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Effectiveness of fluoride varnish four times a year in preventing caries in the primary dentition: A 2 year randomized controlled trial

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Objectives: To test the effectiveness of fluoride varnish in preventing caries in early childhood in children at high risk of caries. **Basic research design**: Randomized controlled trial. **Participants:** 504 participants, with mean age of 21 months at baseline randomly allocated into a test and a control group. 427 children remained in the study after two years. **Intervention:** Fluoride varnish applied four times a year, every three months. The intervention lasted for two years. **Main outcome measures**: Dental status was recorded based on the International Caries Detection and Assessment System (ICADS). **Results:** Mean dmfs was similar in the control and test groups at baseline (1.0 and 1.2 respectively) but was significantly different (10.1 and 5.2, $p < 0.001$, ANOVA) at endpoint. The proportion caries free in the two groups was 40% and 69.4% after two years. **Conclusions**: The application of fluoride varnish four times a year prevented the incidence and reduced the severity of caries in pre-school children. Trial registration number: DRKS00013980.

Keywords: *preschool children, early childhood caries, fluoride varnish, prevention*

Introduction

Caries is a disease that can generally be prevented. The time when preventive measures are taken is very important. The possibility of preventing dental caries may reach 96% when the application of preventive measures begins during the first year of life and decreases to 72% if they are applied after the second year (Melhado *et al*., 2003).

The appearance of caries decreases with increased fluoride exposure whether measured by dose or number of agents applied (Marinho *et al*., 2004; Walsh *et al*., 2019). It is generally considered that the preventive effect of fluoride is higher if applied before the initiation of dental caries (Association of State and Territorial Dental Directors, 2007). Recently the fluoride effect paradigm has changed from systemic to local action due to the biological effect on the enzymatic system of the cariogenic bacteria. The topical application of fluoride after tooth eruption has the highest impact in caries prevention (Hellwig, 2004).

One successful way of local application of fluoride is the use of varnish (F-varnish) (Weintraub *et al*., 2006; Adair *et al*., 2006). The caries-preventive effects of fluoride result from its topical contact with enamel and through its antibacterial actions. Through the varnish the fluoride concentration increases in the outermost and deeper layers of the enamel (Adair *et al*., 2006). Many studies have tested the effectiveness of F-varnish on caries prevention in permanent teeth in school-age children, with the benefits being very positive, but the evidence about the effectiveness of F-varnish in primary teeth is insufficient (Weintraub *et al*., 2006). Repeated Cochrane Reviews suggest that the caries preventive fraction of F-varnish is 43% (95% CI 30% to 57%) for the permanent dentition and 37% (95% CI 24% to 51%) for the deciduous dentition (Marinho *et al*., 2002; 2013). Furthermore, several other studies confirm that F-varnish is effective in reducing caries in the primary dentition of children with a high caries risk (Marinho *et al*., 2002; Petersson *et al*., 2004; Weintraub *et al*., 2006; Marinho *et al*., 2013).

According to Weintraub (2006), more frequent varnish applications were more beneficial and one application was preferable to none. Holve (2008) also confirmed that four applications a year is more beneficial for children at high-risk of caries compared to none or three. The Nevada State Health Division (2008) concluded that F-varnish should be applied at three-month intervals for high-risk children and at six-month intervals for children who are not at high risk. The American Dental Association (ADA, 2006) recommended that children with high caries risk can benefit more if F-varnish is applied at intervals every three months, while moderate risk children should have F-varnish applied every 6 months, even though the optimal number of fluoride applications has not yet been established (Gomez *et al*., 2010).

Dental caries is a great concern for the oral health of Kosovar children. Its prevalence in pre-school children (2 to 6 years), in 2005, was 91.2%, increasing to 94.4% in school-aged children. The prevalence of early childhood caries is 17.6%, which is considered very high when compared to 5% in developed countries (Begzati *et al*., 2011). Therefore, the aim of this study was to test the effectiveness of fluoride varnish application four times a year in preventing caries in a community of young children (aged 6-30 months) at high risk for caries. As a developing country such a contemporary measure has never before been tested or implemented, despite the fact that the children belong to the fluoride-deficient community.

