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Caries prevention and treatment in early childhood: comparing strategies. A systematic review

A.M. INCHINGOLO[1], A.D. INCHINGOLO[1], G. LATINI[1], G. GAROFOLI[1], R. SARDANO[1], N. DE LEONARDIS[1], L. DONGIOVANNI[1], E. MINETTI[2], A. PALERMO[3], G. DIPALMA[1], F. INCHINGOLO[1]

[1]Interdisciplinary Department of Medicine, University of Bari "Aldo Moro", Bari, Italy
[2]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy
[3]College of Medicine and Dentistry, Birmingham, UK

A.M. Inchingolo and A.D. Inchingolo contributed equally to this work as first authors
G. Dipalma and A. Patano contributed equally to this work as last authors

Abstract. – OBJECTIVE: Early childhood caries is a common condition that poses a serious risk to children's health because it can progress quickly, resulting in pain, abscesses, and a general decline in health. As a result, invasive therapies are needed, which call for highly skilled personnel. This systematic review of the literature aims to identify the most recent and widely applied early childhood caries (ECC) prevention and treatment approaches. Only substances that act topically and minimally invasive interventions were considered.

MATERIALS AND METHODS: The database search was restricted to randomized clinical trials completed within the last five years, specifically those that examined the following procedures: sodium fluoride (NaF) varnish, alternative restorative technique (ART), nano-silver fluoride, silver diamine fluoride, and silver modified atraumatic restorative treatment sealants (SMART).

RESULTS: A total of 815 articles were found. After removing duplicates, 584 articles were included, and 567 of them were excluded due to not meeting the predefined inclusion criteria.

CONCLUSIONS: Every method considered has been proven to be successful in halting the progression of ECC and is well-liked by patients, even those who are unwilling to cooperate, as well as by parents. The most common unfavorable effect of SDF is irreversible black discoloration in treated tooth surfaces, but this is typically not a problem. They are all low-cost, minimally invasive techniques that might also be widely used in large communities and low socioeconomic settings.

Key Words:
Early childhood caries (ECC), Silver diamine fluoride (SDF), Sodium fluoride varnish, Alternative restorative technique (ART).

Abbreviations

ECC: Early Childhood Caries; SDF: Silver diamine fluoride; ART: Atraumatic restorative therapies; MIH: Molar incisors hypomineralization; ICDAS: International Caries Detection and Assessment System; WHO: World Health Organization; SEM: Sound Eye Motor Scale; SMART: Silver modified atraumatic restorative treatment sealants; HVGIC: High viscosity glass ionomer cement; HRQoL: Oral health-related quality of life; NaF: Sodium fluoride; TCP: tricalcium phosphate; CXP: xylitol-coated calcium and phosphate; CPP-ACP: casein phosphopeptide-amorphous calcium phosphate; AgNO3: Silver nitrat; NFG: Neutral fluoride gel; FV: Varnish fluoride.

Introduction

Dental caries is the world's most frequent pediatric disease. As a matter of fact, early childhood caries (ECC) is a significant public health issue[1]. Caries-affected teeth can degenerate fast within a few months, and treatments are intrusive and difficult to handle, both because they require experienced medical professionals and because children are unwilling to cooperate[2]. Caries prevention at school is recommended by the Centers for Disease Control and Prevention, and the World Health Organization advocates the adoption of broad-based preventative techniques that are easy, minimally intrusive, and low-cost[3]. It all starts with encouraging children and families to practice good dental hygiene and nutritional habits, including limiting sugar and cariogenic foods. Except for oral hygiene maintenance, the incidence of ECC is

