Fluoride varnishes and caries incidence decrease in preschool children: a systematic review

Abstract

The objective of this systematic review was to evaluate whether conclusive evidence exists that the professional application of fluoride varnish decreases dental caries incidence in preschool children. We searched the electronic databases BBO, LILACS, MEDLINE and Cochrane to identify controlled clinical trials that evaluated the development of cavitated caries lesions in children up to six years of age. Two researchers performed a critical appraisal of the studies selected for inclusion. Five-hundred and thirteen articles were found but only eight met our inclusion criteria. Most of these eight studies were of poor methodological quality. They were also heterogeneous in relation to participants' previous caries experience, type of intervention administered to the control group, children's exposure to other sources of fluoride, and varnish application interval. The absolute differences between caries incidences in the control and test groups ranged from 0.30 to 1.64 and the preventive fractions varied from 5% to 63%. Fluoride varnish may be effective to decrease dental caries incidence in preschoolers, but more randomized clinical trials of better methodological quality are necessary to provide conclusive evidence in this respect.

Keywords: Fluoride. Dental caries. Primary Dentition. Preschool Child. Literature review.

Denise Martins Carvalho*

Master's Candidate in Dentistry, field of Pediatric Dentistry; Department of Preventive and Community Dentistry; School of Dentistry. State University of Rio de Janeiro (UERJ)

Mariana Salazar*

Master's in Dentistry, field of Pediatric Dentistry; Department of Preventive and Community Dentistry; School of Dentistry. State University of Rio de Janeiro (UERJ)

Branca Heloísa de Oliveira*

Doctor of Public Health. Associate Professor; Department of Preventive and Community Dentistry; School of Dentistry. State University of Rio de Janeiro (UERJ)

Evandro Silva Freire Coutinho**

Senior Researcher at the National School of Public Health at the Oswaldo Cruz Foundation (Fiocruz)

* Department of Preventive and Community Dentistry; School of Dentistry of the State University of Rio de Janeiro (UERJ). Address: Boulevard 28 de Setembro, 157 – Vila Isabel – Rio de Janeiro – RJ - CEP: 20551-030.

** National School of Public Health at the Oswaldo Cruz Foundation (Fiocruz). Address: Rua Leopoldo Bulhões, 1480 – Manguinhos – Rio de Janeiro – RJ – CEP: 21041-210.

Address for correspondence: Denise Martins Carvalho. Av. Prefeito Dulcídio Cardoso 3.333/bl.3/apto. 502 – Barra da Tijuca. Rio de Janeiro – RJ – 22.630-022. Tel. 21- 2434-1211/21-8884-4169. E-mail:denise_dentist@yahoo.com.br

INTRODUCTION

In Brazil, 27% of children ages 18 to 36 months have dental caries. At age five, 60% of the population experience dental caries and every child has, on average, three carious, missing or filled primary teeth.[1]

Dental caries is also one of the most common chronic diseases among North American children, with the prevalence of this condition equal to 28% for the two to five-year old age group. Untreated caries lesions occur twice as frequently in children of low socioeconomic levels, and may cause pain, affect how they look and interfere in a child's daily activities.[2]

The use of fluoride in water supplies, toothpastes and professionally applied by dentists is considered to be a key means of preventing dental caries.[3] Children 5 to 16 years of age who are exposed to fluorides regularly through their toothpaste, mouthwashes, gels or varnishes show 26% fewer carious, missing or filled permanent teeth, regardless of their having access to fluoridated water.[4] However, little information exists on how effective these products are in primary dentition.[3] The earliest fluoride varnishes were developed in the 1960's so that dentists could perform topical applications of fluoride in a way that provided more prolonged contact of this substance with dental enamel without increasing the time involved in a visit to the dentist. There are currently various commercial formulations of fluoride varnishes, such as: Duraphat® (5% NaF - Sodium fluoride), Duraflor® (5% NaF) and Fluor Protector® (1% Difluorsilano).[5]

Fluoride varnishes have been described as the most convenient means of having preschoolers use professionally-applied topical fluoride, based on the premise that they are easy to apply and well tolerated. The time required to apply the varnish varies from 1 to 4 minutes per patient, depending on the number of teeth present, and immediately following application the child can close his mouth because the varnish hardens on contact with saliva and forms a film that adheres to tooth surfaces. It is, however, recommended that patients avoid eating for two hours following application of the varnish and not brush their teeth that same day. This allows the varnish to remain in contact with the dental enamel for several hours.[3,5,6]

Given that dental caries still represent a public health problem that negatively affects the lives of many children and their families, and that the use of fluoride varnishes has been proposed as a means of preventing and limiting this disease in preschoolers, it is critical that dentists and health services planners be familiar with the true range of benefits that fluorides offer for primary teeth.

