Professional fluoride varnish treatment for caries control: a systematic review of clinical trials

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The aim of this paper was systematically to evaluate the caries-preventive effect of professional fluoride varnish treatments. A search of the literature for articles published between 1966 and August 2003 was carried out in electronic databases, reference lists of articles, and selected textbooks in accordance with the strategy of the Swedish Council on Technology Assessment in Health Care. Out of 302 identified papers, 24 randomized and controlled clinical trials comparing fluoride varnish with placebo, no active treatment or other fluoride preventive regimens of at least 2 years' study duration were included. The trials that met the inclusion criteria were assessed independently and systematically by at least two reviewers and scored from A to C according to predetermined criteria for methodology and performance. The main outcome measure was the preventive fraction expressed as a percentage. The results displayed limited evidence (evidence level 3) for the caries preventive effect of topical applications of fluoride varnishes in permanent teeth. The average prevented fraction was 30% (0–69%) when compared with untreated controls. Inconclusive evidence (evidence level 4) was found for fluoride varnish treatment in the primary dentition and in adults. This systematic review reinforces the need for future clinical research of high quality, incorporating modern concepts of clinical performance and evaluation to assess dental caries control using professional fluoride varnish. □ *Clinical trials; dental caries; fluoride varnish; professional fluoride; systematic review*

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The purpose of professional topical fluoride application is to treat the tooth surfaces so that dental caries lesions are controlled in an optimal way and progression is retarded, arrested, or even reversed efficiently. Since the introduction in the 1960s, fluoride varnish regimens have been documented in the literature and are widely used as a professional preventive treatment method in Europe (1). The main advantage of fluoride-containing varnishes has been ascribed to the anticipated prolonged fluoride slow-release feature but also its easy application technique, the independence of patient compliance, and its suitability for use in targeted individuals and risk groups has been advocated. There are three main fluoride varnishes available on the market; Duraphat (Colgate Oral Pharmaceuticals, Cologne, Germany) containing 2.26% fluoride, Fluor protector (Vivadent, Schaan, Liechtenstein) containing 0.1% F, and Bifluoride (Voco, Cuxhafen, Germany) containing 5.6% fluoride. The characteristics and efficacy of these fluoride varnishes have been described in previous reviews (2, 3). Two systematic reviews and one meta-analysis of fluoride varnish have recently been published showing a caries preventive effect varying between 33% and 46% (4–6). Although local guidelines may exist, there are at present no general recommendations issued by Swedish health authorities for the use of fluoride varnish in clinical practice.

In 1999, the Swedish Council on Technology Assessment in Health Care (SBU) commissioned a project group to undertake a systematic review of clinical trials and evaluation of the existing literature on caries preventive methods of fluoride varnish. The objective of this paper was to report the findings concerning the caries preventive effect of topical fluoride varnish applications applied by professionals in patients of various ages.

Methods

Literature search strategies

Relevant literature was identified in cooperation with an information specialist at SBU by searching in MEDLINE and the Cochrane library databases from 1966 to November 2001 with a later update in April 2003. The

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main search terms were 'fluoride varnish', 'fluoride lacquer', and 'dental caries'. A total of 302 records were originally identified and filters were then used to allow only for clinical trials resulting in 243 articles. These were printed as abstracts or full-text articles if the abstract was missing. In a second step, two examiners selected relevant records independently and the papers that were considered of interest for the project were ordered in full-text versions. The search was limited to randomized, controlled trials (RCT) or controlled clinical trials (CCT) of at least 2 years and with coronal caries increment in the permanent (ΔDMFS/T) and deciduous dentition (Δdmfs/t) as outcome measures. Only original papers were considered and double publications, interim reports, abstracts, letters, short communications, and chapters in textbooks were discarded. Articles in Swedish, Danish, Norwegian, English, German, French, Italian, and Spanish were accepted. If multiple reports of the same material had been published, only the last publication based on the longest follow-up period was included. During the evaluation process, reference lists were searched by hand. A total of 73 papers were selected and ordered in full text. At this stage, it was also decided not to include studies utilizing the split-mouth technique.