Corresponding Author: F. Inchingolo, MD; e-mail: francesco.inchingolo@uniba.it

related to additional characteristics, such as underprivileged socioeconomic status (SES) and education status. It has been reported that SES of the child's parents/guardians during early childhood can significantly influence the child's oral health status[4]. Topical fluoride mainly exploits the mechanisms of action of remineralization and bacterial inhibition[5] (Figure 1). In the past 70 years, the frequency and severity of dental caries have significantly decreased as a result of the widespread use of fluoridated water and fluoride-containing oral products[6]. Remineralization has taken a leading role in caries prevention strategy. The widespread use of fluoride-containing toothpaste is probably the main cause of this condition. Fluoride promotes the precipitation of calcium and phosphate ions in the form of apatite rather than soluble calcium phosphates, which leads to true remineralization of the first carious core in the same foci of carious demineralization[7,8]. Fluoride functions for bacteria as a true "cellular poison" in bacterial inhibition. Indeed, it slows the formation of pyruvate, which lowers salivary pH by inhibiting the primary enzyme systems of glycolysis[9]. In addition, this process causes a decrease in ATP generation and an overall decrease in the metabolic activity of the bacterial cell[10,11]. The development of extracellular polysaccharides, which serve as a structure for bacterial plaque layering and hinder bacterial adhesion, is one of the processes that fluoride inhibits by competing with plaque matrix surface proteins. Topical fluoride is applied with different indications for use and dosages, including toothpastes with low concentrations for home use, mouthwashes with low concentrations for home use, gels with high concentrations for professional use, and varnishes with high concentrations for professional use[7,12,13]. Inappropriate use of these compounds, whose concentrations range from 500 to 20,000 ppm, can result in acute and/or chronic intoxication. To reduce the risk of overdose, it is critical to have a good understanding of the administration protocols. Early diagnosis is critical for early intervention: in the early stages of caries, toothpastes and mouthwashes for home use, or sodium fluoride varnishes and gels for professional use can be used[14-16]. Early detection is critical for early intervention: in the early stages of caries, remineralizing agents, most notably fluoride, can be used topically in the form of toothpaste and mouthwash for home use, or sodium fluoride varnish and gel for professional usage. Inappropriate use of these compounds, whose concentrations range from 500 to 20,000 ppm, can result in acute and/or chronic intoxication. To reduce the risk of overdose, it is critical to have a good understanding of the administration protocols[17,18]. Several materials are mentioned in the literature,

