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Comparative effect of fluoridated toothpaste with or without arginine on the remineralization of white spot lesions in primary teeth: a randomized controlled clinical trial

Efeito comparativo de dentifrício fluoretado com ou sem arginina na remineralização de lesões de mancha branca em dentes decíduos: um ensaio clínico controlado randomizado

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ABSTRACT

Objective: To compare the remineralizing effect of a toothpaste containing 1,450 ppm sodium monofluorophosphate (MFP) (control), with or without 1.5% arginine (test), on active white spot lesions (WSLs) in primary teeth of preschool children (4-5 years) in a double-blind, randomized controlled clinical trial. **Material and Methods:** Upper primary anterior teeth with WSLs (control: 47; test: 41) from 35 children were analyzed at baseline and after 3 months of supervised toothbrushing performed three times daily. Examinations were conducted in a school setting by a calibrated examiner using the dmft index. WSLs were assessed visually with ICDAS criteria, including caries activity, and monitored using a laser fluorescence device (LFpen). The lesion area (mm^2) was measured using digital photographs with ImageJ. **Results:** The dmft index increased in both groups after 3 months ($p = 0.0084$), with no significant difference between them ($p > 0.05$). No significant differences were observed in WSLs area and LFpen values for treatment type, phase, or interaction ($p > 0.05$). WSLs' activity showed significant differences between study phases for each treatment ($p < 0.0001$). The progression or regression of WSLs did not differ significantly ($p > 0.05$), regardless of caries experience (odds ratio [OR] = 1.65; 95% confidence interval [CI] = 0.59-4.65, low experience OR = 1.33; 95% CI = 0.20-9.08; high experience OR = 1.63; 95% CI = 0.45-5.82). **Conclusion:** The addition of 1.5% arginine to toothpaste containing 1,450 ppm sodium monofluorophosphate did not provide an additional remineralizing effect on active WSLs in primary teeth of preschool children after 3 months of follow-up.

KEYWORDS

Arginine; Dental caries; Dentifrices; Fluoride treatment; Tooth remineralization.

RESUMO

Objetivo: Comparar o efeito remineralizante de um dentifrício contendo 1.450 ppm de monofluorfosfato de sódio (MFP) (controle), associado ou não a 1,5% de arginina (teste), sobre lesões de mancha branca ativas (LMBs) em dentes decíduos de crianças pré-escolares de 4 a 5 anos, em um ensaio clínico randomizado, controlado e duplo-cego. **Material e Métodos:** Os dentes anteriores superiores decíduos com LMBs (controle: 47; teste: 41) de 35 crianças foram analisados no início do estudo e após 3 meses de escovação supervisionada, realizada três vezes ao dia. Os exames foram conduzidos em ambiente escolar por um examinador calibrado utilizando o índice ceo-d. As LMBs foram avaliadas visualmente pelos critérios ICDAS, incluindo atividade de cárie, e monitoradas por meio de um dispositivo de fluorescência a laser (LFpen). A área das lesões (mm^2) foi medida a partir de fotografias digitais utilizando o software ImageJ. **Resultados:** O índice ceo-d aumentou em ambos os grupos após 3 meses ($p = 0.0084$), sem diferença significativa entre eles ($p > 0.05$). Não foram observadas diferenças significativas na área das LMBs e nos valores do LFpen quanto ao tipo de tratamento, fase ou interação ($p > 0.05$). A atividade das LMBs apresentou diferenças significativas entre as fases do estudo para cada tratamento ($p < 0.0001$). A progressão ou regressão das LMBs não diferiu significativamente ($p > 0.05$), independentemente da experiência de cárie (razão de chances [RC] = 1.65; intervalo de confiança [IC] de 95% = 0.59-4.65; baixa experiência RC = 1.33; IC 95% = 0.20-9.08; alta experiência RC = 1.63; IC 95% = 0.45-5.82). **Conclusão:** A adição de 1,5% de arginina a um dentifrício contendo 1.450 ppm de monofluorfosfato de sódio não proporcionou efeito remineralizante adicional de LMBs ativas em dentes decíduos de crianças pré-escolares após 3 meses de acompanhamento.

PALAVRAS-CHAVE

Arginina; Cárie dentária; Dentifrícios; Tratamento com flúor; Remineralização dentária.

INTRODUCTION

Dental caries is a biofilm-diet dysbiosis characterized by dynamic cycles of demineralization and remineralization that result in mineral loss of hard dental tissues [1]. Socioeconomic, demographic, behavioral, and biological factors play key roles in its development [2,3]. Although its prevalence had declined over recent decades, dental caries remains a major global public health concern, particularly in primary teeth [4,5]. The polarization of early childhood caries (ECC) among socially vulnerable groups highlights regional disparities and higher sucrose consumption, with most children remaining caries-free while a small subset of preschoolers presents multiple lesions [6].

The initial clinical sign of dental caries manifests as non-cavitated white spot lesions (WSLs) in specific areas of the teeth. The prevalence of WSLs in primary teeth is 14.0% among preschool children, with higher rates in countries with low-income economies (24.0%) [7]. Detecting WSLs enables conservative management through remineralization process with fluoride, oral hygiene practices, and dietary control [7]. Effective oral hygiene procedures play a crucial role in caries control, particularly when biofilm removal is carried out meticulously and combined with fluoride toothpaste [8].

Fluoride exists in various reactive forms in toothpaste, with sodium monofluorophosphate (MFP or Na_2FPO_3) considered the primary contributor to the release of fluoride ions for its anti-caries effect [9]. Diverse formulations of fluoride toothpaste have the potential to enhance dental caries management [10]. In this regard, arginine (Arg), a semi-essential amino acid termed as prebiotic, appears promising for caries prevention associated with fluoride by targeting biofilm pathogenicity [11,12]. This is attributed to its ability to produce ammonia when metabolized by microorganisms, thereby increasing local pH (neutralizing biofilm acids) and promoting the selection of non-cariogenic bacteria [11,13,14].

Studies have demonstrated that arginine-fluoride-based toothpaste can modulate cariogenic biofilms, enhance fluoride uptake, and promote remineralization [15-21]. It should be noted that some investigations may present a risk of bias due to industrial collaboration. However, other studies suggested a lack of conclusive evidence to support the anticaries benefits of products containing arginine [22-24]. Additionally, up to now, the actual impact of combining fluoride toothpaste with arginine on the management of enamel caries in primary teeth remains uncertain.

Thus, this study aimed to compare the remineralizing effect of a toothpaste containing 1,450 ppm sodium monofluorophosphate, with or without 1.5% arginine, on active WSLs in primary teeth of preschool children in a double-blind, randomized controlled clinical trial. The null hypothesis is that there is no difference between fluoride toothpaste with or without arginine in remineralizing active WSLs in primary teeth.

MATERIAL AND METHODS

Ethical aspects

This study was approved by the local Institutional Review Board (IRB) (protocol #65790317.3.0000.8084) and registered in the Brazilian Registry of Clinical Trials (ReBEC) (identifier #RBR-2G9VBX). The study protocol was explained to the parents or legal guardians of the participants, and enrollment was conducted only after written informed consent was obtained.

