adjusting for duplicates, 74 publications remained. The abstracts of these articles have been reviewed, after which 23 studies were discarded because they did not meet the inclusion criteria.

Inclusion criteria

The following criteria were considered essential for the inclusion into the systematic review: (1) case-control or cohort or controlled or randomized control studies, (2) published between 2010 and 2020, (3) included the previously mentioned key words, (4) English language of the publication, (5) studies involved humans only.

Exclusion criteria

The exclusion criteria were as follows: (1) systematic reviews or meta-analyses, (2) expert opinions or narrative reviews, (3) article language other than English, (4) in vitro research articles, (5) studies conducted on both children and adults, (6) enamel caries. More detailed description of inclusion and exclusion conditions may be found in Table 1. 46 articles were eliminated from the list as they have met the exclusion criteria and the remaining five articles were then analyzed via full-text systematic review. Fig. 1 demonstrates the full process of study selection.

RESULTS

Through the literature search, five articles have met all pre-set criteria. All of them were published between 2010 and 2020

and included four randomized controlled clinical trials, one of which was followed-up in a fifth study included.

In 2012, Liu et al. have conducted a randomized-controlled trial aimed to investigate the effectiveness of silver diamine fluoride solution, sodium fluoride varnish, and resin fissure sealant in fissure and pit caries avoidance in permanent teeth of school students. Their hypothesis stated that all three treatments did not have any caries-preventive influence compared to a placebo control. In total, the researcher recruited 501 children (mean age = 9.1 years) with at least one permanent first molar, which has deep fissures or the signs of early caries. 485 children (97%) remained in the study after 24 months and were a subject of examination.

The proportion of the surface of pit/fissure loci with dentin caries in the sealant, silver diamine fluoride solution, sodium fluoride varnish, and control groups were 1.6%, 2.2%, 2.4%, and 4.6%, respectively. Liu et al. (2012) concluded that semi-annual application of sodium fluoride varnish, application of silver diamine fluoride solution once a year, and placement of resin sealant are all effective in preventing pit and fissure caries in children's permanent molars. Importantly, the ratio of fissure/pit areas with dentin caries did not present a significant difference ($p > 0.05$) in sodium fluoride, sealant, and silver diamine fluoride groups.

Duangthip et al. (2016) compared the performance of the following topical fluoride administration protocols: annual application of 30% silver diamine fluoride solution (Group 1); three administrations of 5% sodium fluoride varnish at a weekly interval (Group 2), and three applications of 30% silver diamine fluoride solution every seven days (Group 3) in arresting dentine caries in primary teeth of preschool-aged children. A total of 304 children in the age of 3-4 years old were treated at baseline. 18 months later, 275 children (91%) were examined in the study. The caries arrest rates at the tooth level among them were 40%, 27%, and 35% for Groups 1, 2, and 3 respectively ($p < 0.001$). The researchers suggested that either annual or three consecutive weekly administrations of silver diamine fluoride solution are more sufficient in arresting dentine caries in primary teeth than three following weekly treatments with sodium fluoride varnish.

Another study by Duangthip et al. (2018) is a 30-month follow-up of the previous manuscript published in 2016. After 30 months, 309 (83%) children were still included in the research project. For cavitated lesions, the caries arrest rate of Group 1 (48%) was significantly more efficient than it was found in Group 2 (34%) and Group 3 (33%), ($p < 0.001$), though for moderate caries lesions where the dentine is not observed the caries arrest rates were calculated as 45%, 51% and 44% in Groups 1, 2, and 3 respectively ($p > 0.05$). The researchers reached the conclusion that the annual administration of silver diamine fluoride solution is superior in arresting active cavitated dentine caries in primary teeth compared to three consecutive weekly applications of sodium fluoride varnish or silver diamine fluoride solution.