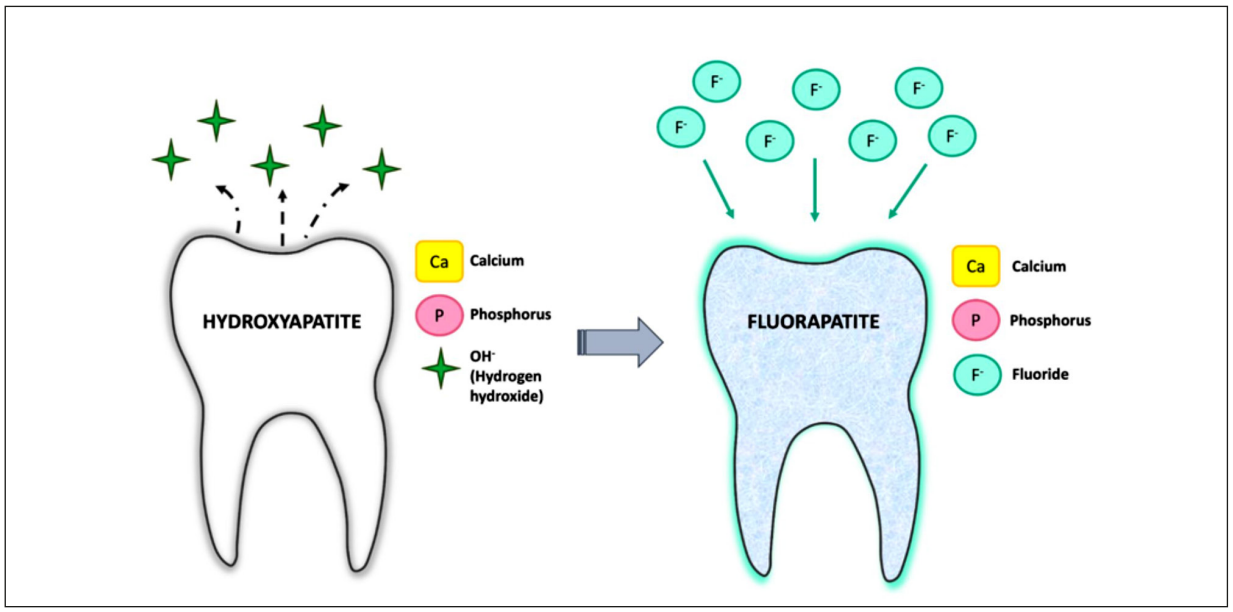

Figure 1. Fluorapatite *vs*. hydroxyapatite.

including silver diamine fluoride (SDF) and glass ionomer cement, which are employed in atraumatic restorative therapies (ART)[19,20]. Certain atraumatic restorative materials and glass ionomer sealants may be optically undetectable. Silver diamine fluoride is a non-invasive caries prevention and control treatment that may be used well in community settings; it works in stopping cavitated dentine carious lesions and preventing the onset of new caries[21]. However, it creates persistent black discoloration of the caries and may stain good tooth tissue. SDF is more effective as a caries therapy since it may be delivered in a lot shorter time and with less clinical expertise than atraumatic restorative therapies[22]. Researchers were motivated to create a material with comparable performance without sacrificing aesthetics as a result of these negative effects. Several methods have been described that might be used to reduce the problem of spotting, including the use of silver, gold, or platinum nanoparticles as well as other metals with antimicrobial properties[23]. Silver nanofluoride has become a novel anti-caries agent as a result of the use of nanoscience and technology in dentistry[24]. Anti-caries agents based on silver nanoparticle (AgNP) technology are non-irritating and have a powerful bactericidal impact on the dynamic *S. mutans* biofilm[25].

Materials and Methods

Protocol and Registration

The current review was carried out in compliance with the standards of Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)[26] and the International Prospective Register of Systematic Review Registry guidelines.

Search Processing

Topical fluoride, preventive, and prophylaxis were the search terms utilized on the databases (Scopus, Web of Science, and Pubmed) to select the papers under evaluation, with the Boolean operators "AND" and "OR" The search was restricted to just items released in English during the previous five years (March 2018-March 2023) (Table I).

Eligibility Criteria

The reviewers, who worked in pairs, chose works that satisfied the following criteria for inclusion: (1) Human subjects-only research; (2) clinical studies or case reports (3) research done on people receiving treatment with topically acting agents or minimally invasive interventions.

Exclusion criteria were: (1) studies involving systemic fluoroprophylaxis; (2) *in vitro* studies; (3) animal studies; (4) systematic reviews, narrative reviews, and meta-analyses. The review followed the PICO criteria: Population (children aged 0-15 years), intervention (caries prevention and treatment), omparison (comparison of different strategies) and outcome (effectiveness).

Data Processing

The screening procedure, which was carried out by reading the article titles and abstracts chosen in the earlier identification step, allowed for the exclusion of any publications that varied from the themes looked at.

The complete text of publications that had been determined to match the predetermined inclusion criteria was then analyzed.

Reviewer disagreements on the choice of the article were discussed and settled.

Results

Keyword searches of the Web of Science (112), Scopus (244) and Pubmed (459) databases yielded a total of 815 articles.

The subsequent elimination of duplicates (231) resulted in the inclusion of 584 articles. Of these 584 studies, 567 were excluded because they deviated from the previously defined inclusion criteria. The screening phase ended with select-

Table I. Database search indicators.

Article screening Strategy	Database: Scopus, Web of Science and Pubmed Keywords: A "Topical fluoride"; B "preventive"; C" prophylaxis" Boolean variable: "AND" "OR" Timespan: 2018-2023 Language: English

ing 25 publications for this work (Figure 2). The results of each study were reported in the **Supplementary Table I**.

Discussion

The term "molar incisor hypomineralization" (MIH) refers to a developmental defect of the enamel with a clinical view of enamel hypomineralization affecting one or more first permanent molars that are frequently associated with affected incisors[27].

