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Clinical Technique

Molar Incisor Hypomineralization: Etiology, Clinical Aspects, and a Restorative Treatment Case Report

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Clinical Relevance

Total-etch adhesive systems and resin composite are clinically viable dental materials for esthetic restorations in teeth presenting white/yellow/brown hypomineralization stains.

SUMMARY

Molar-incisor hypomineralization (MIH) is a condition that negatively affects enamel and dentin, especially the first molars and permanent incisors, causing esthetic and functional problems. The present clinical case report presents and discusses the etiology and clinical characteristics of MIH and describes a restorative protocol for MIH-affected teeth.

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INTRODUCTION

Among the pathologies that may negatively affect the smile and dental structures, molar incisor hypomineralization (MIH) is defined as a systemic hypomineralization of qualitative character that directly affects the enamel and dentin of the first molars, with or without the involvement of the incisors.[1] Less frequently, MIH-like defects have been reported in permanent canines, premolars, and primary second molars.[2-4] As result of an altered (or disturbed) matrix production, secretion, arrangement, crystal formation, or matrix resorption, a compromised enamel structure may be observed.[5] Defects during calcification/maturation stages usually lead to normal volumes of enamel with insufficient mineralization (hypomineralization) and, consequently, altered translucency. MIH, amelogenesis imperfecta, and dental fluorosis are examples of such qualitative alterations.[4,6,7] On the other hand,

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quantitative defects (hypoplasia) are caused by a disturbance during the amelogenesis matrix secretion phase.[8,9]

MIH-affected teeth usually present the enamel with opaque-white, yellow, or brown colorations, with or without posteruptive degradation (PED), varying according to its severity.[1,5,10-12] The mild form of MIH is associated with delimited opaque areas, varying from white to brown, in nonstress areas on first permanent molars, with no structural loss and no dental sensitivity.[10,13-15] Moderate (with slight or no dental sensitivity)[15] and severe forms of MIH are associated with opaque areas at the occlusal/incisal third of teeth. This area occasionally undergoes PED due to reduced hardness and high porosity of enamel, leading to functional and esthetic complications and dental sensitivity.[15-17] PED commonly leads to surfaces that are more susceptible to biofilm accumulation and development of carious lesions.[18] In severe cases, PED may lead to dental sensitivity due to dentin exposure.[1,19] MIH usually presents asymmetrically, affecting two-thirds of the crowns of molars and incisors. One group of teeth may be more affected than the other.[20]

There are multiple treatment options for MIH-affected teeth, which include preventive, desensitizing, and remineralizing products; calcium and vitamin supplements; resin infiltration; fissure sealants; enamel microabrasion; direct or indirect restorations; extractions; and orthodontic alignment.[4,19] The choice and indication of treatment depend on the severity, patient age, socioeconomic factors, and treatment expectations.[21,22] Restorative procedures are great treatment options for teeth with structure loss, requiring restoration of function and esthetics. Some materials and procedures may be considered, including resin composite direct restorations, ceramic indirect restorations, and prefabricated metallic crowns (posterior teeth).[23] However, adhesive procedures on MIH-affected teeth are critical and may affect the bond strength and longevity of these restorations.[16,24-26] More invasive procedures, such as extractions, are adopted for teeth with major structural impairment, aiming for a future orthodontic/prosthetic rehabilitation after dental surgery.[22]

Therefore, the aim of the present clinical case report is to demonstrate an esthetic restorative procedure performed on MIH-affected teeth. The 18-month clinical follow-up and articles concerning MIH are presented and discussed.

CLINICAL CASE REPORT

A 17-year-old female patient presented to the Restorative Dentistry Clinic of Ingá University Center–UNINGÁ (Maringá, PR, Brazil) with a chief complaint of poor esthetics. The patient presented with stains on the maxillary and mandibular anterior teeth (Figures 1 and 2). During anamnesis, the patient's guardian reported that she was born with low birth weight and was hospitalized due to a severe condition of anemia during childhood (when she was about 1 year old) and had antianemic injections, recommended in cases of iron deficiency. The use of amoxicillin was also frequent because of respiratory tract infections (chronic bronchitis) that affected her during infancy (18 months old until 8 years old), and associated with the use of nebulizers to help the pulmonary air ventilation as well.

During dental examination, white, yellow, and brown stains were observed on the buccal surfaces of the maxillary canines, laterals, and central incisors (Figures 1 and 2). On the mandibular teeth, white/"creamy" stains were found on the facial surface of the left lateral incisor and in both central incisors (Figures 1 and 2A). Milder enamel stains were observed on both mandibular canines and on the right lateral incisor. Residual bonding materials were found after bracket debonding on the right maxillary lateral incisor and canine and on the maxillary left lateral incisor. The guardian also reported that the patient's first mandibular permanent molars presented severe structure loss and were submitted to surgical extractions when the patient was 10 years old. The depths of each stain were assessed by positioning the tip of a light-emitted diode (LED) light-curing unit from the palatal/lingual surfaces (Figure 3). Considering both clinical and medical history, MIH was diagnosed. The clinicians proposed the following treatment plan, which was accepted by the patient and guardian: 1) at-home vital dental bleaching; 2) enamel microabrasion on teeth #6, #7, and #10; and 3) direct composite resin restorations on teeth #8, #9, and #11.