In 2019, Gao et al. conducted a no inferiority double-blind randomized clinical trial, which was aimed to evaluate the effect of the topical semiannual administration of a 38% silver diamine fluoride solution (Group B) versus a 25% silver nitrate solution accompanied by a 5% sodium fluoride varnish (Group A) in arresting dentin caries in preschool-aged children. 1,070 children were included in the study with 535 of them in both treatment groups. In 18 months, the mean \pm SD number of arrested dental surfaces in Group A was 3.3 ± 3.4 . The effect observed in Group B equaled to 3.2 ± 3.5 ($P = 0.664$). The difference between the groups' mean number of arrested surfaces equaled to 0.092 (95%CI, -0.322 to 0.505).

Table 1. Inclusion and exclusion criteria

No	Inclusion criteria	Exclusion criteria
1.	Case-control or cohort or controlled or randomized control studies	Systematic reviews or meta-analyses or expert opinions or narrative reviews
2.	Published between 2010 and 2020	Out of the specified time range
3.	English language of publication	Language other than English
4.	Dentin caries	Enamel caries
5.	Children	Children and adults
6.	Comparison of Silver diamine fluoride versus Sodium fluoride	Only one of the treatments tested with no comparison
7.	In vivo (humans)	In vitro

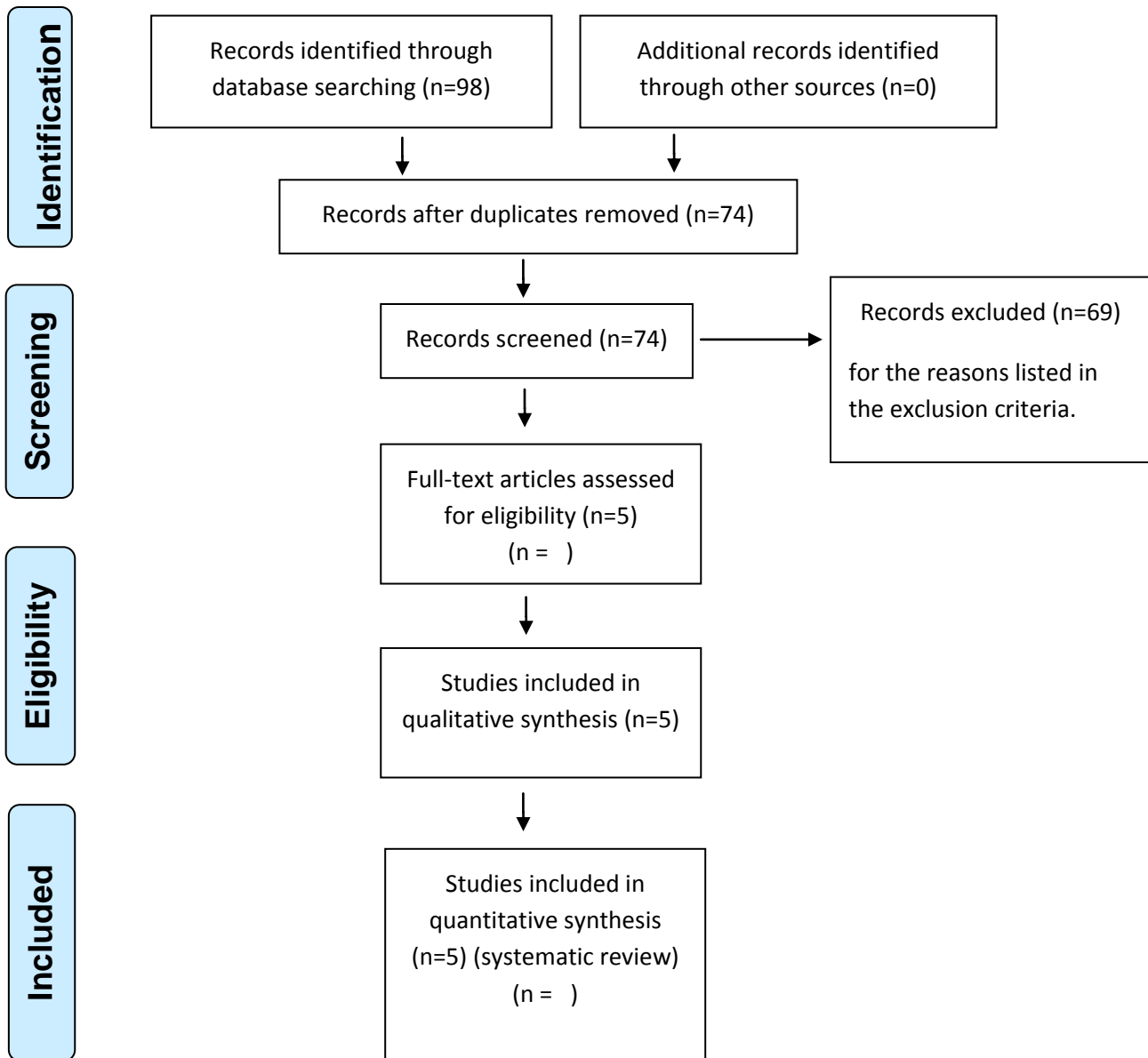


Figure 1. PRISMA flowchart

Table 2. The summary of the studies included into the systematic review and their findings.

#	Authors, year of publication	Inclusion criteria	Results and findings
1.	Duangthip, D, Chu, C & Lo, E 2016	RCT, compares administration of 30% silver diamine fluoride solution once a year (Group 1), three applications of 5% sodium fluoride varnish weekly (Group 2), and three applications of 30% silver diamine fluoride solution weekly (Group 3).	The caries arrest rates at the tooth level among them were 40%, 27%, and 35% for Groups 1, 2, and 3 respectively (p < 0.001). The results suggest that either yearly or three consecutive weekly applications of silver diamine fluoride solution are more successful in arresting dentine caries than three administrations of sodium fluoride varnish made within 3 consecutive weeks.
