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Promoting Caries Arrest in Children With Silver Diamine Fluoride: A Review

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Summary: Although there has been a decrease in the prevalence and the severity of dental caries in children over the past few decades, the benefits have not been equally shared by many low-income or underserved children in many industrialised countries, or children in developing countries. Dental caries is still the most common and challenging dental disease in children for a clinician to treat. Silver diamine fluoride (SDF) has been in use to arrest dental caries in many countries. A 38% (44,800 ppm fluoride ions) SDF solution is commonly used to arrest caries in primary teeth of children, especially those children who are young and difficult to manage. Application of SDF to arrest dental caries is a non-invasive procedure that is quick and simple to use. However, it stains the carious teeth and turns the arrested caries black. It also has an unpleasant metallic taste that is not liked by patients, especially children. The low cost of SDF and its simplicity in application suggest that SDF is an appropriate therapeutic agent for use in community dental health projects. Reports of available studies found no severe pulpal damage after SDF application. The current literature suggests that SDF can be an effective agent in preventing new caries and in arresting dental caries in the primary teeth of the children. It can be used to arrest caries progression in very young children who are less cooperative, and it allows definitive restoration to be performed when they grow older and become more receptive to dental procedures.

Key words: arrested caries, children, silver diamine fluoride

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International data on caries epidemiology confirm that dental caries remains a significant disease of childhood that is found in a subset of at-risk children in both developing and developed countries (Edelstein, 2005). It is still a major problem in many societies and in children belonging to disadvantaged communities. The prevalence of caries in children is high in families with low income, lower education level of parents, poor parental dental attitude and single parent families (Chu et al, 1999). Treatment of dental caries in young children is very challenging and it may require advanced skills of clinicians and high cost of general anaesthesia for patient management (Chu, 2000). The prevailing methods adopted in industrialised countries for the prevention and treatment of dental caries are neither available nor affordable in developing countries where there are inadequate financial resources, dental manpower and facilities.

The use of topical fluorides may be a useful measure to arrest caries lesions because fluorides used in various forms have proven to be effective in dental caries prevention (Hiiri et al, 2006). Fluoride exerts its caries-protective properties in several ways. The primary anti-caries effect is a topical effect on erupted teeth (Featherstone, 1999). Fluoride concentrated in plaque and saliva can inhibit demineralisation of dental hard tissue (Hamilton, 1990). Fluoride taken up along with calcium and phosphate by demineralised dental hard tissue forms a crystalline structure (remineralisation) that is more resistant to the challenges of bacterial acid (ten Cate, 1999). Fluoride has also been shown to inhibit the process by which cariogenic bacteria metabolise carbohydrates to produce acids, and thus affect the bacterial production of adhesive polysaccharides (Hamilton, 1990). The current view, however, is that the antibacterial effects of fluoride occur at higher levels than those that prevail in the oral cavity (ten Cate, 1999).

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Silver diamine fluoride (SDF) is a colourless solution containing fluoride ions. It is used in dentistry to promote remineralisation of tooth mineral hydroxyapatite that is under constant acid challenge in the oral cavity. SDF has been used to deal with high caries prevalence by arresting or slowing down the rate of caries progression (Li, 1984; Gotjamanos, 1996). It is also used in the management of dental caries in young children (Yamaga and Yokomizo, 1969), to arrest root caries (Tan et al, 2006), to prevent pit and fissure caries (Nishino and Yoshida, 1969), to prevent secondary caries (Yamaga et al, 1972), to desensitise sensitive teeth (Liu et al, 1995), to treat infected root canals (Yamashita, 1985) and to prevent the fracture of endodontically treated teeth (Yokoyama et al, 2001).