The objective of this systematic review is to assess whether there is evidence that professional application of fluoride varnish reduces the incidence of dental caries in primary dentition in children of up to six years of age.

METHODOLOGY

A systematic review of the literature was conducted following the methodology proposed in Higgins & Green.[7]

Inclusion criteria

Articles were included based on the following criteria:

- Type of study: randomized, controlled clinical trials or *quasi*-randomized studies.
- Type of population: children of up to six years of age, regardless of their caries experience at the start of the study (initial dmfs ≥ 0).
- Type of intervention: application of topical fluoride in the form of a varnish, to primary dentition, in any quantity, concentration or application interval, on surfaces selected or not, using any application technique.
- Outcome: incidence of caries, given the presence of a cavitated lesion (level of detection C2 - enamel caries, or C3

- dentine caries) in primary dentition (dmfs).
- Languages: English, Spanish or Portuguese;

It was also determined that if we found:

- More than one article that referred to the same study, the one with the longest follow-up period would be included.
- Studies assessing caries incidence in primary and permanent teeth, only those showing specific results for primary dentition would be included.

Exclusion criteria

Publications excluded were those that used the split-mouth design and intentionally administered other fluoride products, in addition to the varnish, to the test or control group (unequal co-intervention).

Search strategy

Bibliographic searches were conducted of the BBO and LILACS databases using the terms "fluoride varnish", "barnices fluorados" and "verniz fluoretado". The terms "fluoride varnish" and "dental caries" were used on the Medline database and, in order to increase the specificity of the search, the filters "humans" and "all child" were added. Next, a search was performed of the Cochrane Library, using the expressions "fluoride varnish", "dental caries" and "child". We sought to identify all articles related to the topic published up to December 2008. The titles and abstracts of the articles thus identified were independently evaluated by two researchers in order to verify whether they met the criteria for inclusion in the review. Using this process, in cases where it was not possible to determine whether or not an article should be included, it was called up and read in full. The final decision on which articles would be included in the review was made by consensus.

Method for evaluating the studies

The articles included in this review were analyzed according to the following aspects:

a) Type of population and sample size: age group, geographic location (country and city), information on access to a fluoridated water supply and number of participants;
b) Randomization and allocation concealment: description of the method used to assign the individuals to test and control groups.
c) Type of intervention used in the test group (type of product applied, concentration, periodicity, means of application) and in the control group (no treatment, placebo or water).
d) Comparability between the test and control groups at the baseline: description of the characteristics of the test and control groups in order to assess their equivalence at the start of the trial.
e) Masking: the means used to blind the examiners, the caregivers and the children receiving treatment.
f) Quality of outcome assessment: intra and inter-examiner reliability.
g) Duration of the study: duration of the follow-up period.
h) Attrition: number of dropouts and description of what caused them.
i) Results: increase in caries in the test and control groups, along with their respective standard deviations and preventive fraction.
1) Adherence to treatment and side effects: complaints from the subjects about side effects or discomfort caused by the treatment.

Jadad's scale[8] was used for qualitative ranking of the publications. This instrument was used to assign ratings to the studies, which varied from zero to five, based on the following criteria: method of randomization, method of blinding and description of withdrawals and dropouts.

RESULTS

Out of 513 articles identified in the bibliographic searches of the LILACS, BBO and Medline databases, only eight were

selected for inclusion in this review. In the Cochrane database, we found 10 full, systematic reviews and their bibliographic references were checked, but no new article was found that met our criteria for inclusion in this review. (Figure 1)

The controlled clinical trials included were conducted in four countries: China, the United States, Poland and Sweden. The oldest article was published some 30 years ago and the most recent one was published in 2006. In these clinical trials, 2,501 children, aged six months to five years, were assigned to the test (fluoride varnish) and control groups. The follow-up periods varied from 9 to 30 months and 75% of the studies covered a period of 24 months. (Table 1)

