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ORIGINAL RESEARCH

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Effect of two remineralization agents on mild and moderate Molar Incisor Hypomineralization defects in Mexican schoolchildren: a double-blind randomized controlled clinical trial

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Abstract

Background: Remineralization is the process of depositing calcium and phosphate ions into crystal voids in demineralized dental enamel preventing early enamel lesions progression. To evaluate, via laser fluorescence, the effect of the two remineralizing agents Fluor protector™ and Clinpro White Varnish™ on the permanent molars and incisors of 8–12-year-old Mexican schoolchildren with mild and moderate Molar Incisor Hypomineralization (MIH). **Methods**: The study was conducted on 78 children divided randomly into three groups: Group I—Oral-B kids™ toothpaste (sodium fluoride at 1100 ppm), which was used as the control group; Group II—Fluor protector™; and Group III—Clinpro White Varnish™. The remineralization effect was evaluated via Laser Fluorescence (LF) on commencement of the treatment, then one and three months later. The paired samples *t*-test was used to evaluate the changes observed in the LF average values during the monitoring period, an intragroup one-way repeated-measures analysis of variance (ANOVA) was carried out to evaluate the effectiveness of the remineralizing agents, and the Greenhouse-Geisser correction was applied to evaluate sphericity. **Results**: Both agents obtained higher levels of remineralization, than the control treatment, of the mild and moderate MIH defects after three months of monitoring ($p < 0.001$). The difference observed among the LF average values were similar for both treatment groups. **Conclusions**: The results obtained enable the conclusion that fluoride varnishes such as Fluor Protector™ and Clinpro White Varnish™ are effective in remineralizing mild and moderate MIH lesions evaluated via LF. **Clinical Trial Registration**: The protocol was also registered on the ClinicalTrials.gov Identifier, under the reference NCT06362681.

Keywords

Molar Incisor Hypomineralization; Laser fluorescence; Remineralization; Fluoride varnish; Children

1. Introduction

Developmental defects of enamel (DDE) are alterations in the formation of the matrix and the mineralization of the hard tissues of the teeth and mainly present as enamel hypoplasia, Molar Incisor Hypomineralization (MIH), amelogenesis imperfecta, and dental fluorosis [1]. A qualitative defect of the dental enamel with a multifactorial etiology, characterized by marked white/cream or yellow/brown opacities [2], mainly affecting the incisors and first permanent molars but also, according to recent reports, the second permanent molars, the severity defects vary between teeth, even in the same person [3]. While the precise etiology of MIH remains unclear, recent researches based on the available scientific evidence indicates that MIH has a multifactorial etiology [4]. Research has reported on the ultrastructural and biochemical characteristics of the interior of enamel presenting MIH [5, 6]. Moreover, mineral content studies have reported that enamel affected by MIH is characterized by lower mineral (Ca, P and Cl) quality and quantity, higher carbon and oxygen concentrations, and a higher protein content than healthy enamel, resulting in increased porosity, more fissures, and deep pits [7, 8]. Therefore, MIH patients may present enamel structure loss caused by masticatory force and may develop dental caries.

Preventive treatments play a significant role in teeth affected by MIH, given that they reduce the probability of tooth loss at a young age. Recent years have seen the increasing use of non-invasive or minimally invasive approaches, such as the utilization of remineralizing agents, in order to conserve as much of the tooth structure as possible in the treatment of teeth affected

by MIH [9, 10]. Remineralizing agents are used to treat caries by controlling the demineralization/remineralization cycle, in accordance with the microenvironment surrounding the tooth. Although the treatment of MIH has been recommended in order to protect damaged enamel and increase the mineral content of hypomineralized surfaces, research remains limited on the effectiveness of remineralizing agents on teeth presenting MIH [11, 12]. The discipline of dentistry uses various fluoride systems to remineralized tooth surfaces, either topically or systemically [13]. Topical fluorides can be used for improving remineralization, as they are able to increase the availability of fluoride ions in the saliva and improve the formation of fluorapatite [14]. Fluoride varnishes have been used as a caries prevention strategy, wherein, on application they adhere to the tooth surface for a prolonged period releasing the fluoride effectively. They are also used to inhibit desmineralization and improve remineralization [15]. Research on the use of remineralizing agents, such as Clinpro White Varnish™, Duraphat™ and Fluor Protector™, has demonstrated the efficacy of fluoride varnish in promoting the remineralization of carious lesions [16, 17].