SILVER DIAMINE FLUORIDE IN DENTISTRY FOR CHILDREN

When children are too young to have their carious teeth restored by conventional methods, SDF can be used to slow down or arrest the caries progression. In addition, SDF application can be a cost-effective means of treatment for many disadvantaged children or in areas where there is a great shortage of dental personnel. SDF has been in use in many countries (including Australia and China) to arrest dental caries for many years (Li, 1984; Gotjamanos, 1996). In Japan, it has been accepted as a therapeutic agent by the Central Pharmaceutical Council of the Ministry of Health and Welfare for dental treatment for more than 40 years (Yamaga and Yokomizo, 1969). A solution of 38% SDF was used in China to arrest caries (Li, 1984). A clinical trial conducted in China reported that SDF was effective in preventing and arresting caries in primary anterior teeth of preschool children (Lo et al, 2001; Chu et al, 2002). Another clinical trial in Cuba also found that SDF is effective in caries reduction in primary teeth and first permanent molars in schoolchildren (Llodra et al, 2005). A clinician in Mexico had reported that a 2-year-old child who had caries in the incisors associated with a nursing bottle had the caries arrested and hardened after the use of sodium fluoride (NaF) and silver nitrate solution (Aron, 1995). SDF in various concentrations has been used in community dental health projects in Argentina, Brazil and Spain; and further community projects were planned for sub-Saharan Africa and for several other African countries (Bedi and Infirri, 1999). Although an article in an American journal mentioned that there were clinicians in Southern California who used SDF to arrest caries and to harden the demineralised dentine of young children with early childhood caries (Duperon, 1995), SDF is not widely available in many countries in Europe and in the USA.

The school dental service in Western Australia used 40% silver fluoride (AgF) as the standard treatment for deep caries lesions in primary teeth (Gotjamanos, 1996). AgF solution requires a two-stage application procedure using stannous fluoride (SnF_2) as a reducing agent. Beneficial results were reported by Craig et al (1981) when using AgF followed by SnF_2 solution to arrest caries in primary molars in very young children who were difficult to manage.

Although AgF is much more soluble in water (1820 g/L at 15 °C) than the other silver halides, it forms colourless cubic crystals. SDF contains ammonia and AgF. The ammonia ions combine with the silver ions to produce a complex ion called the diamine–silver ion, $[Ag(NH_3)_2]^+$. This formation of diamine–silver ions is a reversible reaction. The complex is very stable, and the position of equilibrium lies with in the diamine–silver ions. As many silver ions are removed from the solution producing a value less than the solubility product, there is less precipitation of AgF. The SDF is claimed to be more stable than AgF, and it can be kept in a constant concentration for a longer time. In addition, SDF is not as alkaline (pH 8 to 9) as AgF solution (pH 11).

While AgF is becoming less readily available in dentistry, SDF is commonly used in 38% solution as a commercial preparation and is marketed in Japan as Saforide (Toyo Seiyaku Kasei Ltd, Osaka, Japan). Saforide contains 380 mg water-soluble SDF in 1 ml colourless aqueous solution, or about 44,800 ppm of fluoride ions. SDF is also commercially made and marketed in South America as Fluoroplat (Laboratorios Naf, Buenos Aires, Argentina) and Safluoride di Walter in 10% solution (Polidental, Rio de Janeiro, Brazil). A solution of 38% SDF is also available in Australia (Creighton Pharmaceutical, Sydney, Australia). The SDF solutions used in the clinical studies in China were prepared by the Medical Faculty of Peking University and by other universities (Li, 1984).

There are several advantages of using SDF in caries treatment. Firstly, SDF kills cariogenic bacteria. It precipitates on carious dentine and provides instant caries arrest. Its application does not require injection and drilling, and hence can be used to treat caries in apprehensive young children with intense dental fear. The patient compliance is good. Several studies have reported its successful use in young children (Shimizu and Kawagoe, 1976; Chu et al,

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2002; Llodra et al, 2005). Finally, SDF has long-proven success; that is, it has been used since the 1960s, especially in Asian countries, with no reports of major or severe complications (Chu et al, 2002; Llodra et al, 2005).

SDF can be used to tackle the caries problem in community dental health programmes in developing countries. The main advantages as pointed out by Bedi and Infirri (1999) are as follows.

- Control of pain and infection. SDF is effective in arresting caries progression that if left untreated will cause pain and infection.
- Affordable cost. The cost of SDF treatment is low and should be affordable in most communities.
- Simplicity of treatment. The procedures are simple. This allows non-dental professionals including primary health care workers to be easily trained to apply SDF to children.
- Minimal support required. The treatment does not require expensive equipment or support infrastructure such as piped water and electricity. Therefore, the programme is easy and inexpensive to set up. The simple armamentarium needed also allows the trained workers to deliver the treatment to people who live in remote areas.
  As the treatment is non-invasive, the risk of spreading the infection is very low.