At-home dental bleaching was performed by using 10% carbamide peroxide (Opalescence PF, Ultradent Inc, South Jordan, UT, USA) for 2 hours per day, for 20 days. Alginate impressions of the maxillary and mandibular arches were made, and stone models were poured and used to fabricate the custom acetate bleaching trays. The patient was instructed to place a small drop of bleaching product into each tooth section and to contact the clinician if any discomfort or sensitivity occurred. The bleaching treatment

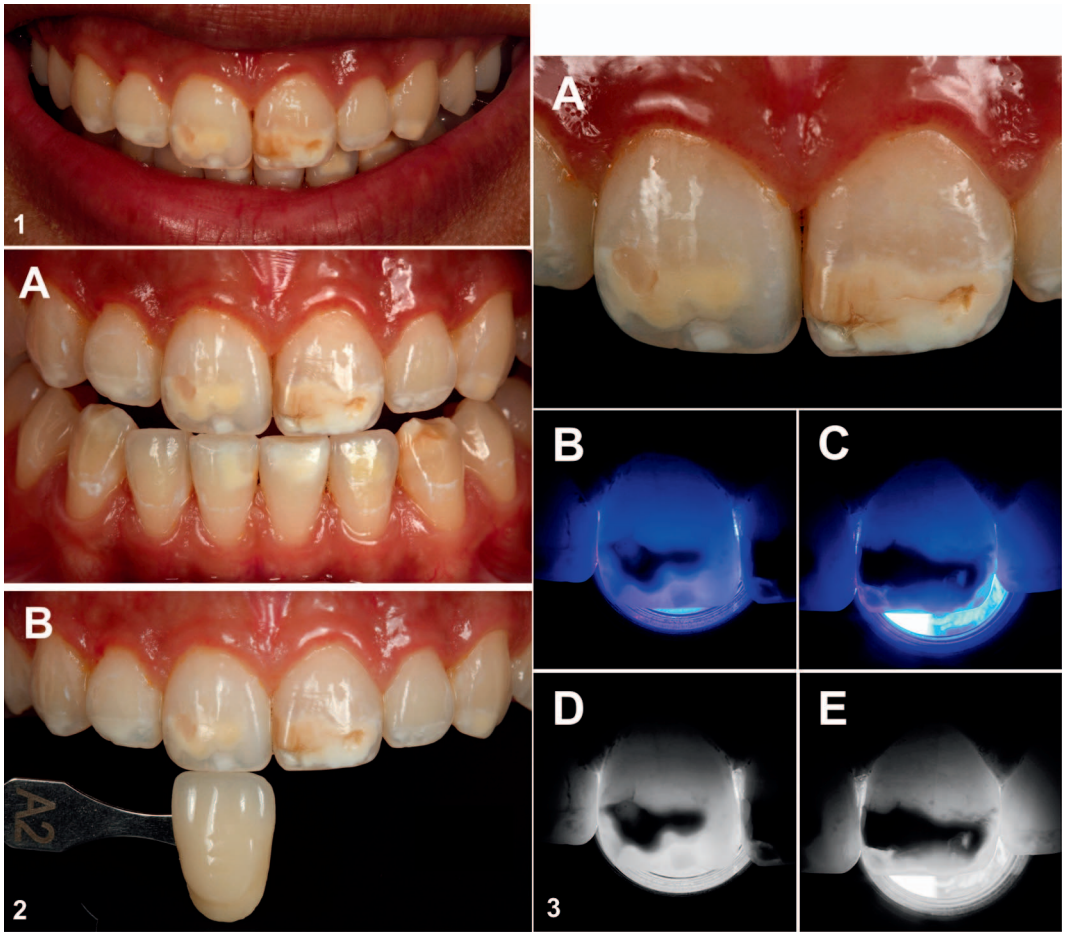

Figure 1. *Initial clinical aspect showing white/yellow/brown stains in maxillary and mandibular anterior teeth.*

Figure 2. *(A): Intraoral view during mandibular protrusion (note the white/yellow/brown stains in maxillary and mandibular anterior teeth). (B) Initial teeth shade evaluation (color A2 using Ivoclar shade guide).*

Figure 3. *(A): Close-up view of stained central incisors. Transillumination assessment positioning the tip of the light-curing unit at the palatal surface on the right (B and D) and left (C and E) maxillary central incisors. Dark and intense color indicates deep stains.*

resulted in a color alteration from A2 to B1 (Ivoclar Shade Guide, Vita Shade System) using a visual assessment method (Figure 4).

After 1 month, the restorative procedures with resin composite were performed. The chromatic mapping was made by placing small resin composite increments (Vit-l-escence, Ultradent Inc) on the buccal surface of the maxillary incisors (Figure 5). After rubber dam isolation, the hypomineralized stains were removed using a spherical diamond bur (#1014, KG Sorensen, Cotia, SP, Brazil) coupled to a high-speed handpiece with water irrigation (Figure 6). After complete removal, the enamel was etched for 30 seconds and dentin for 15 seconds using 35% phosphoric acid (Ultra-Etch, Ultradent Inc; Figure 7). Then, the primer (step 2) of a total-etch three-step adhesive system (Adper Scotchbond Multi-Purpose, 3M ESPE, St Paul, MN, USA) was applied only to dentin. Solvent from the primer was allowed to evaporate using air from the syringe for 15 seconds, followed by the unfilled adhesive resin application (adhesive, step 3; Figure 8). The adhesive was light activated for 10 seconds using a polywave LED light-curing unit (Valo Cordless, Ultradent Inc) in the regular mode (1,000 mW/cm^2). Resin composite restoration (Vit-l-escence) was made using an incremental technique, respecting the original dental anatomy (Figure 9).[27]

The enamel microabrasion was performed for residual orthodontic bonding materials, intrinsic stain removal, and regularization of the enamel surface (Figure 10).[28,29] The surface layers of the stained enamels located on the buccal surface of both maxillary lateral incisors and right maxillary canine

