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MOLAR-INCISOR HYPOMINERALIZATION: WHY DOES IT OCCUR? / WHAT TO DO?

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ABSTRACT

Introduction: Molar Incisor Hypomineralization (MIH) is defined as a qualitative defect resulting from the decrease in inorganic content and lack of mineralization in enamel layer of affected tooth. Its characterization is presence of opacities/pores of varying sizes from white to yellowish brown in color. Loss of tooth substance, plaque accumulation, caries formation started and progressed rapidly short after tooth eruption in majority of patients with MIH. Additionally to esthetics and sensitivity problems in patients, it presents treatment challenges for dentists. Therefore, understanding its etiology is important to prevent.

Aim: This study aims to raise awareness of etiologic factors related to MIH and to determine necessary measures for prevention.

Method: We performed a literature review of potential etiologic factors of MIH, which involve one or more permanent first molars, and may also affect permanent incisors.

Results: Limited information is available regarding etiology of MIH. Observational studies have been conducted to determine etiological factors, and diseases occurring postnatally are found more effective considering prenatal/perinatal/postnatal periods. Various factors such as systemic diseases, drug use, malnutrition, preterm birth, low birth weight, long-term lactation, dioxins, and bisphenol A (BPA) have been associated with MIH. Respiratory tract diseases, certain antibiotics, calcium deficiency, and BPA in materials in contact with infants have been particularly emphasized. Genetic factors are also reported by some studies.

Conclusion: Further studies are required to determine clear-cut etiologic factors for MIH. Systemic diseases, applied treatments, malnutrition, chemical agents, genetic factors, and other possible conditions occurring during prenatal/perinatal/postnatal periods should be discussed in detail.

INTRODUCTION

A structural defect of the enamel which includes one to four permanent first molars and may also affect the permanent incisors is named as Molar Incisor Hypomineralization (MIH). The enamel of the affected teeth has loss of component and discoloration due to lack of inorganic content and mineralization and it has been described to be a qualitative defect (1). Although this pathology has commonly been known to affect the first molars and incisors, it has recently been reported to affect any of the primary or permanent teeth (2). Epidemiological studies in different parts of the world have revealed that the prevalence of MIH varies widely between 2.8%-40.2% (3,4) and it is estimated to affect one of six children in the world (5).

Clinically, hypomineralization is characterized by the presence of opacities of varying sizes from white to yellowish brown in color. Since hypomineralized enamel has a high protein content, it is softer than normal enamel. While normal enamel shows a well-arranged prism and crystal structure, hypomineralized enamel has less prominent prism crystals. Therefore, the structure of hypomineralized enamel is more porous than normal enamel. Due to these characteristics, in most patients with MIH, loss of substance and plaque accumulation have started and progressed rapidly after a short period of tooth eruption. This situation leads to esthetical and sensitivity

problems for the patients, as well as treatment challenges for the dentists (6).

There is limited available information regarding the certain etiology of MIH. Observational studies have been conducted to determine the etiological factors. Despite the association of several diseases of prenatal, perinatal or postnatal periods, the causes have not been determined clearly. Considering the difficulties experienced by patients and dentists related to MIH, knowing the etiology of MIH is important in preventing its formation or developing new treatment approaches. In this respect, this study aims to create an awareness revealing the etiologic factors related to MIH and to determine the necessary measures for its prevention.

MIH Etiology

Although the causative factors of MIH are unclear, the clinical appearance of localized and asymmetric lesions has been indicated to occur as a result of damage to secretory ameloblasts during the formation and maturation stages of enamel layer (6). This has been reported to be caused by multiple factors as long as the last trimester of pregnancy and first three years after birth, such as acute/chronic diseases or exposure to environmental agents (7). The number of affected teeth has been related to the time in which systemic problems occur, and postnatal diseases have been found to be more effective (8). Several factors have been proposed in literature such as systemic diseases and drug use, malnutrition, preterm birth and low birth weight, long-term breastfeeding and dioxins, and bisphenol A (BPA) (6). In some studies, genetic factors have also been reported to play a role (9,10).