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Methods

This randomized clinical trial was approved by the Pristina University Ethics Committee (Ethic Committee Medical Faculty, University of Pristina, Ref.Nr.1851). The project took place in eleven Pristina preschool institutions. Institutions were selected in different parts of the city to cover all neighbourhoods. Both public and private institutions were involved to reduce sampling bias with respect to socio-economic status. The criteria for inclusion in the study was the child's age (6 to 30 months) and parental permission for their child to participate.

Sample Size: The data (Begzati *et al*., 2010; 2011) available for power calculations were insufficient as dmft was used instead of dmfs and no variance (SD) data were provided. In addition, no data were specified for children under three years old. We therefore estimated mean dmfs and SD, based on Sheiham (2010) and Jarvinen (1983). The previous studies of the oral health of Kosovar children (Begzati *et al*., 2010; 2011) did not use standard caries experience criteria when presenting dmft data. The initial and dentinal stages were summarized to express the d component of dmft, whereas modern systems such as the International Caries Detection and Assessment System (ICDAS) include pre-cavitated enamel stages. We therefore estimated, for comparison reasons, the clinical stages of these publications with the stages of Lafiti-Xhemajli (2013) using the ICDAS classification. We assumed that Begzati and colleagues included cavitated enamel within their dentinal caries estimates. We used the dmft trends from Begzati and colleagues for the expected baseline values in 1-2-year old participants, but used the endpoint estimates from the ICDAS values reported by Lafiti-Xhemajli (2013) since they used a SD and an optimal method. We set the meaningful difference for dmfs at three surfaces and a difference in caries prevalence at 30%, based on the preventive fraction for F-varnish estimated by Marinho and colleagues (2002).

Thus, setting the power at 90%, with an alpha (a) of 5% and using the data from the aforementioned studies, the required sample size was 250 per group. The anticipated loss to follow-up was 20%, so a sample size target of 600 participants was set to enable us to have the required sample at study completion. After recruitment started it became evident that it would be impossible to recruit more than 504 participants.

A total of 504 children aged 6 to 30 months were included at baseline. Participants were allocated into the test (N=255) and control group (N=249). Children whose parents agreed and signed the consent form, progressed to the next stage. Participants were randomly assigned to one of the groups: test or control by the statistician using randomization lists generated by the computer. Randomization occurred within each centre to ensure similar numbers of participants in the two groups.

During the intervention phase two pediatric dentists applied the F-varnish but baseline and endpoint recordings of dental status were by dentists masked to participants' group allocation.

Participants were examined at baseline and follow up using a mirror and a non-sharp dental probe under artificial lighting in the knee-to-knee position. Data were recorded using the ICADS-index. The examinations were conducted by the same examiner/dentist who was trained by a core member of the ICDAS Coordinating committee, in 2012. The ICDAS (2009) codes for coronal caries are: 0-sound, caries free surface; 1-first visual change in enamel; 2-distinct visual change in enamel; 3-localized enamel breakdown; 4-underlying dark shadow from dentin; 5-distinct cavity with visible dentin and 6-extensive distinct cavity with visible dentin.

After baseline examination and every three months thereafter for two years, F-varnish was applied to participants in the test group. Before each application the teeth were wiped cleaned and dried with a gauze pad and F-varnish (Fluor Protector S, Ivoclar Vivadent) was applied to all tooth surfaces with a brush. The children's parents were advised not to give the children anything to eat or drink for at least one hour afterwards. Participants in the control group had no F-varnish applied, unless their parents were advised for their child's basic oral health care.

Three months after the last application of F-varnish, dental status was recorded in all children in both the control and the test groups.

Descriptive statistics were calculated for all variables using SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA). ANOVA, Chi square and Fisher's Exact tests were used for bivariate analyses.

Results

Of the 504 children recruited, 77 (15.5%) were lost from the research for various reasons (changing residence, lack of further attendance at the preschool institute or others) (Figure 1). The average age of children at baseline was 21 months, while at the endpoint it was 45 months (about 4 years).

Mean baseline dmfs in the control group was 1.0 (sd 2.2) and 1.2 (3.5) in the test group (Table 1).