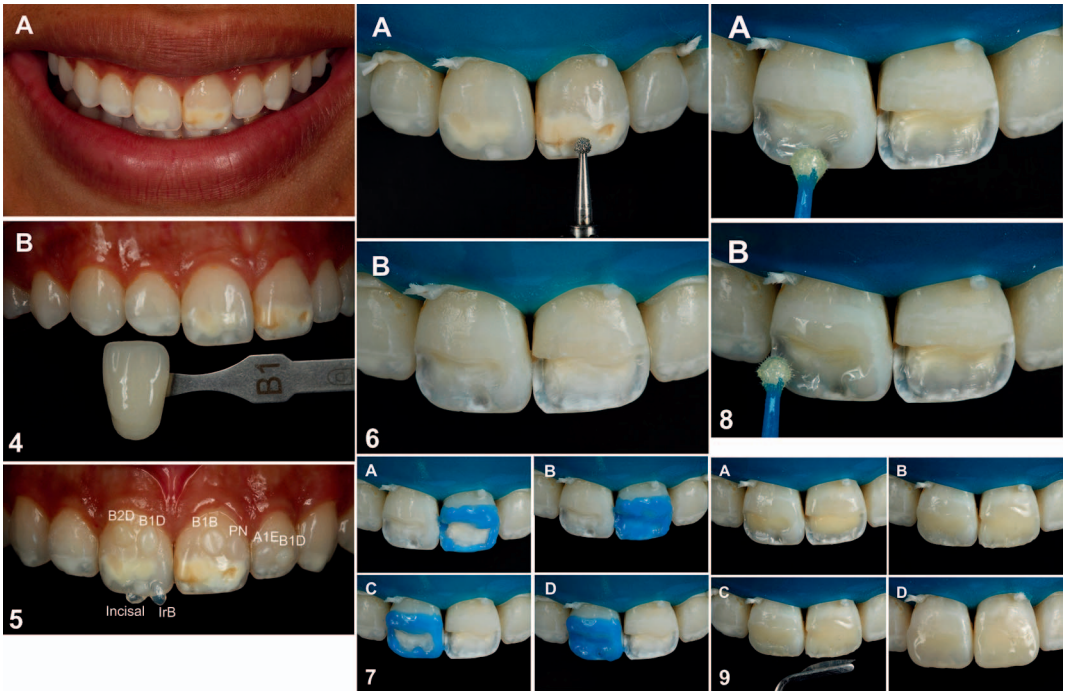

Figure 4. *(A): Clinical aspect after at-home dental bleaching. (B) Teeth shade selection using a visual color scale (color B1 using Ivoclar shade guide).*

Figure 5. *Resin composite (Vit-l-escence, Ultradent Inc) color mapping prior to direct restorations: [B2D] Dentin, B2; [B1D] Dentin, B1; [PN] Enamel, Pearl Neutral; [IrB] Incisal, Iridescent Blue; [A1E] Enamel, A1; [B1D] Dentin, B1; [Incisal] Incisal shade (Forma, Ultradent Inc.).*

Figure 6. *Complete removal of hypomineralized stains using a spherical diamond bur (#1014, KG Sorensen) on the buccal surface of both maxillary central incisors.*

Figure 7. *(A, C): Acid etching with 35% phosphoric acid for 30 seconds on enamel. (B, D): Acid etching with 35% phosphoric acid for 15 seconds on dentin.*

Figure 8. *(A): Application of primer (step 2) on dentin only. (B): Application of the unfilled adhesive (step 3) on the entire preparation. Same protocol was adopted for the left maxillary central incisor.*

Figure 9. *(A): Increment of B2 Dentin resin composite. (B): Increment of B1 Dentin resin composite. (C): Increment of Iridescent Blue at the incisal third. (D): Increment of Pearl Neutral Enamel shade as the last increment.*

were removed using a super-fine (macroabrasion) tapered bur (#3195FF, KG Sorensen) under copious water irrigation attached to a high-speed handpiece (Figure 10A,C). A microabrasive product (Opalustre, Ultradent Inc) was used to remove the remaining stains, using a specially designed rubber cup (Opal-Cups, Ultradent Inc) with a low-speed handpiece (Figure 10B,D). After two weeks, it was observed that the incisal stains were not completely removed on teeth #6 and #7 since they were deeper than the enamel microabrasion was able to remove. Thus, direct resin composite restorations were made on both maxillary lateral incisor and right maxillary canine (Figure 11) following the technique described above for both maxillary central incisors.

Finishing and polishing procedures were performed using an aluminum oxide disc (Sof-Lex, 3M ESPE), followed by abrasive rubber discs (Jiffy, Ultradent Inc; Figure 12). Later, a silicon-carbide–impregnated brush (Jiffy Brush, Ultradent Inc) was used, followed by the application of a diamond paste (Diamond Polish, Ultradent Inc) using a goat-hair brush. The patient was satisfied with the treatment (Figure 13) and did not want to remove the stains located in the mandibular teeth. Figure 14 represents the 18-month follow-up of the procedures.

