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Sealant and Fluoride Varnish in Caries: a Randomized Trial

ABSTRACT

Little is known about the effect of discontinuation of sealant or fluoride varnish. The purpose of this study was to compare sealant with fluoride varnish in the prevention of occlusal caries in permanent first molars of children over a nine-year period: 4 yrs for program evaluation plus 5 yrs of discontinuation. A clinical trial was conducted on three groups of six- to eight-year-old schoolchildren: a control group (n = 45); a group (n = 37) in which sealant was applied and re-applied up to 36 mos; and a group (n = 38) in which fluoride varnish was applied and re-applied up to 42 mos. Percent caries reduction was studied in these initially healthy molars with complete occlusal eruption: 129 (control), 113 (sealant), and 129 (varnish) molars met inclusion criteria. Of these, 76.7%, 26.6%, and 55.8% had developed occlusal caries at 9 yrs, which implies caries reductions of 65.4% (SE = 8.5%) for sealants *vs.* control and 27.3% (SE = 10.2%) for varnish *vs.* control. Furthermore, the varnish program was not effective during the discontinuation period.

KEY WORDS: dental caries, pit and fissure sealant, fluoride varnish, clinical trial.

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INTRODUCTION

Fissure sealants and fluoride varnishes are preventive procedures for dental caries developed in the 1960s and widely used in public dental programs. Many narrative reviews (*e.g.*, Simonsen, 2002; Donly, 2003) have shown both techniques to be effective. Meta-analyses of controlled clinical trials on sealants (Llodra *et al.*, 1993; Mejàre *et al.*, 2003; Ahovuo-Saloranta *et al.*, 2004) and varnish (Helfenstein and Steiner, 1994a,b; Strohmenger and Brambilla, 2001; Marinho *et al.*, 2002, 2003) confirmed their effectiveness, but described significant heterogeneity and indicated the need for further studies.

The effect of the discontinuation of preventive programs is an important issue, mainly related to measures that require continual re-applications. Although reports on the impact of discontinuing fluoride applications other than varnish—such as tablets, water, rinses, or toothbrushing—have been inconsistent, most described a slow and gradual loss of preventive effect over the years (*e.g.*, Haugejorden *et al.*, 1990; McDonagh *et al.*, 2000). Duraphat® fluoride varnish (Colgate-Palmolive Co., New York, NY, USA) has been reported to provide a protective effect after 2 yrs of discontinuation (Seppä *et al.*, 1984). Sealants are considered a more definitive preventive treatment, although periodic replacement or repair is recommended (Simonsen, 2002).

In 1990, a clinical trial was initiated in Granada, a non-fluoridated city in Spain, comparing six- to eight-year-old children receiving sealants with a group receiving fluoride varnish and a control group. Follow-up at 24 mos showed a reduction in occlusal caries in permanent first molars of 76.8% for the sealant group *vs.* controls, and 37.7% for the varnish group *vs.* controls (Bravo *et al.*, 1996a). A survival analysis of the results at 48 mos yielded similar findings (Bravo *et al.*, 1997b). The purpose of this study was to compare sealant with fluoride varnish in the prevention of occlusal caries in permanent first molars after a nine-year period: 4 yrs for evaluation of the active programs, plus 5 yrs of discontinuation.

MATERIALS & METHODS

Design and Sampling

A detailed description of the clinical trial at 48 mos after its commencement has been published previously (Bravo *et al.*, 1996a,b, 1997a,b). A brief description, completed following the suggestions of the CONSORT Statement (Moher *et al.*, 2001), is also provided here, including a flow-chart (Fig.). The original study was designed for a two-year follow-up. Sample sizes were calculated according to Fleiss (1981) for the comparison of caries incidence in molars without considering the clustering of molars in the children. The key percentages were alpha-error = 5%, beta-error = 20%, and maximum error in risk difference = 0.15, giving the most conservative values to the unknown caries incidence in the two groups, *i.e.*, 0.575 and 0.425. The result

was a sample of 186 permanent first molars *per* group, *i.e.*, 93 children/group with 2 sound molars *per* child. For an estimated annual attrition rate of 10%, and assuming parental authorization for 80% of subjects, we sought informed consent for approximately 144 children *per* group in 1990.

