Randomized trial of silver nitrate with sodium fluoride for caries arrest

Gao SS, Duangthip D, Wong MCM, Lo ECM, Chu CH

Faculty of Dentistry, The University of Hong Kong

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Corresponding to : CHU Chun Hung,
3/F Prince Philip Dental Hospital
34 Hospital Road, Hong Kong
E-mail: chchu@hku.hk
Tel : +852 2859 0287
Fax: +852 2858 2532

Abstract

This non-inferiority, double-blind, randomized clinical trial aimed to compare the effectiveness of a 25% silver nitrate ($AgNO_3$) solution followed by a 5% sodium fluoride (NaF) varnish with a 38% silver diamine fluoride (SDF) solution in arresting caries among preschool children over 18 months. Healthy 3-year-old children with active dentine caries were randomly allocated into 2 groups by a computer-generated random-number table. Group A received a semi-annual application of the 25% $AgNO_3$ solution followed by the 5% NaF varnish. Group B received a semi-annual application of the 38% SDF solution followed by a placebo varnish. Caries and oral hygiene status were recorded by a trained examiner at baseline and follow-up examinations. The examiner, children and their caretakers were blinded to the intervention allocation. A questionnaire was used to obtain the child's oral-health-related habits and socio-economic background. This study adopted an intention-to-treat analysis. A non-inferiority test and a logistic regression analysis were conducted for data processing. Group A's non-inferiority was accepted if the lower limit of a 95% confidence interval (CI) for the difference of mean arrested carious surfaces was greater than -0.5. A total of 1,070 children were recruited at baseline with 535 children in each group. After 18 months, 484 and 476 children remained in Group A and B. The mean arrested carious surfaces in Group A and B were 3.29±3.42 and 3.21±3.48, respectively (p=0.690). The estimated difference of mean arrested carious surfaces between the two groups was 0.084 (95% CI: -0.329 to 0.498). The arrested carious surfaces were stained black. No other significant side effect was observed. In conclusion, a semi-annual application of 25% $AgNO_3$ followed by 5% NaF is no worse than a 38% SDF in arresting dentine caries among preschool children over 18 months.

Introduction

Early childhood caries (ECC) is defined as the presence of at least one decayed, missing (due to caries) or filled tooth surface in the primary teeth of a child aged 71 months or under (American Academy of Paediatric Dentistry 2008). The problem of ECC is one of the major health issues affecting many young children worldwide. The prevalence of dental caries among 2–5-year-old children in the United States (US) increased between 1988–1994 and 1999–2004, and nearly half of the children had ECC before entering kindergarten (Dye et al. 2007). More than 70% of children in most Southeast Asian countries suffer from ECC (Duangthip et al. 2017). Advanced ECC causes pain and infection, progresses into pulp and eventually forms a dental abscess or fistula. Poor dentition not only influences children's oral health, but also it affects their general health in terms of absorbing nutrition, growth, cognitive development and quality of life. Restorative treatment for young children is always challenging because of their uncooperative behaviours. Moreover, conventional treatment for advanced ECC is neither accessible nor affordable to many children, particularly those from disadvantaged communities. Thus, alternative strategies are essential to manage advanced ECC.

Clinical studies reported the success of silver diamine fluoride (SDF) in arresting caries in primary teeth of young children (Chu et al. 2002; Duangthip et al. 2016; Fung et al. 2016). The caries-arresting rate is about 80% (Gao et al. 2016a). Although SDF is available in Australia, the United States and some countries in Asia and Latin America, its use is not yet available in a number of countries. Sodium fluoride (NaF) varnish is effective in preventing caries and treating white spot enamel lesions (Gao et al. 2016b). However, NaF varnish is not effective in arresting caries (Chu et al. 2002). A laboratory study found that the remineralization of artificial dentine caries was possible after an application of a silver nitrate ($AgNO_3$) solution followed by a NaF varnish (Zhao et al. 2017). $AgNO_3$ solution and NaF varnish are available worldwide, hence they may be used to arrest caries when SDF is not available. A literature search found there is no well-designed clinical trial that has studied the effectiveness of $AgNO_3$ and NaF in managing ECC.