Clinically speaking, MIH is distinguished by clearly defined opacities on affected teeth that can range in color from white to yellow to brown[28].

Numerous clinical problems are common in children with MIH, including rapid enamel loss, increased risk of caries (10 times higher than in normal teeth), and subsequent need for treatment[29,30]. More porous enamel makes teeth more sensitive to cold air, water, and brushing[31].

The prevention of caries in hypomineralized molars has been proposed using a number of non-invasive and minimally invasive techniques[32].

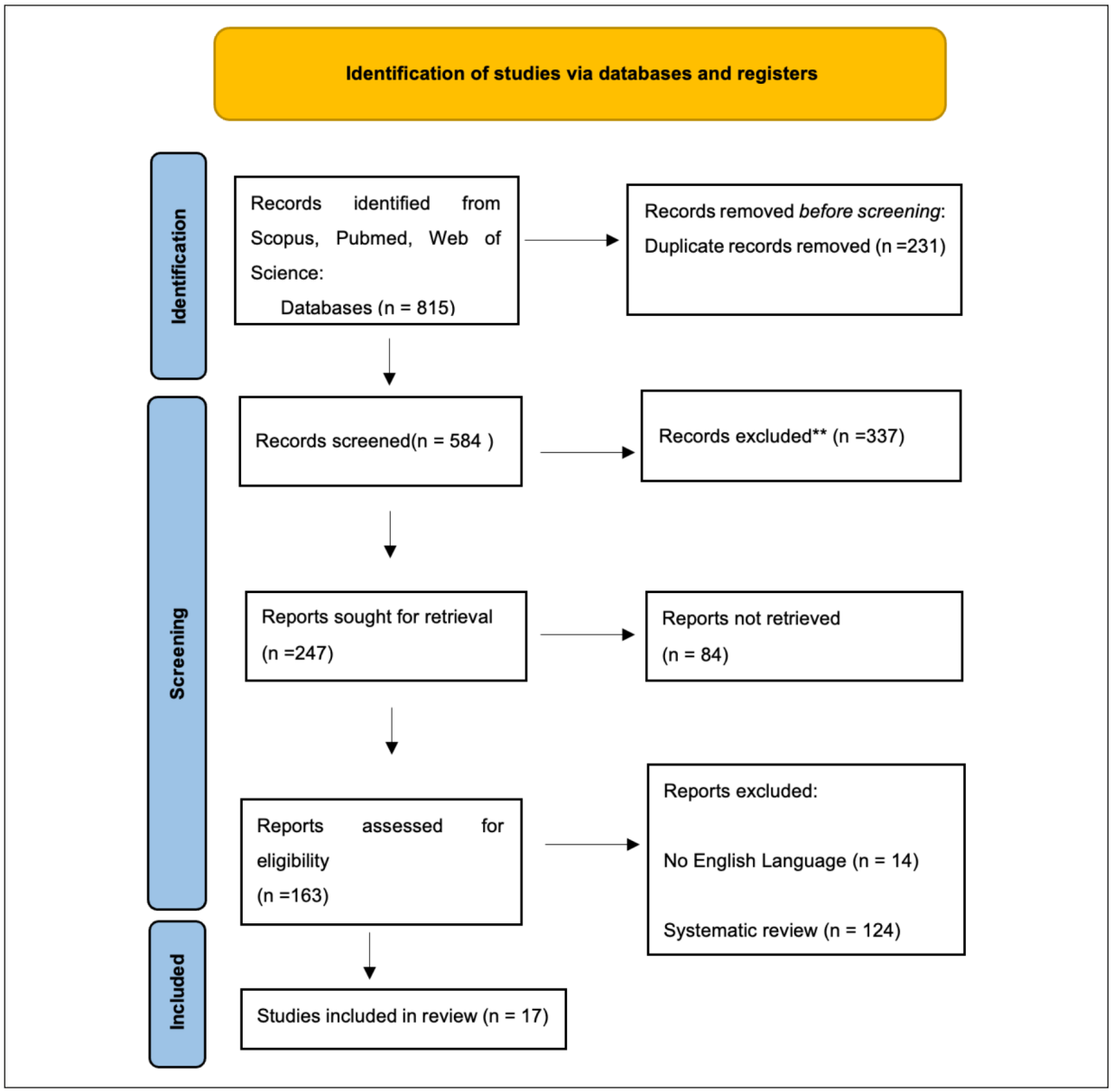

Figure 2. PRISMA flowchart.