Evaluation of scientific papers and levels of evidence

The papers that met the inclusion criteria were subjected to a critical appraisal, carried out independently by at least two members of the project group. Data were extracted using a pilot-tested form and each paper was assessed with a score of A to C according to predetermined criteria for methodology and performance, as defined in Table 1. In the case of disagreement among the examiners, the paper was re-evaluated and discussed by the entire group until consensus was reached. If, for some reason, a selected paper was found irrelevant for the research question, the article was excluded. The primary measure of effect was the preventive fraction (PF) calculated as the difference in mean caries increment between the treatment and control groups expressed as a percentage of the increment in the control group. Statistically non-significant treatment effects were calculated as 'zero'. A P value <0.05 was considered statistically significant. Based on the evaluated literature, the final level of evidence was judged according to the protocol of the Swedish Council on Technology Assessment in Health Care, as described in Table 2 (7).

Table 1. Criteria for grading of assessed clinical trials

Grade A	Grade B	Grade C
High value as evidence	Moderate value as evidence	Low value as evidence
All criteria should be met	All criteria should be met	One or more of conditions below
Randomization by subject	Randomization by subject, school class, clinic, etc.	No or unclear randomization
Diagnostic reliability described	Diagnostic reliability described	Diagnostic reliability not described
Baseline value described	Baseline value described	Baseline value not described
Attrition explained	Attrition explained	Attrition not explained or
<10% per year	>10% per year	>10% per year
Blinded outcome assessment	Blinded outcome assessment	Non-blinded outcome assessment
Representative sample of population under study, results can be generalized	Population under study defined, results cannot fully be generalized	Population under study not defined, results cannot be generalized
Bias and confounders considered	Bias and confounders considered	Bias and confounders not considered

Results

Out of the 73 papers that were critically assessed, 24 studies involving more than 12,000 children were included for evaluation of evidence as presented in Table 3 (8–31). The discarded reports are listed in Table 4 along with the main reasons for exclusion (32–80). Studies of fluoride varnish treatments performed in adults were not included.

Table 2. Definitions of evidence level (7)

1. Strong evidence	At least two studies assessed with level 'A'
2. Moderate evidence	One study with level 'A' and at least two with level 'B'
3. Limited evidence	At least two studies with level 'B'
4. Inconclusive evidence	Less than two studies with level 'B'

Regarding levels 1–3, there should be no major study disclosing contra-dictionary results.

The calculated mean prevented fraction was 30.0% (0–69%) when professional fluoride varnish treatments in young permanent teeth were compared with placebo or untreated controls and 17.8% (0–52%) in comparison to other fluoride regimens. The average number of saved permanent tooth surfaces was 0.4 (0–1.6) per child and year when compared with controls and 0.3 (0–1.6) in favor of other fluoride regimens. None of the included trials had a grade A score. Of the 12 studies with placebo varnish or untreated controls, 6 were scored with 'B' (11, 15, 16, 24, 26, 27). The evidence for caries prevention by professional topical fluoride varnish applications was therefore rated as limited (evidence level 3) in permanent teeth in children and adolescents. In 9 studies fluoride varnish was compared with other fluoride regimens and 8 studies were scored with grade 'B'. Conflicting findings were reported and the majority (12, 13, 18, 22, 23) demonstrated non-significant results. Therefore, the evidence for a superior effect of fluoride varnishes compared to other fluoride regimens was inconclusive (evidence level 4). Three clinical trials were conducted in the primary dentition (10, 28, 30) and one was graded as 'B', with a significant outcome (30), suggesting inconclusive evidence (evidence level 4) for an anti-caries effect of fluoride varnish in the primary dentition.

Discussion

The systematic search for literature, data extraction, and subsequent quality assessment of included papers are now well-established measures for evidence-based medicine. However, the precise methods for the process differ between various organizations, and the methodology used in the present paper was adopted from the guidelines of the Swedish Council on Technology Assessment in Health Care. The efficacy of preventive regimens usually comes from results of clinical trials with varying entry criteria and different characteristics, including methods of randomization. In this analysis, the main reasons for exclusion were unclear clinical intervention design, a large number of drop-outs, uncontrolled compliance, and interaction or combination of other preventive measures. The decision to exclude the split-mouth design was motivated by the obvious carry-over risk with an uncontrolled fluoride distribution in the oral cavity. A notable finding was the rare use of placebo varnish in the performed studies. It should also be underlined that none of the included papers reported any serious adverse effects. Fluoride varnish treatments seemed safe, with few side effects when used routinely in dental practice (81, 82). The topical applications could be carried out by dental assistants and dental hygienists, in order to increase efficiency (83).