Recent studies have evaluated the effects of remineralizing agents on teeth affected by MIH by comparing the application of fluoride varnish with that of other remineralizing agents, such as pastes containing casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and CPP-ACP with fluoride (CPP-ACFP). These studies reported that both the varnishes and the agents derived from CPP-ACP strengthened and remineralized the teeth presenting MIH, reducing the extent of the porous structure along the length and depth of the lesion and across the tooth surfaces affected [18–20]. For some time now, there has been interest in the literature in non-destructive methods for the evaluation and monitoring of mineral changes in enamel, using laser fluorescence (LF). DIAGNOdent™ has recently become the most accurate tool to detecting enamel demineralization. The DIAGNOdent™ has the advantage is more informative for the patient and can be used in the clinic. It is more reproducible and accurate; however, its higher cost is a disadvantage [19]. Therefore, with the aim of improving the mechanical properties of teeth affected by MIH, remineralization, when used as a preventive treatment, is able to increase the mineral content of the enamel affected, preventing fractures from presenting once the eruption process has been completed. Exploring the possible advantages of increasing the mineral content of the teeth affected by MIH via the use of remineralizing agents, the present study applied Laser Fluorescence to evaluate the effects of two remineralizing agents, Clinpro White Varnish™ and Fluor protector™, on the permanent molars and incisors with mild and moderate MIH, in 8–12-year-old Mexican schoolchildren. The research hypothesis was that Fluor protector™ and the fluoride varnish Clinpro White Varnish™ are equally effective in remineralizing enamel affected by MIH, for both mild and moderate lesions.

2. Material and methods

The research protocol was reviewed and approved by the Ethics Committee at the Iztacala Faculty of Higher Studies of the National Autonomous University of Mexico (CE/FESI/062022/1520). The corresponding authorities at the public primary schools and the parents/guardians of the children were informed of the study objectives and the procedures to be followed as part of the research. Those parents/guardians who agreed to the participation of their children gave their signed informed consent, with the children themselves also providing their signed informed assent to participate in the study. The protocol was also registered on the ClinicalTrials.gov Identifier, under the reference NCT06362681.

2.1 Sample power calculation

The sample size was calculated based on that reported in a previous study [21]. A sample size of at least 75 teeth (25 for each of the three study groups) was required for the clinical trial, with a power of 0.85 and significance level (α) of 0.05 [22]. However, the clinical trial comprised at least 30 teeth per treatment group as a contingency against the possible withdrawal of a patient during the monitoring period.

2.2 Study population

One hundred children enrolled in a public primary school at a location (in which no private schools are located) in the municipality of Ayala, in the state of Morelos, Mexico, were invited to participate in the present study. The following inclusion criteria were applied for the schoolchildren participating in the present study: 8–12 years old; of either gender; a recent diagnosis of MIH in erupted permanent molars or incisors, with creamy-white and/or yellow-brown lesions and either with or without post-eruptive breakdown of the enamel; no caries present; and no previous restorations, according to the European Academy of Paediatric Dentistry (EAPD) criteria [23]. Only mild and moderate MIH lesions were considered by the present study. The following exclusion criteria were applied: the use of a fixed orthodontic appliance; the presence of a systemic disease; the presence of another DDE, such as fluorosis or amelogenesis imperfecta; a history of dental trauma; the presence of an allergy; and uncooperative behavior during the application of the remineralizing agents. 22 children were excluded because they did not meet the inclusion criteria and total sample was 78 children.

2.3 Assignation and intervention procedure to the treatment group

From January to June 2024, the present study conducted a three-armed randomized controlled clinical trial, wherein a block randomization technique was applied to assign each participant to a particular group at a 1:1 allocation ratio, using the online tool found at https://www.randomizer.org. The random allocation sequence was performed by the blinded investigator. The data was captured and coded according to the child's identification number, while the allocation to each treatment group was blinded. Those children diagnosed with MIH that presented a creamy-white or a yellow-brown color were placed in random order and divided into two treatment groups, while the control group comprised children with teeth presenting