Studies have shown that 38% SDF is an effective agent in arresting caries amongst children. Since it was not ethical to conduct a clinical trial where children did not receive treatment or were given a placebo as a control, this study adopted a non-inferiority design using SDF as a control group. The aim of this non-inferiority randomized clinical trial is to systematically compare the effectiveness of an adjunctive application of a 25% $AgNO_3$ solution followed by a 5% NaF varnish with a 38% SDF solution in arresting dentine caries of young children when applied twice a year over an 18-month period.

Materials and Methods

Trial design

This study is a non-inferiority, double-blind, randomized clinical trial comparing the effectiveness of caries arrest by using a 25% $AgNO_3$ solution followed by a 5% NaF varnish versus a 38% SDF solution. The non-inferiority margin was set as -0.5 for the difference in mean arrested carious surfaces (MAS) between the two groups, which was considered clinically negligible (effect size was 0.25, standard deviation of mean was 2.5 and the true difference was 0) (Chu et al. 2015). The sample size calculation was done by G*Power (version 3.1.7; Franz Faul, Universität Kiel, Kiel, Germany). The statistical power was set at 90%. In total, the analysis accounted for at least 856 children. The overall dropout rate was anticipated to be 20%. Therefore, a total of 1,070 participants needed to be recruited at the baseline examination with 535 children allocated in each intervention group. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW 13-569) and registered in ClinicalTrials.gov (NCT02019160).

Participant recruitment and randomized allocation

An invitation letter and consent form was sent to the parents of kindergarten children participating in this trial. The inclusion criteria were children: a) generally healthy with parental consent, b) attending the first year of kindergarten and aged 3–4 years old and c) with at least one untreated cavitated active caries during the baseline examination. Children who were uncooperative during the dental examination, who had severe oral diseases other than dental caries, who wore orthodontic devices or were under other dental treatment, who had major systemic diseases and/or were under long-term medication were excluded. The baseline screening was conducted at the kindergartens. A stratified randomization method was adopted in this study. To balance the baseline caries status between the two intervention groups, the recruited children were firstly allocated into two categories: i) low caries rate—children with a decayed, missing or filled surfaces (dmfs) score lower or equal to 3, and ii) high caries rate—children with a dmfs score higher than 3. After that, a randomized allocation for two intervention groups was conducted separately in the aforementioned two categories by using a computer-generated random-number table with a block size of 8. The randomized allocation procedure was conducted by an independent assistant. The examiner, the children and their parents were blinded to the treatment allocation. Treatment was applied by an independent operator after the clinical examination. The operator did not know the treatment allocation until a child was ready for the intervention application.

Clinical examination

Clinical examinations were conducted at the kindergartens by a trained examiner. A World Health Organization Community Periodontal Index ball-end probe and a disposable dental mirror with a light-emitting diode for intra-oral illumination were used for the dental examination. Teeth with carious lesions extending into pulp or any signs suggesting a tooth was non-vital at baseline (discoloration, hyper-mobility or abscess/fistula formed) were excluded for further analysis. The surfaces of each tooth were assessed, and caries were diagnosed at the cavitation level. A carious lesion was recorded as being active if softness was detected upon probing. If the lesion was hard when probing, it was classified as an arrested caries (Chu et al. 2002; Duangthip et al. 2016; Fung et al. 2016). The number of active and arrested surfaces for each child was recorded. Oral hygiene was measured using the visible plaque index (VPI) on the buccal and lingual surfaces of 6 index teeth (55, 51, 63, 71, 75 and 83). Intra-examiner reliability was evaluated through duplicate examinations on 10% of the randomly selected children. The same examiner performed a follow-up examination every 6 months at the kindergartens.

Interventions

The two intervention groups were: Group A— a semi-annual application of a 25% $AgNO_3$ solution (25% silver nitrate, Gordon Labs, Carson, CA, US) followed by a 5% NaF varnish (Duraphat Varnish, Colgate-Palmolive, Endicott, NY, US), and Group B— a semi-annual application of a 38% SDF solution (Saforide, Toyo Seiyaku Kasei Co., Osaka, Japan) followed by a placebo varnish (Vaseline, Unilever, Englewood Cliffs, NJ, US). An independent operator used a microbrush to apply the appropriate solution and varnish on the carious lesions according to the assigned treatment group. Interventions were conducted every 6 months right after the oral examination. Kindergarten teachers were informed not to let the children eat or drink for half an hour after the treatment application. The caries surfaces became hard (and often black) if the caries were arrested after treatment.