DISCUSSION

The present clinical case report describes the esthetic restorative treatment of MIH-affected teeth using a combination of dental bleaching, direct resin composite restorations, and enamel microabrasion. The last procedure was performed to remove resid-

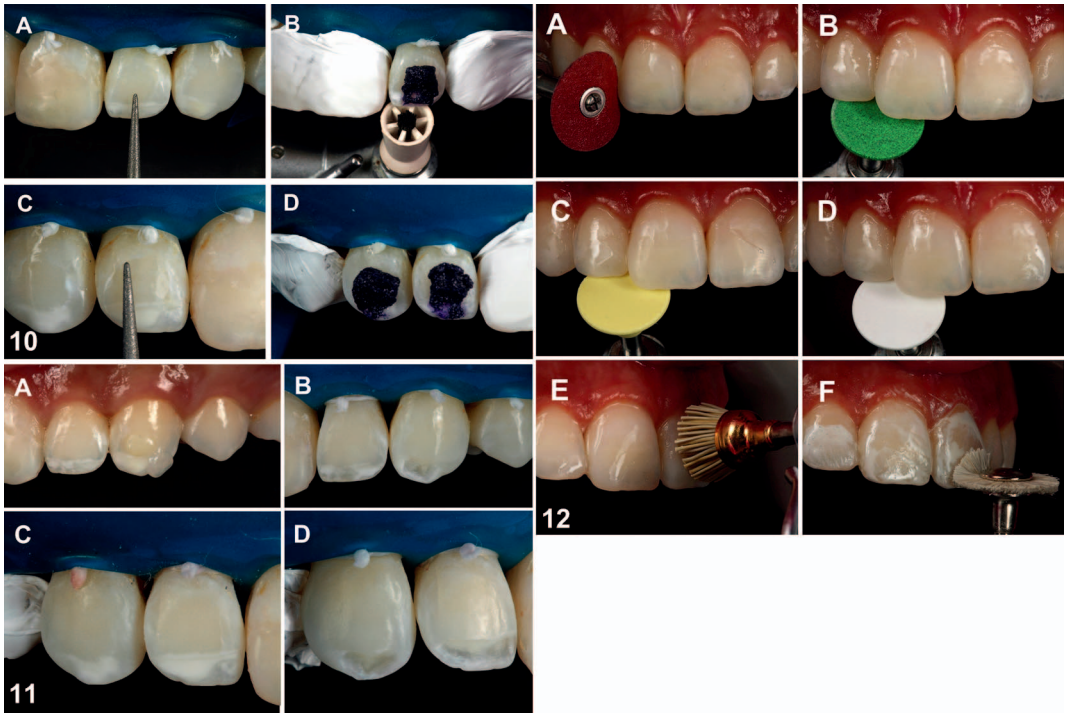

Figure 10. *(A, C): Macroabrasion using a super-fine tapered diamond bur (#3195, KG Sorensen) on the buccal surface of both maxillary lateral incisors and right maxillary canine. (B): Application of the microabrasive product (Opalustre, Ultradent Inc) using the specific rubber cup (Opalcup, Ultradent Inc).*

Figure 11. *(A): Resin composite shade mapping on the left maxillary canine before direct resin composite restoration ([B2D] Dentin, B2 and Pearl Neutral Enamel shade). (B): Complete removal of the stained opacity at the incisal third. (C): Stained buccal surface at the incisal surface. (D): Removed stains prior to direct resin composite restoration. Although the stain is evident in the left lateral incisor during rubber damn isolation, it was not necessary to perform a direct restoration since the stain disappears when hydrated in saliva.*

Figure 12. *(A): Finishing using aluminum oxide disc. (B-D): Abrasive rubber discs with progressive reduction of abrasive size. (E): Impregnated silicon carbide brush. (F): Use of a diamond paste associated with a goat-hair brush.*

ual orthodontic bracket bonding materials and white remineralized stains around them and, consequently, smoothening the enamel surface after bracket debonding.[29] The patient was satisfied with the clinical esthetic outcomes from the described techniques.

Disturbance (ie, illness) during the late enamel maturation phase of amelogenesis may negatively affect the function of ameloblasts (which are very sensitive to changes in their surrounding environment),[30] leading to the qualitative defects found in MIH.[31] The MIH diagnosis was based on medical and dental history. The best age for a correct diagnosis of MIH is about eight years, as the maxillary and mandibular permanent incisors and first molars are fully erupted.[32] The patient's guardian reported that the patient presented with severe anemia during early childhood. This information is of great value, since the etiology of MIH may be related to some systemic factors and changes/problems during the prenatal (ie, hypocalcemia and/or diabetes), perinatal (ie, premature birth or prolonged delivery), and/or postnatal periods (ie, antibiotic use and/or nutrition problems).[33] The severe anemia reported was framed as one of the possible causes of MIH.[34] The etiology of MIH is not fully elucidated,[5,33,35] and it is difficult to obtain scientific evidence on the origins/causes of MIH development because of the lack of standardized measurement protocols/guidelines. Therefore, well-designed future cohort studies are required.[36-38]

Scientific reports[37,39-41] found that premature birth and low birth weight are associated with MIH. Moreover, there is considerable evidence of an association between early childhood illness (fever, asthma, and pneumonia, up to three or four years of age) and MIH.[38,42] A positive correlation was reported between respiratory disease and a severe variant of MIH with incisor involvement,[43] including bronchitis,[39,44] and ear, nose, and throat diseases.[11] A genetic