Considering that the participants were preschool children aged 4-5 years, the study procedures were also explained to them in simple and age-appropriate language before the clinical examinations and supervised toothbrushing sessions. Illustrative drawings displayed on a poster were used to facilitate the children's understanding of the research procedures. Due to their young age and limited ability to read and understand a formal written assent document, written assent was not obtained from the children. Nevertheless, their verbal assent and willingness to participate were respected throughout the study, and any sign of refusal, discomfort, or lack of cooperation would have led to interruption of the procedure.

Study design

This study was a parallel-randomized, double-blind, controlled clinical trial and an equivalence trial. The methodology of the present study followed the CONSORT (Consolidated Standards of Reporting Trials) 2025 statement [25] for randomized clinical studies.

Study population

Preschool children with complete primary dentition were recruited from four public municipal preschools located in the eastern region of São Paulo, Brazil. The participating schools were selected among those authorized by the Regional Directorates of Education responsible for public preschools in this region. The schools were located in the same low-income area of the city and shared similar socioeconomic, organizational, and environmental characteristics. As municipal institutions, they had comparable administrative structures, basic facilities, daily routines, and meal services, which helped reduce variability among study settings.

In addition, all selected schools had appropriate facilities for supervised toothbrushing, allowing standardized implementation of the intervention protocol. The schools were regularly monitored by local public health professionals, including nurses and dentists from public health units, as well as municipal health inspectors. Importantly, no fluoride-based interventions were provided during the study period to avoid interference with outcomes. It is also important to note that the public water supply in São Paulo is fluoridated at a concentration of 0.7 ppm fluoride.

Children of both sexes, aged 4-5 years, in good general health, presenting at least one visible active white spot lesion (WSL) (ICDAS code 2 – International Caries Detection & Assessment System) on the buccal surface of their primary maxillary anterior teeth, and with a signed informed consent form provided by their legal guardians.

Children were excluded if they were participating in other clinical trials; were undergoing ongoing orthodontic or orthopedic treatment, had a diagnosis of cognitive impairments or syndromes, required continuous use of medication, were undergoing dental treatment, did not allow clinical examinations, or were participating in fluoride-based dental programs.

Before the beginning of the study, educational sessions were scheduled at each school, first with teachers and subsequently with parents or guardians. These sessions provided information about the research and addressed key topics in oral health for preschool-aged children, including the concept of dental caries, main risk factors such as diet and oral hygiene, recommendations for a healthy diet and toothbrushing practices, proper use of dental floss, and guidance on fluoride toothpaste, including concentration, amount, initiation of use, and prevention of dental fluorosis.

At the end of each session, details about the study protocol, including its phases, potential risks, and expected benefits, were presented. Parents and guardians received the informed consent form, which did not require immediate signature. For those unable to attend, the informed consent form and the same written information about the study and oral health recommendations were also sent home via the children's planners. Parents were given sufficient time to read the material and clarify doubts with the researchers before returning the signed form during the week of child assessments.

Although parental guidance was important to reinforce oral hygiene practices at home, the toothbrushing intervention evaluated in this trial was performed under supervision at school, according to a standardized protocol. Therefore, possible differences in attendance at the educational sessions were minimized and were not expected to substantially affect the intervention outcomes.

Sample size calculation

The required sample size was calculated using the Sealed Envelope online software [26]. The number of caries lesions (one lesion per tooth) was used as the unit of analysis for estimating the required number of observations. A minimum of 52 teeth (26 per group) was required, considering a significance level (α) of 5%, a statistical power of 80%, and a 1:1 allocation ratio between groups. A 30% anticipated dropout rate was also considered. Sample size estimation for the mean and standard deviation of caries lesion area was based on data from a pilot study evaluating the test toothpaste in preschool children, following a 3-month follow-up protocol.

Randomization, allocation concealment, and blinding

Regarding group randomization, participants were allocated using the block randomization method, with blocks defined by municipal preschools that shared similar characteristics. Simple randomization was then applied within blocks to ensure homogeneity between the test and control groups. Allocation by school was adopted to prevent the exchange of toothpaste between participants, thereby ensuring group integrity.

To ensure blinding, allocation was conducted by a team collaborator who prepared sealed, opaque, tamper-proof envelopes containing the names of the preschools. The envelopes were opened through a simple random draw, giving each school the same probability of being assigned to either group. The collaborator maintained confidentiality regarding treatment allocation throughout the study.

Within each block, participants were randomly allocated to one of two treatment groups: the test group (TG), which received a toothpaste containing 1,450 ppm fluoride as sodium monofluorophosphate (MFP) combined with 1.5% arginine (Colgate Máxima Proteção Anticárie mais NeutrAçúcar®, Colgate-Palmolive Company, Brazil) (n = 41 caries lesions in 21 children), or the control group (CG), which received a toothpaste containing 1,450 ppm MFP alone (Colgate Máxima Proteção Anticárie®, Colgate-Palmolive Company, Brazil) (n = 47 caries lesions in 17 children).

The study followed a double-blind design in which both the examiner and participants were unaware of group assignments. The toothpastes were identical in consistency, color, and odor, and were packaged in indistinguishable tubes labeled only with character stickers. To maintain blinding, labeling was performed by an external researcher.

Study instructions were provided to parents/guardians, who supervised toothbrushing at home, and to teachers, who supervised brushing at school. Participants received prior training in the Fones toothbrushing technique and were subsequently instructed to brush their teeth three times daily, for approximately one to two minutes, using the allocated toothpaste at school and at home.

Oral hygiene kits were distributed to all participants, each consisting of one toothbrush and one 120 g tube of the assigned toothpaste for school use. An additional home kit with the same contents was also provided, and parents/guardians were informed through written communication sent via the children's planners. At home, parents were instructed to brush their children's teeth after meals, avoid using other oral hygiene products, and ensure proper expulsion of the toothpaste after brushing.

All toothbrushes and toothpastes were provided throughout the study. If toothpaste replacement was necessary, the participant received a new tube of the same coded toothpaste according to the original group allocation, thereby maintaining blinding and avoiding cross-use between treatment groups. During supervised toothbrushing sessions at school, the amount of toothpaste used was standardized and monitored by the research team.

Compliance with the study protocol was monitored through monthly visits and biweekly telephone contact with school staff. During school visits, interviews were conducted with teachers, coordinators, and children to verify the correct use of the provided toothpaste. Written reminders were also sent monthly to parents/guardians via the children's planners. Harms were defined as any oral or systemic adverse effects related to toothpaste use (i.e., signs of irritation), and caregivers were asked about symptoms; any events would be recorded and evaluated.

Baseline assessments

All clinical examinations were conducted by a single examiner who had been previously trained and calibrated by a senior researcher with recognized expertise in dental caries epidemiological indices. Calibration was performed for both the dmft index (decayed, missing, and filled primary teeth) and ICDAS criteria, achieving an intra-examiner Kappa coefficient greater than 0.80, indicating substantial to excellent reliability.