After applying the F-varnish four times a year for 24 months, the control group had on average 4.9 more carious surfaces than the test group (10.1 (12.9) and 5.2 (10.5) respectively, $p<0.001$, ANOVA) representing a 49% reduction in dmfs scores between the groups (Table 1).

There were also significant differences in the presence of all types of ICDAS lesions (01-06) between the test and control groups. The same structure was found in all others type of lesions, ranging from initial (01-02) to the deep lesions (05-06). The average of the extracted and filled tooth surfaces was 0.3 (0.7) for the test and 0.8 (1.2) for the control group (Table 2).

At endpoint the proportion of participants' who were caries free was 42.6% in the control group, while in the test group it was 69.4%. Differences were also shown in the prevalence of the different lesions. The presence of all types of ICDAS lesions (01-02, 03-04 & 05-06) was significantly higher in the control group than the test group ($p<0.001$). An absence of initial lesions (01-02) was manifested by 43.0% for the control group and 70.0% for the test group. While the absence of deep lesions (05-06) was manifested with 52.3% for the control and 78.0% for the test group (Table 3).

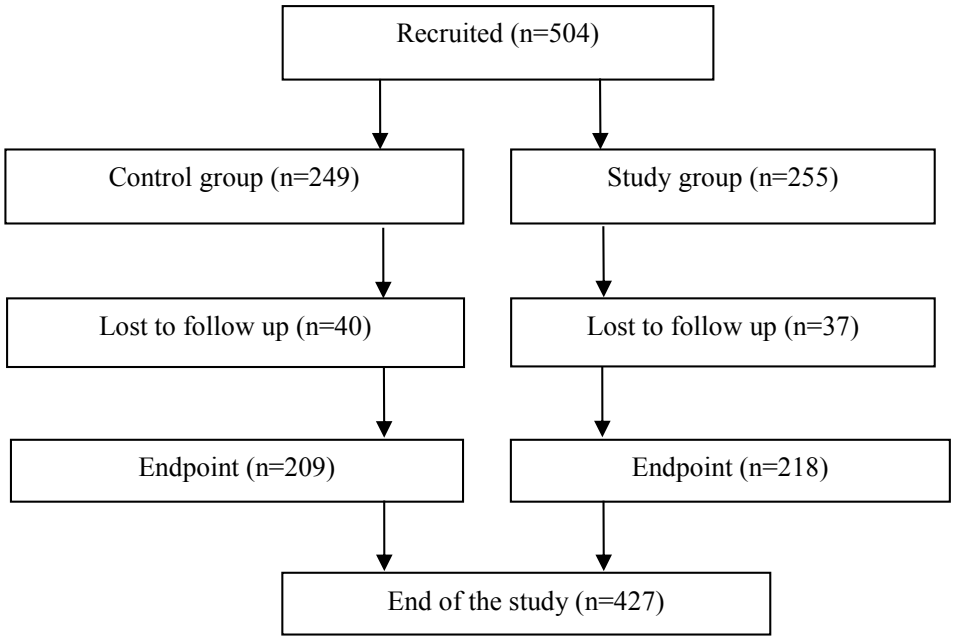

Figure 1. *Trial Profile*

Table 1. Decayed, missing and filled surfaces at baseline and 2 year follow up

	Test Mean (sd)	**Control** Mean (sd)	*P* (ANOVA)
Baseline	1.2 (3.5)	1.0 (2.2)	
Endpoint	5.2 (10.5)	10.1 (12.9)	<0.001

Table 2. Distribution of ICDAS lesions in two groups

ICDAS lesions	**Control group** Mean (sd)	**Test group** Mean (sd)	**Reduction of caries surfaces**	***P* (ANOVA)**
All lesions from 01 to 06/dmfs≠0	10.1 (12.9)	5.2 (10.5)	4.9	
First visual/distinct change in enamel (01-02)	2.8 (3.3)	1.3 (2.5)	1.5	< 0.001
Enamel breakdown/ Underlying dentine shadow (03-04)	7.0 (10.0)	3.5 (7.8)	3.5	
Distinct cavity/extensive distinct cavity with visible dentin (05-06)	3.3 (6.4)	1.7 (5.4)	1.6	
Filling/Missing	0.8 (1.2)	0.3 (0.7)	0.5	< 0.001