In terms of the concomitant exposure of participants to other sources of fluoride, in two studies it was reported that they were exposed to water supplies with adequate fluoride levels[9,10] and in three other studies[11,12,13] it was mentioned that most of the children regularly used fluoridated toothpaste. In one of the studies[12], 27% of the participants regularly used fluoride tablets and in another[14], the subjects used

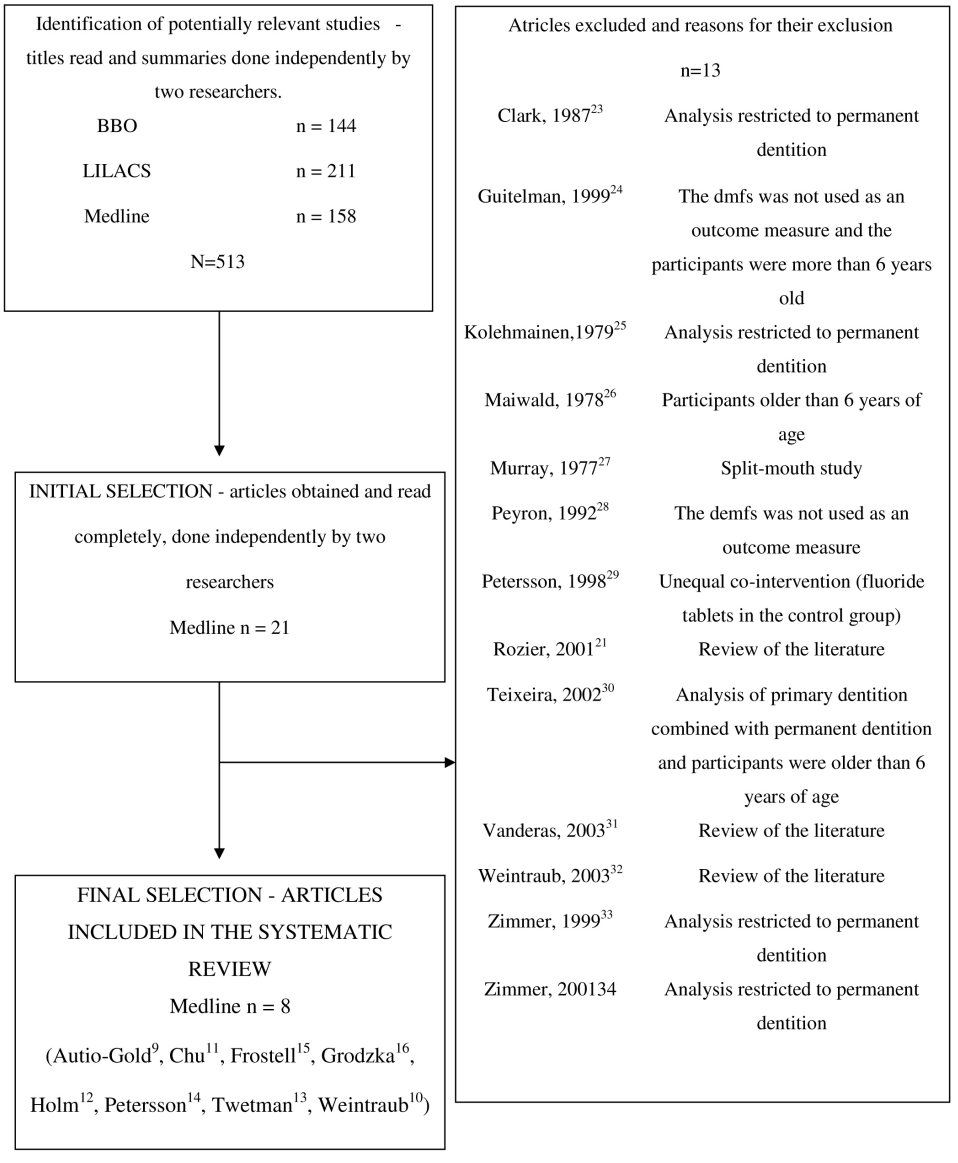

Figura 1 - Flowchart of the search strategy.

Table 1 - Characteristics of the clinical trials included.