Prior to the baseline clinical examination, each child received a toothbrush and toothpaste for supervised toothbrushing to remove dental biofilm. Examinations were performed on school premises, with children seated in classroom chairs under natural lighting, supplemented with a flashlight. Sterile gauze, a dental mirror, and a WHO (World Health Organization) ball-ended probe were used.

Caries experience was assessed using the dmft index, following WHO guidelines. The dmft index was used only to characterize the caries experience of the participants and to verify group comparability, and was not used as an outcome measure for the remineralization of white spot lesions. For analysis, caries experience was further categorized according to the number of teeth with a "d" component: "very mild" (1 tooth), "mild" (2-3 teeth), "moderate" (4-5 teeth), and "severe" (≥6 teeth), as described by Hallett and O'Rourke [27]. In addition, participants were classified according to Hallett and O'Rourke [28], where low and moderate categories were combined as "low caries experience" (dmft ≤ 6) and "high caries experience" (dmft > 6).

To evaluate initial caries lesions using the ICDAS visual criteria, tooth surfaces were carefully dried with a portable air nebulizer, and surface texture was assessed with a WHO probe [29]. The buccal surfaces of all primary maxillary anterior teeth were examined. Caries lesion activity was classified as "active" (+) when presenting an opaque and rough surface, usually with mature biofilm, or "inactive" (−) when presenting a smooth and shiny surface [30]. Children with at least one visible WSL (ICDAS code 2) on the buccal surface of their primary maxillary anterior teeth were selected to continue in the study evaluations.

The area of each white spot lesion (WSL) (mm^2) was determined by photographic documentation with a digital camera (Canon EOS Rebel T3i 600D, Ohta-ku, Tokyo, Japan) equipped with a macro lens. Flash settings, illumination, and framing of the maxillary incisors were standardized (ISO 100, shutter speed 1/100, aperture f/20). Children were seated with their heads supported and the Frankfurt plane parallel to the ground. Teeth were allowed to undergo natural dehydration, and a millimeter calibration scale was included adjacent to the tooth in each image. The camera was positioned at a 45° angle (12 o'clock position) to minimize specular reflection and lip shadow, following Cochran et al. [31]. All photographs at baseline and follow-up were taken by the same trained operator, following protocols for smooth-surface caries diagnosis [32], to minimize variability in image acquisition. The images were transferred to a computer and analyzed using ImageJ software (version 2.0, San Antonio Dental School, University of Texas Health Science, TX, USA). The "analyze" and "measure" tools were applied to quantify the area of structural enamel demineralization (mm^2). Lesion area assessments were performed independently by two examiners blinded to the treatment allocation, and the mean value of the two measurements was used for analysis.

The DIAGNOdent 2190 laser fluorescence device (DIAGNOdent pen, LFpen, KaVo, Biberach, Germany) was used for additional evaluation and monitoring of WSLs. Measurements were taken with the cylindrical sapphire tip for smooth surfaces, following the manufacturer's instructions. A schematic sketch of each lesion was recorded to assist in subsequent evaluations.

After the 3-month follow-up, changes in WSL area and DIAGNOdent pen (LFpen) values were classified as “progression”, “no change”, or “regression”. For WSL area, alterations smaller than 10% were categorized as arrest, whereas larger changes were classified as progression or regression depending on the direction of the variation. For LFpen values, stability was defined as no change from baseline, while increases indicated progression and decreases indicated regression.

Follow-up

A 3-month follow-up was conducted after the baseline intervention. Caries experience was assessed using the dmft index. The severity of caries lesions was recorded according to ICDAS scores, and their activity was determined clinically (active vs. inactive). In addition, lesion area (mm^2) was measured, and laser fluorescence values (LFpen) were obtained for monitoring.

At the end of the longitudinal follow-up, all participating preschools received an educational banner and brochures summarizing the oral health topics previously presented in the introductory lecture. The material addressed dental caries, appropriate use of fluoride toothpaste (including label information, recommended concentration, and age-appropriate amounts), toothbrushing technique, and use of dental floss, myths regarding antibiotics and dental caries, and dietary guidance.

Statistical analysis

The distribution of age, sex, and number of teeth with active WSLs between groups was analyzed using the Chi-square test. Data normality was assessed using the Shapiro-Wilk test. Two-way ANOVA followed by Tukey’s post hoc test was applied to evaluate differences between groups, follow-up assessments, and their interactions for caries experience (dmft), WSL area (mm^2), and LFpen values. Student’s t-test was used to compare the percentage change in lesion area between groups after 3 months. Fisher’s exact test was applied to analyze the severity of the decayed “d” component of the dmft index (no exposure, very mild, mild, moderate, or severe), as well as WSL activity (active or inactive) at baseline and follow-up in relation to the treatment group.

Changes in caries lesion and fluorescence area (no change, progression, or regression) were also evaluated using Fisher’s exact test and the Chi-square test. Logistic regression was used to assess the transition of WSLs (no change, progression, or regression) according to baseline caries experience (independent, low, or high experience) across groups. Odds ratios (OR) and corresponding 95% confidence intervals (CI) were calculated. Missing data were handled by complete-case analysis; only caries lesion data from children who completed the 3-month follow-up were included in the analyses

All statistical analyses were performed using MedCalc for Windows, version 12.3.0 (MedCalc Software, Mariakerke, Belgium), Statistica for Windows, version 8.0 (StatSoft Inc., Tulsa, OK, USA), and Social Science Statistics [33]. A significance level of 5% was adopted for all tests.

RESULTS

Among the 440 children enrolled in the four participating preschools. Of these, 244 children were initially assessed for eligibility because parental/legal guardian authorization for the initial evaluation was obtained. The remaining children were not screened because written authorization for the initial assessment was not provided. Of these, 209 were excluded: 138 did not meet the inclusion criteria, 68 declined to participate, and 3 were excluded for other reasons. Therefore, 35 children, corresponding to 88 teeth with active white spot lesions, were randomized and included in the study. In the test group (TG), 18 children from two schools were enrolled, comprising 41 teeth with active WSLs at baseline. After 3 months, there was a sample loss of 26.8% (6 children and 11 lesions). In the control group (CG), 17 children from the other two schools were enrolled, comprising 47 teeth with active WSLs at baseline. After 3 months, there was a sample loss of 27.7% (5 children and 13 teeth). During follow-up, 11 children did not attend the 3-month follow-up mainly due to children transferring or leaving school without justification. No adverse events or harms related to the toothpastes were observed in any participant during the trial period. Recruitment took place from [May/2018] to [November/2018], with outcomes assessed during a 3-month follow-up

A CONSORT flowchart of the study can be observed in Figure 1. Regarding compliance, the response rate from interviews, notes, and school visits was satisfactory. Teachers and coordinators reported on toothpaste use at school, while some parents/guardians provided information on home use through the school planners.