The inherent disadvantage of using SDF to arrest caries is that the lesions will be stained black. SDF stops caries progression by forming a hard, black, impermeable layer on the tooth surface that is resistant to caries. It has been suggested that when carious dentine is treated with SDF, silver phosphate (Ag_3PO_4) is formed and this is weakly soluble (Yamaga et al, 1972). Ag_3PO_4 is yellow when it is first formed, but readily turns black under sunlight or under the influence of reducing agents. In addition, the precipitation of silver sulphide also contributes to the blackening of caries lesions (Llodra et al, 2005). Some children and their parents may not be pleased with the aesthetics of this treatment outcome. Moreover, SDF can stain clothes and the skin of the body. The stain caused by SDF on the skin, although does not cause any pain or damage, cannot be easily washed away and it takes some time for it to disappear. SDF solution also has a metallic taste that is not too pleasant. Furthermore, gingival and mucosal irritation may occur. In most cases, the affected tissue turns white and the change is transient (Llodra et al, 2005). The white marks (burning) on the gingiva usually heal within 1 to 2 days. Other disadvantages include its sensitivity to light, and hence it must be kept in dark/opaque container. Its high fluoride concentration can be toxic when swallowed in large doses, hence precaution must be taken especially when it is used on very small children.

As SDF stains skin, clothes and even dental instruments black, it must be handled with care by using protective gloves. The cotton pellets soaked in SDF must be disposed of properly after use to avoid staining. If there is accidental ingestion of large amount of SDF, it is important to call for medical assistance. Vomiting can be induced to avoid its absorption in the body; a 10% calcium gluconate (10 ml) solution can be administered. The calcium ions will react with fluoride ions to form insoluble calcium fluoride (CaF_2), which cannot be absorbed in the gastrointestinal tract.

A suggestion to manage the staining problem of SDF is to use potassium iodide (KI), which reacts with the free silver ions to form a creamy white substance of silver iodide. An *in vitro* study has shown that this SDF/KI application has no significant difference in preventing biofilm formation (Knight et al, 2005) and bacterial inhibition compared with those of SDF alone (Knight, 2006). Another suggestion to prevent the black staining is to replace the silver ion of AgF with a silicon ion using ammonium hexafluorosilicate, $(NH_4)_2SiF_6$, or in short form, SiF. An *in vitro* study reported that SiF increased acid resistance of bovine enamel and dentine as well as SDF (Kawasaki et al, 2005). However, the acid resistance of the SiF-treated teeth was inferior to that of the SDF-treated teeth. There is no clinical trial on either the SDF/KI or SiF that is published in English. Further studies are necessary to substantiate the promising results of these *in vitro* studies before successful use in clinical practice.

SAFETY OF SDF

Studies in Japan investigating the oral tissue response to SDF applications found transient gingival irritation, but no severe pulpal damage and no severe reaction was reported (Nishino et al, 1974; Suzuki et al, 1974). A study of SDF application to 225 schoolchildren of 6 years of age in Cuba reported that three children had a small, mildly painful white lesion in the mucosa that disappeared within 48 h without treatment (Llodra et al, 2005). Another study on 55 primary carious teeth of children

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aged 6 to 13 years in Australia, found that over 90% of the teeth treated with AgF showed histologically the presence of abundant reparative dentine, a wide odontoblast layer, and hence a favourable pulpal response (Gotjamanos, 1996).

Like the use of silver amalgam in dentistry, SDF has a long-proven success. However, there is a concern that the use of 40% AgF will induce fluorosis. A laboratory study in Australia found that a sample of 24 commercial preparations of 40% AgF had a significantly higher concentration of fluoride than the expected fluoride level of 60,000 ppm (Gotjamanos and Afonso, 1997). The study concluded that the amount of fluoride in commercially available 40% AgF in Australia was too high for treatment and that it carried a high risk of causing dental fluorosis when used on young children. In response to the study, the Dental Services of the Health Department of Western Australia carried out an investigation and found no evidence that proper use of AgF would cause fluorosis (Nelsham, 1997). There was no clinical report on the high prevalence of fluorosis that was found in children who received SDF treatment despite the common use of SDF in the school dental service in Western Australia. Although there were laboratory studies that demonstrated the hypothetical risk of possible toxicity and fluorosis on children (Gotjamanos and Afonso, 1997; Gotjamanos and Orton, 1998), this concern was not observed in two clinical trials on children (Chu et al, 2002; Llodra et al, 2005). At present, the safety of the use of SDF is not conclusive.