Main author	Year/Country	Duration of the study (in months)	Randomi-zation	Age	Type of intervention Control group	Interval between varnish application (in months)	Number of participants at the end of the study		Widrawal (%)	Jadad clasification
							t	c		
Weintraud[10]	2006/EUA	24	Yes	6 a 44 months	Oral health counselling	6	70		46	4
						12	69	63		
Chu[11]	2002/China	30	No	3 a 5 years	Water	3	61	62	16	0
Autio-Gold[9]	2001/EUA	9	Yes	3 a 5 years	NT	4	59	83	22	2
Twetman[13]	1996/Sweden	24	No	4 a 5 years	NT	6	442	374	2	1
Frostell[15]	1991/Sweden	24	Yes	4 years	NT	6	113	93	0	2
Petersson[14]	1985/Sweden	24	No	3 years	Oral health counselling	6	88	85	4	0
Grodzka[16]	1982/Poland	24	No	3 a 4 years	NT	6	148	100	23	1
Holm[12]	1979/Sweden	24	No	3 years	NT	6	112	113	10	1

NT – No Treatment. This group was not submitted to any treatment. t – test group. c – control group

a low concentration fluoridated toothpaste (0.025% sodium fluoride - NaF) supplied by the researchers themselves.

Among commercially existing products, the fluoride varnish Duraphat® (5% NaF) was used in seven studies[9,10,11,12,14,15,16] and Fluor Protector® (1% Difluorsilano) was used in a single study[13]. No study used a placebo in the control group. In all of the clinical trials analyzed, except one[11], the varnish was applied to all of the primary teeth. In the one exception, only the caries lesions present on the upper incisors were treated.

In five studies[12,13,14,15,16], the application of fluoride varnish took place every six months, and in two[9,11], the interval between applications was four and three months, respectively. In the most recent study[10], there were two test groups: one received yearly applications and the other received 6-month applications.

Assessment of the quality of the clinical trials, using Jadad's scale[8], showed that most of them presented problems in terms of their design. (Table 1)

Of the works included, only two[10,15] were described as being double-blind, but in one[15], it was reported that they were unable to maintain the masking of parents and children throughout the entire study. Three studies[9,11,14] used masking of the examiners and one study[12] resorted to masking the children's parents. Two articles[13,16] made no mention of the use of any blinding strategy at all.

Intra-examiner and inter-examiner reliability were measured in three studies[9,10,11] and the Kappa coefficient values reported were in a range of 0.71 to 0.96.

Of the three studies[9,10,15] that mentioned having assigned participants to the test and control groups using a randomization process, only one[10] adequately described how the process was carried out. This study also adequately described how the assignment concealment was done. The others[9,15] reported that randomization was used, but did not describe how it was done. In two studies[13,16], the intervention was assigned by school or health center.

The rate of loss to follow-up was reported in all the studies, but many did not report the reasons why such losses occurred. The latter turned out to be related to change of address, lack of cooperation or refusal to take the treatment, and truancy. In one study[9], the researchers excluded six children from the control group because they required immediate restorative treatment, and in another[10], all participants who developed

caries lesions were excluded from the study in the course of the follow-up.

The initial oral health condition of the children in terms of caries experience was reported in all of the studies and the initial dmfs values varied from zero to 9.90 (Table 2). In one clinical trial[10], all of the subjects were caries-free at the beginning of the study and in the rest[9,11,12,13,14,15,16], the test and control groups were comparable in terms of caries experience.

Broad diversity was found between the trials in terms of caries increment in the test and control groups, with the average increase in the number of cavitated carious surfaces varying from 0.5 to 6.3 in the test group and from 1.4 to 6.7 in the control group. The differences between the test and control groups in the increment in cavitated carious lesions varied from 0.30 to 1.64. The prevented fraction, which is the difference in the caries increment between the test and control groups expressed as a percentage of the caries increment of the control group, varied from 5 to 63% and the highest values were found in the most recent studies. (Table 2) (Figure 2)

Examination of Table 2 suggests a major asymmetry in the distribution of the data on the mean number of carious, missing and filled dental surfaces (dmfs). Several means showed values less than twice the standard deviation[17], which ruled out the calculation of combined means using the weighted mean difference and the standardized mean difference. It was not possible to perform transformations to make the data more symmetrical since the raw data from the studies was not available. For the same reason, meta-regression was not used to assess sources of heterogeneity between the studies.

One study[11] mentioned that no side effects were observed, such as gingival tissue damage, and another[10] reported that no side effect associated with the intervention was

Table 2: Mean number of decayed, missing and filled surfaces (dmfs), initial and final, mean caries increment in test and control groups (standard deviation), *P*-values for the difference in caries increment between test and control groups and prevented fractions.