Five of the 21 primary schools in the Northern district of Granada (Spain) were selected at random. First-year (n = 6) and second-year (n = 9) classes (six- to eight-year-old children) were randomly assigned to one of three independent groups (control, sealant, and fluoride varnish) until 144 children *per* group were enrolled. The study was approved by the University of Granada Faculty of Dentistry Ethics Committee, and informed consent from the parents was sought at the beginning of the study and again for the follow-up visit at 9 yrs. Consent was initially obtained for 362 (84%) of the selected children. The children received no toothbrushing, fluoride rinse, or fluoride tablet programs, and no sealants were present at the beginning. Three controls moved to fluoride classes and received the varnish, but were considered as controls in the analysis ("intention to treat" strategy). Of the 362 children, 186 could be found in secondary schools in the Northern district of Granada 9 yrs later, and 177 (48.9% of the 362) agreed to the follow-up examination. Of these, 120 (67.8%) (45 controls, 37 with sealant, and 38 with varnish) had presented with at least 1 healthy and fully erupted permanent first molar at study commencement and had been examined at 4 yrs.

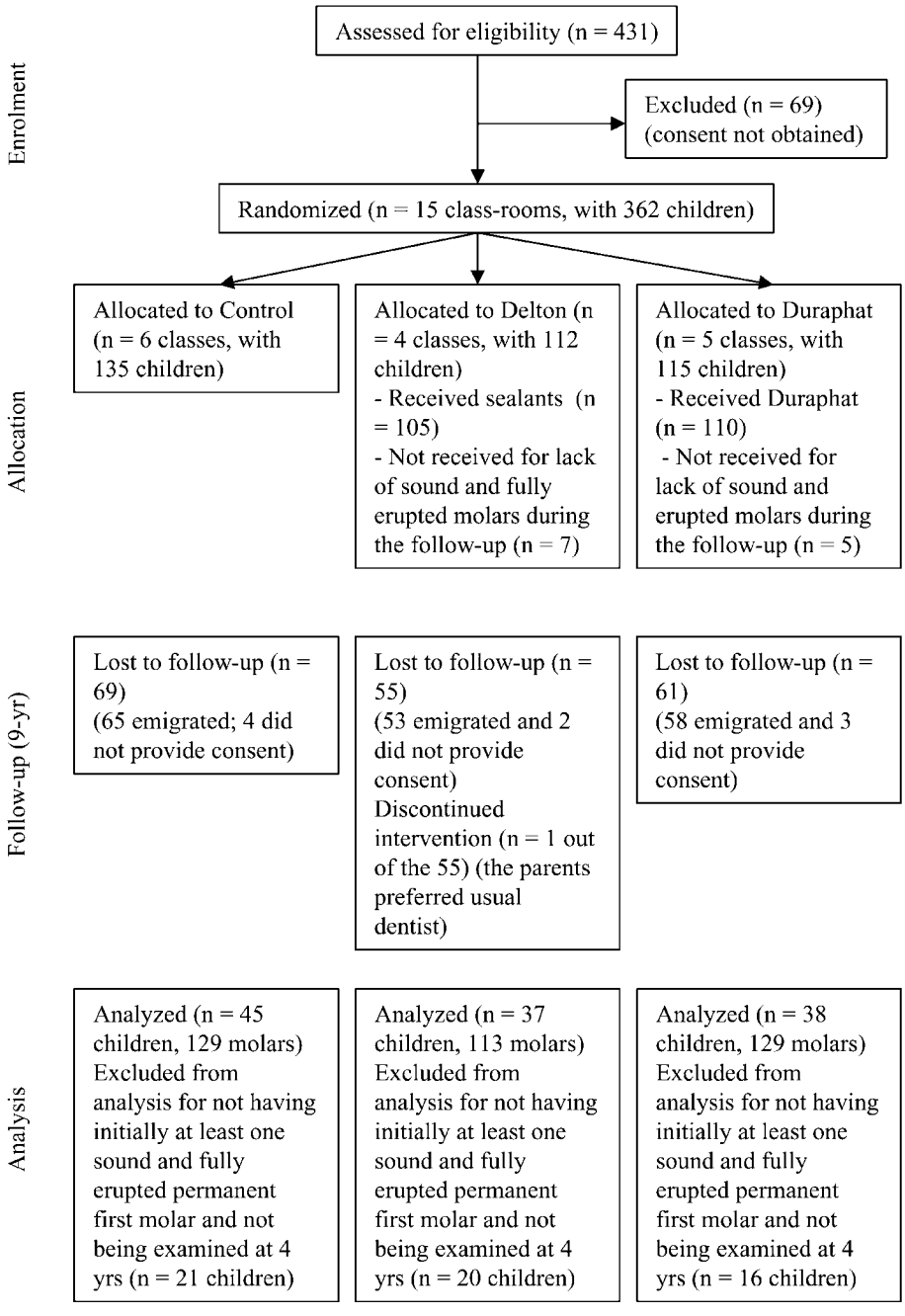

Figure. Flow diagram of the progress through the study phases according to the CONSORT statement (Moher *et al.*, 2001).

Description of Programs

Application of the sealant and fluoride varnish was carried out in the schools by one dentist plus an assistant, using portable equipment. Sealant (Delton® light-polymerized opaque fissure sealant: Johnson & Johnson Dental Products Co., East Windsor, NJ, USA) was applied to all healthy, permanent, and fully erupted first molars. After 6, 12, 18, 24, and 36 mos, sealant was applied to molars that had not previously erupted and was replaced if there had been partial or total loss (Bravo *et al.*, 1996b). In the fluoride varnish group, Duraphat was applied to all healthy permanent first molars with partially or fully erupted occlusal surfaces. After 6, 12, 18, 24, 30, 36, and 42 mos, varnish was applied to newly erupted molars and was re-applied to all molars that had remained healthy. No adverse effects were detected or reported by the patients.