Questionnaire survey

A modified validated questionnaire (Chen et al. 2017; Chu et al. 2012a; Chu et al. 1999) was used to study the child's oral-health-related habits (e.g. bottle-feeding and tooth-brushing history, dental visit behaviours) and socio-economic backgrounds (e.g. birthplace, parental condition, family total income, parental educational level, main caretaker) at baseline. A follow-up questionnaire survey was performed after 18 months to study the child's oral-health-related habits.

Statistical methods

The primary outcome measurement was the number of active carious surfaces at baseline that became arrested for each child during the follow-up examinations. Data was analysed using the Stata 13.1 (William Gould, Texas, US) and a Statistical Package for the Social Sciences 24.0 (SPSS Inc., Chicago, US). An intention-to-treat (ITT) analysis was performed. Missing cases were tested for randomness by using the Little's missing completely at random (MCAR) test. A last observation carried forward (LOCF) method was adopted for inputting the missing data. A non-inferiority test was conducted to compare the difference of MAS between two groups at an 18-month follow-up. With the non-inferiority margin set to -0.5 (Group A minus Group B), the non-inferiority of Group A to Group B could be claimed if the lower limit of the 95% confidence interval (CI) for the difference of MAS was greater than the -0.5. An independent t-test was performed to compare dmfs scores, the number of active decayed surfaces (ds) at baseline, the number of newly developed dmfs and the VPI between the two groups. Chi-square tests were used to compare the baseline oral-health-related habits and socio-economic backgrounds between Group A and Group B. An intra-examiner agreement in caries diagnoses was assessed by Cohen's Kappa statistics. The level of statistical significance for all tests was set at 0.05.

Since multiple carious lesions could be observed in one child, generalized estimating equations (GEE) with a logit link and two-level clusters (subject level and surface level) was adopted to investigate the effects of confounding factors (intervention group, related clinical characteristics, oral-health-related habits and socio-economic background) on caries arrest after adjusting the effect of correlation between variables. GEE model for a bivariate logistic regression was used to analyse each variable. Variables with p-values less than 0.05 were included to form a base model. Variables with p-values less than 0.2 but higher than 0.05 were considered potential variables and were entered into subset models. Multivariable logistic regressions were conducted on the subset models. Models with the smallest quasi-likelihood information criterion (QICC) was presented as the best-fit model for reporting. A Bonferroni test for pairwise comparisons was conducted for an inner-variable analysis.

Results

A total of 1,070 children with 535 children in each intervention group were recruited (Figure 1). The dmfs score of Group A and Group B were 5.87±6.26 and 5.96±6.11, respectively (p=0.828) (Table 1). There is no significant difference in oral-health-related habits or socio-economic background between the two groups at baseline (Appendix 1). The dropout rate after 18 months was 9.5% (51/535) and 11.0% (59/535) in Group A and B, respectively (p=0.421). Quitting school was the major reason children dropped out of the study. Missing data was completely random. During the follow-up examinations at 6 months, 12 months and 18 months, there were no significant differences between Group A and B regarding the dmfs, the number of arrested decayed surfaces, the number of newly developed dmfs or VPI, except for the VPI during the 12-month follow-up (Table 1). The VPI at the 12-month follow-up for Group A and B was 55.0%±17.3% and 52.4%±17.9%, and the difference was considered clinically insignificant. The Kappa values for the duplicated examinations of caries status were higher than 0.9 at all examinations.

Non-inferiority test for the 25% $AgNO_3$ followed by a 5% NaF with 38% SDF

During the 18-month examination, the MAS of Group A and B was 3.29±3.42 and 3.21±3.48, respectively (p=0.690). The estimate mean difference of MAS between the two groups (Group A minus Group B) was 0.084 (95% CI: -0.329 to 0.498) (Table 2). As the lower limit of 95% CI was higher than -0.5, the non-inferiority regarding the effectiveness of Group A's caries arrest compared to Group B was accepted. Arrested carious lesions were stained black. The examiner did not observe any other significant side effects.