Author	Test group				Control group				*P*-value	Prevented fraction
	N	initial dmfs (SD)	final dmfs (SD)	mean caries increment (SD)	N	initial dmfs (SD)	final dmfs (SD)	mean caries increment (SD)		
Weintraub[10]	69[a]	0.00 (ni)	0.70 (1.80)	0.70 (ni)	63	0.00 (ni)	1.70 (3.10)	1.70 (ni)	p≤ 0.01	58%
	70[b]	0.00 (ni)	0.70 (2.10)	0.70 (ni)						
Chu[11]	61	4.71 (ni)	4.33 (ni)	0.70 (ni)	62	4.36 (ni)	4.24 (ni)	1.58 (ni)	p< 0.001	56%
Autio-Gold[9]	59	2.51 (4.02)	3.05 (4.25)	0.54 (ni)	83	2.58 (3.27)	4.05 (4.40)	1.47 (ni)	p< 0.05	63%
Twetman[13]	442	1.00 (2.36)	2.07 (ni)	1.07 (1.96)	374	0.95 (2.14)	2.48 (ni)	1.53 (2.55)	p< 0.01	30%
Frostell[15]	113	2.75 (ni)	5.01 (ni)	2.26 (ni)	93	3.34 (ni)	6.94 (ni)	3.60 (ni)	p <0.01	37%
Petersson[14]	88	0.90 (ni)	2.60 (ni)	1.70 (ni)	85	0.90 (ni)	2.90 (ni)	2.00 (ni)	ni	15%
Grodzka[16]	148	9.90 (7.96)	16.25 (ni)	6.35 (4.98)	100	9.70 (7.19)	16.41 (ni)	6.71 (5.22)	p>0.1	5%
Holm[12]	112	1.05 (2.34)	3.15 (4.12)	2.10 (2.75)	113	0.71 (1.62)	4.47 (5.29)	3.74 (4.62)	p <0.05	44%

SD– standard deviation, **ni-** not informed [a]-Annual application of the varnish [b]- Semiannual application of the varnish

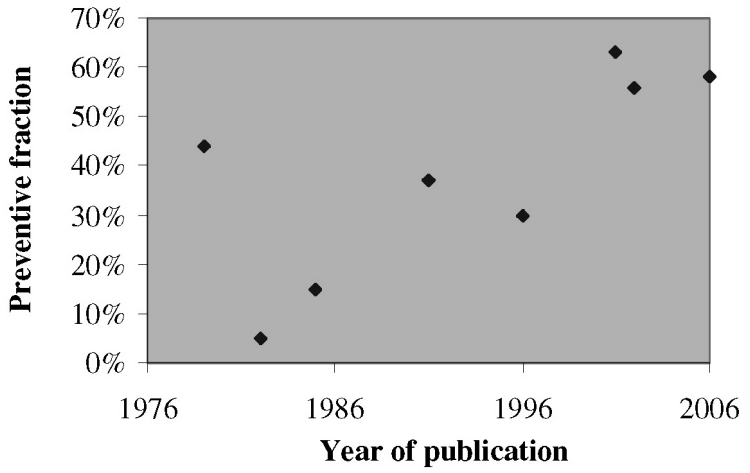

Figure 2 - Prevented fractions by year of publication of the study.

described by the children's caregivers.

DISCUSSION

Those controlled clinical studies that assessed the effectiveness of the fluoride varnish in primary dentition and were included in this review showed differences in relation to various aspects likely to affect their results, which make it difficult to compare their results. For example, there was no homogeneity between the studies concerning: previous caries experience of the subjects, the type of treatment administered to the control group, the children's exposure to other sources of fluoride and the interval between varnish applications. Nevertheless, all of the studies, except one[16], showed some benefit from using the varnish.

Of the eight studies, four[12,13,14,15] were conducted in Sweden and mainly involved population groups with little caries experience. Only two clinical trials, one conducted in China[11] and the other in Poland[16], studied children with a high prior disease experience. In those children with high dmfs at the outset of the study, the prevented fractions were 5%[16] and 56%[10], and in those where the initial dmfs values were low, preventive fractions of 15%[14] and 58%[10] were observed. It was not possible to conclude whether or not the magnitude of the fluoride varnish effect is related to previous caries experience.