Comparison of Silver Diamine Fluoride and Alternative Restoration Technique

Abdellatif et al[33], in a 2021 clinical study, compared the effect of a six-month application of 38% SDF with an ART on caries arrest in the primary dentition.

A well-accepted minimal intervention approach for the management of cavitated carious lesions in both clinical and community settings is the WHO-approved atraumatic/alternative restorative technique (ART). The sample analyzed was 79 children aged from 3 to 8 years with at least one active carious lesion and International Caries Detection and Assessment System (ICDAS) score 4-5-6. They were divided into 2 groups, the first treated with SDF in the test group and with ART in the control group. The treated surfaces were followed up at 6 and 12 months. The clinical procedure of ART consists of the removal of carious enamel and dentin with hand instruments, cleaning and drying of the cavity, and then restoration with glass ionomer cement followed by protective varnish. Based on the results of this study, it can be concluded that SDF and ART are both effective in stopping caries in deciduous teeth. However, it can be said that the highchair time and cost required for ART make SDF the modality of choice, especially in public health settings for disadvantaged populations. The best decision regarding disease management and application of SDF or ART must be made by both the dentist and the patient/parent recognizing the differences and preferences of individuals[34].

The 2019 clinical study by Vollù et al[22] also aimed to compare the efficacy of 30% SDF with ART on stopping caries in preschool deciduous molars[22]. In addition, the time required for treatment, children's anxiety before and after treatment, possible adverse events, aesthetic perception, and impact on the quality of life of treatments were also evaluated. SDF is a preventive procedure with black discoloration of the teeth as the only real undesirable effect. ART is a low-cost alternative to conservative treatment of caries in children, which is well accepted even by uncooperative individuals and is easy to administer even in places where there is a lack of electricity and running water; it has been shown to be effective in controlling caries. A similar rate of dentinal caries arrest was observed in both SDF and ART groups. Considering that SDF is cheaper, less dependent on the skill of the operator, and requires almost half the treatment time compared to ART, the study suggests that SDF should be chosen as a treatment option, at least in situations where access to treatment is rather difficult[22].

Another randomized clinical trial conducted by Ali et al[35] in 2021 compared the pain perception of young children treated with SDF and ART, along with parental acceptance of both modalities. Eighty children from 3 to 8 years with at least one asymptomatic deciduous tooth with active caries as defined by ICDAS II scores 4, 5, 6 were randomly assigned to two groups: SDF for the test group's caries arrest and ART for the control group's caries eradication. Parental approval was evaluated using a self-administered questionnaire, and pain perception was evaluated using the Sound, Eye, Motor scale (SEM). Patients treated with SDF reported significantly less discomfort and pain than the ART group, so this treatment was better accepted by parents, also considering the shorter intervention time and higher quality of treatment[35].

Comparison of SDF and Silver Modified Atraumatic Restorative Treatment

In a 2022 prospective randomized study, Ballikaya et al[34] assessed and contrasted the effects of silver-modified atraumatic restorative therapy sealants (SMART) and SDF for the treatment of first carious lesions of permanent molars with MIH[34].

