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Original Article

Adverse Effects of Application of Fluoride Varnish versus Resin-Based Fissure Sealant in Newly Erupted Permanent Molars in Group of Egyptian Children: A Randomized Clinical Trial

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Abstract

Aim: This study aims to determine the adverse effects of fluoride varnish (FV) versus resin-basedfissure sealant (RBS) required to prevent caries in newly erupted first permanent molars in a group of Egyptian children.
Subjects and methods: This is a randomized clinical trial with two arms, parallel groups, and allocation-blinded. The total number of participants was calculated as 182 children. The calculated sample size was divided equally among two postgraduate students; this part included 91 participants, with ages ranging from 6 to 8 years. The participants were randomly assigned to one of two groups: RBS as a control and FV as an intervention. (45) children were in the FV group, and (46) children were in the RBS group. Of the 91 children, only 89 completed the follow-up at 6 and 12 months. The findings measured were the adverse effects of FV & RBS using a custom-made questionnaire for the parent and visually at the clinic.
Results: In this study, 91 children were randomly allocated to both tested groups. There were 28 (56.0%) males and 18 (43.9%) females in the FV group, while in the FS group, there were 22 (44.0%) males and 23(56.1%) females. The mean age in the FV was (7.00±1.12) years, while in FS it was (7.29±1.42) years. There was no significant difference between both groups regarding demographic data ($p>0.05$). The results showed that there were no adverse effects in both groups.
Conclusion: Based on the 12-month results The two preventive methods had no adverse effects.

Keywords: : Fluoride Varnish, Children, Fissure Sealant, Adverse effects

I. INTRODUCTION

Dental caries, often referred, to as tooth decay is an infectious disease distinguished by the destruction of dental enamel. Caries is caused by a complex combination of cariogenic acid, fermentable carbohydrates, and a multitude of other dietary, social, behavioral, genetic, and cultural factors. Caries is a risk for children when their first tooth starts to erupt, which usually occurs at 6 months. Early childhood caries (ECC) is defined as the presence of one or more decayed primary teeth (cavities) of children under the age of 5 (Arroyo Buenestado & Ribas-Pérez, 2023).

The importance of first permanent molars (FPMs) in caries prevention cannot be overstated (Wright *et al.*, 2016). FPMs decay accounts for the majority of the decayed,

missing, and filled tooth index (DMFT). Caries of FPMs is not only common, but it also causes a significant disease burden. The keys to establishing persistent occlusion are FPMs. Severe FPMs caries frequently results in discomfort and infection, as well as a reduction in nutritional intake and malocclusion (Li *et al.*, 2020).

Current raises in caries prevalence in children, particularly among many minorities and low-income countries, have highlighted the necessity for early application of dental homes and simple, easy, effective preventive programs for oral care for any young children as aspects of a medical prevention management model of disease (Youssefi and Afroughi, 2020). A significant rate of dental caries in mixed dentition was related to the sociodemographic characteristics of children. Has highlighted the necessity to develop and execute preventative, therapeutic, and educational programs for reducing dental caries at the individual, family, and educational levels (Ramos-Gomez *et al.*, 2010).

Preventive measures include Fissure sealant (FS) and Fluoride varnish (FV). FS is a one- time application of a coating consisting of an adhesive substance such as glass ionomer or resin which is applied to the tooth surface. It protects the teeth by sealing off the grooves that tend to accumulate food, on the other hand, FV is a sticky paste that includes quantities of fluoride that increase tooth resistance to caries. Application of fluoride varnishes should be done by a dentist 2to 4 times a year (Kashbour *et al.*, 2020).

The current trial aims to investigate the adverse effects of resin sealants versus fluoride varnish for the prevention of dental caries on newly erupted permanent molars.

II. SUBJECTS AND METHODS

Our research was a randomized clinical trial (RCT): allocation-blinded, two-arm, parallel- group trial. As the fissure sealant was apparent to the patient, parent, operator (investigator), and outcome assessor (supervisor), no one was blinded; only the statisticians could be blinded. This study was performed in the outpatient diagnostic clinic of Pediatric Dentistry and Dental Public Health Department within the Faculty of Dentistry at Cairo University.

A power analysis was designed to have adequate power to apply a one-sided statistical test of the null hypothesis that both treatments have the same clinical effect but fluoride varnish is more cost-effective. By adopting an alpha (α) level of 0.05 (5%), a beta (β) level of 0.20 (20%), i.e. power =80%, and an effect size of (d =0.459) calculated based on the results of (Arruda, Airton O., et al.), the predicted sample size (n) was found to be a total of (152) children, i.e. (78) children per group. The sample size was increased by 20% to account for possible dropouts, for a total of 182 children. The calculated sample size was divided equally among two postgraduate students So in this trial (part 2), 91 children were enrolled in this study. Sample size calculation was performed using PS software version 3.0 for Windows.