Table 3. Prevalence of lesions by ICDAS category in the control and test groups

Variable		*Control* %	*Test* %	*All*
Without lesions (01-06)	Baseline	80.3	79.6	80.0
dmfs = 0	Endpoint	40.0	69.4	56.2
Without lesions and first visual/distinct change in enamel (01-02 lesions)		42.0	70.0	57.0
Without enamel breakdown/ Underlying dentine shadow (03-04 lesions)		43.5	72.9	58.5
Without distinct cavity/ extensive distinct cavity with visible dentin (05-06 lesions)		52.3	78.0	65.3

Discussion

In this study F-varnish applied four times per year reduced the incidence and severity of caries among pre-school children at high risk of caries.

Our findings support the use of F-varnish to prevent early childhood caries and reduce the caries increment in very young children with a high caries risk. The prevention and reduction of caries in the permanent dentition after F-varnish application has been demonstrated in numerous studies. These studies conducted over several decades have shown that the reduction of caries in the permanent dentition by using F-varnishes, ranges from approximately 20-70% (De Bryne *et al*., 1987; Eugenio *et al*., 2000; Marinho *et al*., 2013).

Fewer studies can be found testing F-varnish in the primary dentition and their results indicate differing effectiveness depending on the type of study, whether they were randomized and the age of the children. Eugenio and colleagues (2000) reported an 8% caries reduction among high caries risk children aged 12 to 24 months. A Canadian study provides different results among preschool children, with an 18% reduction for high caries risk children and a 25% reduction overall (Lawrence *et al*., 2008). Marinho and colleagues' (2013) meta-analysis suggested that the caries preventive fraction was 37% (95% CI 24% to 51%). In a study by Weintraub (2006) this value ranged from 52 to 92%, which supports the use of fluoride varnish to prevent early childhood caries and reduce the caries increment in children 1.8 years old. In our study, the caries preventive fraction was 49%. Similar to the study by Weintraub (2006), we also found a significant decrease in caries experience with and without pre-cavitated lesions in the test group compared to the control group.

We have shown a caries increment of 9 surfaces in the control group and only 4.8 for the test group over two years. Although there are insufficient data on the epidemiology of caries in young children in our country, Begzati and colleagues (2010) reported a very high incidence of caries in young children with a rapid progression. The mean dmft in 2-year old children was reported to be 6.47, which increased 12.8 in 6-year-olds. These reports used other indices such as dmft but did not analyse the number of tooth surfaces with caries. Therefore, our results with an incremental change in the number of surfaces with caries from 1.0 to 10.0 in a group without treatment within two years, support earlier studies and once again show the poor oral health of our children. However, these results show that this condition can be improved and that our children can benefit from the application of F-varnish.

The Fluoride varnish efficacy in our study may be due to the young age of the children and the frequent, four times a year application. Regarding the frequency of F-varnish application, Holve (2008) found that children at high caries risk aged 9-30 months benefitted more from four treatments per year, with overall caries reduced by 35%. Children with four or more fluoride varnish treatments had 15.5 dmfs versus children with 0-3 treatments who had a mean dmfs of 23.4, which presents higher dmfs values than in our study where the fluoride varnish treatment group had a 5.2 dmfs versus the zero treatments group who had a mean dmfs of 10.1.

Our study has some limitations as the frequency of exposure to cariogenic foods, the home oral hygiene and fluoride exposure of the children were not recorded. Whilst we were not able to recruit our intended incept cohort, this was mitigated to some extent by the lower loss to follow up (15%) than was anticipated. Furthermore, the positive findings of the study indicate that the sample size was adequate.

Conclusion

This trial showed that use of fluoride varnish applications was associated with a preventive (fraction of 49%) reduction in caries, compared to the control group. Caries reduction was manifest in terms of incidence and severity of disease. Our findings suggest that fluoride varnish should be given to children who are at an increased risk of early childhood caries.

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