SDF is a very good agent to block the evolution of caries due to the remineralizing action of fluoride and silver's antibacterial properties. SDF also effectively reduces hypersensitivity because it produces fluorohydroxyapatite, raises mineral density, and hardens minerals, sealing dentinal tubules. A carious lesion is first treated with SDF using the SMART approach, and then it is sealed or repaired using either regular or high-viscosity glass ionomer cement (HVGIC). By chemical and micromechanical adhesion, HVGICs adhere to dental hard tissues and release fluoride that may help prevent the growth of biofilm and recurrent caries. Fifty-six patients with molars with hypomineralization and ICDAS code 1 and 2, were selected. The patients were randomly divided into 2 groups: SDF group and SMART group, and follow-ups were done after treatment at 1, 6 and 12 months. Since the first follow-up, a significant reduction in hypersensitivity was found. In hypomineralized molars with early lesions, hybrid glass ionomer sealants placed just after SDF administration demonstrated a respectable retention rate of 88.7%. After one year, SMART sealants and SDF application alone both showed compa-

rable clinical effectiveness. The most frequent problem with SMART sealants was marginal discolouration linked to prior SDF treatment[34].

The randomized clinical trials by Ruff et al in 2022[36] and 2023[37] also showed similar conclusions. The first study's goal was to compare a typical package of glass ionomer sealants and ART in children aged 5 to 13 to the short-term effects of SDF therapy on oral health-related quality of life (OHRQoL). Six months following treatment, they discovered that children receiving SDF did not have lower life quality than those getting ART and sealants[36]. In the second study[37], a sample of 2,998 children, with a mean age of 6.6 years, was divided into 2 groups and analyzed: experimental treatment consisted of 5% fluoride varnish applied to all teeth and 38% SDF applied to all asymptomatic cavitated lesions and brushed over all dimples and fissures of premolars and molars. Standard treatment included identical application of fluoride varnish, glass ionomer sealants applied to all dimples and fissures of premolars and molars, and placement of atraumatic restorations on all frankly asymptomatic cavitated lesions. Follow-up at approximately 2 years showed that both approaches were effective; however, sealant treatments are more expensive and require trained clinicians to administer, making SDF treatment more likely to be used in caries prevention programs on very large populations[37].

Comparison of SDF and Sodium Fluoride Varnish

Mabangkhru et al[38], in a 2020 randomized clinical trial, compared the efficacy of 38% SDF solution and 5% sodium fluoride (NaF) varnish applied, preventing dentin caries in young infants at high risk of caries semi-annually. A sample of children aged from 1 to 3 years at high risk of caries was selected and randomly divided into 2 groups. Group 1 (153 children) = 38% SDF and Group 2 (149 children) = 5% NaF varnish. Both agents were applied every 6 months to the carious surface, and follow-up was performed at 1 year[38].

In children younger than 71 months, ECC is characterized by the presence of one or more decaying, missing (due to decay), or obturated tooth surfaces in any deciduous tooth. ECC is a serious global health problem, especially in the most disadvantaged socioeconomic groups, where adequate prevention is lacking and access to treatment is also particularly difficult. The etiology of the disease is associated with frequent consumption of sugary drinks or foods, prolonged breastfeeding, and poor oral hygiene[39,40]. Children with ECC are at increased risk for pain or discomfort, abscesses, delayed growth/development, and oral health-related quality of life impairment. In addition, ECC is an important predictor for the development of dental caries in permanent dentition. Fluoride in various formulations has been widely used for the prevention and control of caries. Sodium fluoride (NaF) varnish has been one of the most widely used topical fluorides for more than 50 years. It can adhere to the tooth surface and release fluoride ions into the oral cavity for several hours. However, a recent systematic review showed that NaF varnish had a modest benefit in preventing new carious dentin lesions. SDF is a topical fluoride solution containing a high concentration of fluoride and silver that has recently attracted much attention from both clinicians and researchers. Its anti-caries efficacy is promising due to the synergistic effects of silver, which acts as an antimicrobial agent, and fluoride, which promotes remineralization, while ammonia helps stabilize solution concentrations. In the present study, treatment with SDF proved to be 2 times more effective than NaF varnish in blocking the evolution of ECC. The dose used is well below the toxicity levels of fluoride and silver, and the only undesirable effect is the blackish discoloration that remains on treated teeth.