Data Collection

For the first 4 yrs, the children received six-monthly caries examinations according to standardized criteria (World Health Organization, 1987). For the purpose of this study, initial and four-year caries status was noted, along with initial age, sex, and socio-economic group (Registrar General, 1980). At the nine-year follow-up, a different dentist examined the subjects in a blinded fashion, according to the same criteria, and administered a brief questionnaire on toothbrushing frequency and visits to the dentist. In 20 children, the examination was repeated after 7 days by the same dentist and by

Table 1. Baseline Characteristics by Group of Children Followed for 4 and 9 Yrs, with at Least 1 Healthy Permanent First Molar with Complete Occlusal Eruption at Baseline

Variable	Control (n = 45)	Sealant (n = 37)	Varnish (n = 38)	Comparison[e]
Age (yrs), mean (SD)[a]	7.4 (0.7)	7.3 (0.8)	7.6 (0.7)	Wald F = 0.24 (2 df), $p = 0.790$
Sex (% of female)	51.1%	67.6%	47.4%	Chi-square$_{adj}$ (2 df) = 5.09, $p = 0.114$
Social level[b], median	middle	middle	middle	Chi-square$_{adj}$ (2 df) = 1.55, $p = 0.479$[f]
dft[c], mean (SD)	2.98 (2.90)	2.24 (2.59)	2.42 (3.26)	Wald F = 0.90 (2 df), $p = 0.427$
DMFT(M1)[d], mean (SD)	0.64 (0.96)	0.46 (0.87)	0.29 (0.69)	Wald F = 1.46 (2 df), $p = 0.266$
DMFT(M1) = 0, %	62.2%	73.0%	81.6%	Chi-square$_{adj}$ (2 df) = 3.05, $p = 0.252$

[a] SD, standard deviation.
[b] Missing in five and four children from Control and Varnish groups, respectively.
[c] Decayed and filled deciduous teeth.
[d] Decayed, missing, and filled permanent first molars.
[e] Adjusted for the cluster (school classes, rather than children) random allocation (see MATERIALS & METHODS).
[f] After categories were collapsed for scarcity of data, the social level was classified into two categories: High/High-Middle/Middle *vs.* Low-Middle/Low.

another experienced dentist, yielding intra- and interexaminer kappa coefficients greater than 0.68 in all measurements, indicating that examiner reliability was adequate (Landis and Koch, 1977).