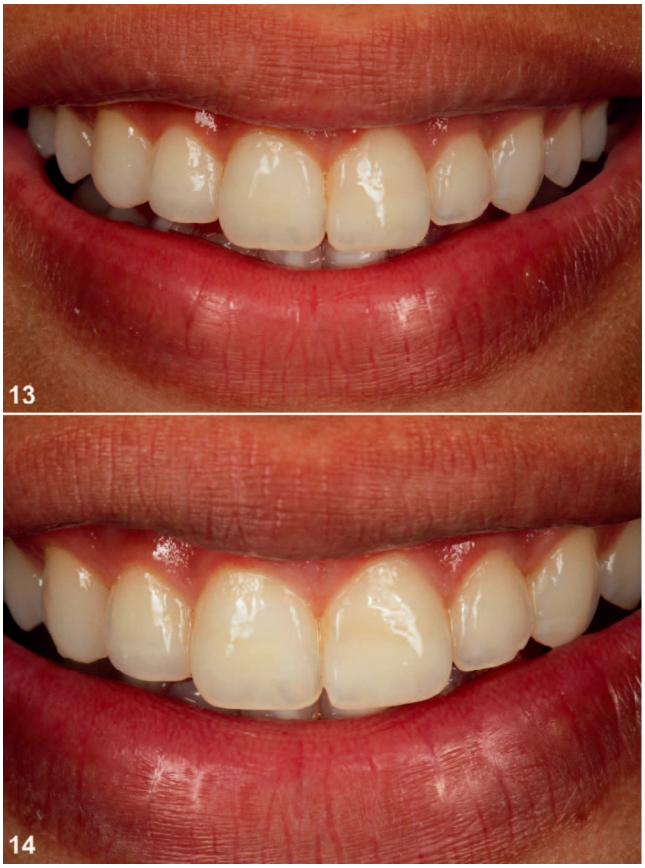

Figure 13. *Clinical aspect after 1 week.*

Figure 14. *Clinical aspect after 18 months (resin composite restorations were repolished).*

component from multifactorial pathogenesis was also hypothesized.[37,42,45] A systematic review[42] reported several studies indicating that chickenpox, renal disease, measles, gastrointestinal disease, tonsillitis, otitis, and adenoiditis might be related to the etiology of MIH. Medication intake (eg, antibiotics such as amoxicillin or penicillin) is strongly associated with MIH etiology and development.[11,46-48] Corticosteroids and bronchodilators (asthma drugs) were related to enamel defects as well.[49] It is noteworthy to state that the mineralization of the first permanent molars usually starts at birth and is fully completed at four to five years of age.[50] The early use of those drugs may have a negative influence on the amelogenesis process. Many of those factors may have influenced or increased the odds of MIH development for the patient presented in this case report, including low birth weight, bronchitis, anemia, and antibiotic intake.

The human dental enamel, in its normal state, has a mineral content of 95%, which leads to a high hardness that can withstand occlusal forces and chewing. The other 5% consists of water (4%) and traces of organic content.[51,52] Generally, the MIH-affected enamel presents a reduction in the quantity and quality of mineral content compared with normal enamel. Thus, MIH-affected enamel has a reduced content of calcium and phosphate, and consequently, there is a reduction in the hardness and elasticity, increased porosity,[31,53-56] increased carbon and carbonate concentrations, and greater protein content,[31,45,54,55,57] which hamper the growth of hydroxyapatite crystals.[58,59] Also, the MIH-affected enamel is not organized into hydroxyapatite crystals, usually presenting loosely packed crystals, less-dense prismatic structure, partial loss of the prismatic pattern, less distinct prism borders, and more evident interprismatic space.[53,55,57,60,61] Studies[54-57] have demonstrated that MIH lesions start at the enamel-dentin junction and end at the enamel surface; thus, MIH lesions are located throughout the whole enamel thickness. All of this information attests to the fact that hypomineralized enamel is more fragile than sound enamel.

The degree of lesion opacities is directly related to the degree of porosity: creamy/white lesions and those without posteruptive breakdown are less porous when compared with yellow/brown–colored enamel.[55,56,62] Thus, yellow/brown opacities are more prone to evolve into PED when compared with white/creamy opacities.[12] Dentin may also be negatively affected by MIH, presenting lower mineral density when compared with nonaffected dentin, at the cervical region.[56] Heijs and colleagues[63] reported that MIH-affected dentin under MIH-affected enamel presents few morphological alterations, of which the most significant is the increased interglobular dentin compared with a normal dentin. However, no structural differences were verified when compared with nonaffected enamel.

In MIH-affected teeth, the restoration stage is problematic because of the micromorphological changes found in the hard tissues, which may adversely affect the adhesion between the restorative materials and these substrates.[24,25] A significantly higher bond strength to sound enamel when compared with MIH-affected enamel has been reported, regardless of the type of adhesive system used (total-etch or self-etch systems).[23,25] The explanation is that a conventional phosphoric etching pattern on MIH enamel is much less pronounced, and this etching also exposes porosities and voids resulting in a "weak link for enamel-resin bond."[25] An abnormal etching pattern in MIH-affected enam-

el compared with sound enamel was found in other studies.[54,61] Moreover, total-etch adhesive systems demonstrated higher bond strength to MIH-affected enamel when compared with self-etch adhesive systems.[25] On the other hand, dentin adhesion beneath hypomineralized enamel seems not to be negatively affected and may be performed using either total-etch or self-etch adhesive systems.[25]

Considering all of this information, all MIH-affected enamel was removed so as not to jeopardize the bonding quality between the adhesive system and enamel. This procedure ensured that margins were in sound enamel since the cavosurface margins in hypomineralized enamel show less bonding capability[16] and may be more susceptible to marginal breakdown. An *in vivo* study[26] found increased restoration failures in first permanent molars when the hypomineralized tissue was left surrounding the cavities, which means that the complete removal of hypomineralized enamel significantly increases the success of MIH-affected teeth restored with resin composite compared with a noninvasive/conservative group (hypomineralized tissue was left in the cavity). Similarly, Fagrell and others[64] also recommended the need for removal of MIH-affected areas up to healthy enamel to ensure adequate adhesion and less chance of bacterial invasion,[5,64] but with more tooth structure loss.