1. Systemic Diseases and Drug Usage

The incidence of MIH was found to be high in children with systemic diseases. Gastrointestinal problems, celiac disease, lead poisoning, nephrotic syndrome, cystic fibrosis, diabetes, thyroid and parathyroid diseases, brain injury, neurological defect, epilepsy, epidermolysis bullosa, rubella, oncological cases treated with radiotherapy, ophthalmic disorders, and treated cleft lip-palate were found to be associated with MIH (1,11,12). In previous studies, the majority of children with MIH have been presented to have otitis media and upper respiratory tract diseases, such as asthma, bronchitis, and pneumonia, as well as high fever (13,14). Due to the infectious nature of the respiratory tract diseases, it is controversial whether the diseases themselves or the drugs used are the primary factor for the development of tooth hypomineralization. Pelisson-Guergolette et al. (15) associated the enamel defects observed in asthmatic children with reduced oxygen supply to ameloblasts at amelogenesis. In a retrospective study evaluating the relationship between antibiotic use and MIH, it was reported that there was a significant relationship between antibiotic use during the first year of life and MIH (13). At a study in which the age of antibiotic use for children with MIH was assessed, the authors stated that the highest risk of MIH was between 1-2 years of age (16). Laisi et al. (17) determined that children who use amoxicillin or erythromycin in the first year of life were found to develop enamel hypomineralization more often as compared to those who did not use. Amoxicillin was shown to induce enamel formation increasing amount of enamel formed and resulting irregular hard tissue formation in animal experiments (17). Possibility of occurrence of MIH was also found to be significantly higher in children used much macrolide in the first 3 years after the birth. These observations suggested that antibiotic treatment rather than the disease itself may be a key factor for the induction of enamel hypomineralization (18). It is important to seek and record the systemic diseases and treatment approaches in detail within the researches studying the main factors that are effective for MIH.

2. Malnutrition

Malnutrition seen in early childhood has been associated with the enamel defects of permanent central incisors. It has been reported that calcium and phosphate deficiency due to malnutrition leads to MIH (6). The absence of calcium in tooth structure with MIH has given rise to thought that ameloblasts form defective enamel structure as a result of impaired calcium metabolism (13). Hypocalcemia can occur in cases of pregnancy diabetes, vitamin D deficiency in the prenatal and/ or perinatal period, and prematurity (19). In addition, a genetic action leading to a gluten-specific immune response in celiac patients has been pointed out to cause MIH (20). Attention to nutrition during pregnancy and early childhood is essential for both general and oral health.

3. Preterm Birth and Low Birth Weight

Children with a birth weight <1500 g and gestational period <38 weeks are termed as premature. It has been reported that children with a very low birth weight have a risk of developing opacities in their teeth due to the disturbances in calcium metabolism (13). There are limited studies suggesting the association between MIH and perinatal factors such as prematurity, low birth weight, cesarean delivery, and delivery complications. In a study performed in Finland, enamel defects were observed in 36% of children born in time and in 84% of preterm children (19). Brogardh-Roth et al. (21) stated that an increase of 100 g per body weight for preterm infants with a low birth weight may reduce the number of cases of MIH by 4.5%. Along the studies suggesting that low birth weight or preterm birth is related to MIH, there are also studies indicating that it is not (22,23). Further studies are needed to identify possible relationships on this subject.

4. Long-term Breastfeeding and Dioxins

It has been remarked that dibenzo-p-dioxin (PCDD) known as a polyhalogenated aromatic hydrocarbon causes environmental pollution, and its presence in breast milk may lead to enamel hypomineralization. Depending on its lipophilic nature, this substance can pass through the breast milk and accumulate in the adipose tissue resulting in chronic exposure of infants. More enamel defects have been stated to occur in children exposed to high amounts of PCDD by breast milk, compared to children not exposed (24). Long-term breastfeeding has been suggested to increase the risk of MIH due to environmental toxicants present in breast milk (25). In a study conducted in Sweden, it was reported that breast milk is devoid of nutrients necessary for enamel development and that breastfeeding for more than 6 months may delay transition to additional nutrients and increase the risk of MIH (26). In order to reduce the risk of MIH related to breastfeeding, it is important to consider protecting the mother against environmental factors and regulating her diet.