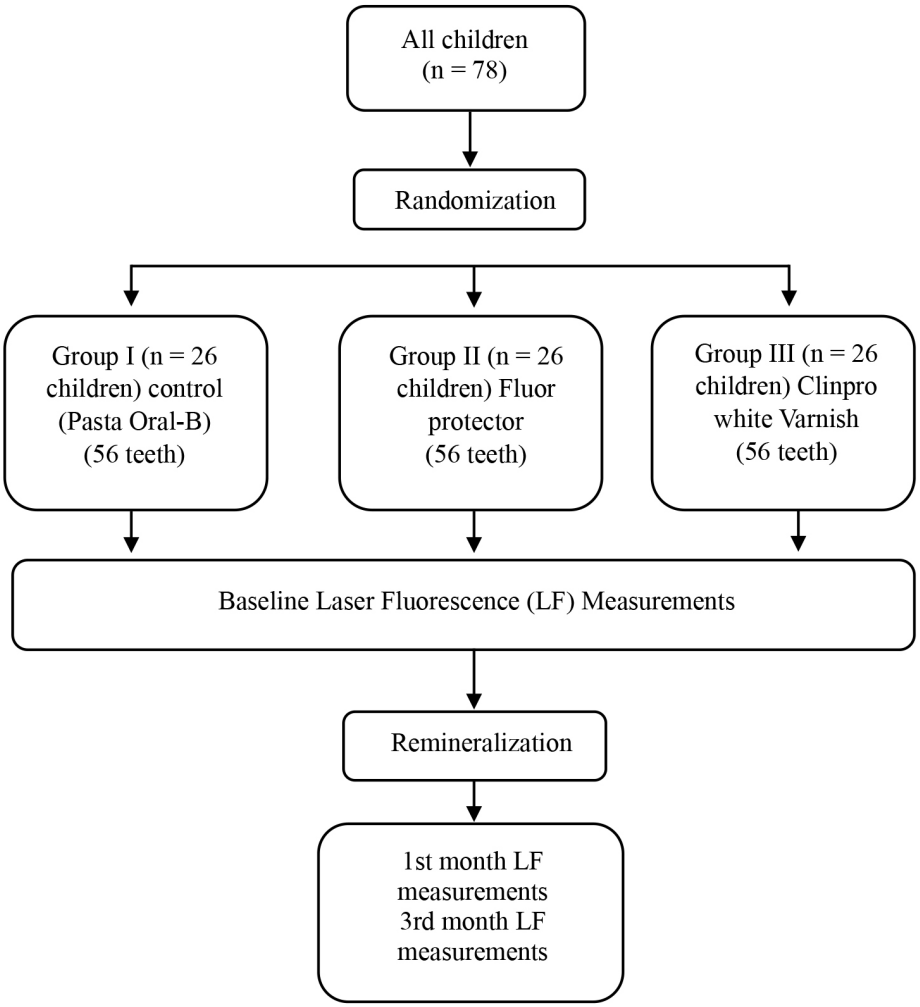

FIGURE 1. Flowchart for treatment assignment in children with MIH.

healthy enamel. The three groups were as follows: Group I (control)—Oral-B Kids™ toothpaste (sodium fluoride at 1100 ppm) (Fig. 1) (26 children); Group II—Ivoclar Vivadent™ fluor protector (0.9% difluorosilane on a polyurethane varnish base with ethyl acetate and isoamyl propionate solvents) (26 children); and Group III—Clinpro White Varnish 3M™ (5% sodium fluoride and tricalcium phosphate) (26 children). Both varnishes were applied once every four weeks for three months for each group. The teeth and molars presenting MIH were not cleaned professionally prior to the application of the varnishes and, instead, were simply brushed without toothpaste and then dried. The remineralizing agents were applied in accordance with the manufacturer's instructions.

Procedure Ivoclar Vivadent™ fluor protector (Liechtenstein): The teeth were isolated with cotton rolls; a thin layer of Fluor Protector was applied using a suitable single-use applicator (Vivabrush™). The varnish was spread and allowed to dry, finally, the cotton rolls were removed after 1 minute.