For anterior teeth, the removal of all white/yellow/brown stains is also reasonable because of esthetic concerns. Sönmez and others[26] recommended a more conservative technique by treating the hypomineralized enamel with NaOCl instead of removing all the MIH-affected enamel. However, leaving white/yellow/brown stains around the margins of the preparation may affect the esthetic quality, especially on the facial surfaces of incisors. Future studies should describe and standardize guidelines for assessing the causes of MIH and surface treatments prior to bonding, in order to achieve more conservative dental preparations for resin composite restorations in MIH-affected teeth.

CONCLUSIONS

Regardless the cause of MIH, the restorative treatment should comprise the removal of all MIH-affected dental hard tissues (enamel and dentin) prior to bonding procedures for resin composite restorations. After 18 months, satisfactory bonding to MIH-affected teeth using a total-etch adhesive system was observed. Preventive treatments (topical fluoride application, glass-ionomer restorations) should be adopted as soon as the MIH is diagnosed in order to avoid PED, development of caries lesions and pain, and, consequently, invasive treatments such as root canal treatments or extractions.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the Ingá University Center–UNINGÁ, Brazil.

Conflict of Interest

The authors of this article certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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REFERENCES

1. Weerheijm KL, Jälevik B, & Alaluusua S (2001) Molar-incisor hypomineralization *Caries Research* **35(5)** 390-391.
2. Elfrink ME, ten Cate JM, Jaddoe VW, Hofman A, Moll HA, & Veerkamp JS (2012) Deciduous molar hypomineralization and molar incisor hypomineralization *Journal of Dental Research* **91(6)** 551-555.
3. Negre-Barber A, Montiel-Company JM, Boronat-Catalá M, Catalá-Pizarro M, & Almerich-Silla JM (2016) Hypomineralized second primary molars as predictor of molar incisor hypomineralization *Scientific Reports* **6** 31929.
4. da Cunha Coelho ASE, Mata PCM, Lino CA, Macho VMP, Areias CMFGP, Norton APMAP, & Augusto APCM (2019) Dental hypomineralization treatment: a systematic review *Journal of Esthetic and Restorative Dentistry* **31(1)** 26-39.
5. Elhennawy K, Manton DJ, Crombie F, Zaslansky P, Radlanski RJ, Jost-Brinkmann PG, & Schwendicke F (2017) Structural, mechanical and chemical evaluation of molar-incisor hypomineralization-affected enamel: a systematic review *Archives of Oral Biology* **83** 272-281.
6. Wright JT (2006) The molecular etiologies and associated phenotypes of amelogenesis imperfecta *American Journal of Medical Genetics Part A* **140(23)** 2547-2555.
7. Jacobsen PE, Haubek D, Henriksen TB, stergaard JR, & Poulsen S (2014) Developmental enamel defects in children born preterm: a systematic review *European Journal of Oral Sciences* **122(1)** 7-14.
8. Clarkson J (1989) Review of terminology, classifications, and indices of developmental defects of enamel *Advances in Dental Research* **3(2)** 104-109.
9. Mahoney E, Ismail FS, Kilpatrick N, & Swain M (2004) Mechanical properties across hypomineralized/hypoplastic enamel of first permanent molar teeth *European Journal of Oral Sciences* **112(6)** 497-502.
10. Bullio Fragelli CM, Jeremias F, Feltrin de Souza J, Paschoal MA, de Cassia Loiola Cordeiro R, & Santos-Pinto L (2015) Longitudinal evaluation of the structural integrity of teeth affected by molar incisor hypomineralisation *Caries Research* **49(4)** 378-383.