In the control group, the mean age of the children was 4.6 ± 0.5 years, while in the test group it was 4.4 ± 0.5 years. The groups were homogeneous with respect to age, sex, and tooth type, with active WSL ($p > 0.05$) (Table I).

The results for dmft, WSL area (mm²), and LFpen values at both study phases are presented in Table II. For the dmft index, a statistically significant difference was observed between baseline and 3 months ($p = 0.0084$), while no significant differences were found between treatment groups ($p = 0.5094$) or for the interaction between factors ($p = 0.9682$). Tukey's post hoc analysis revealed that the dmft

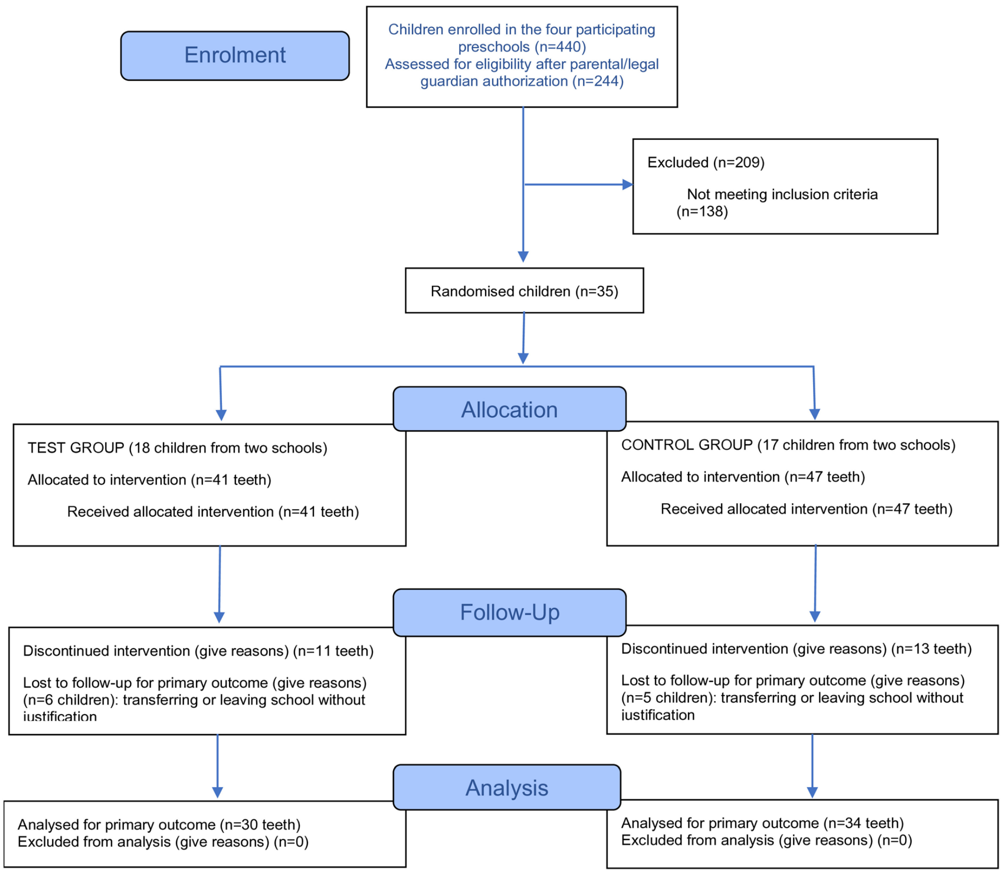

Figure 1 - Consort Flow Diagram.

Table I - Sample characteristics by group according to age, sex, and primary maxillary anterior teeth affected by active WSLs in the control and test groups

Characteristics	Control Group n (%)	Test Group n (%)	p-value*
Age			
4 years	7 (41.2)	11 (61.1)	0.2383
5 years	10 (58.8)	7 (38.9)	
TOTAL	17 (100.0)	18 (100.0)	
Sex			
female	5 (29.4)	6 (33.3)	0.8028
male	12 (70.6)	12 (66.7)	
TOTAL	17 (100.0)	18 (100.0)	

*Chi-square test.

Table I - Continued...

Characteristics	Control Group n (%)	Test Group n (%)	p-value*
Primary upper anterior teeth with active WSLs			
Central incisor	14 (29.8)	13 (31.7)	
Lateral incisor	15 (31.9)	12 (29.3)	0.9611
Canine	18 (38.3)	16 (39.0)	
TOTAL	47 (100.0)	41 (100.0)	

*Chi-square test.

Table II - Mean ± standard deviation of the dmft index, WSLs area (mm²), and laser fluorescence values (LFpen) at baseline and after 3 months of clinical follow-up in the control and test groups

Clinical variables and groups	Study phase	
	Baseline	3-month follow-up
dmft index		
Control group	5.0 ± 4.0^{A,a}	5.6 ± 3.5^{A,b}
Test group	6.0 ± 4.0^{A,a}	6.6 ± 4.1^{A,b}
WSLs area (mm²)		
Control group	5.5 ± 4.6^{A,a}	6.2 ± 5.9^{A,a}
Test group	3.9 ± 4.2^{A,a}	3.8 ± 3.9^{A,a}
LFpen values		
Control group	7.4 ± 11.3^{A,a}	5.4 ± 7.9^{A,a}
Test group	4.1 ± 5.0^{A,a}	3.2± 5.2^{A,a}

Statistically significant differences are indicated by different uppercase letters within the same column and by different lowercase letters within the same row (two-way repeated measures ANOVA followed by Tukey's post hoc test; p < 0.05).

index increased after 3 months in both groups ($p < 0.05$). For WSL area and LFpen values, no statistically significant differences were detected between treatment groups ($p = 0.0800$ and $p = 0.1095$, respectively), between study phases ($p = 0.2840$ and $p = 0.1468$, respectively), or for the interaction between factors ($p = 0.1930$ and $p = 0.5857$, respectively).

Regarding the percentage change in WSL area after 3 months, the control group (CG) showed an average increase of 10.25%, while the test group (TG) showed an increase of 3.87%. This difference was not statistically significant (Student's *t*-test, $p = 0.9620$).

Table III shows the frequency (%) of dental caries severity (decayed "d" component of the dmft index) and WSLs activity classification at both study phases in the control and test groups. Across the different categories of dental caries severity determined by the decayed "d" component of the dmft index, no statistically significant differences were found between study phases (baseline vs. 3-month follow-up) within each group ($p > 0.05$).

It is noteworthy that the "severe" category of dental caries was the most prevalent in both groups: 41.2% at baseline and 41.6% after 3 months in the control group (CG), and 50.0% at baseline and 66.8% after 3 months in the test group (TG). For WSLs' activity, a statistically significant difference was observed between baseline and 3-month follow-up within each treatment group ($p < 0.05$). At the 3-month evaluation, 58.8% of WSLs had become inactive in the control group (CG) and 43.3% in the test group (TG).