Procedure Clinpro White Varnish 3M™ (United States): The teeth were not isolated, using the applicator brush to thoroughly mix Clinpro varnish 3M™, since components of all sodium fluoride varnishes can separate during storage. A dose of 0.40 mL was used for use in children with mixed dentition who required extensive tooth surface or cavity area coverage. Clinpro White Varnish 3M™ will uniformly set to dentition in the presence of saliva. With the children asked not to brush their teeth, eat or drink, or rinse their mouths for two hours after the application of the remineralizing agent.

During the study, all the children attended a session on tooth-brushing, while the participants in the two treatment groups used a fluoride toothpaste (1110 ppm) to maintain their oral hygiene three times per day.

2.4 Evaluation LF

The LF evaluation was conducted using the DIAGNOdent Pen™ (2190, KaVo, Biberach, BW, Germany), as it enables the identification of the smallest modifications to the tooth surface via its special Type A tip. The DIAGNOdent™ scores range between 0 and 99. This number offers the possibility to monitor lesion behavior (0–12 sound, 13–24 enamel and 24–99 dentin involvement). All the measurements were taken by one examiner, who had been calibrated following the manufacturer's instructions for the use of the DIAGNOdent Pen™. Once the teeth had been isolated with cotton roll, LF was used to evaluate of the smooth surfaces of the enamel presenting creamy-white and/or yellow-brown opacities, with the Type A probe able to explore the entire tooth surface and

then register the highest score on the screen of the apparatus. The remineralizing agents were applied immediately after the LF readings, firstly after the base-level measurement of the MIH defects and then every month for three months.

2.5 Statistical analysis

All the statistical analysis was carried out using the Stata 18 program (Stata Corp, College Station, TX, USA). Descriptive statistics (frequencies, percentages, means and standard deviations) were used to summarize the characteristics of the study population, while the Shapiro-Wilk test was applied to ascertain the normal distribution of the quantitative variables (LF values). The paired samples *t*-test was applied in accordance with the distribution of the data showing the differences between the initial base-level measurements and the mean values obtained during the monitoring period. A repeated-measures analysis of variance (ANOVA) was carried out to determine whether three or more means for the group were different when the children in each group were the same, while sphericity (equal variances) was evaluated using the Greenhouse-Geisser correction. All the hypothesis tests were conducted with a $p \leq 0.05$ significance level.

3. Results

3.1 Description of the study population

The total number of participants in the study was 78 children, 46 (59.0%) of whom were male and 32 (41.0%) were female, with an average age of 9.50 (±1.35). Fifty-two of the participants presented, in total, 112 teeth diagnosed with mild and moderate MIH (delimited white/cream and yellow/brown lesions) and were divided randomly into two groups: Group II (Fluor Protector™), comprising 26 children and 56 teeth; and Group III (Clinpro White Varnish™), comprising 26 children and 56 teeth. Group I (toothpaste) was used as the control and comprised 26 children and 56 teeth. The 1:1 allocation ratio applied ensured that all three groups comprised the same number of teeth and children.

In the base-level measurements obtained, the average LF scores did not present statistically significant differences (31.3 (±11.8) for Group II *vs.* 29.9 (12.2) for Group III; $p > 0.05$). Table 1 shows the significant changes observed for the measurements obtained over the study period for both treatment groups, wherein the mean LF scores at the beginning of the study were higher, with those obtained for the first month found to be higher than those obtained for the third. Remineralization was achieved in a period of three months in teeth with both mild and moderate MIH, while a significant improvement was observed in the LF scores for both treatment groups ($p < 0.05$).

The one-way repeated-measures ANOVA conducted for the intragroup comparison of the LF values over time revealed changes in the average values, over time, for both treatment groups, in contrast to those observed for the control group ($p < 0.001$) (Table 2).

The one-way repeated-measures ANOVA conducted for 78 children and 112 of their teeth presenting MIH (both mild and moderate) sought to identify any differences in the LF scores due to the application of the remineralizing agents for three months. The results obtained showed statistically significant differences in the LF scores for the remineralizing agents over time—$F_{(2,146)} = 79.05$, $p < 0.001$ (Table 2).

3.2 Adverse effects on the study population

The present clinical trial found neither adverse effects nor damage affecting the general and oral health of the children in both treatment groups.

4. Discussion

The present clinical trial comprised a prospective longitudinal evaluation of the effects of remineralizing agents, such as Fluor Protector™ and Clinpro White Varnish™, on the defects in the teeth and molars of Mexican children with mild and moderate MIH. After three months of monitoring, while significant differences were found in the reduction of the LF scores obtained for both treatment groups, both agents increased the amount by which the MIH defects were remineralized, thus verifying the hypothesis of the present study.