Statistical Analysis

SPSS-Windows v.10.0 (SPSS Inc., Chicago, IL, USA) was used for the descriptive statistics, with the child as the unit of analysis. Comparison among groups was done by SUDAAN v.7.0 (Research Triangle Institute, Research Triangle Park, NC, USA), based on the cluster (school classes rather than children) random allocation by means of REGRESS and CROSSTAB procedures for quantitative and categorical variables, respectively.

When the molar was considered as the unit of analysis, only molars that were healthy and fully erupted at the beginning of the study, and were followed at both 4 and 9 yrs, were included. With caries incidence as the dependent variable, the group (control, sealant, and varnish) by time (four- and nine-year) interaction was evaluated by the LOGISTIC procedure of SUDAAN; since results were significant ($p < 0.001$), further analysis was performed for each time point (four- and nine-year). Caries incidences at 4 yrs, 4-9 yrs, and 9 yrs were calculated for each preventive technique. Standard errors and chi-square statistics were adjusted for multiple molars in the child and school-classes random allocation, by the CROSSTAB procedure of SUDAAN. In sealed molars, the percentage with complete retention of sealant at 9 yrs was also calculated.

Percent change in one group compared with another was calculated as [(mean2-mean1)/mean1] x 100, where mean1 and mean2 were the mean caries incidences in the two groups being compared

Table 2. Occlusal Caries Incidence over 9 Yrs in Initially Healthy Molars with Full Occlusal Eruption

			Occlusal DMF[c]					
			Total			Components		
Group	No. Children	No. Molars	n	% ± SE[d]	Design Effect[e]	D	M	F[f]
0-4 yrs								
Control	45	129	82	63.6 ± 6.8	2.60	67	0	15 (6)
Sealant	37	113	17	15.0 ± 4.7	1.97	9	0	8 (2)
Varnish	38	129	46	35.7 ± 5.3	1.57	35	0	11 (6)
Comparison[a]	chi-square$_{adj}$ (2 df) = 34.22, $p < 0.001$							
4-9 yrs[b]								
Control	20	47	17	36.2 ± 9.6	1.85	10	0	7 (7)
Sealant	34	96	13	13.5 ± 3.7	1.09	10	1	2 (2)
Varnish	32	83	26	31.3 ± 6.9	1.81	17	0	9 (9)
Comparison[a]	chi-square$_{adj}$ (2 df) = 8.37, $p = 0.018$							
0-9 yrs								
Control	45	129	99	76.7 ± 6.4	2.92	59	4	36 (12)
Sealant	37	113	30	26.6 ± 6.1	2.15	17	1	12 (4)
Varnish	38	129	72	55.8 ± 6.3	2.10	40	0	32 (13)
Comparison[a]	chi-square$_{adj}$ (2 df) = 31.47, $p < 0.001$							

[a] Adjusted for multiple molars within the child and cluster (school classes, rather than children) random allocation.
[b] Based on molars that remained sound at 4 yrs. Note that there were no reversals (*i.e.*, molars detected as sound at 9 yrs, but not sound at 4 yrs).
[c] DMF = decayed (D), missing (M), and filled (F) permanent first molars.
[d] SE = standard error.
[e] Ratio of %variance (CS) to %variance (SRS), where CS is complex sampling and SRS is simple random sampling, *i.e.*, assuming that the molars are independent observations.
[f] Filling. In brackets are the filled occlusal surfaces that had been declared sound at the previous visit.

(see Dubey *et al.*, 1965, for standard error formula). Statistical power for non-significant comparisons was calculated by SamplePower v.2.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

There were no significant differences in sex, age, social level, or baseline caries scores between the 177 followed children and the 185 lost to follow-up (results not shown). A description of the 120 children included in this analysis is presented, with non-significant differences among the groups at baseline (Table 1). Regarding oral hygiene (not shown in Table 1), eight (6.7%) children never brushed their teeth, and a frequency of 1-2 times/week was reported by 15 (12.5%), 1-2 times/day by 83 (69.2%), and 3 or more times/day by 14 (11.7%). Thirty-five children (29.2%) had visited the dentist in the previous 24 mos. There were no significant differences in these variables among the groups (results not shown).