The product has been proven to be useful and easy to use even at such a young age when it is very difficult to have cooperation for more invasive treatments, and it has been successful with parents[41-45].

Slightly different results were reached in the 2022 clinical study by Phonghanyudh et al[46]. They randomly assigned 290 enamel-carious youngsters between the ages of one and three into two groups. The study's objective was to determine if semi-annual treatments of 38% SDF varnish and 5% NaF were effective at slowing the advancement of enamel caries in children between the ages of 1 and 3 who were at high risk for developing the condition. Follow-up at 6-12-18 months showed that the 2 products had similar efficacy in stopping enamel caries. Both products were safe, no notable adverse reactions were reported, and satisfied parents[46].

Adverse Effects OF SDF Treatment

Duangthip et al[47], in a 2017 randomized clinical trial, focused on evaluating adverse effects and parental satisfaction with SDF treatment administered to preschool children.

A sample of 888 children with an average age of 3.8 years was considered and randomly divided into 4 groups with follow-up from 6-month up to 30 months.
Group 1: 12% SDF applied once a year.
Group 2: 12% SDF applied twice a year.
Group 3: 38% SDF applied once a year.
Group 4: 38% SDF applied twice a year.

The following adverse effects were evaluated:
- Tooth or gum pain: no significant difference between groups at all follow-ups (rate between 3.7% and 7.0%);
- Gum swelling: no significant difference between groups at all follow-ups (percentage between 1.5% and 2.8%);
- Gum whitening: spontaneous resolution within 2 days, no significant difference between groups at all follow-ups (percentage between 3.0% and 5.7%);
- Systemic toxicity: not detected;
- Black staining: greater blackening of lesions treated with 38% SDF than others, especially after half-yearly administration[47].

Applications of SDF in the various concentrations were effective: at 30-month follow-up, 74.2% of lesions showed caries arrest. Parents show a good degree of satisfaction related to the treatments performed, and the side effects found do not affect their confidence in the treatment[47].

Comparison of Nano-Silver Fluoride and Silver Diamine Fluoride

An alternative to SDF has been suggested: nano-silver fluoride (NSF) to bypass its most common undesirable effect, namely black discoloration of treated teeth.

Ammar et al[48], in a 2022 randomized clinical trial, compared the two agents, evaluating their antibacterial action and impact on caries activity. The short-term antibacterial efficacy of NSF was similar to that of SDF. In both groups, there was a significant reduction in *S. mutans* and lactobacilli counts in active dentinal caries, and two-thirds of the lesions became inactive, with no differences between the two interventions. Further research is needed to study the long-term efficacy of NSF and its suitability for clinical use in caries management[48].

Comparison of Fluoride Varnish Pure and Fortified with Various Agents

Erkmen Almaz et al[49], in a 2020 clinical study, compared the antibacterial activity of fluoride varnishes containing different agents in children with severe early childhood caries (S-ECC). They considered a sample of 92 children with S-ECC. The patients were randomly divided into four groups: control group with 5% sodium fluoride (SF) (n = 23), 5% SF with tricalcium phosphate (TCP) (n = 23), 5% SF with xylitol-coated calcium and phosphate (CXP) (n = 23), and 5% SF with casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) (n = 23). Saliva mutans streptococci (MS) and lactobacilli (LB) levels were assessed by taking saliva samples at baseline (T0), 1 month (T1) and 3 months (T2) after treatment. Fluoride varnish with TCP showed good antibacterial activity against cariogenic bacteria. In contrast, that with CXP did not show any efficacy[49].

Comparison Between 25% Silver Nitrate Solution (Agno 3) + 5% Sodium Fluoride (Naf) Paint and 38% Silver Diamine Fluoride Solution

Gao et al[50], in a 2020 clinical trial, compared the efficacy of semiannual (every six months) applications of a 25 percent silver nitrate ($AgNO_3$) solution followed by a 5 percent sodium fluoride (NaF) varnish *vs.* semiannual applications of a 38% silver diamine fluoride (SDF) solution in stopping early childhood caries (ECC). Silver nitrate ($AgNO_3$) has been used to manage dental caries because of its disinfectant properties. A total of 1,070 children randomly divided into 2 groups were analyzed: the 2 approaches were equally effective in stopping ECC. Both silver and fluoride treatment protocols are simple, inexpensive, and noninvasive and are a promising strategy for the management of ECC in young children[50].