The Research Ethics Committee at the Faculty of Dentistry, Cairo University, granted ethical approval, approval number(6521). This study was registered on clinical trial.gov with the identifier:NCT04793256. The investigator discussed the trial with the legal guardian of each participating child, Verbal permission was taken orally from participating child, and written informed consent was taken from the legal guardian of each participating child willing to participate in the trial.

The total number of participants was 91 participants selected from the outpatient clinic. The participants were randomized on a 1: 1 allocation ratio to receive one of the following interventions: RBS OR FV. participants that were included in the trial were randomly assigned one of the experimental groups using closed white opaque envelopes (simple randomization 1:1 ratio), by randomly selecting an envelope for each patient after their enrollment after shuffling the envelopes. Four-folded numbered papers were packed in opaque sealed envelopes to be dragged by the patients. The written number on the paper assigned the patient to either the experimental or control group according to the randomization table.

Inclusion criteria included: newly fully erupted FPMs in children aged 6–8, healthy children with no physical or mental disorders, and no sex predilection was determined. Exclusion criteria involved: children with dental decay in enamel, a history of pain or swelling, or parents refusing their children's participation in the trial.

Clinical procedures

In both groups, prior to commencing the procedures, the surface of FPMs was cleaned using a brush or cotton, The FPMS was isolated using a cotton roll and a saliva ejector to control moisture. In the FS group, the procedure started with the application of etchant for 30 seconds, followed by rinsing and drying until a frosted appearance was achieved. Bond was then applied and cured for 20 seconds per surface. The sealant was applied to the occlusal surface and cured for 20 seconds. In the FV group, a thin layer of FV was applied to pits, fissures, and smooth surfaces using a disposable micro brush. This procedure was repeated for all FPMs(Chestnutt et al., 2017).At the end of the procedures, postoperative instructions were given to both groups, which included guidance on maintaining good oral hygiene and dietary instructions.

Adverse effect binary outcome was measured with a questionnaire for the parent (allergy, diarrhea, bad taste or vomiting) and visually at the clinic (white, brown or black discoloration). Assessment and collection of the outcome were done at treatment visit (baseline), 6 and 12 months clinically (using custome-made questionnaire for parents to measure the adverse effects). (Chestnutt et al., 2017).

Baseline data were collected by the operator through a paper-based form. The full detailed personal data of the patient was written in a separate sheet having the patient's serial number for further contact with patient, this sheet can be only seen by the operator and the assistant.

Principle investigator informed participants about the possible harms if present. Participants were allowed to contact the operator at any moment through telephone. The data was reported to the Main Supervisor.

Suppose the patient showed complications such as Bad taste, Hypersensitivity, Discolouration, and Vomiting. The patient was excluded from the trial, and all the needed management was done. There was no pain or bad taste, but the varnish may have made teeth look yellowish or less shiny after it was put on. These changes were regular and would disappear when the child brushed their teeth the next day.

The investigator discussed the trial with the legal guardian of each participating child: Verbal permission was taken orally from participating child and written informed consent was obtained from the legal guardian of each participating child who was willing to participate in the trial. The consent form was written in Arabic.

The name and personal data of the participants did not appear on the protocol form. All these data will be securely stored and maintained for 10 years after the trial. This is done for the protection of participants' privacy and civil rights.

Statistical analysis

Categorical data was represented as frequency (n) and percentage (%) and was analyzed using chi square test. Numerical data was explored for normality by checking the data distribution, calculating the mean and median values and using Kolmogorov- Smirno and Shapiro- Wilk tests. The data was found to be normally distributed, it was presented as mean and standard deviation values, independent t-test was used for the intergroup comparisons, and paired t-test was used for intragroup comparisons. The assumption of normality was found to be violated; the data was presented as median and range values and was analyzed using Mann-Whitney U test for intergroup comparisons while Wilcoxon signed rank was used for intragroup comparisons. The significance level was set at $p \leq 0.05$ for all tests.

III. RESULTS

The study was conducted on 91 children that were randomly allocated to both tested groups (i.e.46 children in the fluoride varnish group and 45 children in resin-based fissure sealant group). Demographic data for different groups were presented in Table (1) and Figures (1) and (2). There were 28(56.0%) males and

18(43.9%) females in the fluoride varnish group, while in resin-based fissure sealant group there were 22(44.0%) males and 23(56.1%) females. The mean age in the fluoride varnish was (7.00±1.12) years, while in resin-based fissure sealant, it was (7.29±1.42) years. There was no significant difference between both groups regarding demographic data (p>0.05).