The average number of examination visits *per* child, excluding the nine-year follow-up visit, was 8.75 (SD = 0.55) (maximum 9), with no significant differences among the three groups. The average number of treatment visits *per* child during the active phase of the programs was 2.24 (SD = 1.14) (maximum 6) for children with sealant and 7.26 (SD = 0.98) (maximum 8) for children with varnish. This difference is great, because the sealant was re-applied only when a partial or total loss occurred, whereas the varnish was systematically re-applied and was also re-applied at 30 and 42 mos.

Three hundred and 71 molars could be included in the analysis (129 control, 113 sealed, and 129 varnished). Of these, 76.7%, 26.6%, and 55.8%, respectively, had developed occlusal caries at 9 yrs (Table 2). The effect of clustering on the standard error of the percent of molars becoming carious is measured by the design effect (Table 2), indicating a loss of precision.

The effectiveness of the treatments was 76.3% for sealant and 43.9% for varnish at 4 yrs, and 65.4% and 27.3%, respectively, at 9 yrs (Table 3). Comparison between the sealant and the varnish showed that the performance of the former was superior at 4 and 9 yrs, because zero was not included in the 95% confidence interval (CI) (Table 3). Statistical power for the only non-significant comparison (Varnish *vs.* Control from 4 to 9 yrs [Table 3]) was 45.4% (see footnote c, Table 3.

At the nine-year examination, 5 control (3.9%), 55 sealed (48.7%), and 5 varnished (3.9%) molars presented partial or complete sealant. It should be noted that sealants in control and varnish groups had been placed outside the program. Of the 113 sealed molars, 44 (38.9%) remained sealed (complete retention) and were sound.

Table 3. Relative Risk and Percent Effectiveness of Sealants and Varnish over 9 Yrs in Initially Healthy Molars with Full Occlusal Eruption

Comparison	Relative Risk	% Caries Reduction Mean ± SE[a]	95%-CI[b]
0-4 yrs			
Sealant *vs.* control	0.24	76.3 ± 7.9	57.5 - 95.1
Varnish *vs.* control	0.56	43.9 ± 10.3	19.3 - 68.5
Sealant *vs.* varnish	0.42	57.8 ± 14.7	22.8- 92.9
4-9 yrs			
Sealant *vs.* control	0.37	62.6 ± 14.1	28.8 ± 96.4
Varnish *vs.* control	0.87	13.4 ± 29.7	- 57.6 - 84.4[c]
Sealant *vs.* varnish	0.43	56.8 ± 15.0	20.9 - 92.7
0-9 yrs			
Sealant *vs.* control	0.34	65.4 ± 8.5	45.2 - 85.6
Varnish *vs.* control	0.73	27.3 ± 10.2	2.8 - 51.7
Sealant *vs.* varnish	0.47	52.4 ± 12.2	23.3 - 81.6

[a] SE = standard error adjusted for multiple molars within child and cluster (school classes, rather than children) random allocation.

[b] After Bonferroni's corrections for three comparisons, the significance level is $p < 0.017$ (for an uncorrected level of 0.05), 95%-CI = mean ± 2.39 x SE.

[c] Power calculation to detect effectiveness of 46% for fluoride varnish (Marinho *et al.*, 2002): For a 36.2% caries increase in the control group with effective sample sizes (= sample size/design effect) (Dean, 1993) of 25 control molars (≈ 47/1.85) and 46 varnished molars (≈ 83/1.81) (Table 2), the power was 45.4%.

DISCUSSION

Validity

The validity up to 48 mos was previously described and discussed (Bravo *et al.*, 1996a,b, 1997a,b). At 9 yrs, 51.1% of the children could not be examined. However, this should not represent a selection bias, because the main reason was that the children had moved to other districts or cities. Little effect appears to have been produced by restorative treatment, *i.e.*, the increment in DMF (Decayed, Missing and Filled permanent teeth) due to fillings placed according to other caries criteria. Of the total of 201 occlusal surfaces that became DMF at 9 yrs, 80 were fillings, and 29 (36.3%) had been placed in molars assessed as sound at the previous visit (Table 2), resulting in a maximum bias of 14.4% (29/201) in the caries incidence estimates. Finally, only a low proportion of sealants were placed outside the study (see last paragraph of RESULTS).