An interesting finding is that no work used a placebo in the control group. In one study[11], the dental surfaces of the children in the control group were painted with water, and in another[10], these surfaces were rubbed with the back side of a gauze compress containing the varnish. Although one cannot rule out the possibility that these strategies may have worked, being considered by the parents and the children to be a form of treatment, it should be noted that they do not simulate the yellowish appearance of the teeth and the change in taste following application of the varnish.

As for the effect of the varnish in children who are regularly exposed to fluoride from other sources, the results suggest that having the fluoride varnish applied professionally provides additional protection against dental caries in populations that consume fluoridated water[9,10] and/or use fluoridated toothpaste[11,12,13]. From the clinical perspective, this information is quite relevant to the current situation in which children are routinely exposed to fluoridated water and/or use fluoridated toothpastes.

It was not possible to determine whether the fluoride concentration in the varnish affects its prophylactic capacity, since only one study[13] used the product FluorProtector® (1% Difluorsilano), while the others used Duraphat® (5% NaF), but the studies

that obtained the highest preventive fractions used the product with the highest concentration. It was also not possible to conclude what the ideal interval is for varnish applications, but in those studies that used intervals of four and three months between applications[9,11], the preventive fractions were higher than in five studies with 6-month applications[12,13,14,15,16]. Nevertheless, this conclusion should be evaluated with caution, given that only two studies used intervals of less than six months.

Despite professional application of fluoride varnish being cited as a safe method with broad acceptance by patients[3,5], this review was unable to assess whether these allegations are true since only two of the most recent studies[10,11] supplied data on the absence of side effects immediately after application. No study considered the possibility that using fluoride varnish might increase the risk of dental fluorosis.

The problems associated with the design of the clinical studies included in this review should also be taken into consideration.

The random assignment of subjects to the test and control groups through the use of proper randomization procedures was apparent in only one study[10]. Even so, that study suffered a high dropout rate and, at the end of the first year of follow-up intentionally excluded any children who had developed dental caries. This exclusion was unequal since it involved more participants in the control group than in each of the test groups (yearly and 6-month varnish application). It is thus not possible to guarantee that the dropouts and exclusions in question had no effect on the results. It is also relevant to highlight that, in two studies[13,16], assignment of the intervention was done by groups and not individuals, without this factor being taken into consideration in the statistical analyses.

It is interesting to note that, although Weintraub's study[10] presents the abovementioned limitations, it is cited as a basis for recommendations related to the professional use of fluorides for preventing caries in children as part of policies and practice guidelines such as those developed by the American Academy of Pediatric Dentistry[18], for example.

Other problems that may have contributed to compromising the internal validity of the studies were: the absence of masking[12,13,16] and calibration[12,13,14,15,16] of the examiners, and the lack of use of a placebo in the control group.[9,10,11,12,13,14,15,16]

Unfortunately, in the course of conducting the present review, we found only a small number of publications on the effect of fluoride varnish on the incidence of dental caries in primary teeth. An especially important finding for Brazilian professionals was the absence of controlled clinical studies using locally manufactured products, such as Fluorniz® (5.0% NaF) and Biophat® (6.0% NaF and 6.0% CaF - calcium fluoride), which generally cost less than the product found to be most often evaluated (Duraphat®).

It was also found that most of the publications do not meet the basic requirements for producing high-quality scientific evidence, which is shown by the fact that only one of the trials included obtained a rating higher than 2 according to the ranking criteria proposed by Jadad[8]. We also found impediments to performing metanalysis, such as asymmetry and the lack of information on standard deviations.

The conclusions from three systematic reviews[19,20,21] published up to December 2008 on the strength of available evidence for the preventive effects of fluoride varnishes in primary dentition do not match up. Marinho et al.[19] suggested that professional application of fluoride varnish might offer a substantial benefit for primary dentition. However, Petersson et al.[20] and Rozier[21] state that there is no conclusive evidence that treatment with fluoride varnish reduces caries incidence in primary dentition. In contrast, the American Academy of Pediatric Dentistry[18] recommends professional use of fluoride varnish to prevent or reverse the demineralization of dental enamel in children with a moderate to high risk of dental caries. Finally, in addition to there being