Frequency and percentage values of treatment adverse effects for different groups were presented in Table (2) In both groups none of the children suffered from any adverse effects such as bad taste, hypersensitivity, discoloration, and vomiting. There was a strong agreement between both raters (weighted kappa=0.815 [95%CI (0.750:0.986)], p<0.001).

Table (1): Demographic Data of study sample for both groups

Parameter			Fluoride varnish	Resin based fissure sealant	p-value
Sex	**Male**	**n**	28	22	**0.251**
		%	56.0%	44.0%	
	Female	**n**	18	23	
		%	43.9%	56.1%	
Age	**Mean±SD**		7.00±1.12	7.29±1.42	**0.284**

Table (2): Frequency and percentage values of treatment adverse effects for both groups

Treatment adverse effects		Fluoride varnish	Resin-based fissure sealant	Odds ratio [95%CI]	P-value
No	**n**	46	45	**NA**	**NA**
	%	50.5%	49.5%		
Yes	**n**	0	0		
	%	0%	0%		

NA: Not Applicable

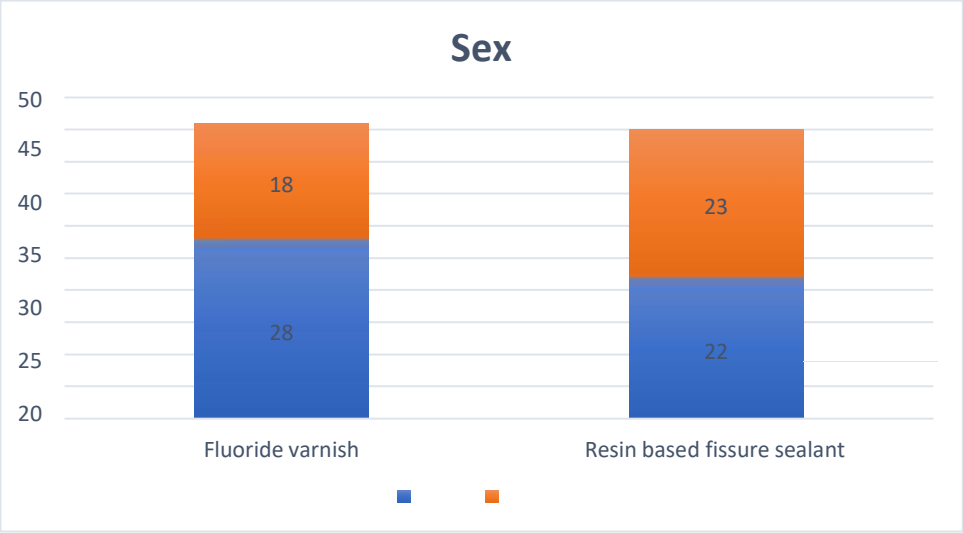

Figure (1): Bar chart showing gender distribution.

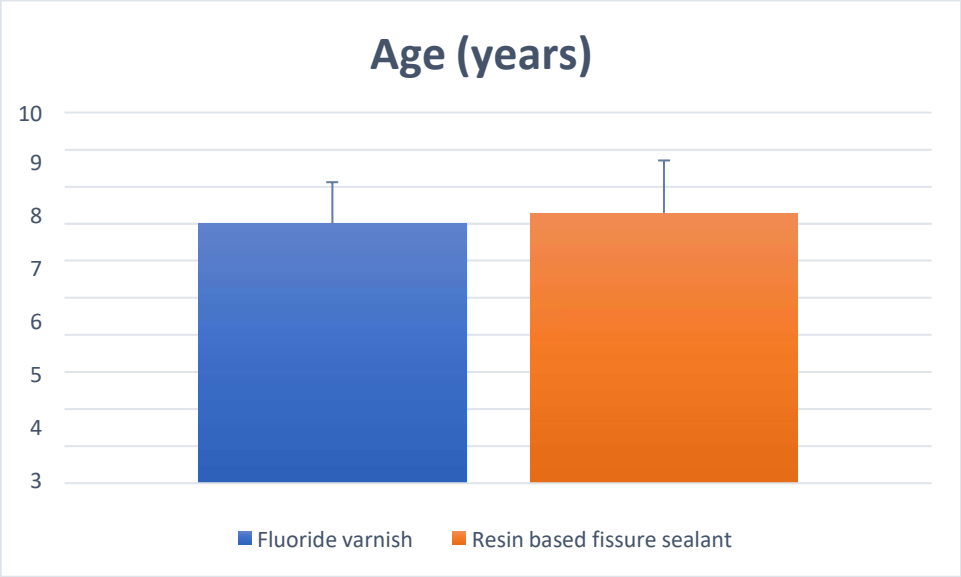

Figure (2): Bar chart showing mean and standard deviation values (error bars) for age (years)

IV. DISCUSSION

Dental decay is considered a critical oral health problem. It affects hundreds of millions of people worldwide. It is Initiated by acidic by-products from bacterial fermentation of carbohydrates leading to localized destruction of dental tissues. Despite the availability of evidence-based, easy, and economical preventive interventions, untreated caries of permanent teeth impacted 2.3 billion individuals globally in 2017, making it the most prevalent disease afflicting humanity (Wen et al., 2022).