Table IV shows the frequency (%) of changes in WSL area and LFpen values after a 3-month follow-up in the control and test groups. No statistically significant differences were found between treatment groups regarding WSL changes ($p > 0.05$). Similarly, no statistically significant differences were observed between treatment groups in LFpen values ($p > 0.05$).

Table III - Frequency (%) of dental caries severity (decay "d" component of the dmft index) and WSLs activity at both phases of the study in the control and test groups

Clinical variables Baseline n (%)		Control group (CG)		Test group (TG)		p-value*
		3-month follow-up n (%)	Baseline n (%)	3-month follow-up n (%)		
Dental caries severity (decayed "d" Component of the dmft index)§	No exposure	4 (23.5)	3 (25.0)	4 (22.2)	3 (20.0)	0.2067
	Very mild (1 tooth)	5 (29.4)	0 (0.0)	1 (5.5)	0 (0.0)	
	Mild (2-3 teeth)	0 (0.0)	2 (16.7)	1 (5.5)	1 (6.6)	
	Moderate (4-5 teeth)	1 (5.9)	2 (16.7)	3 (16.8)	1 (6.6)	
	Severe (≥6 teeth)	7 (41.2)	5 (41.6)	9 (50.0)	10 (66.8)	
TOTAL CHILDREN		17 (100.0%)	12 (100.0%)	18 (100.0%)	15 (100.0%)	
p-value*		0.1277		0.7470		
WSLs Activity§§	Active	47 (100.0%)	14 (41.2%)	41 (100.0%)	17 (56.7%)	< 0.0001*
	Inactive	0 (0.0%)	20 (58.8%)	0 (0.0%)	13 (43.3%)	
TOTAL TEETH		47 (100.0%)	34 (100.0%)	41 (100.0%)	30 (100.0%)	
p-value*		< 0.0001*		< 0.0001*		

*Fisher's exact test. §Children included in the study. §§Teeth with WSLs included in the study. * indicates a statistical significant difference

Table IV - Frequency (%) of changes in WSLs area and LFpen values after 3 months of clinical follow-up in the control and test groups

Change		Control Group n (%)	Test Group n (%)	p-value
WSLs area§	No change	2 (5.9)	3 (10.0)	0.5291*
	Progression	17 (50.0)	11 (36.7)	
	Regression	15 (44.1)	16 (53.3)	
TOTAL		34 (100.0%)	30 (100.0)	
LFpen values§	No change	7 (20.6)	5 (16.7)	0.3233**
	Progression	17 (50.0)	10 (33.3)	
	Regression	10 (29.4)	15 (50.0)	
TOTAL		34 (100.0%)	30 (100.0%)	

*Fisher's exact test. **Chi-square test. §WSLs included in the study.

Table V - Distribution of WSLs transition (regression or progression) after 3 months of clinical follow-up according to baseline caries experience (dmft index) in the control and test groups

WSLs transition	Control Group	Test Group	OR*	95% CI	p-value
Regardless of caries experience					
WSLs regression	15	16	1.65	0.59-4.65	0.3439
WSLs progression	17	11			
Low caries experience§					
WSLs regression	6	3	1.33	0.20-9.08	0.7689
WSLs progression	8	3			
High caries experience§§					
WSLs regression	9	13	1.63	0.45-5.82	0.4560
WSLs progression	9	8			

*OR indicates the chance/probability of WSLs progression in relation to regression. 95% CI = 95% Confidence Interval. §Low caries experience = decayed "d" component of the dmft index between 0 and 3. §§High caries experience = decayed "d" component of the dmft index ≥4.

In general, after 3 months of clinical follow-up, the distribution of WSL transitions (progression or regression) did not differ significantly between groups ($p > 0.05$), regardless of children's caries experience (OR = 1.65; 95% CI 0.59-4.65), low caries experience (OR = 1.33; 95% CI 0.20-9.08), or high caries experience (OR = 1.63; 95% CI 0.45-5.82) in the baseline (Table V).

DISCUSSION

The main finding of this randomized clinical trial was that the addition of 1.5% arginine to a toothpaste containing 1,450 ppm sodium monofluorophosphate (MFP) did not provide an additional remineralizing effect on active white spot lesions (WSLs) in primary teeth after 3 months of follow-up. Although WSLs represent the earliest clinically detectable stage of dental caries and may be arrested or reversed through non-invasive remineralization strategies [7,34], the present findings suggest that the clinical response observed in both groups was mainly associated with the fluoride-containing formulation. This result is clinically relevant for preschool children, whose primary enamel is thinner and more prone to rapid demineralization [35], as it indicates that the inclusion of arginine did not enhance the short-term remineralizing performance of a conventional fluoride toothpaste under the conditions evaluated in this trial.

After three months of supervised toothbrushing, no significant differences were observed between the arginine-fluoride-based toothpaste and the conventional MFP formulation regarding changes in lesion area (mm^2), laser fluorescence readings, or lesion transition (progression and regression). Nevertheless, both groups exhibited a significant reduction in lesion activity, suggesting that regular, supervised exposure to fluoride effectively promotes the arrest of early enamel lesions in primary teeth, although the addition of arginine did not enhance the remineralizing potential under the study conditions.

The lack of a significant difference between the arginine-fluoride and conventional fluoride toothpastes observed in this study aligns with previous systematic reviews [22,23], which have highlighted the limited and low-quality evidence supporting the additional benefits of arginine in caries prevention. According to a comprehensive systematic overview [23], there is currently no scientific basis to recommend arginine-fluoride toothpaste over standard fluoride formulations for either preventing or arresting dental caries in children. The review emphasized that most available studies had methodological shortcomings, including inadequate randomization procedures, lack of pre-registered trial protocols, and potential conflicts of interest related to industry involvement in the research process. Moreover, questionable detection methods and limited generalizability further weaken the existing evidence base. Collectively, these issues indicate that the suggested advantages of arginine remain unconfirmed, and fluoride alone continues to represent the most reliable and evidence-based agent for caries control in pediatric populations.

Although arginine has been shown to contribute to biofilm alkalinization and modulation of the oral microbiota, favoring the growth of arginolytic bacteria and inhibiting acidogenic species [11,13], its clinical impact may depend on factors such as exposure time, frequency of toothbrushing, and formulation characteristics. It may be that higher concentrations of arginine have an additional protective effect.

In the present study, both groups were instructed to brush their teeth three times daily under supervision, which optimized fluoride efficacy during the relatively short observation period and may have masked any additional effects of arginine. Furthermore, the fluoride concentration used (1,450 ppm MFP) is well established as effective for caries prevention in both permanent and primary dentitions [36]. The strong remineralizing effect of fluoride may therefore have limited the detection of slight differences between formulations. Nevertheless, arginine-fluoride toothpaste is more expensive than conventional fluoride formulations, which may represent an additional barrier to its widespread adoption, particularly in low-income populations [23].