One of the aims of the present study was to evaluate the effect of fluoride varnish applications in patients of various ages. However, following the inclusion criteria no clinical trials were found on adult subjects and only three clinical trials with fluoride varnish were included in the primary dentition (10, 28, 30). Holm (30) found a significant caries reduction of 44% when preschool children were treated twice a year with fluoride varnish, but other studies have not been able to verify those results in preschool children with a low caries prevalence (10) or in a population with a high caries prevalence (28). Therefore, the evidence for an anti-caries effect of fluoride varnish in the preschool ages was inconclusive.

In the young permanent dentition, we found an average preventive fraction of 30% in the selected papers that was considerably less than that reported earlier by Marinho et al. (4). In their systematic review, the average caries preventive fraction was estimated at 46% (95% CI 30–63%). However, if the outcome measure was calculated from only the clinical trials graded as 'B' (11, 15, 16, 24, 26, 27), an average preventive fraction of 33% in young permanent teeth was obtained. This value was in fair agreement with the meta-analysis of Helfenstein & Steiner (6). The average number of saved tooth surfaces per year was 0.3–0.4 in the present review, which was comparable with previous reports (4). Our value was strongly influenced by the findings of one single study from India (21) that was conducted in a study group with a high level of caries increment. On the other hand, no significant association was found by Marinho et al. (4) between estimates of DMFS-prevented fractions and severity of baseline caries.

It is generally thought that professional fluoride varnish treatment is indicated as a caries preventive measure in subjects with a high caries risk. We included three clinical trials performed in high-risk patients and none of them demonstrated a significant caries reduction (8, 13, 19). The question of whether or not fluoride varnish treatments are superior to other fluoride supplements is an interesting one but contradictory results were displayed. Semi-annual varnish treatments were compared with fluoride rinses twice a month in four clinical trials graded as 'B' (20, 22, 23, 31), and two of these showed a statistically significant caries reduction (20, 31). Furthermore, no differences between fluoride varnish treatments twice or

Table 3. Clinical trials with fluoride varnish in the primary and permanent dentition in children and adolescents