Pits and fissures have a plaque-retentive characteristic that makes them challenging to clean, making them more prone to caries than smooth surfaces and possibly not protected by a fluoride treatment. Pits and fissures sealant prevents dental caries by creating a physical barrier that prevents food stagnation (Naaman et al., 2017).

Fluoride acts in several ways to protect against tooth decay by reducing acid production by interfering with various bacterial strains' metabolic activity and enhancing remineralization. Fluoride varnish is the optimal solution for topical fluoride treatments due to its high fluoride concentration and long-lasting effects on the teeth. In addition, the simplicity, acceptability, economy, less time of application, and less sensitivity technique of FV compared to fluoride foam made us choose FV in our study (Munteanu et al., 2022).

This study was designed to be a randomized control trial on children with newly erupted first permanent molars. The participants were randomized on a 1: 1 allocation ratio to receive one of the following materials: RBS OR FV. The study design was the most appropriate, as it is the mostreliable and strict design to identify the relationship between the intervention and outcome. The RCT design is known to be at the highest level of the evidence pyramid because it is designed to be unbiased and has less risk of systematic errors (Bhide *et al.*, 2018).

Before collecting data, researchers should determine the ideal sample size to prevent making mistakes due to insufficient sample size and wasting resources and time

due to excessive sample size. In addition, a well-conducted study may not be able to answer the research question or may not be able to identify significant effects and associations in a clinical trial if the sample size is too small to address the research hypothesis. Any research project must include the optimal sample size (Pourhoseingholi *et al.*, 2013).

The allocation concealment procedure helps prevent selection bias in Randomized Clinical Trials (RCTs) by keeping the allocation sequence hidden from those responsible for allocating participants in the intervention groups until the time of assignment (Doig and Simpson, 2005). In this study, the allocation concealment was conducted by Four-folded numbered papers packed in opaque sealed envelopes to be dragged by the patients.

When comparing groups to examine the impact of an intervention, it is critical to ensure that the groups are as similar as possible. Typically, this is accomplished using randomization, a process in which individuals are assigned to groups by the opportunity to eliminate bias. There are various randomization techniques, such as a coin toss, a block Computerized allocation, randomization (randomization by groups), etc. Theoretically, Random groupings should consist of similar individuals *(Glynn, 2006)*. In this study, the FPMs that were included were randomly assigned to one of the experimental groups using closed white opaque envelopes (simple randomization 1:1 ratio). Sequence generation was conducted by randomly selecting an envelope for each patient after their enrollment after shuffling the envelopes

In this study, according to the questionnaire answered by the parents, no body of the participant in both groups suffered from any adverse effects such as bad taste, hypersensitivity, discoloration,and vomiting. These results agree with (Deery, 2016; Chestnutt et al., 2017 and Kashbour et al., 2020) they reported and confirmed no adverse effect in connection with using either RBS or FV.

Fluoride varnish is very safe for children as it has a low amount of fluoride ingestion due to its short setting time and the prolonged contact time between the varnish and enamel surface, leading to the slow release of fluoride. These facts are consistent with the findings reported in the current study (Baik et al., 2021).

To the best of our knowledge, there are rare adverse effects of fluoride varnish, and they were only reported in conjunction with the use of Duraphate.(Isaksson et al.,1993) reported two cases of hypersensitivity, skin dermatitis, and contact stomatitis, resulting from the use of Duraphat. This could be explained by Colonophy, which is a component of Duraphet, that may cause an allergic reaction in individuals with a known sensitivity to it. Also, Colonophy can cause a burning sensation in the gingival tissue (Baik et al., 2021).

Also, asthmatic attack and urticaria were only reported once in a case report in 1993 by Hallström when using Delton, a fissure sealant material (Hallström,1993), lake of reports displaying the adverse effect of the fissure sealant could be taken as evidence of its safety, which goes in accordance with the current study results.

V. CONCLUSION

Based on the 12 months results and within the limitations of this study, it is concluded that:

The two preventive methods are acceptable, and no adverse effect was detected.

Recommendations:

As the caries progression rate in permanent teeth is difficult to predict, further studies are needed to assess the effectiveness with long-term follow- up.

Conflict of Interest:

The authors declare no conflict of interest.

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Ethics:

This study protocol was approved by the ethical committee of the faculty of dentistry-Cairo university on:25\5\2021, approval number:(6521)

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