Multi-level logistic regression of confounding factors on caries arrest

A bivariate logistic regression using GEE for individual variables found that several confounding factors, including newly developed dmfs, VPI, tooth and surface location of the carious lesions, dental treatment after the study and monthly family income during the 18-month follow-up were associated with the status of surface-level caries arrest (arrested or not arrested) (Table 3). These variables and the intervention group were included in the base model for a multi-variable logistic regression. Variables with p-values less than 0.2 (bottle-feeding before sleep, assisted tooth-brushing, parental status and mother's education level) were considered as potentially significant variables. They were added with different combinations to the base model for analysis. Thus, 16 possible models (1 base model plus 15 subset models) were computed for a multi-variable logistic regression. Amongst the 16 models, the base model plus the variable of bottle-feeding before sleep presented the smallest QICC (5024.256), which was accepted as the best-fit model. The results of multi-variable logistic regression based on the best-fit model are shown in Table 4.

Caries arrest was negatively related to newly developed dmfs (Odds ratio: 0.944, p=0.038) and VPI (Odds ratio: 0.991, p=0.005) at the 18-month follow-up. Tooth location and surface location of the carious lesions were significantly associated with caries status (i.e. active or arrest [p<0.001]). Carious lesions on lower anterior teeth and on buccal surfaces had the highest chance of being arrested. Children who had a monthly family income lower than HK$ 20,000 and those who did not seek dental treatment after the study had a higher chance of having their caries arrested (Table 4).

Discussion

Silver is a disinfectant, and fluoride is a remineralizing agent. This could be the basic principle of SDF for its caries arresting effect. Using a 25% $AgNO_3$ solution followed by a 5% NaF follows the same principle for caries arrest. A laboratory study showed that a 25% $AgNO_3$ solution and a 5% NaF varnish could remineralize both inter- and intra-tubular demineralized dentine and prevent the collagen fibres from exposure on dentine surfaces (Zhao et al. 2017). A clinical observation of community dental care for more than 5,000 US children also reported that an adjunctive application of a 25% $AgNO_3$ solution followed by a 5% NaF varnish could arrest active caries in almost all the caries lesions (Duffin 2012). This non-inferiority, double blind, randomized clinical trial found that a 25% $AgNO_3$ solution followed by a 5% NaF varnish was not worse than 38% SDF in clinically arresting dentine caries among preschool children. Therefore, this adjunctive treatment could be used to arrest caries, especially when SDF is not available.

A non-inferiority trial was adopted in this study. It tests whether a new treatment is less effective than a positive control treatment, which is already in use (Walker and Nowacki 2011). There are several advantages in adopting a non-inferiority trial in a study design. Firstly, it address the ethical concern for clinical trials, because it is more desirable to conduct a clinical trial where the control group also receives treatment. Secondly, it is more favourable to compare the new treatment with a currently available standard treatment to prove its effectiveness, especially when the new treatment may offer important advantages over the standard treatment such as a lower cost (Hahn 2012). Last but not least, non-inferiority trials have considerably larger sample sizes than placebo control trials, which enhances the study’s reliability (Snapinn 2000). Nevertheless, the large size required can also be a limitation in implementing a non-inferiority clinical studies. In the clinical trial, it was very challenging to recruit more than 1,000 3-year-old children with untreated cavitated caries for longitudinal follow-ups. More than 5,000 children were screened to identify the required 1,070 children in this clinical trial. In countries or areas with smaller populations, a non-inferiority trial can be an insurmountable difficulty. A multi-centre clinical trial can be a solution, but the cost would increase significantly.

This clinical trial used an ITT analysis to avoid misleading artefacts such as non-random participant dropouts from the study. ITT includes all children who were randomized into the two intervention groups at baseline for data processing, regardless of their adherence to the assigned treatment group or subsequent withdrawal from this study. The Consolidated Standards of Reporting Trials (CONSORT) guidelines recommend reporting randomized clinical trials (Moher et al. 2001). The ITT analysis reflects the practical scenario, as it includes noncompliance, dropouts and admits protocol deviation. Moreover, ITT analysis preserves the sample size to maintain statistical power. As all noncompliance and dropouts are included into analysis, an ITT analysis can always provide a relatively conservative estimate of treatment effectiveness (Gupta 2011). It is noteworthy that a full application of the ITT analysis requires complete outcome data for all participants. The presence of missing data and adherence to a 6-month treatment protocol can impose difficulties in completing an ITT analysis. In this study, the LOCF method was adopted for inputting the missing data; hence, the missing values were replaced by the last available measurement. Clinical studies have shown that caries arresting rates increased over follow-up periods when the SDF application was repeated annually or semi-annually (Duangthip et al. 2016; Fung et al. 2016; Zhi et al. 2012). Thus, inputting the missing values by using the LOCF method in this study could prevent the overestimation of treatment effectiveness.