Comparison of Fluoride Varnish and Neutral Fluoride Gel

Sousa et al[51] 2022 conducted a randomized clinical trial to compare two strategies for the management of ECC: topical application of neutral fluoride gel (NFG group) and varnish (FV group) every four months for a period of one year in a sample of 240 children aged three to four years. The follow up was done at 12 months. In this 12-month randomized clinical trial, the efficacy of neutral fluoride gel was shown to be similar to that of varnish[51].

Wang et al[52] in a 2021 randomized clinical trial evaluated the effect of fluoride varnish in preventing dental caries in the first permanent

molars. The sample analyzed was very large, of more than 5,000 children, with a follow-up of 36 months. Six-monthly application of fluoride varnish can effectively prevent dental caries in children aged six to seven years. However, additional treatments (fissure sealing and dimpling) should be considered for optimal benefit after 24 months[52,53].

Fluoride varnish was also the subject of a 2023 randomized controlled trial by Latifi-Xhemajli et al[54] who tested its efficacy in reducing early childhood tooth decay in kids who are at a high risk for caries. The sample of 504 children, average age 21 months, was divided into 2 groups: in the test group, fluoride varnish applied was used every three months. In contrast to the control group, this study demonstrated that using fluoride varnish applications was linked to a preventive reduction in caries. This research indicates that children who are more likely to develop early childhood caries should receive fluoride varnish[54].

The recommended frequency of varnish application can range from 1 to 4 times per year. Given the paucity of long-term efficacy results of fluoride varnish application, the 2022 study by Agarwal et al[52] evaluated the efficacy of fluoride varnish in the prevention of early childhood caries in 3-4-year-old children over a period of 3 years. Fluoride varnish was found to be an effective and safe mode of early childhood caries prevention in children[52].

Poza-Pascual's 2021 study[55] showed that quarterly application of calcium phosphate varnish for 12 months did not change the pH, lactic acid concentrations and most chemical elements in the saliva of children at high risk of caries. However, it did have a positive influence on the occurrence of new caries[56,57].

Conclusions

Early Childhood Caries (ECC) is a chronic infectious disease affecting young children, a major global health concern. It results from cariogenic microorganisms, incorrect dietary behaviors, and social factors. Preventive measures include adopting simple behaviors, promoting proper dental hygiene, and reducing sugar intake. Topical fluoride, like Sodium Fluoride (NaF) Varnish and Silver Diamine Fluoride (SDF), is widely used for caries prevention due to its remineralization and antibacterial properties. Nano-Silver Fluoride (NSF) is an alternative to SDF, avoiding staining while maintaining efficacy. The SMART procedure combines SDF treatment with sealing using glass ionomer cement to reduce recurrent caries. Some authors suggest enhancing fluoride varnishes' antibacterial effect with chemical agents like Tricalcium Phosphate (TCP).

Conflict of Interest

The Authors declare that they have no conflict of interests.

Authors' Contribution

Conceptualization, A.P., and A.M.I.; Methodology, G.L., and R.S.; Software, N.D.L., L.D., and G.D.; Validation, F.I. and S.B.; Formal analysis, R.S. and G.G.; Resources, A.D.I. and G.L.; Data curation, S.B. and A.M.I., L.D.; Writing-original draft preparation, E.M., N.D.L., A.P., and G.G.; Writing-review and editing, A.P. and A.M.C.; Visualization, E.M., N.D.L, and A.D.I.; Supervision, A.P., F.I., and A.M.I.; Project administration, F.I., and G.D. All authors have read and agreed to the published version of the manuscript.

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Ethics Approval

Not applicable.

Informed Consent

Not applicable.

Data Availability

Not applicable.

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