One of main oral prevention measures is the use of fluorides on the surface of the teeth, as its application can help to strengthen and remineralized compromised areas of the enamel [24].

In vitro and *in vivo* studies conducted on the remineralization of the enamel/dentin have shown that elevated fluoride concentrations reversed calcium loss in the enamel and dentin, promoting remineralization and inhibiting demineralization [25]. Fluoride varnish is a remineralizing agent recommended for caries prevention, given that it prolongs the contact time between the fluoride and the enamel. Moreover, the fluoride released by the varnishes increases fluoride concentration in the saliva, interacts with the hydroxyapatites of the enamel, interferes in the bacterial metabolism, and accumulates on the tooth surface in the form of calcium fluoride [26]. Bijle *et al.* [27], using two experimental varnishes on healthy enamel, found that the Mineral Density (MD) of the treated enamel was significantly higher than that of the untreated enamel.

Mineral density deficiencies in enamel with MIH occurs during amelogenesis, in the initial maturation phase [28]. The effects of mineral loss may deteriorate both the superficial and sub-superficial enamel and result in changes to the hardness, form, function, and esthetic qualities of the teeth, increasing sensitivity and causing tooth loss [29]. The agents that have been used to intervene in the demineralization/remineralization process are fluoride varnishes, which increase MD in the enamel and eliminate tooth hypersensitivity [30].

As stated above, the remineralizing agents used in the present study, such as Fluor Protector™ and Clinpro White Varnish™, show a reduction in LF scores for mild and moderate MIH defects after three months of monitoring. Olgen *et al.* [18] evaluated the long-term efficacy of fluoride varnish and toothpastes containing CPP-ACP and CPP-ACP with fluoride (CPP-ACFP) in remineralizing molars with MIH, finding that all the remineralizing agents tested intensified the remineralization of MIH defects. Furthermore, Biondi *et al.* [20] evaluated MD after the application of CPP-ACP

TABLE 1. Comparison of means of laser fluorescence by severity of MIH and treatment group in Mexican schoolchildren aged 8–12 years.

Groups	Baseline to 1st month Mean (SD)		Mean Difference	(95% CI)	*p*	Baseline to 3rd month Mean (SD)		Mean Difference	(95% CI)	*p*
MIH mild										
Clinpro white varnish	28.36 (13.1)	21.84 (3.2)	6.52	(3.0–10.0)	0.002	28.36 (13.1)	13.29 (4.3)	15.06	(8.4–21.7)	0.001
Fluor protector	28.90 (10.7)	23.22 (8.4)	5.68	(2.6–8.8)	0.005	28.90 (10.7)	10.86 (2.3)	18.03	(6.9–19.1)	0.008
MIH moderate										
	Baseline to 1st month		Mean Difference	(95% CI)	*p*	Baseline to 3rd month		Mean Difference	(95% CI)	*p*
Clinpro white varnish	31.96 (11.9)	23.7 (11.5)	8.26	(5.3–11.2)	0.001	31.96 (11.9)	13.77 (6.7)	18.19	(12.8–23.5)	0.001
Fluor protector	31.81 (8.1)	23.65 (5.8)	8.16	(4.1–12.1)	0.002	31.81 (8.1)	11.96 (3.5)	19.85	(13.2–26.4)	0.001

The paired samples t-test. SD: Standard Deviation; CI: Confidence Interval; MIH: Molar Incisor Hypomineralization.

TABLE 2. Intergroup comparison of laser fluorescence values in teeth with MIH by over studied time in Mexican schoolchildren aged 8–12 years.