Suzuki et al (1974) showed that after SDF application, fluoride ions penetrated the enamel diffusely to a depth of about 25 μm, whereas silver ions were mainly deposited on the surface and some penetrated as far as 20 μm into the enamel. SDF is often used to deal with dentine caries, which present a greater amount of protein substrate, carbonates and phosphates for the reaction (Delbeml et al, 2006). Another study found that when SDF is applied onto caries lesions of primary teeth, silver ions penetrate deeper than the fluoride ions in four patterns of deposition (Okuyama, 1974). Concentric layers of silver ions were observed on the superficial layer of the exposed carious dentine and there could be further penetration of silver ions pulpally through the dentinal tubules into the pulp. Gotjamanos (1996) reported that there was penetration of silver ions to the coronal pulp after the application of AgF in cavities close to the pulp. However, the silver ion deposits remained localised at the base of the cavity preparation, and only an insignificant amount of fluoride penetrated into the pulp (Afonso and Gotjamanos, 1996).

A study of 55 teeth with deep caries in children attending the School Dental Service in Australia found that 50 teeth had a favourable pulpal response from 3 to 56 months after AgF application and glass ionomer restoration (Gotjamanos, 1996). Although not all carious dentine was removed, there was a normal appearance and arrangement of connective tissue, blood vessels and nerves in the coronal pulp and the presence of a well-defined predentine layer under the reparative dentine and an adjacent continuous layer of odontoblasts. Silver granules were noted in the odontoblastic and subodontoblastic layers and in the coronal pulp of some teeth but not in the radicular pulp.

It has been reported that SDF ($Ag(NH_3)_2F$) reacts with the tooth mineral hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) to release CaF_2 and Ag_3PO_4 that are responsible for the prevention and the hardening of dental caries (Duperon, 1995). A simplified chemical equation has been suggested as follows (Yamaga et al, 1972; Okuyama, 1974):

$$Ca_{10}(PO_4)_6(OH)_2 + Ag(NH_3)_2F \rightarrow CaF_2 + Ag_3PO_4 + NH_3(H_2O)$$

The CaF_2 thus formed provides a reservoir of fluoride for the formation of fluoroapatite ($Ca_{10}(PO_4)_6F_2$), which is more resistant to acid attack than hydroxyapatite. Another study had found similar fluoride uptake by enamel with SDF (370 ppm fluoride ions) and NaF (420 ppm fluoride ions), but there was a significant difference in the percentage ratio of retained fluoride after 1 week (Suzuki et al, 1974); 41% for SDF versus 17% for NaF. The Ag_3PO_4 that precipitates on the tooth surface is weakly soluble. Its antibacterial properties act by inhibiting the enzyme activities on dextran-induced agglutination of cariogenic strains of *Streptococcus mutans* (Suzuki et al, 1976; Knight et al, 2005). An *in vitro* study found that after SDF treatment, the number of microorganisms present on the tooth surface was significantly lower (Knight et al, 2005). The presence of silver and fluoride in the outer surface layers had been suggested as the likely cause of preventing biofilm formation (Murata et al, 1996).

CLINICAL STUDIES OF AGF ON CARIES

In a search on the Medline database, which was carried out in August 2007, eight articles on seven clinical studies on AgF or SDF in children written in English or that had an English abstract were found (Table 1).