Regarding the statistical analysis, two issues deserve attention: first, the importance of adjusting the analysis, as with SUDAAN in this study, for the lack of independence of molars in the children. Considering the molars as independent observations would have led to a misleading increase in precision (lower standard errors) (Koch and Paquette, 1997). Second, clinical trials can have multiplicity problems, such as multiple outcomes, subgroup analyses, interim analyses of accumulating data, multiple treatment comparisons, and repeated measurements over time (Pocock, 1997). The last two issues affect this trial, since we have three groups and two clinical examinations (48-month and nine-year). The statistical analysis should avoid loss of validity from the inflation of Type I error, while simultaneously avoiding power loss by excessive Type II error (Koch and Paquette, 1997). We used the Bonferroni correction to solve the multiple treatment comparisons (see footnote b of Table 3). However, we decided not to correct the p-values for the two repeated measurements over time, since the measurement at 9 yrs is the only one that evaluates efficacy after the discontinuation period, which is the central outcome in this study. Nevertheless, the Bonferroni correction can again be applied. In Table 2, the corrected p-value would be 0.025 (for an uncorrected level of 0.05), and in

Table 3, the significance level reflected in footnote b would be 0.0085 for 6 comparisons - 3 treatment groups by 2 repeated measures, with a factor of 2.63 to calculate the 95% CI. These new figures do not change the conclusions.

Effectiveness

Results of the active period of the project at both 24 (Bravo *et al.*, 1996a, 1997a) and 48 mos (Bravo *et al.*, 1997b) indicated that both treatments were effective, and that the sealants performed better than the varnish. Furthermore, the caries reduction figures up to 48 mos were within the published range of pooled preventive fractions in available meta-analyses (see INTRODUCTION). The same conclusions apply to the nine-year results, with a higher loss in preventive effect for varnish (43.9% at 4 yrs and 27.3% at 9 yrs) *vs.* sealant (76.3% at 4 yrs and 65.4% at 9 yrs) (Table 3).

The long-term success, measured by retention and caries prevention, of second-generation (chemically cured) fissure sealants has been well-documented (Romcke *et al.*, 1990; Simonsen, 1991; Wendt *et al.*, 2001). However, to our knowledge, 9 yrs is the longest follow-up period to date in a study of caries reduction with a third-generation (visible-light-cured) sealant or fluoride varnish, although comparisons of varnish with other studies should be interpreted with caution because of the 5 yrs of discontinuation.

Discontinuation

The key finding is the incidence of occlusal caries among the three groups at 4 yrs and during the discontinuation period (4-9 yrs). The caries risk in molars can be observed in control group results, which showed a significant reduction (43.1%, SE = 16.2%, $p < 0.05$) between the first (four-year) period (63.6%) and the second (five-year) period (36.2%), which cannot be explained by the different number of years in each period. A plausible explanation derives from the greater susceptibility of human teeth to dental caries shortly after eruption (up to 2-4 yrs), a well-documented phenomenon (Carvalho *et al.,* 1989).

The changes in caries incidence between 0-4 yrs and 4-9 yrs were non-significant in both Sealant (15.0% to 13.5%, a change of 10.0%, SE = 37.3%) and Varnish (35.7% to 31.3%, a change of 12.1%, SE = 23.2%) groups. However, the incidence of occlusal caries in the discontinuation period was similar between the Control and Varnish groups, but was significantly lower in the Sealant group (Tables 2, 3). An explanation of this important finding is that the sealant continues to protect the molar after discontinuation of the re-application protocol, since sealants appear to last for many years (Simonsen, 2002).

The preventive effect of the varnish appeared to cease during the discontinuation period, since there were similar occlusal caries incidences between molars in varnish and control groups. Importantly, however, there was no rebound effect. After discontinuation of varnish treatment, the molars did not show the high risk found for control molars during the maturation period (approximately the first 4 yrs), and the progressive loss of the preventive effect was very slow. Thus, after 5 yrs of discontinuation, the overall effect of the four-year varnish program remained significant (Table 3). This observation is in agreement with findings of the fluoride studies cited in the INTRODUCTION. It should also be borne in mind that fluoride varnish allows for a high uptake of fluoride into the enamel (Strohmenger and Brambilla, 2001).

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