First author	Year	Ref.	Intervention test	Intervention control/placebo	Study design	Subjects	Age year	Drop-outs, %	Effect ΔDMFS/T (Δdmfs/t), PF %	Saved tooth surfaces/year	Grading of studies
Primary dentition											
Petersson	1998	(10)	Fp 2/yr	Control	CCT	4,161	4–5	19	1.3/1.4; NS		C
Grodzka	1982	(28)	D 2x/yr	Control	CCT	321	3–4	25	6.4/6.7; NS		C
Holm	1979	(30)	D 2x/yr	Control	RCT	250	3	10	2.1/3.7; 44%	0.8	B
Young permanent dentition											
Zimmer	2001	(8)	Fp 4x/yr	Control	CCT	419	9–10	23	2.2/2.6; NS		C
Zimmer	1999	(9)	D 3x/yr	Control	CCT	269	7	28	0.9/1.4; 30%	0.13	C
Bravo	1997	(11)	D 2x/yr	Control	CCT	362	6–8	19	1.3/2.2; 37 %	0.45	B
Borutta	1991	(15)	BF 4x/yr	Placebo	RCT	400	12–14	10	1.9/2.9; 35%	0.5	B
Tewari	1991	(16)	D 2x/yr	Control	RCT	1,335	6–12	8	0.4/1.3; 69%	0.36	B
Lindquist	1989	(19)	D 4x/yr	Control	CCT	256	13	26	5.9/6.3; NS		C
Shobha	1987	(21)	D 4x/yr	Control	RCT	396	9–12	2	5.6/10.4; 46%	1.6	C
Clark	1985	(24)	D/Fp 2x/yr	Control	RCT	787	6–7	14	2.6/2.4/3.1; 19%	0.2	B
Holm	1984	(25)	D 2x/yr	Control	RCT	120	6	9	1.4/3.3; 56%	0.95	C
Modeér	1984	(26)	D 4x/yr	Control	RCT	236	14	18	1.2/2.0; 40 %	0.27	B
van Eck	1984	(27)	Fp 1x/yr	Control	RCT	649	10,12	9	8.4/8.8, NS		B
Schiöth	1981	(29)	D 2x/yr	Control	CCT	93	13–14	7	4.8/6.7; 28%	0.76	C
Young permanent dentition-comparison with other fluoride regimens											
Seppä	1995	(12)	D 2x/yr	APF-gel	RCT	254	12–13	12	3.1/3.6; NS		B
Seppä	1994	(13)	D 3x/yr	D 3x/yr	RCT	326	12–14	16	5.5/5.3; NS		B
Sköld	1994	(14)	D 3x/w/1x/yr	D 1x/yr	RCT	134	11	12	1.5/3.1; 52%	0.4	B
Petersson	1991	(17)	D 3x/w/1x/yr	D 2x/yr	CCT	160	11	5	1.3/2.4; 46%	0.36	C
Seppä	1990	(18)	D 2x/yr	D 4x/yr	RCT	254	9–13	7	2.9/2.9; NS		B
Seppä	1987	(20)	D/Fp 2x/yr	F-rinse/ 2x/m	CCT	204	10–13	9	6.7/9.0/9.9; 32%	1.6	B
Kirkegaard	1986	(22)	D 2x/yr	F-rinse/ 2x/m	CCT	426	9	42	3.0/2.8; NS		B
Bruun	1985	(23)	Fp 2x/yr	F-rinse/2 x/m	CCT	359	9–12?	16	3.5/3.3; NS		B
Koch	1979	(31)	D 2x/yr	F-rinse/2x/m	CCT	200	14		2.4/3.5; 30%	0.55	B

PF = preventive fraction; RCT = randomized controlled trial; CCT = controlled clinical trial; 1 BF = Bifluoride varnish; D = Duraphat varnish; Fp– = fluor protector varnish; F-rinse = fluoride rinsing; yr = year; m = month; d = day; NS = not significant. Grading A–B, see Table 1 for details.

Table 4. Excluded papers

Reason for exclusion	Reference no
Small study, selected subjects, teeth (split-mouth) or short duration	(35, 36, 62–67, 72–75, 77, 79)
Large drop-out, bias or confounders	(47, 68, 69, 76, 79)
No or clear, controlled or actual clinical intervention(s) or agent(s) or output measure	(34, 38, 40, 47, 49, 52, 53, 61, 80)
Interactive or combined preventive program(s), retrospective-, follow-up-, cross-sectional study	(50, 51, 55, 58, 71)
No or lack of original or relevant data, data in other study	(37, 44, 49, 70)
Thesis, meta-analysis, survey, review, post-intervention study, guideline, earlier-, repeated-, later study, other publication, or other reason	(3, 32, 33, 39, 41–43, 46, 48, 54, 56, 57, 59, 60, 65, 68–70, 78)

four times a year, fluoride gel (12), or fluoride varnishes with different fluoride concentrations (13, 18) were revealed. Two clinical trials graded as 'B' with an 'intensive fluoride varnish protocol' indicated an enhanced caries inhibiting effect on proximal tooth surfaces compared with fluoride varnish treatment once or twice per year (14, 17). It must, however, be noted that the comparative studies of fluoride varnish regimens and other fluoride supplements were all conducted in study populations with an almost mandatory and regular use of fluoride-containing toothpaste. In a systematic review of selected caries prevention methods, the strength of the evidence was judged to be *fair* for fluoride varnish, equal to that, efficacy has not been clearly established (84).

In conclusion, there was limited evidence (evidence level 3) that professional fluoride varnish treatment has a caries preventive effect in permanent teeth in children and adolescents. In primary dentition as well as for adults, the evidence for using fluoride varnish was inconclusive (evidence level 4). The evidence was also inconclusive for the efficacy of different fluoride varnishes as well as for various application frequencies.

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