Group	Baseline Mean (SD)	1st month Mean (SD)	3rd month Mean (SD)	*p*
Clinpro white varnish	29.9 (12.2)	22.6 (10.5)	13.3 (5.3)	<0.001
Fluor protector	31.3 (11.8)	24.6 (9.8)	13.8 (8.6)	
Control	6.7 (1.5)	7.3 (0.8)	5.8 (0.8)	

SD: Standard Deviation.

and the fluoride varnishes Duraphat™ and Clinpro™ on mild and moderate MIH defects at 15, 30 and 45 days, finding that Clinpro™ was the most effective for mild lesions, while Duraphat™ was more effective for moderate MIH lesions. Contradictory results for the use of fluoride varnish on MIH defects have been reported, however. Restrepo *et al.* [12] evaluated the effect of fluoride varnish on teeth affected by MIH, using LF to evaluate the MD of the enamel, but not obtaining favorable results for the remineralization of MIH lesions after four applications of fluoride varnish. However, they do mention that one of the reasons for this finding may be the architectural organization and protein/mineral content of the enamel affected, which would impede the success of any attempt at mineral incorporation [18].

The present study evaluated MIH lesions the use of LF, observing an almost 18-point reduction in the average LF score after three months of treatment. Recently, satisfactory results have been obtained for the use of LF in clinical studies evaluating MIH [18–20]. Beyond clinical evaluation, which is one of the most common tools for this purpose, enamel lesions produced by MIH can be evaluated using various methods [31], one of which is the DIAGNOdent pen™, which functions via the LF diagnostic method. The light absorbed by the teeth is reflected in the form of fluorescence, while the intensity of the fluorescent light increases with the depth of the lesion [32]. Therefore, in teeth with MIH, the irregular structure of the enamel increases the amount of fluorescence reflected by the tooth surface and, therefore, the organic content increases and the mineral hardness of the enamel is reduced [18]. Farah *et al.* [33] studied the relationship between the mechanical properties of the hypomineralized enamel and LF in extracted teeth with MIH, finding a correlation between the measurements obtained with the DIAGNOdent pen™ and the mechanical properties of enamel with MIH. They also state that the increased LF values in hypomineralized enamel may be related to the proteins it contains and/or the light dispersed by the inhomogeneous enamel [33].

To date, a large part of the research carried out to evaluate MIH has focused on the prevalence of and risk factors related to this alteration [34, 35]. Significant information is available on the mechanical, physical, and morphological properties of the hard tissues affected by MIH, mainly indicating the reduced mineral content, increased porosity, and reduced microhardness [36]. Fluoride varnish has not only been used as a remineralizing agent for MIH. In an *in vitro* study on teeth with MIH conducted using polarized Raman microscopy and scanning electron microscopy, Cardoso-Martins *et al.* [37] found improvements in MD and the organization of hypomineralized

enamel after treatment with CPP-ACP.

There are limitations to the present study, among which are the use of a limited number of teeth and molars with MIH and a short monitoring period for evaluating the remineralizing agents. Another limitation is that when applying fluoride varnish, complete isolation was not achieved, and saliva could also influence possible remineralization. Finally, the control group was given toothpaste, and it is not possible to know whether the children used the toothpaste correctly at home. However, other clinical studies have observed that short monitoring periods have enabled the positive evaluation of the effectiveness of remineralizing agents [19].

5. Conclusions

The use of remineralizing agents, such as Fluor Protector™ and Clinpro White Varnish™, in children with mild and moderate MIH lesions, was shown, via laser fluorescence, to achieve an increased level of remineralization after a three-month monitoring period.

Obtaining information on the physical, mechanical and morphological properties of teeth affected by MIH reported in the literature will help to improve clinical results in these patients.

Moreover, the information obtained can be used to help identify better treatment strategies with non-invasive or minimally invasive approaches to oral health prevention, thus improving quality of life for child patients.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

AUTHOR CONTRIBUTIONS

AGP—designed the study, contributed to analyze the data, led the writing, reviewed the manuscript and contributed to discussion. JARC, HMFR, TVG and KAMN—reviewed the manuscript and contributed to discussion.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The research protocol was reviewed and approved by the Ethics Committee at the Iztacala Faculty of Higher Studies of the National Autonomous University of Mexico (CE/FESI/062022/1520). The corresponding authorities at the public primary schools and the parents/guardians of the children were informed of the study objectives and the procedures to be followed as part of the research. Those parents/guardians who agreed to the participation of their children gave their signed informed consent, with the children themselves also providing their signed informed assent to participate in the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Seow WK. Developmental defects of enamel and dentine: challenges for basic science research and clinical management. Australian Dental Journal. 2014; 59: 143–154.