Some carious surfaces after fluoride treatments were found to be filled by other dentists in the follow-up examinations. These filled surfaces were considered “failed” in the analysis. Thus, children who had other dental treatments after this study showed a lower caries arresting rate than those children who had no other dental treatment after the study. Children from higher monthly income families were more likely to visit a dentist to receive a filling; this could be a reason why children who were from higher monthly income families had lower caries arresting rates.

The results of the non-inferiority test suggested that the 25% $AgNO_3$ solution followed by the 5% NaF varnish was not worse than the 38% SDF for the caries arresting effectiveness amongst kindergarten children. Results from the multivariable logistic regression showed that the intervention group ($AgNO_3$ + NaF vs SDF) was not an affecting factor for caries arrest; whereas other confounding factors, such as newly developed dmfs, VPI, tooth and surface location of the carious lesions, could influence the outcome of caries arrest. Caries on anterior teeth are more likely to be arrested than caries on lower posterior teeth. This finding was consistent with previous studies (Fung et al. 2016; Zhi et al. 2012). The fluoride solution could be readily diluted when applied to lower posterior teeth, because there was no moisture (saliva) control during this study’s treatment application. This might be a reason for the outcome. Furthermore, the children’s oral hygiene (VPI) and their caries incidence (newly developed dmfs at the18-month follow-up) were negatively related to the treatment’s effectiveness. Thus, developing and maintaining good oral hygiene is crucial for caries arrest.

Conclusion

In conclusion, a semi-annual application of a 25% $AgNO_3$ solution followed by a 5% NaF varnish was not worse than the 38% SDF in arresting dentine caries among preschool children over 18 months. The caries arresting rate was influenced by the child's oral hygiene and the location of the carious surface.

Conflicts of interest

The authors declare no potential conflicts of interest.

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Table 1. Caries experience (dmfs) and oral hygiene status (VPI) at baseline and follow-up examinations

Examination	Variables	Group A 25% $AgNO_3$ + 5% NaF	Group B 38% SDF	p-value
Baseline	dmfs	5.87 (6.26)	5.96 (6.11)	0.828
	active ds	5.18 (4.64)	5.18 (4.72)	1.000
	VPI (%)	62.8 (17.6)	60.9 (18.1)	0.092
6-month follow-up	MAS	2.14 (2.53)	2.00 (2.51)	0.370
	dmfs	6.58 (6.56)	6.64 (6.43)	0.869
	New dmfs	0.71 (1.24)	0.68 (1.16)	0.741
	VPI (%)	54.7 (15.6)	53.2 (15.6)	0.108
12-month follow-up	MAS	3.23 (3.37)	3.10 (3.41)	0.522
	dmfs	7.45 (7.10)	7.45 (6.88)	0.993
	New dmfs	0.86 (1.58)	0.80 (1.29)	0.484
	VPI (%)	55.0 (17.3)	52.4 (17.9)	0.015
18-month follow-up	MAS	3.29 (3.42)	3.21 (3.48)	0.690
	dmfs	8.36 (7.57)	8.28 (7.57)	0.856
	New dmfs	0.96 (1.59)	0.83 (1.91)	0.251
	VPI (%)	54.1 (16.9)	53.8 (16.9)	0.733

dmfs, decayed, missing (due to caries) and filled surfaces; ds, decayed surfaces; MAS, mean arrested carious surfaces; VPI, visible plaque index.

Table 2. Non-inferiority test of MAS difference between the two groups

Follow-up Examination	Estimated Mean Difference	95% Confidence Interval		p-value
		Lower	Upper	
6-month	0.138	-0.164	0.441	0.370
12-month	0.132	-0.274	0.540	0.522
18-month	0.084	-0.329	0.498	0.690

MAS, mean arrested carious surfaces.