2.	Duangthip, D, Wong, M, Chu, C & Lo, E 2018	RCT, compares yearly application of 30% silver diamine fluoride solution (Group 1); three applications of 5% sodium fluoride varnish at weekly (Group 2), and three administrations of 30% silver diamine fluoride solution weekly (Group 3).	For cavitated lesions, the rate of caries arrest in Group 1 (48%) was significantly higher than in Group 2 (34%) and Group 3 (33%), (p<0.001), though for mild caries lesions without visible dentine the caries arrest rates were 45%, 51% and 44% in Groups 1, 2, and 3 respectively (p>0.05). The results suggest that the application of silver diamine fluoride solution once a year is more beneficial than three consecutive weekly applications of sodium fluoride varnish or silver diamine fluoride solution.
3.	Gao, S, Duangthip, D, Wong, M, Lo, E & Chu, C 2019	RCT, compares the effectivity of the administration of a 25% silver nitrate solution accompanied by a 5% sodium fluoride varnish semiannually (Group A) versus 38% silver diamine fluoride solution (Group B).	The mean ± SD value of the surfaces effected was 3.3 ± 3.4 for group A (n = 484) and 3.2 ± 3.5 for group B (n = 476; P = 0.664). The mean value of the influenced surfaces between the groups had a difference of 0.092 (95% CI, -0.322 to 0.505). The results of the study suggest that the application of 25% silver nitrate solution every 6 months followed by a 5% sodium fluoride varnish is no worse than semiannual application of a 38% silver diamine fluoride solution.
4.	Liu, B, Lo, E, Chu, C & Lin, H 2012	RCT, compares the influence of silver diamine fluoride solution, sodium fluoride varnish, and resin fissure sealant on the caries arrest in the pediatric patients.	Proportion of pit/fissure areas with dentin caries in the sealant, silver diamine fluoride solution, sodium fluoride varnish, and control groups were 1.6%, 2.2%, 2.4%, and 4.6%, respectively. The results suggest that the administration of sodium fluoride varnish every 6 months, annual application of silver diamine fluoride solution, and placement of resin sealant present rather similar benefits in arresting dentin carious lesions in permanent molars.
5.	Mabangkru, S, Duangthip, D, Chu, C, Phonghanyudh, A & Jirarattanasopha, V 2020	RCT, compares the effect of 38% silver diamine fluoride solution and 5% sodium fluoride varnish applied semiannually.	The caries arrest rate of Group 1 (35.7%) had a significant over the Group 2 (20.9%) (p < 0.001). The data suggests that the treatment with 38% silver diamine fluoride solution had superior efficacy in arresting dentin carious sites comparing to 5% sodium fluoride (OR = 2.04; 95% CI, 1.41-2.96).