[2] Zameer M, Birajdar SB. The ‘mysterious aetiology’ of molar incisor hypomineralisation. European Archives of Paediatric Dentistry. 2022; 23: 987–988.

[3] de Farias AL, Rojas-Gualdrón DF, Girotto Bussaneli D, Santos-Pinto L, Mejía JD, Restrepo M. Does molar-incisor hypomineralization (MIH) affect only permanent first molars and incisors? New observations on permanent second molars. International Journal of Paediatric Dentistry. 2022; 32: 1–10.

[4] Sluka B, Held U, Wegehaupt F, Neuhaus KW, Attin T, Sahrmann P. Is there a rise of prevalence for molar incisor hypomineralization? A meta-analysis of published data. BMC Oral Health. 2024; 24: 127.

[5] Neboda C, Anthonappa RP, King NM. Tooth mineral density of different types of hypomineralised molars: a micro-CT analysis. European Archives of Paediatric Dentistry. 2017; 18: 377–383.

[6] Fagrell TG, Dietz W, Jälevik B, Norén JG. Chemical, mechanical and morphological properties of hypomineralized enamel of permanent first molars. Acta Odontologica Scandinavica. 2010; 68: 215–222.

[7] Farah RA, Swain MV, Drummond BK, Cook R, Atieh M. Mineral density of hypomineralised enamel. Journal of Dentistry. 2010; 38: 50–58.

[8] Bozal CB, Kaplan A, Ortolani A, Cortese SG, Biondi AM. Ultrastructure of the surface of dental enamel with molar incisor hypomineralization (MIH) with and without acid etching. Acta Odontológica Latinoamericana. 2015; 28: 192–198.

[9] Bhandari R, Thakur S, Singhal P, Chauhan D, Jayam C, Jain T. *In vivo* comparative evaluation of esthetics after microabrasion and microabrasion followed by casein phosphopeptide-amorphous calcium fluoride phosphate on molar incisor hypomineralization-affected incisors. Contemporary Clinical Dentistry. 2019; 10: 9–15.

[10] Gatón-Hernandéz P, Serrano CR, da Silva LAB, de Castañeda ER, da Silva RAB, Pucinelli CM, *et al*. Minimally interventive restorative care of teeth with molar incisor hypomineralization and open apex—a 24-month longitudinal study. International Journal of Paediatric Dentistry. 2020; 30: 4–10.

[11] Rao A, Malhotra N. The role of remineralizing agents in dentistry: a review. Compendium of Continuing Education in Dentistry. 2011; 32: 26–33; quiz 34, 36.