Table 3. Bivariate logistic regression using the GEE model with a logit link and two-level clusters (surface level and subject level) for individual factor

Explanatory variables	Odds ratio	95% Confidence Interval	p-value
Clinical parameters			
Intervention group (ref: 38% SDF + placebo)			0.107
- 25% $AgNO_3$ + 5% NaF	1.153	0.970-1.371	
Baseline dmfs	0.998	0.987-1.008	0.679
18-month new dmfs	0.957	0.916-0.999	0.047
18-month VPI	0.995	0.989-1.000	0.045
Tooth location (ref: lower posterior tooth)			<0.001
- Upper anterior tooth	6.735	5.490-8.262	
- Upper posterior tooth	1.968	1.551-2.498	
- Lower anterior tooth	27.081	14.571-50.332	
Surface location (ref: occlusal surface)			<0.001
- Buccal surface	10.545	8.232-13.507	
- Mesial surface	5.329	4.435-6.403	
- Distal surface	5.898	4.742-7.337	
- Lingual surface	4.625	3.554-6.018	
Oral-health-related habits			
Age of stop bottle-feeding (ref: after 24 months)			0.557
- Breast feeding only	1.140	0.836-1.554	
- 1 to 12 months	0.947	0.563-1.594	
- 13 to 24 months	1.153	0.920-1.445	
Current bottle-feeding before sleep (ref: no)			0.052
- Yes	0.804	0.645-1.002	
Daily snack intake (ref: no)			0.390
- Yes	0.771	0.426-1.395	
Daily snack intake frequency	0.956	0.871-1.049	0.341
Age of start tooth-brushing (ref: after 24 months)			0.965
- 1 to 12 months	1.037	0.758-1.417	
- 13 to 24 months	1.018	0.850-1.221	
Daily tooth-brushing (ref: twice per day or more)			0.693
- Less than once per day	1.238	0.633-2.422	
- Once per day	1.070	0.867-1.322	
Assisted tooth-brushing (ref: no)			0.123
- Yes	0.864	0.717-1.040	
Use of fluoride toothpaste (ref: no)			0.255
- Yes	1.158	0.900-1.490	
Dental treatment after start of study (ref: no)			<0.001
- Yes	0.582	0.469-0.724	
Socio-economic backgrounds			
Sex (ref: female)			0.693
- Male	1.036	0.870-1.234	
Birthplace (ref: mainland)			0.274
- Hong Kong	0.846	0.628-1.141	
Parental status (ref: single parent)			0.116
- Both parents	0.699	0.448-1.092	
Monthly family income (ref: HK$ 40,001 or above)			0.012
- HK$ 20,000 or less	1.563	1.157-2.113	
- HK$ 20,001 to 40,000	1.383	1.002-1.910	
Father's education level (ref: higher education)			0.592
- Mandatory education	1.054	0.870-1.277	
Mother's education level (ref: higher education)			0.193
- Mandatory education	1.129	0.940-1.356	
Main caretaker (ref: maid)			0.647
- Parents	1.044	0.689-1.584	
- Relatives	0.943	0.603-1.475	