11. Giuca MR, Cappè M, Carli E, Lardani L, & Pasini M (2018) Investigation of clinical characteristics and etiological factors in children with molar incisor hypomineralization *International Journal of Dentistry* **2018** 7584736. doi:10.1155/2018/7584736
12. Cabral RN, Nyvad B, Soviero VLVM, Freitas E, & Leal SC (2019) Reliability and validity of a new classification of MIH based on severity *Clinical Oral Investigations*. In press.
13. Da Costa-Silva CM, Ambrosano GM, Jeremias F, De Souza JF, & Mialhe FL (2011) Increase in severity of molar-incisor hypomineralization and its relationship with the colour of enamel opacity: a prospective cohort study *International Journal of Paediatric Dentistry* **21(5)** 333-341.
14. Fragelli CM, Souza JF, Jeremias F, Cordeiro Rde C, & Santos-Pinto L (2015) Molar incisor hypomineralization (MIH): conservative treatment management to restore affected teeth *Brazilian Oral Research* **29** 1-7.
15. Pasini M, Giuca MR, Scatena M, Gatto R, & Caruso S (2018) Molar incisor hypomineralization treatment with casein phosphopeptide and amorphous calcium phosphate in children *Minerva Stomatologica* **67(1)** 20-25.
16. de Souza JF, Fragelli CB, Jeremias F, Paschoal MAB, Santos-Pinto L, & de Cássia Loiola Cordeiro R (2017) Eighteen-month clinical performance of composite resin restorations with two different adhesive systems for molars affected by molar incisor hypomineralization *Clinical Oral Investigations* **21(5)** 1725-1733.
17. Raposo F, de Carvalho Rodrigues AC, Lia ÉN, & Leal SC (2019) Prevalence of hypersensitivity in teeth affected by molar-incisor hypomineralization (MIH) *Caries Research* **53(4)** 424-430.
18. Americano GC, Jacobsen PE, Soviero VM, & Haubek D (2017) A systematic review on the association between molar incisor hypomineralization and dental caries *International Journal of Paediatric Dentistry* **27(1)** 11-21.
19. Lygidakis NA, Wong F, Jälevik B, Vierrou AM, Alaluusua S, & Espelid I (2010) Best clinical practice guidance for clinicians dealing with children presenting with molar-incisor hypomineralization (MIH): an EAPD policy document *European Archives of Paediatric Dentistry* **11(2)** 75-81.
20. Jälevik B (2010) Prevalence and diagnosis of molar-incisor-hypomineralization (MIH): a systematic review *European Archives of Paediatric Dentistry* **11(2)** 59-64.
21. Weerheijm KL, Duggal M, Mejàre I, Papagiannoulis L, Koch G, Martens LC, & Hallonsten AL (2003) Judgement criteria for molar incisor hypomineralization (MIH) in epidemiologic studies: a summary of the European meeting on MIH held in Athens, 2003 *European Journal of Paediatric Dentistry* **4(3)** 110-113.
22. Kotsanos N, Kaklamanos EG, & Arapostathis K (2005) Treatment management of first permanent molars in children with molar-incisor-hypomineralisation *European Journal of Paediatric Dentistry* **6(4)** 179-184.
23. William V, Burrow MF, Palamara JE, & Messer LB (2006) Microshear bond strength of resin composite to teeth affected by molar hypomineralization using 2 adhesive systems *Pediatric Dentistry* **28(3)** 233-241.
24. Jälevik B & Klingberg GA (2002) Dental treatment, dental fear and behavior management problems in children with severe enamel hypomineralization of their permanent first molars *International Journal of Paediatric Dentistry* **12(1)** 24-32.
25. Krämer N, Bui Khac NN, Lücker S, Stachniss V, & Frankenberger R (2018) Bonding strategies for MIH-affected enamel and dentin *Dental Materials* **34(2)** 331-340.
26. Sönmez H & Saat S (2017) A clinical evaluation of deproteinization and different cavity desgins on resin restoration performance in MIH-affected molars: two-year results *Journal of Clinical Pediatric Dentistry* **41(5)** 336-342.
27. Yanikian C, Yanikian F, Sundfeld D, Lins R, & Martins L (2019) Direct composite resin veneers in nonvital teeth: a still viable alternative to mask dark substrates *Operative Dentistry* **44(4)** E159-E166.
28. Sundfeld RH, Croll TP, Briso AL, de Alexandre RS, & Sundfeld Neto D (2007) Considerations about enamel microabrasion after 18 years *American Journal of Dentistry* **20(2)** 67-72.
29. Sundfeld RH, Franco LM, Machado LS, Pini N, Salomao FM, Anchieta RB, & Sundfeld D (2016) Treatment of enamel surfaces after bracket debonding: case reports and long-term follow-ups *Operative Dentistry* **41(1)** 8-14.
30. Tung K, Fujita H, Yamashita Y, & Takagi Y (2006) Effect of turpentine-induced fever during the enamel formation of rat incisor *Archives of Oral Biology* **51(6)** 464-470.
31. Farah RA, Monk BC, Swain MV, & Drummond BK (2010) Protein content of molar-incisor hypomineralisation enamel *Journal of Dentistry* **38(7)** 591-596.
32. Garg N, Jain AK, Saha S, & Singh J (2012) Essential of early diagnosis of molar incisor hypomineralization in children and review of its clinical presentation, etiology and management *International Journal of Clinical Pediatric Dentistry* **5(3)** 190-196.
33. Vieira AR & Kup E (2016) On the etiology of molar-incisor hypomineralization *Caries Research* **50(2)** 166-169.
34. Onat H & Tosun G (2013) Molar incisor hypomineralization *Journal of Pediatric Dentistry* **1(3)** 53-57.
35. Serna C, Vicente A, Finke C, & Ortiz AJ (2016) Drugs related to the etiology of molar incisor hypomineralization: a systematic review *Journal of the American Dental Association* **147(2)** 120-130.
36. Crombie F, Manton D, & Kilpatrick N (2009) Aetiology of molar-incisor hypomineralization: a critical review *International Journal of Paediatric Dentistry* **19(2)** 73-83.
37. Alaluusua S (2010) Aetiology of molar-incisor hypomineralisation: a systematic review *European Archives of Paediatric Dentistry* **11(2)** 53-58.
38. Fatturi AL, Wambier LM, Chibinski AC, Assunção LRDS, Brancher JA, Reis A, & Souza JF (2019) A systematic review and meta-analysis of systemic exposure associated with molar incisor hypomineralization *Community Dentistry and Oral Epidemiology* **47(5)** 407-415.
39. Souza JF, Jeremias F, Costa-Silva CM, Santos-Pinto L, Zuanon AC, & Cordeiro RC (2013) Aetiology of molar–

incisor hypomineralisation (MIH) in Brazilian children *European Archives of Paediatric Dentistry* **14** 233-238.