[12] Restrepo M, Jeremias F, Santos-Pinto L, Cordeiro RC, Zuanon AC. Effect of fluoride varnish on enamel remineralization in anterior teeth with molar incisor hypomineralization. Journal of Clinical Pediatric Dentistry. 2016; 40: 207–210.
[13] Pollick H. The role of fluoride in the prevention of tooth decay. Pediatric clinics of North America. 20148; 65: 923–940.
[14] Baik A, Alamoudi N, El-Housseiny A, Altuwirqi A. Fluoride varnishes for preventing occlusal dental caries: a review. Dentistry Journal. 2021; 9: 64.
[15] Donly KJ. Fluoride varnishes. Journal of the California Dental Association. 2003; 31: 217–219.
[16] Mohd Said SN, Ekambaram M, Yiu CK. Effect of different fluoride varnishes on remineralization of artificial enamel carious lesions. International Journal of Paediatric Dentistry. 2017; 27: 163–173.
[17] Byeon SM, Lee MH, Bae TS. The effect of different fluoride application methods on the remineralization of initial carious lesions. Restorative Dentistry & Endodontics. 2016; 41: 121–129.
[18] Olgen IC, Sonmez H, Bezgin T. Effects of different remineralization agents on MIH defects: a randomized clinical study. Clinical Oral Investigations. 2022; 26: 3227–3238.
[19] Sezer B, Kargul B. Effect of remineralization agents on molar-incisor hypomineralization-affected incisors: a randomized controlled clinical trial. Journal of Clinical Pediatric Dentistry. 2022; 46: 192–198.
[20] Biondi AM, Cortese SG, Babino L, Fridman DE. Comparison of mineral density in molar incisor hypomineralization applying fluoride varnishes and casein phosphopeptide-amorphous calcium phosphate. Acta Odontológica Latinoamericana. 2017; 30: 118–123.
[21] Gutiérrez TV, Ortega CCB, Pérez NP, Pérez AG. Impact of molar incisor hypomineralization on oral health-related quality of life in Mexican schoolchildren. Journal of Clinical Pediatric Dentistry. 2019; 43: 324–330.
[22] Billings M, Lopez Mitnik G, Dye B. Sample size for clinical trials. Oral Diseases. 2017; 23: 1013–1018.
[23] Lygidakis NA, Dimou G, Marinou D. Molar-incisor-hypomineralisation (MIH). A retrospective clinical study in Greek children. II. Possible medical aetiological factors. European Archives of Paediatric Dentistry 2008; 9: 207–217.
[24] Inchingolo AM, Inchingolo AD, Viapiano F, Ciocia AM, Ferrara I, Netti A, *et al*. Treatment approaches to molar incisor hypomineralization: a systematic review. Journal of Clinical Medicine. 2023; 12: 7194.
[25] Bizhang M, Kaleta-Kragt S, Singh-Hüsgen P, Altenburger MJ, Zimmer S. Effect of 10% fluoride on the remineralization of dentin *in situ*. Journal of Applied Oral Science. 2015; 23: 562–570.
[26] Piesiak-Pańczyszyn D, Zakrzewski W, Piszko A, Piszko PJ, Dobrzyński M. Review on fluoride varnishes currently recommended in dental prophylaxis. Polymers in Medicine. 2023; 53: 141–151.
[27] Bijle MN, Ekambaram M, Lo EC, Yiu CKY. The enamel remineralization potential of fluoride varnishes containing arginine. Journal of Dentistry. 2020; 99: 103411.
[28] Koruyucu M, Özel S, Tuna EB. Prevalence and etiology of molar-incisor hypomineralization (MIH) in the city of Istanbul. Journal of Dental Sciences. 2018; 13: 318–328.
[29] West NX, Joiner A. Enamel mineral loss. Journal of Dentistry. 2014; 42: S2–S11.
[30] Sezer B, Tuğcu N, Calışkan C, Durmuş B, Kupets T, Bekiroğlu N, *et al*. Effect of casein phosphopeptide amorphous calcium fluoride phosphate and calcium glycerophosphate on incisors with molar-incisor hypomineralization: a cross-over, randomized clinical trial. Bio-Medical Materials and Engineering. 2022; 33: 325–335.
[31] Lygidakis NA, Garot E, Somani C, Taylor GD, Rouas P, Wong FSL. Best clinical practice guidance for clinicians dealing with children presenting with molar-incisor-hypomineralisation (MIH): an updated European Academy of Paediatric Dentistry policy document. European Archives of Paediatric Dentistry. 2022; 23: 3–21.
[32] Altan H, Yilmaz RE. Clinical evaluation of resin infiltration treatment masking effect on hypomineralised enamel surfaces. BMC Oral Health. 2023; 23: 444.
[33] Farah RA, Drummond BK, Swain MV, Williams S. Relationship between laser fluorescence and enamel hypomineralisation. Journal of Dentistry. 2008; 36: 915–921.
[34] Juárez-López MLA, Salazar-Treto LV, Hernández-Monjaraz B, Molina-Frechero N. Etiological factors of molar incisor hypomineralization: a systematic review and meta-analysis. Dentistry Journal. 2023; 11: 111.
[35] Garot E, Rouas P, Somani C, Taylor GD, Wong F, Lygidakis NA. An update of the aetiological factors involved in molar incisor hypomineralisation (MIH): a systematic review and meta-analysis. European Archives of Paediatric Dentistry. 2022; 23: 23–38.
[36] Crombie FA, Manton DJ, Palamara JE, Zalizniak I, Cochrane NJ, Reynolds EC. Characterisation of developmentally hypomineralised human enamel. Journal of Dentistry. 2013; 41: 611–618.
[37] Cardoso-Martins I, Pessanha S, Coelho A, Arantes-Oliveira S, Marques PF. Evaluation of the efficacy of CPP-ACP remineralizing mousse in molar-incisor hypomineralized teeth using Polarized Raman and Scanning Electron Microscopy—an *in vitro* study. Biomedicines. 2022; 10: 3086.

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