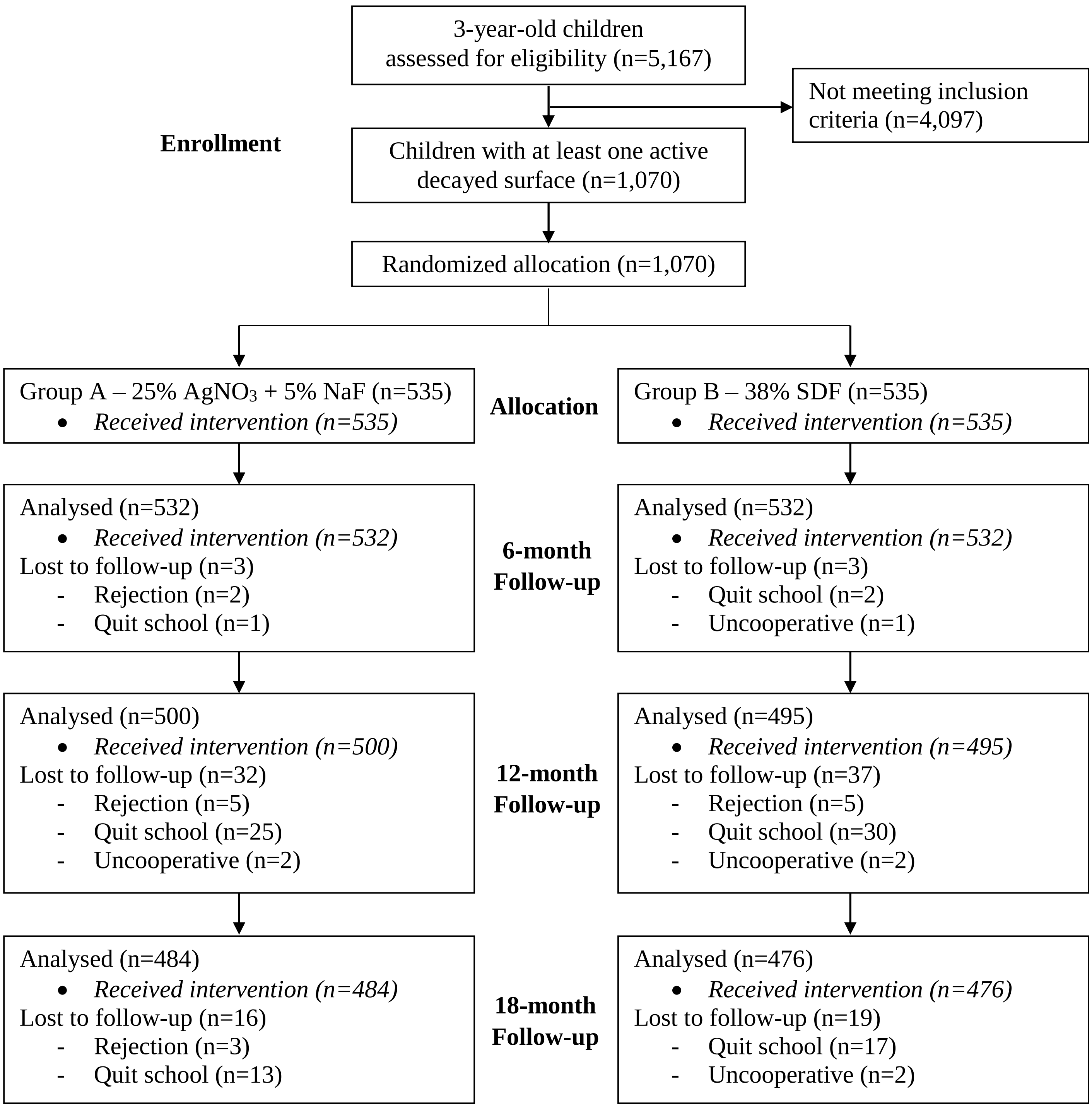
ref, reference group; SDF, silver diamine fluoride; $AgNO_3$, silver nitrate; NaF, sodium fluoride; dmfs, decayed, missing (due to caries) and filled surfaces; VPI, visible plaque index; HK$, Hong Kong dollars.

Table 4. Multivariable logistic regression model with the best estimated fit by quasi-likelihood information criterion

Explanatory variables	Odds ratio	95% CI	p-value	Pairwise comparison
Intervention group			0.577	
(1) 25% $AgNO_3$ + 5% NaF	1.062	0.860-1.312		
(2) 38% SDF + placebo (ref)				
18-month new dmfs	0.944	0.894-0.997	0.038	
18-month VPI	0.991	0.984-0.997	0.005	
Tooth location			<0.001	(3)>(1)>(2)>(4)
(1) Upper anterior tooth	4.818	3.567-6.507		
(2) Upper posterior tooth	1.763	1.347-2.308		
(3) Lower anterior tooth	35.426	17.173-73.083		
(4) Lower posterior tooth (ref)				
Surface location			<0.001	(1)>(2),(3),(4)>(5)
(1) Buccal surface	4.305	3.194-5.802		
(2) Mesial surface	2.058	1.545-2.741		
(3) Distal surface	1.926	1.369-2.710		
(4) Lingual surface	1.735	1.323-2.276		
(5) Occlusal surface (ref)				
Monthly family income			0.024	(1)>(3)
(1) HK$ 20,000 or less	1.689	1.150-2.480		
(2) HK$ 20,001 to HK$ 40,000	1.480	0.982-2.230		
(3) HK$ 40,001 or above (ref)				
Current bottle-feeding before sleep				
(1) Yes	0.796	0.613-1.034	0.088	
(2) No (ref)				
Dental treatment after start of the study			0.001	
(1) Yes	0.614	0.466-0.809		
(2) No (ref)				

ref, reference group; AgNO3, silver nitrate; NaF, sodium fluoride; SDF, silver diamine fluoride; dmfs, decayed, missing (due to caries) and filled surfaces; VPI, visible plaque index; HK$, Hong Kong dollars.

Figure 1. Flow diagram of this trial



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