no evidence on the magnitude of benefit offered by the varnish in terms of individual caries risk, the efficacy of the disease control strategy based on individual risk has been the subject of criticism. The idea underlying the high-risk approach is that by tracking the most susceptible individuals, prevention can be directed toward those who will benefit the most, thus promoting the optimal use of available resources. However, for this to occur, there must be valid and reliable ways to estimate individual risk and it must be the case that a small number of individuals with a high risk of disease is responsible for a substantially higher number of carious lesions rather than a large number of individuals with a low risk of disease. Thus, currently, from a public health point of view, population and population-targeted strategies would seem to be more appropriate as an approach to dealing with dental caries. In the population-risk strategy, actions target the entire population and in the population-targeted strategy, groups of more vulnerable individuals constitute the targets of the actions[22]. In the present review, we found that the highest preventive fractions were obtained in the most recent studies, which were conducted with population groups more prone to disease and regularly exposed to fluorides through toothpastes or public water supplies, which suggests that the professional use of fluoride varnish may be useful when one opts for a caries control strategy based on a population-targeted strategy. Nevertheless, caution should be taken before reaching a positive conclusion on implementing the use of this measure in public health since, in absolute terms, each child treated with the varnish had, on average, one less carious dental surface than a child not treated. Furthermore, there is still a lack of data on the possible side effects of fluoride varnishes.

CONCLUSION

The results of the controlled clinical trials published in the research literature and included in the present review suggest that fluoride varnish is capable of reducing the incidence of caries in the primary teeth of children six years of age or younger, but provide no conclusive scientific evidence in this respect. It is recommended that well-designed, randomized clinical trials be conducted along this line of investigation. Such clinical trials should seek to assess: whether there is an ideal interval for applying the varnishes - taking into consideration the cost-benefit ratio, whether the magnitude of the beneficial effect of fluoride varnish is associated with prior caries experience and what magnitude of additional benefit is derived from the application of fluoride varnish in populations exposed to fluoridated water and toothpastes. Moreover, it is important to investigate whether fluoride varnishes are, in fact, well accepted by children and their parents, and whether or not they cause side effects.

Collaborators

Denise Martins Carvalho and Branca Heloisa de Oliveira performed the bibliographic searches and article selection. All of the authors participated in the critical evaluation of the publications included in the review and in writing the article.

References

1. BRASIL. Ministério da Saúde. Coordenação Nacional de Saúde Bucal. Projeto SB Brasil 2003. *Condições de saúde bucal da população brasileira. Resultados prin*cipais. Brasília; 2004.

2. National Center for Caries Disease Prevention and Health Promotion. *Oral Health Resources – Children's Oral Health Overview*; 2006.

3. National Institutes of Health (NIH). Consensus Development Conference on Diagnosis and Management of Dental Caries Throughout Life. Bethesda, MD, March 26-28, 2001. Conference Papers. *J Dent Educ* 2001; 65(10): 935-1179.

4. Marinho VC, Higgins JP, Sheiham A, Logan S. Fluoride toothpastes for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2003(1): CD002278.

5. Beltran-Aguilar ED, Goldstein JW, Lockwood SA. Fluoride varnishes. A review of their clinical use, cariostatic mechanism, efficacy and safety. J Am Dent Assoc 2000; 131(5): 589-96.

6. Petersson LG, Twetman S, Pakhomov GN. *Fluoride varnish for community-based caries prevention in children.* Geneva: WHO; 1997.

7. Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.1 [updated September 2008]. The Cochrane Collaboration; 2008. Available from www.cochrane-handbook.org.

8. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; 17(1): 1-12.

9. Autio-Gold JT, Courts F. Assessing the effect of fluoride varnish on early enamel carious lesions in the primary dentition. *J Am Dent Assoc* 2001; 132(9): 1247-53; quiz 317-8.

10. Weintraub JA, Ramos-Gomez F, Jue B, Shain S, Hoover CI, Featherstone JD et al. Fluoride varnish efficacy in preventing early childhood caries. *J Dent Res* 2006; 85(2): 172-6.

11. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. *J Dent Res* 2002; 81(11): 767-70.

12. Holm AK. Effect of fluoride varnish (Duraphat) in preschool children. *Community Dent Oral Epidemiol* 1979; 7(5): 241-5.

13. Twetman S, Petersson LG, Pakhomov GN. Caries incidence in relation to salivary mutans streptococci and fluoride varnish applications in preschool children from low- and optimal-fluoride areas. *Caries Res* 1996; 30(5): 347-53.