Moreover, the similarity in outcomes observed between the two toothpaste formulations may be attributed to the characteristics of the study population, which consisted predominantly of children with high caries experience, poor oral hygiene habits, and residence in an area of socioeconomic vulnerability. Previous studies have demonstrated that children from socioeconomically disadvantaged backgrounds, particularly those whose mothers have lower educational levels, exhibit higher prevalence and severity of dental caries [37,38]. In addition, parents or caregivers with limited socioeconomic resources often display lower awareness of their children's oral health, reduced understanding of caries-related risk factors, and greater barriers to accessing preventive or restorative care [39,40]. These contextual factors may have influenced the overall treatment response, thereby minimizing the potential differences between the toothpaste formulations. Nevertheless, the significant reduction in lesion activity in both groups highlights the effectiveness of supervised toothbrushing with fluoride toothpaste, even among populations experiencing social and economic disadvantages.

Our results cannot be directly compared with those of previous studies [16-18], in which the evaluated population consisted of children with mixed and permanent dentition. It is worth noting that these investigations assessed the remineralizing potential of toothpastes on the anterior permanent teeth of children aged 7 to 14 years and were conducted in China [16,17] and Thailand [18] by the same group of researchers. This difference in study populations contrasts with previous reports using arginine-based toothpastes, which demonstrated favorable results in the regression of WSLs [16-18].

The use of multiple detection methods by a trained and calibrated examiner—visual-tactile criteria (ICDAS) [41], laser fluorescence device (LFpen) [42], and digital image analysis for the lesion area (ImageJ) [31,32]—represents a major methodological strength of this study in assessing caries lesions on primary teeth. Similar to Kargul et al. [43], who also evaluated preschool children, detailed ICDAS-based visual examinations were performed only on the upper anterior teeth, while the entire dentition was assessed using the dmft index. This approach was chosen due to behavioral management challenges and field conditions, with all assessments conducted by a single calibrated examiner. These complementary methods enabled a multidimensional evaluation of lesion dynamics, increasing data robustness. Moreover, the supervised toothbrushing protocol implemented in the school setting ensured standardized oral hygiene and adherence to the study regimen. The double-blind design and random allocation of participants further minimized selection and measurement bias, strengthening internal validity.

Despite these strengths, certain limitations should be considered when interpreting the results. The three-month follow-up may have been insufficient to capture long-term remineralization or sustained effects on biofilm metabolism attributable to arginine. Additionally, testing a single fluoride-arginine concentration precluded dose-response analysis. Previous studies using arginine-containing toothpastes have had longer follow-ups (6 months to 2 years) and examined populations with mixed or permanent dentition. To our knowledge, this is the first study to assess an arginine-based toothpaste in preschool children with primary dentition over three months. Although shorter than those in the literature, this follow-up was sufficient to detect changes in WSLs, consistent with the results of Sugiura et al. [44] and Kitasako et al. [45], who investigated other remineralizing agents in young permanent teeth over similar time frames.

Dietary habits, salivary flow, and buffering capacity—factors known to influence enamel remineralization—were not strictly controlled and may have contributed to interindividual variability. Other potential confounders, such as socioeconomic status, access to dental care, previous fluoride exposure, and oral hygiene practices, may also have affected caries development and lesion behavior [36]. In addition, because the study was conducted in a single geographic region, the findings should be interpreted with caution regarding their external validity. Regional differences in socioeconomic conditions, dietary habits, fluoride exposure, access to dental care, and oral health-related behaviors may limit the extrapolation of the results to other populations. Although parents/guardians who attended the initial meeting received dietary guidance, particularly regarding healthy eating habits and reduction of sugar intake frequency, this recommendation was provided equally to both groups as part of standardized preventive and ethical care. Therefore, although dietary counseling may have contributed to the arrest or regression of active WSLs in both groups, it is unlikely to explain the absence of an additional remineralizing effect associated with the arginine-containing toothpaste.

Adherence to the intervention is another relevant aspect in longitudinal studies [46]. In the present study, compliance was monitored through interviews with parents/caregivers and school visits. Nevertheless, home-based toothbrushing could not be fully standardized, since parental/caregiver supervision may have varied, and differences in brushing frequency, toothpaste amount, brushing time, and technique may have occurred. This is particularly relevant in preschool children, who do not yet have fully developed motor coordination and therefore depend on adult supervision for effective oral hygiene [47]. In the school setting, toothbrushing was mainly performed by the children under teacher supervision, which increased ecological validity but may also have introduced slight variations in brushing technique and exposure to fluoride and/or arginine. These factors may have influenced the remineralization response of WSLs and should be considered methodological limitations. In addition, because more than one tooth/lesion was included per child, the statistical analysis may have involved dependent observations. Future studies should consider analytical approaches that account for clustering within participants to provide more robust estimates.

Within the limitations of this study, the findings provide valuable evidence on the clinical performance of arginine-fluoride toothpaste in preschool children. Clinically, the results reinforce the effectiveness of supervised toothbrushing with fluoride toothpaste as a fundamental strategy for controlling early carious lesions. The addition of 1.5% arginine to an MFP-based formulation did not produce superior outcomes within the study period but did not compromise fluoride efficacy. These findings suggest that consistent, supervised oral hygiene exerts the greatest influence on caries control in early childhood. For clinicians and public health professionals, this evidence highlights the importance of structured, school-based preventive programs emphasizing regular fluoride exposure and supervision by caregivers or teachers.

Future studies including diverse socioeconomic populations, longer follow-ups, multiple formulation concentrations, and microbiological analyses of oral biofilm would enhance the external validity and public health relevance of these results. A comprehensive evaluation of WSLs on all teeth and surfaces would also provide a broader understanding of the remineralization potential of arginine-containing toothpastes.

CONCLUSION

It can be concluded that the addition of 1.5% arginine to a toothpaste containing 1,450 ppm MFP did not enhance the remineralizing potential for active WSLs in the primary teeth of preschool children after three months of follow-up. Both formulations were effective in reducing the activity of active WSLs, demonstrating that fluoride remains the principal agent for enamel remineralization in preschool children. In contrast, the fluorescence values obtained with the LFpen and the measurements of lesion area showed no significant differences across study phases or between the types of toothpaste evaluated. The findings highlight that fluoride exposure, toothbrushing frequency, and supervision remain the key determinants for the successful management of early caries lesions in this age group.

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Data availability

Institutional Repository. Submitted article is derived from a Thesis. https://repositorio.cruzeirodosul.edu.br/items/fc5482d3-9dac-402f-adf4-33d5a5122db8.
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Author's Contributions

PHC: Data Curation, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Software, Writing – Original Draft Preparation. MMP: Data Curation, Investigation, Methodology, Writing – Original Draft Preparation. ROG: Data Curation, Investigation, Methodology, Visualization, Writing – Original Draft Preparation. AL: Conceptualization, Formal Analysis, Methodology, Validation, Visualization, Writing – Review & Editing. EB: Conceptualization, Data Curation, Formal Analysis, Methodology, Supervision, Validation, Visualization, Writing – Review & Editing. MBD: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Methodology, Project Administration, Resources, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing.

Conflict of Interest

No conflicts of interest declared concerning the publication of this article.