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Duangthip, D 2016							
Duangthip, D 2018							
Gao, S 2019							
Liu, B 2012							
Mabangkru, S 2020							
					Yes	Unclear	No

Table 3. Risk of bias assessment

The results of the study suggest that the semiannual application of 25% silver nitrate solution followed by a 5% sodium fluoride varnish is no worse than the semi-annual application of a 38% silver diamine fluoride solution in arresting dentine caries among preschool-aged children.

The latest study by Mabangkhru et al. (2020) compares the performance of 38% silver diamine fluoride solution versus 5% sodium fluoride varnish applied semiannually for arresting dentin caries in pediatric patients which have a high predisposition of caries development. Initially, 153 and 149 children were included in Group 1 (38% silver diamine fluoride solution) and Group 2 (5% sodium fluoride) respectively. In 12 months, 87.1% of children continued their participation in the project. The caries arrest rate of Group 1 (35.7%) was notably higher than the rate of Group 2 (20.9%) ($p < 0.001$). Mabangkhru et al. (2020) concluded that the treatment with 38% silver diamine fluoride solution was more efficient in arresting dentin carious lesions than 5% sodium fluoride (OR = 2.04; 95% CI, 1.41–2.96). Table 2 summarizes the findings of the studies included in the systematic review.

QUALITY ASSESSMENT

Cochrane risk of bias assessment method has been used to assess the quality of the studies included (Table 3).

DISCUSSION

Dentin caries is one of the leading dental diseases in children. Its adequate treatment and prevention may impact not just the overall health of the teeth but also the compliance of the patients when they face other diseases in the older age. Therefore, it is very important to develop successful strategies and approaches to caries prevention, which would be affordable, minimally invasive, and effective.

Fluoride is a natural element that strengthens enamel and dentin, thus preventing and arresting caries. In children under 6 years, fluoride incorporates into the enamel cover of permanent teeth, thus making them more resistant to acids and bacteria (Medjedovic et al.,). This systematic review was conducted in order to determine and to compare the effectiveness of silver diamine fluoride versus sodium fluoride for arresting dentin caries in children up to 18 years of age.

The findings of the study by Liu et al. (2012) suggest that the administration of sodium fluoride varnish every 6 months, annual administration of silver diamine fluoride solution, and placement of resin sealant have a remarkably similar arresting effect on caries. The 18-month long trial by Duangthip et al. (2016) and its' 30-month update (Duangthip et al., 2018) conclude that the annual application of 30% silver diamine fluoride solution is the most successful strategy in caries arrest. In 2019, Gao et al. published the results of their study, which proved that the semiannual application of 25% silver nitrate solution followed by a 5% sodium fluoride varnish is no worse than semiannual administration of a 38% silver diamine fluoride solution in arresting dentine carious sites among preschool-aged children.

Finally, Mabangkhru et al. (2020, p. 106) suggest that the treatment with 38% silver diamine fluoride solution was more beneficial in arresting dentin carious lesions than 5% sodium fluoride. Thus, three studies proved the superiority of silver diamine fluoride over sodium fluoride, one confirmed that it is not inferior and one stated that they have a similar effect.

The strong side of this research is that it contains only recent randomized clinical trials with well-thought designs and nearly absent bias. There are multiple limitations of the study discovered. First of all, there is a large range of solution concentrations used in the trials as well as there is a difference in the regimens of their application. Secondly, some of the trials include additional chemicals added to one of the compared treatments. Thirdly, a longer-term follow up of the patients is needed in order to evaluate the long-term outcomes of treatment with both silver diamine fluoride solution and sodium fluoride varnish. Lastly, there is a need in a large multicenter study where the children population will be divided accordingly to the age groups, which may reveal age-dependent benefits of one or both therapy options.

CONCLUSION

The studies included in this systematic review demonstrate that silver diamine fluoride solution is more effective in dentine caries arrest than sodium fluoride varnish. However, these results need to be evaluated and used with caution as further research is required to consolidate the findings.

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