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Table 1 Summary of clinical studies on AgF in children

Studies	Site	Subjects	Duration	Intervention	Main findings
Llodra et al (2005)	Santiago de Cuba, Cuba	373 children ≥ 6 years old (mean = 6.3 years)	36 months	Group 1 – 0.2% NaF rinses/2 weeks Group 2 – 0.2% NaF rinses/2 weeks + SDF 2 times/year	Children in Group 2 developed fewer new caries ($P < 0.001$) and more inactive caries at the surface ($P < 0.05$) in both the primary teeth and first permanent molars
Lo et al (2001) and Chu et al (2002)	Guangzhou, China	375 children 3–5 years old (mean = 4.1 years)	18 months 30 months	Group 1 – Caries excavated + SDF once/year Group 2 – SDF once/year Group 3 – Caries excavated + NaF 4 times/year Group 4 – NaF 4 times/year Group 5 – Control	Children in Group 1 developed new caries after 18 months Group 1 and 2 had about twice the number of caries to be arrested than Group 3, 4 and 5 after 30 months ($P < 0.001$)
Gotjamanos (1996)	Western Australia, Australia	55 primary teeth in 6–13 years old (mean = 8.7 years) children	3–56 months (mean = 16.3 months)	The teeth first received AgF followed by ART (atraumatic restorative treatment). They were then extracted for histological examination	50 of the 55 teeth examined showed a favourable pulpal response, inducing the presence of abundant reparative dentine and a wide odontoblast layer
Hihara et al (1994)	Tokushima, Japan	220 children 1–3 years old	Not reported	SDF versus control	52% reduction in caries severity and 47% reduction in new caries development
McDonald and Sheiham (1994)	London, England	191 caries lesions in 52 children, 2–9 years old (mean = 5.3 years)	18 months	Group 1 – SnF_2 Group 2 – SnF_2 SDF Group 3 – SnF_2 + SDF Group 4 – Resin composite Group 5 – Control	No statistical significance between groups in caries progression Progression of caries in combined Group 1 and 2 was faster than in combined Group 3 and 4 ($P < 0.001$)
Shimizu and Kawagoe (1976)	Osaka, Japan	60 caries lesions in 19 children, 3–6 years old	26 months	Split-mouth design Group 1 – amalgam Group 2 – SDF + amalgam	Group 1: 8 of 30 restorations (27%) had recurrent caries Group 2: no recurrent caries were found on the 30 restorations
Nishino and Yoshida (1969)	Osaka, Japan	188 caries lesions in 34 children	6 months	SDF versus control	69% of lesions that received SDF showed no enlargement in surface area of caries lesion versus 52% in control group. 76% of lesions that received SDF showed no increase in pulpal extension versus 65% in control group

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A 36-month controlled clinical trial was conducted in a cohort of 373 schoolchildren in Santiago de Cuba (Llodra et al, 2005). The schoolchildren received an application of 38% SDF solution every 6 months on the caries lesion of primary teeth and all first permanent molars. There were significantly more surfaces with inactive caries and fewer new caries lesion surfaces in children who received SDF during the study. Around 77% of the active caries that were treated became inactive during the study, and the efficacy of preventing new caries was 80% in the primary teeth and 65% in the first permanent molar.

A clinical trial in China applied SDF annually to caries lesions in the anterior primary teeth of preschool children. Results after 18 months showed that there was a mean value of 0.4 new caries per child among the children who received annual SDF application, whereas the mean value of the children in control group was 1.2 (Lo et al, 2001). In addition, SDF was found to be effective in arresting caries and there was no increase in the risk of the tooth becoming non-vital after 30 months (Chu et al, 2002).

A study in Australia reported beneficial results with the use of AgF followed by SnF_2 solution to arrest caries in primary molars on very young children who were difficult to manage (Craig et al, 1981). Later, a study based on the minimal invasion approach was carried out to treat the caries lesions of primary teeth of children attending the School Dental Service of Western Australia (Gotjamanos, 1996). Caries lesions in 55 primary teeth that required extraction for orthodontic reasons were treated in the study. The technique involved removal of some of the carious dentine without local anaesthesia. The deep residual caries that lay close to the pulp was then treated with a 40% AgF solution followed by a glass-ionomer cement restoration. The study reported that all restorations placed were deemed to be satisfactory at the time of orthodontic extraction after a mean of 16 months. Furthermore, the majority (91%) of the teeth studied showed a favourable pulpal response histologically.