5. Bisphenol A

Exposure to endocrine-disrupting chemicals (EDCs) during the prenatal period may cause lesions similar to MIH. Researchers suggest that EDCs can increase the secretion of enamel proteins and reduce the expression of klk4 gene, which produces the organic matrix of enamel, and may lead to albumin accumulation that prevents the growth of enamel crystals (27). A typical EDC commonly used for the production of polycarbonate plastics and epoxy resins is BPA. It affects different components, such as the reproductive organs, breasts and glands, and brain, and physiological functions of the body. It has been expressed that it may increase the risk of breast cancer and cause obesity (28,29). In a study with rats, Bisphenol A-Glucuronide Acid (BPA-GA) in the maternal rat circulation passed through the placenta and turned into BPA in the fetus (30). The mechanism of action of BPA on ameloblasts is not fully understood. However, at the developmental stages of the secretion of ENAM and klk4 genes which are responsible for enamel formation, BPA is thought to affect the secretion of these genes by binding to

estrogen receptor-alpha, vitamin D, and thyroid receptors found in the ameloblasts (31,32). The sensitivity of humans to BPA has been emphasized to be high during the perinatal period (33), which corresponds to the period of formation of the permanent incisors and first molars. The teeth affected by MIH generally come into mineralize at birth and within 5 months after birth. The current data propose that ameloblasts are predisposed to BPA and that BPA may be a factor in the etiology of MIH. Therefore, the content of products such as pacifiers, baby bottles, and plastic toys which are in contact with babies should be considered and BPA-containing products should not be used. BPA-containing products should be considered thoughout pregnancy too.

In the field of dentistry, BPA is utilized to synthesize matrix monomers such as bisphenol A glycidyl methacrylate (bisGMA) used in restorative materials (34). BPA improves handling and resistance properties of the resin-containing materials, and the undesirable feature of such materials is that they cannot be fully polymerized. Correspondingly, shrinkage, microleakage, and degradation can be observed in restorations over time and BPA release may occur. An increase in BPA and other related compounds in saliva 1 hour after the placement of restorative material and an increase in BPA concentration in urine 9-30 hours after the placement of restorative material have been reported (35). Polymerization and polishing of the resin-containing restorations should be done well, isolation should be elaborated, and if possible, the materials containing BPA should be avoided.

6. Genetics

During amelogenesis, especially in the last trimester of pregnancy, genetic variations because of the influence of environmental factors have been suggested to be able to cause MIH (36). Defects in AMELX gene encoding the amelogenin protein, ENAM gene accounting for enamel formation, and TUFT1 gene involving in enamel development and mineralization have been observed in the formation of MIH (8). Ameloblastin gene, which generates about 5% of enamel proteins, has been shown to play a role in the adhesion of ameloblasts at enamel formation process and a defect of this gene has been found to be associated with MIH (9). Studies showed that mutations in the klk4 gene, which produces the organic matrix of enamel, were correlated with MIH (36,37). Defects in SCUBE1, BMP2, BMP4, and BMP7 genes binding to bone morphogenetic protein (BMP) have also been stated to be able to cause MIH (37,38). Teixeira et al. (10) reported that higher incidence of MIH in monozygotic twins in comparison with dizygotic twins indicated a genetic effect, however, environmental effects such as socioeconomic factors were also in question. Studies specify that MIH is a multifactorial genetic disease and that more than one gene may play a role. In future studies, it would be useful to design a gene-environment model that deals with genetic and environmental risk factors together.

CONCLUSION

Further studies are required to determine the clear-cut etiologic factors leading to the MIH defects. In these studies; systemic diseases, applied treatments, malnutrition, exposure to chemical agents, genetic factors, and other possible conditions occurring during the prenatal/perinatal/ postnatal periods should be discussed in detail. On the other hand, necessary measures should be taken to avoid the possible risks associated with these factors.

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