14. Petersson LG, Koch G, Rasmusson CG, Stanke H. Effect on caries of different fluoride prophylactic programs in preschool children. A two year clinical study. *Swed Dent J* 1985; 9(3): 97-104.

15. Frostell G, Birkhed D, Edwardsson S, Goldberg P, Petersson LG, Priwe C et al. Effect of partial substitution of invert sugar for sucrose in combination with Duraphat treatment on caries development in preschool children: the Malmo Study. *Caries Res* 1991; 25(4): 304-10.

16. Grodzka K, Augustyniak L, Budny J, Czarnocka K, Janicha J, Mlosek K et al. Caries increment in primary teeth after application of Duraphat fluoride varnish. *Community Dent Oral Epidemiol* 1982; 10(2): 55-9.

17. Altman DG, Bland JM. Detecting skewness from summary information. *BMJ* 1996; 313: 1200.

18. American Academy of Pediatric Dentistry. Policy on use of fluoride. *Pediatric Dentistry. Reference manual* 2009/2010; 31(6): 34-5.

19. Marinho VC, Higgins JP, Logan S, Sheiham A. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2002(3): CD002279.

20. Petersson LG, Twetman S, Dahlgren H, Norlund A, Holm AK, Nordenram G et al. Professional fluoride varnish treatment for caries control: a systematic review of clinical trials. *Acta odont scand* 2004; 62(3): 170-6.

21. Rozier RG. Effectiveness of methods used by dental professionals for the primary prevention of dental caries. *J Dent Educ* 2001; 65(10): 1063-72.

22. Batchelor P, Sheiham A. The limitations of a "high-risk" approach for the prevention of dental caries. *Community Dentistry and Oral Epidemiology* 2002; 30: 302-12.

23. Clark DC, Stamm JW, Tessier C, Robert G. The final results of the Sherbrooke-Lac Megantic fluoride varnish study. *J Canad Dent Ass* 1987; 53(12): 919-22.

24. Guitelman I, Sebelli P, Delgado S, Medina E, Samuelian C, Ciccorossi E. Efectividad de dos barnices en la remineralización de la mancha blanca. *Bol Assoc Argent Odontol Ninos* 1999; 28(3): 11-3.

25. Kolehmainen L, Kerosuo E. The clinical effect of application of a urethane lacquer containing silane fluorine. A one-year study. *Proc Finn Dent Soc*1979; 75(4): 69-71.

26. Maiwald HJ, Ruiz MS, Despaigne BF. Fluorine varnish application study. Experience after four and half years. *Rev Cubana Estomatol* 1978; 15(3): 109-14.

27. Murray JJ, Winter GB, Hurst CP. Duraphat fluoride varnish. A 2-year clinical trial in 5-year-old children. *Br Dent J* 1977; 143(1): 11-7.

28. Peyron M, Matsson L, Birkhed D. Progression of approximal caries in primary molars and the effect of Duraphat treatment. *Scand J Dent Res* 1992; 100(6): 314-8.

29. Petersson LG, Twetman S, Pakhomov GN. The efficiency of semiannual silane fluoride varnish applications: a two-year clinical study in preschool children. *J Publ Hlth Dent* 1998; 58(1):57-60.

30. Teixeira RTS, Brauna APVS, Pacheco CMF, Aoki MS, Gomes MF. Efeitos do verniz com flúor Duraphat na prevenção da cárie em pacientes com paralisia cerebral. *Rev Assoc Paul Cir Dent* 2002; 56(1): 57-61.

31. Vanderas AP, Skamnakis J. Effectiveness of preventive treatment on approximal caries progression in posterior primary and permanent teeth: a review. *Eur J Paediatr Dent* 2003; 4(1): 9-15.

32. Weintraub JA. Fluoride varnish for caries prevention: comparisons with other preventive agents and recommendations for a community-based protocol. *Spec Care Dentist* 2003; 23(5): 180-6.

33. Zimmer S, Robke FJ, Roulet JF. Caries prevention with fluoride varnish in a socially deprived community. *Community Dent Oral Epidemiol* 1999; 27(2): 103-8.

34. Zimmer S, Bizhang M, Seemann R, Witzke S, Roulet JF. The effect of a preventive program, including the application of low-concentration fluoride varnish, on caries control in high-risk children. *Clin Oral Investig* 2001; 5(1): 40-4.