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Regulatory Statement

This study was conducted in accordance with the guidelines and policies established by the Brazilian CEP/CONEP System (Law No. 14.874/2024) for research involving human subjects. This study protocol was reviewed and approved by the local Institutional Review Board (IRB) under approval number CAAE 65790317.3.0000.8084.

REFERENCES

1. Machiulskiene V, Campus G, Carvalho JC, Dige I, Ekstrand KR, Jablonski-Momeni A, et al. Terminology of dental caries and dental caries management: consensus report of a workshop organized by ORCA and Cariology Research Group of IADR. Caries Res. 2020;54(1):7-14. https://doi.org/10.1159/000503309. PMid:31590168.
2. Martignon S, Roncalli AG, Alvarez E, Aránguiz V, Feldens CA, Buzalaf MAR. Risk factors for dental caries in Latin American and Caribbean countries. Braz Oral Res. 2021;35(Suppl 1):e053. https://doi.org/10.1590/1807-3107bor-2021.vol35.0053. PMid:34076077.
3. Wu J, Chen J, Lv C, Zhou L. Global, regional, and National levels and trends in burden of dental caries and periodontal disease from 1990 to 2035: result from the global burden of disease study 2021. BMC Oral Health. 2025;25(1):844. https://doi.org/10.1186/s12903-025-06108-w. PMid:40442655.
4. Bernabe E, Marcenes W, Abdulkader RS, Abreu LG, Afzal S, Alhalaiqa FN, et al. Trends in the global, regional, and national burden of oral conditions from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2025;405(10482):897-910. https://doi.org/10.1016/S0140-6736(24)02811-3. PMid:40024264.
5. Costa CM, Costa SA, Hugo FN, Paes AMA, Tabchoury CPM, Cury JA, et al. Increasing global trends in Early Childhood Caries prevalence over the last decade: Global Burden of Disease 2021 Study. Caries Res. 2025;1-7. https://doi.org/10.1159/000549128. PMid:41144607.
6. Tinanoff N, Baez RJ, Diaz Guillory C, Donly KJ, Feldens CA, McGrath C, et al. Early childhood caries epidemiology, aetiology, risk assessment, societal burden, management, education, and policy: global perspective. Int J Paediatr Dent. 2019;29(3):238-48. https://doi.org/10.1111/ipd.12484. PMid:31099128.
7. Campos PH, Gimenez T, Rocha RS, Caneppele TMF, Guaré RO, Lussi A, et al. Prevalence of white spot caries lesions in primary teeth in preschool children: systematic review and meta-analysis. Curr Pediatr Rev. 2022;18(1):33-46. https://doi.org/10.2174/1573396317666211202090657. PMid:34856910.
8. Maltz M, Jardim JJ, Alves LS. Health promotion and dental caries. Braz Oral Res. 2010;24(Suppl 1):18-25. https://doi.org/10.1590/S1806-83242010000500004. PMid:20857071.
9. Tenuta LM, Cury JA. Laboratory and human studies to estimate anticaries efficacy of fluoride toothpastes. Monogr Oral Sci. 2013;23:108-24. https://doi.org/10.1159/000350479. PMid:23817064.
10. Lagerweij MD, van Loveren C. Declining caries trends: are we satisfied? Curr Oral Health Rep. 2015;2(4):212-7. https://doi.org/10.1007/s40496-015-0064-9. PMid:26523247.
11. Cummins D. The development and validation of a new technology, based upon 1.5% arginine, an insoluble calcium compound and fluoride, for everyday use in the prevention and treatment of dental caries. J Dent. 2013;41(Suppl 2):S1-11. https://doi.org/10.1016/j.jdent.2010.04.002. PMid:23985433.
12. Assar S, Kristensen MF, Del Rey YC, Lund MB, Raittio EJ, Schramm A, et al. Microscale analyses of the effect of arginine on oral biofilms. J Dent. 2025;160:105863. https://doi.org/10.1016/j.jdent.2025.105863. PMid:40449826.
13. Cummins D. The superior anti-caries efficacy of fluoride toothpaste containing 1.5% arginine. J Clin Dent. 2016;27(2):27-38. PMid:28390204.
14. Goyal V, Damle S, Puranik MP, Nuvvula S, Kakanur M, Marwah N, et al. Arginine: a new paradigm in preventive oral care. Int J Clin Pediatr Dent. 2023;16(5):698-706. https://doi.org/10.5005/jp-journals-10005-2693. PMid:38162235.
15. Kraivaphan P, Amornchat C, Triratana T, Mateo LR, Ellwood R, Cummins D, et al. Two-year caries clinical study of the efficacy of novel dentifrices containing 1.5% arginine, an insoluble calcium compound and 1,450 ppm fluoride. Caries Res. 2013;47(6):582-90. https://doi.org/10.1159/000353183. PMid:23988908.
16. Yin W, Hu DY, Fan X, Feng Y, Zhang YP, Cummins D, et al. A clinical investigation using quantitative light-induced fluorescence (QLF) of the anticaries efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride as sodium monofluorophosphate. J Clin Dent. 2013;24:A15-22. PMid:24156136.
17. Yin W, Hu DY, Li X, Fan X, Zhang YP, Pretty IA, et al. The anti-caries efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride as sodium monofluorophosphate assessed using Quantitative Light-induced Fluorescence (QLF). J Dent. 2013;41(Suppl 2):S22-8. https://doi.org/10.1016/j.jdent.2010.04.004. PMid:23985435.
18. Srisilapanan P, Korwanich N, Yin W, Chuensuwonkul C, Mateo LR, Zhang YP, et al. Comparison of the efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride to a dentifrice containing 1450 ppm fluoride alone in the management of early coronal caries as assessed using Quantitative Light-induced Fluorescence. J Dent. 2013;41(Suppl 2):S29-34. https://doi.org/10.1016/j.jdent.2010.04.005. PMid:23985436.
19. Bijle MNA, Ekambaram M, Lo EC, Yiu CKY. The combined enamel remineralization potential of arginine and fluoride toothpaste. J Dent. 2018;76:75-82. https://doi.org/10.1016/j.jdent.2018.06.009. PMid:29935996.

20. Orilisi G, Vitiello F, Notarstefano V, Furlani M, Riberti N, Monterubbianesi R, et al. Multidisciplinary evaluation of the remineralization potential of three fluoride-based toothpastes on natural white spot lesions. Clin Oral Investig. 2023;27(12):7451-62. https://doi.org/10.1007/s00784-023-05334-2. PMid:37857734.

21. Yin W, Zhou Z, Huang RZ, Sun G, Zhong Y, Yang Z, et al. Arginine dentifrices and childhood caries prevention: a randomized clinical trial. JDR Clin Trans Res. 2026;11(2):204-14. https://doi.org/10.1177/23800844251361471. PMid:40794532.

22. Li J, Huang Z, Mei L, Li G, Li H. Anti-caries effect of arginine-containing formulations in vivo: a systematic review and meta-analysis. Caries Res. 2015;49(6):606-17. https://doi.org/10.1159/000435894. PMid:26536588.