40. de Lima Mde D, Andrade MJ, Dantas-Neta NB, Andrade NS, Teixeira RJ, de Moura MS, & de Deus Moura Lde F (2015) Epidemiologic study of molar-incisor hypomineralization in schoolchildren in North-Eastern Brazil *Pediatric Dentistry* **37(7)** 513-519.
41. Wu X, Wang J, Li YH, Yang ZY, & Zhou Z (2018) Association of molar incisor hypomineralization with premature birth or low birth weight: systematic review and meta-analysis *Journal of Maternal-Fetal & Neonatal Medicine* **29** 1-9.
42. Silva MJ, Scurrah KJ, Craig JM, Manton DJ, & Kilpatrick N (2016) Etiology of molar incisor hypomineralization: a systematic review *Community Dentistry and Oral Epidemiology* **44(4)** 342-353.
43. Kühnisch J, Mach D, Thiering E, Brockow I, Hoffmann U, Neumann C, Heinrich-Weltzien R, Bauer CP, Berdel D, von Berg A, Koletzko S, Garcia-Godoy F, Hickel R, & Heinrich J (2014) Respiratory diseases are associated with molar-incisor hypomineralizations *Swiss Dental Journal* **124(3)** 286-293.
44. Kusku OO, Caglar E, & Sandalli N (2008) The prevalence and aetiology of molar-incisor hypomineralisation in a group of children in Istanbul *European Journal of Paediatric Dentistry* **9(3)** 139-144.
45. Elhennawy K & Schwendicke F (2016) Managing molar-incisor hypomineralization: a systematic review *Journal of Dentistry* **55** 16-24.
46. Whatling R & Fearne JM (2008) Molar incisor hypomineralization: a study of aetiological factors in a group of UK children *International Journal of Paediatric Dentistry* **18(3)** 155-162.
47. Laisi S, Ess A, Sahlberg C, Arvio P, Lukinmaa PL, & Alaluusua S (2009) Amoxicillin may cause molar incisor hypomineralization *Journal of Dental Research* **88(2)** 132-136.
48. Souza JF, Costa-Silva CM, Jeremias F, Santos-Pinto L, Zuanon AC, & Cordeiro RC (2012) Molar incisor hypomineralisation: possible aetiological factors in children from urban and rural areas *European Archives of Paediatric Dentistry* **13(4)** 164-170.
49. Guergolette RP, Dezan CC, Frossard WT, Ferreira FB, Cerci Neto A, & Fernandes KB (2009) Prevalence of developmental defects of enamel in children and adolescents with asthma *Jornal Brasileiro de Pneumologia* **35(4)** 295-300.
50. Caruso S, Bernardi S, Pasini M, Giuca MR, Docimo R, Continenza MA, & Gatto R (2016) The process of mineralisation in the development of human tooth *European Journal of Paediatric Dentistry* **17(4)** 322-326.
51. Simmer JP & Finchman AG (1995) Molecular mechanisms of dental enamel formation *Critical Reviews in Oral Biology and Medicine* **6(2)** 84-108.
52. Schneider PM & Silva M (2018) Endemic molar incisor hypomineralization: a pandemic problem that requires monitoring by the entire health care community *Current Osteoporosis Reports* **16(3)** 283-288.
53. Fagrell TG, Dietz W, Jälevik B, & Nóren JG (2010) Chemical, mechanical and morphological properties of hypomineralized enamel of permanent first molars *Acta Odontologica Scandinavica* **68(4)** 215-222.
54. Fagrell TG, Salmon P, Melin L, & Norén JG (2013) Onset of molar incisor hypomineralization (MIH) *Swedish Dental Journal* **37(2)** 61-70.
55. Crombie FA, Manton DJ, Palamara JE, Zalizniak I, Cochrane NJ, & Reynolds EC (2013) Characterisation of developmentally hypomineralised human enamel *Journal of Dentistry* **41(7)** 611-618.
56. Gambetta-Tessini K, Marino R, Ghanim A, Adams GG, & Manton DJ (2017) Validation of quantitative light-induced fluorescence-digital in the quantification of demarcated hypomineralized lesions of enamel *Journal of Investigative and Clinical Dentistry* **8(4)** e12259.
57. Taube F, Marczewski M, & Nóren JG (2015) Deviations of inorganic and organic carbon content in hypomineralised enamel *Journal of Dentistry* **43(2)** 269-278.
58. Beentjes VE, Weerheijm KL, & Groen HJ (2002) Factors involved in the aetiology of molar-incisor hypomineralisation (MIH) *European Journal of Paediatric Dentistry* **3(1)** 9-13.
59. Jedeon K, De la Dure-Molla M, Brookes SJ, Loiodice S, Marciano C, Kirkham J, Canivenc-Lavier MC, Boudalia S, Bergès R, Harada H, Berdal A, & Babajko S (2013) Enamel defects reflect perinatal exposure to bisphenol A *American Journal of Pathology* **183(1)** 108-118.
60. Baroni C & Marchionni S (2011) MIH supplementation strategies: prospective clinical and laboratory trial *Journal of Dental Research* **90(3)** 371-376.
61. Bozal CB, Kaplan A, Ortolani A, Cortese SG, & Biondi AM (2015) Ultrastructure of the surface of dental enamel with molar incisor hypomineralization (MIH) with and without acid etching *Acta Odontologica Latinoamericana* **28(2)** 192-198.
62. Da Costa-Silva CM, Ambrosano GM, Jeremias F, De Souza JF, & Mialhe FL (2011) Increase in severity of molar-incisor hypomineralization and its relationship with the colour of enamel opacity: a prospective cohort study *International Journal of Paediatric Dentistry* **21(5)** 333-341.
63. Heijs SC, Dietz W, Norén JG, Blanksma NB, & Jälevik B (2007) Morphology and chemical composition of dentin in permanent first molars with the diagnose MIH *Swedish Dental Journal* **31(4)** 155-164.
64. Fagrell TG, Lingström P, Olsson S, Steiniger F, & Norén JG (2008) Bacterial invasion of dentinal tubules beneath apparently intact but hypomineralized enamel in molar teeth with molar incisor hypomineralization *International Journal of Paediatric Dentistry* **18(5)** 333-340.