In Japan, a 30-month field study of SDF on 220 young children was carried out, and a 52% reduction in caries severity was found in children receiving SDF treatment compared with that of children receiving no treatment (Hihara et al, 1994). There was also a 47% reduction in new caries development. Two clinical studies on SDF were conducted in Osaka, Japan (Shimizu and Kawagoe, 1976; Bedi and Infirri, 1999). The first study examined 188 caries lesions in 34 children and found less caries increment in children receiving SDF compared with that in children receiving no SDF therapy (Bedi and Infirri, 1999). The second study found no secondary caries on amalgam restorations on primary teeth pretreated with SDF after 26 months, but 27% of the amalgam restorations without SDF pretreatment showed secondary caries lesion (Shimizu and Kawagoe, 1976).

A clinical study on 191 caries lesions in 52 children in London, UK found no statistically significant difference in caries progression among children receiving either SnF_2, SnF_2 and SDF, and SnF_2, SDF and resin composite restorations, resin composite restorations alone or receiving no intervention (McDonald and Sheiham, 1994).

CONCLUSIONS

Studies have found SDF to be an effective agent in preventing new caries and arresting dentine caries in the primary teeth of children. The reports of the available studies found no severe pulpal damage after SDF applications. SDF is simple and quick to use and is an affordable therapeutic agent in developing countries. It is also a useful caries arresting agent to control caries in young children who are less cooperative. However, like the issue of toxicity of amalgam, results of some laboratory studies have raised the safety issue of SDF in its clinical use in dentistry. The black staining of arrested caries lesion is also not acceptable in many practices. Further studies can be performed to investigate the effectiveness of SDF application prior to atraumatic restorative treatment, or in indirect pulp capping of deep caries lesions.

REFERENCES

1. Afonso F, Gotjamanos T. An *in vitro* study of the distribution of silver and fluoride following application of 40 per cent silver fluoride solution to dentine. Aust Dent J 1996;41:388–392.
2. Aron VO. Porcelain veneers for primary incisors: a case report. Quintessence Int 1995;26:455–457.
3. Bedi R, Infirri JS. Oral Health Care in Disadvantaged Communities. London: FDI World Dental Press, 1999.
4. ten Cate JM. Current concepts on the theories of the mechanism of action of fluoride. Acta Odontol Scand 1999;57:325–329.
5. Chu CH. Treatment of early childhood caries: a review and case report. Gen Dent 2000;48:142–148.
6. Chu CH, Fung DSH, Lo ECM. Dental caries status of preschool children in Hong Kong. Br Dent J 1999;187: 616–620.
7. Chu CH, Lo ECM, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentine caries in Chinese pre-school children. J Dent Res 2002;81:760–770.