23. Ástvaldsdóttir Á, Naimi-Akbar A, Davidson T, Brolund A, Lintamo L, Attergren Granath A, et al. Arginine and caries prevention: a systematic review. Caries Res. 2016;50(4):383-93. https://doi.org/10.1159/000446249. PMid:27403876.

24. Prasad J, Bhojraj N, Shanbhog R, Ashwini KP. Combined remineralizing effect of arginine and fluoride on artificially demineralized human primary dentin evaluated using quantitative light induced fluorescence. J Indian Soc Pedod Prev Dent. 2023;41(1):63-9. https://doi.org/10.4103/jisppd.jisppd_107_23. PMid:37282414.

25. Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 statement: updated guideline for reporting randomized trials. Nat Med. 2025;31(6):1776-83. https://doi.org/10.1038/s41591-025-03635-5. PMid:40229553.

26. Sealed Envelope [Internet]. 2025 [cited 2025 Dec 07]. Available from: www.sealedenvelope.com

27. Hallett KB, O'Rourke PK. Dental caries experience of preschool children from the North Brisbane region. Aust Dent J. 2002;47(4):331-8. https://doi.org/10.1111/j.1834-7819.2002.tb00547.x. PMid:12587770.

28. Hallett KB, O'Rourke PK. Caries experience in preschool children referred for specialist dental care in hospital. Aust Dent J. 2006;51(2):124-9. https://doi.org/10.1111/j.1834-7819.2006.tb00415.x. PMid:16848259.

29. Ekstrand KR, Martignon S, Ricketts DJ, Qvist V. Detection and activity assessment of primary coronal caries lesions: a methodologic study. Oper Dent. 2007;32(3):225-35. https://doi.org/10.2341/06-63. PMid:17555173.

30. Braga MM, Mendes FM, Ekstrand KR. Detection activity assessment and diagnosis of dental caries lesions. Dent Clin North Am. 2010;54(3):479-93. https://doi.org/10.1016/j.cden.2010.03.006. PMid:20630191.

31. Cochran JA, Ketley CE, Sanches L, Mamai-Homata E, Oila AM, Arnadóttir IB, et al. A standardized photographic method for evaluating enamel opacities including fluorosis. Community Dent Oral Epidemiol. 2004;32(Suppl 1):19-27. https://doi.org/10.1111/j.1600-0528.2004.00135.x. PMid:15016113.

32. Palma ABO, Castro C, Imparato JCP, Mendes FM. Photographic method for diagnosis of carious lesions on a smooth surface. Rev Gaucha Odontol. 2011;59(3):397-403.

33. Social Science Statistics [Internet]. 2025 [cited 2025 Dec 07]. Available from: www.socscistatistics.com

34. Roppa KB, Pathak S, Poormina P, Neena IE. White spot lesions: a literature review. J Paediatr Dent. 2015;3(1):1-7. https://doi.org/10.4103/2321-6646.151839.

35. Lynch RJ. The primary and mixed dentition, post-eruptive enamel maturation and dental caries: a review. Int Dent J. 2013;63(Suppl 2):3-13. https://doi.org/10.1111/idj.12074. PMid:24283279.

36. Walsh T, Worthington HV, Glenny AM, Marinho VC, Jeroncic A. Fluoride toothpastes of different concentrations for preventing dental caries. Cochrane Database Syst Rev. 2019;3(3):CD007868. https://doi.org/10.1002/14651858.CD007868.pub3. PMid:30829399.

37. Castilho AR, Mialhe FL, Barbosa TS, Puppin-Rontani RM. Influence of family environment on children's oral health: a systematic review. J Pediatr. 2013;89(2):116-23. https://doi.org/10.1016/j.jped.2013.03.014. PMid:23642420.

38. Moimaz SA, Fadel CB, Lolli LF, Garbin CA, Garbin AJ, Saliba NA. Social aspects of dental caries in the context of mother-child pairs. J Appl Oral Sci. 2014;22(1):73-8. https://doi.org/10.1590/1678-775720130122. PMid:24626252.

39. Corrêa-Faria P, Paixão-Gonçalves S, Paiva SM, Pordeus IA. Incidence of dental caries in primary dentition and risk factors: a longitudinal study. Braz Oral Res. 2016;30(1):S1806-83242016000100254. https://doi.org/10.1590/1807-3107BOR-2016.vol30.0059. PMid:27223127.

40. Setijanto D, Alkadasi BA, Nurrobi LAW, Dewi FL, Firmansyah FF. Caregiver perception of children's dental caries and experience of accessing dental health services for their children. Braz Dent Sci. Braz Dent Sci. 2023;26(2):e3749. https://doi.org/10.4322/bds.2023.e3749.

41. Braga MM, Mendes FM, Martignon S, Ricketts DN, Ekstrand KR. In vitro comparison of Nyvad's system and ICDAS-II with Lesion Activity Assessment for evaluation of severity and activity of occlusal caries lesions in primary teeth. Caries Res. 2009;43(5):405-12. https://doi.org/10.1159/000239755. PMid:19776572.

42. Rodrigues JA, Sarti CS, Assunção CM, Arthur RA, Lussi A, Diniz MB. Evaluation of laser fluorescence in monitoring non-cavitated caries lesion progression on smooth surfaces in vitro. Lasers Med Sci. 2017;32(8):1793-800. https://doi.org/10.1007/s10103-017-2262-2. PMid:28669068.

43. Kargul B, Durmus B, Bekiroglu N. Effect of CPP-ACP on remineralisation of early caries lesions in primary teeth. Oral Health Dent Manag. 2017;16(3):1-4.

44. Sugiura M, Kitasako Y, Sadr A, Shimada Y, Sumi Y, Tagami J. White spot lesion remineralization by sugar-free chewing gum containing bio-available calcium and fluoride: a double-blind randomized controlled trial. J Dent. 2016;54:86-91. https://doi.org/10.1016/j.jdent.2016.09.003. PMid:27639827.

45. Kitasako Y, Sadr A, Shimada Y, Ikeda M, Sumi Y, Tagami J. Remineralization capacity of carious and non-carious white spot lesions: clinical evaluation using ICDAS and SS-OCT. Clin Oral Investig. 2019;23(2):863-72. https://doi.org/10.1007/s00784-018-2503-1. PMid:29948272.

46. Saltaji H, Armijo-Olivo S, Cummings GG, Amin M, Flores-Mir C. Randomized clinical trials in dentistry: risks of bias, risks of random errors, reporting quality, and methodologic quality over the years 1955-2013. PLoS One. 2017;12(12):e0190089. https://doi.org/10.1371/journal.pone.0190089. PMid:29272315.

47. Marshman Z, Ahern SM, McEachan RRC, Rogers HJ, Gray-Burrows KA, Day PF. Parents' experiences of toothbrushing with children: a qualitative study. JDR Clin Trans Res. 2016;1(2):122-30. https://doi.org/10.1177/2380084416647727. PMid:28879241.

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