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8. Craig GG, Powell KR, Cooper MH. Caries progression in primary molars: 24-month results from a minimal treatment programme. Community Dent Oral Epidemiol 1981;9: 260–265.
9. DelbemI ACB, BergamaschiII M, SassakiII KT, CunhaI RF. Effect of fluoridated varnish and silver diamine fluoride solution on enamel demineralization: pH-cycling study. J Appl Oral Sci 2006;14:88–92.
10. Duperon DF. Early childhood caries: a continuing dilemma. J Calif Dent Assoc 1995;23:15–25.
11. Edelstein BL. Pediatric caries worldwide: implications for oral hygiene products. Compend Contin Educ Dent 2005;26 (5 Suppl 1):4–9.
12. Featherstone JD. Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol 1999;27:31–40.
13. Gotjamanos T. Pulp response in primary teeth with deep residual caries treated with silver fluoride and glass ionomer cement (‘atraumatic’ technique). Aust Dent J 1996;41:328–334.
14. Gotjamanos T, Afonso F. Unacceptably high levels of fluoride in commercial preparations of silver fluoride. Aust Dent J 1997;42:52–53.
15. Gotjamanos T, Orton V. Fluoride ion concentration in 40 per cent silver fluoride solutions determined by ion selective electrode and ion chromatography techniques. Aust Dent J 1998;43:55–56.
16. Hamilton IR. Biochemical effects of fluoride on oral bacteria. J Dent Res 1990;69: Spec Issue 660–667.
17. Hihara T, Nishino M, Yasutomi Y, Tominaga T, Mori Y, Arita K. Effects of diamine silver fluoride on arrestment and prevention of caries in primary tooth. Dent Jpn 1994;31:93–95.
18. Hiiri A, Ahovuo-Saloranta A, Nordblad A, Makela M. Pit and fissure sealants versus fluoride varnishes for preventing dental decay in children and adolescents. Cochrane Database Syst Rev 2006;18(4):CD003067 Review.
19. Kawasaki A, Suge T, Ishikawa K, Ozaki K, Matsuo T, Ebisu S. Ammonium hexafluorosilicate increased acid resistance of bovine enamel and dentine. J Mater Sci Mater Med 2005;16:461–466.
20. Knight GM. Inhibition of biofilm formation by silver fluoride and potassium iodide. J Dent Res 2006;85: Spec Issue B Abst 1268.
21. Knight GM, McIntyre JM, Craig GG, Zilm PS, Gully NJ. An *in vitro* model to measure the effect of a silver fluoride and potassium iodide treatment on the permeability of demineralized dentine to *Streptococcus mutans*. Aust Dent J 2005;50:242–245.
22. Li YJ. Effect of a silver ammonia fluoride solution on the prevention and inhibition of caries. Zhonghua Kou Qiang Ke Za Zhi 1984;19:97–100 [in Chinese].
23. Liu Y, Zhai W, Du F. Clinical observation of treatment of tooth hypersensitiveness with silver diamine fluoride and potassium nitrate solution. Zhonghua Kou Qiang Yi Xue Za Zhi 1995;30:352–354 [in Chinese].
24. Llodra JC, Rodriguez A, Ferrer B, Menardia V, Ramos T, Morato M. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. J Dent Res 2005;84:721–724.
25. Lo ECM, Chu CH, Lin HC. A community-based caries control program for pre-school children using topical fluorides: 18-month results. J Dent Res 2001;80:2071–2074.
26. McDonald SP, Sheiham A. A clinical comparison of non-traumatic methods of treating dental caries. Int Dent J 1994;44:465–470.
27. Murata H, Ishikawa K, Tenshin S, Horiuchi S, Nakanishi M, Asaoka K et al. Fluoridation of hydroxyapatite powder by ammonium hexafluorosilicate. Caries Res 1996;30: 465–470.
28. Nelsham DC. Fluoride concentration in AgF and dental fluorosis (Letter to the editor). Aust Dent J 1997;42:268.
29. Nishino M, Ono S, Kita Y, Tsuchitani Y. Caries prevention in pits and fissures with diamine silver fluoride solution and fissure sealant. Sealing properties of pits and fissures and adhesive characteristics to enamel. J Osaka Univ Dent Sch 1974;14:1–7.
30. Nishino M, Yoshida S. The cariostatic effect and pulp reaction of topically applied ammonical silver fluoride on in primary teeth. Jap J Pedodont 1969;7:55–59 [in Japanese].
31. Okuyama T. On the penetration of diamine silver fluoride into the carious dentin of deciduous teeth. Shigaku 1974;61:1048–1071 [in Japanese].
32. Shimizu A, Kawagoe M. A clinical study of diamine silver fluoride on recurrent caries. J Osaka Univ Dent Sch 1976;16:103–109.
33. Suzuki T, Nishida M, Sobue S, Moriwaki Y. Effects of diamine silver fluoride on tooth enamel. J Osaka Univ Dent Sch 1974;14:61–72.
34. Suzuki T, Sobue S, Suginaka H. Mechanism of antiplaque action of diamine silver fluoride. J Osaka Univ Dent Sch 1976.
35. Tan HP, Lo ECM, Luo Y, Dyson JE, Corbet EF. A randomized controlled trial on root caries in institutionalized elders. J Dent Res 2006;85: Spec Issue B Abst 553.
36. Yamaga R, Nishino M, Yoshida S, Yokomizo I. Diamine silver fluoride and its clinical application. J Osaka Univ Dent Sch 1972;12:1–20.
37. Yamaga R, Yokomizo I. Arrestment of caries of deciduous teeth with diamine silver fluoride. Dent Outlook 1969;33:1007–1013.
38. Yamashita H. Penetration of $Ag(NH_3)_2F$ applied to an infected root canal. Gifu Shika Gakkai Zasshi 1985;12: 417–439 [in Japanese].
39. Yokoyama K, Kimura Y, Matsumoto K, Fujishima A, Miyazaki T. Preventive effect of tooth fracture by pulsed Nd:YAG laser irradiation with diamine silver fluoride solution. J Clin Laser Med Surg 2001;19:315–318.