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Molar incisor hypomineralisation: current knowledge and practice

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Background: Molar incisor hypomineralisation (MIH) is a common developmental dental condition that presents in childhood. Areas of poorly formed enamel affect one or more first permanent molars and can cause opacities on the anterior teeth. MIH presents a variety of challenges for the dental team as well as functional and social impacts for affected children. **Objectives:** Here, we provide an up-to-date review of the epidemiology, aetiology, diagnosis and clinical management of MIH. **Materials and methods:** A review of the contemporary basic science and clinical literature, relating to MIH, was undertaken using information obtained (up to 10 April 2020) from the electronic databases PubMed, Scopus, Web of Science and the Cochrane Library. **Results:** There is a growing body of evidence relating to the aetiology, presentation and clinical management of MIH. Current knowledge appears to be focused on potential genetic aspects, as well as the development and validation of indices for the diagnosis and management of MIH. There has also been increasing recognition of the global and individual burden of this common condition. **Conclusions:** Dental health professionals should regularly appraise the basic science and clinical MIH literature to ensure that they provide the best possible short- and long-term care for their young patients.

Key words: Molar incisor hypomineralisation, developmental enamel defect, children, diagnosis, management

INTRODUCTION: SETTING THE SCENE

Molar incisor hypomineralisation (MIH) is a common developmental dental condition that presents in childhood. Well-demarcated areas of hypomineralised enamel affect one or more first permanent molars. Consequently, these teeth may be very sensitive, undergo post-eruptive tissue breakdown and be predisposed to caries (*Figure 1a,b*). Associated opacities on anterior teeth are less likely to have functional problems but may result in cosmetic and psychosocial issues (*Figure 1c*). The potential burden relating to MIH, from both an individual and a population perspective, is well recognised and continues to stimulate wide public and professional interest^{1–3}. Although an excellent review article has been published recently⁴, it is important to regularly update knowledge and practice because new research continues to emerge at a rapid rate. A useful online resource for the latest MIH-related information, for both patients and clinicians, is hosted by the D3 Group for Developmental Dental Defects⁵.

There can be considerable disparity in the management of children with MIH. Expert groups, such as the European Academy of Paediatric Dentistry, have established MIH clinical guidelines⁶, but oral health professionals are exposed to diverse societal, cultural and health service factors that influence treatment approaches in different countries and settings. Furthermore, the evidence base to support treatment decisions for both hypomineralised first permanent molars (FPMs) and anterior teeth is surprisingly sparse for such a universal and challenging condition. The aim of this review article was to provide an overview of contemporary thinking and knowledge on the epidemiology, aetiology, diagnosis, management and psychosocial aspects of MIH.

EPIDEMIOLOGY: MIH IS A WORLDWIDE PROBLEM

Since the original definition of MIH as a distinct clinical entity in 2001⁷, numerous studies, reporting on the prevalence of MIH in both general and clinical populations, have been conducted around the world.



Figure 1. Examples of clinical presentations of molar incisor hypomineralisation in children. (a) Ten-year-old girl with severely hypomineralised lower first permanent molars showing posteruptive enamel breakdown. She also has a discrete white opacity on her lower left permanent central incisor. (b) Fourteen-year-old boy with a severely hypomineralised upper-right first permanent molar showing posteruptive enamel breakdown; his upper-left first permanent molar is intact but has yellow/cream enamel opacities. (c) Nine-year-old boy with a large white/cream opacity involving his upper-left permanent central incisor and yellow opacities involving lower permanent lateral incisors. He reportedly would not smile for school photographs. (d) Ten-year-old boy with hypomineralised upper first permanent molars and second primary molars. He also has white opacities evident on his permanent central incisors. (e) Eleven-year-old girl who requested treatment of the ‘white marks’ affecting her upper permanent central incisors. She had previously had preformed metal crowns placed on her hypomineralised first permanent molars. (f) Following treatment of the patient in (e) with resin infiltrant (ICON; DMG), the white opacities became much less visible and she was reportedly much more confident in social interactions.

The reported prevalence of MIH varies widely, from 3%–40%, depending on the population and country studied⁸. However, recent meta-analyses suggest that MIH affects around 13%–14% of the world’s children^{1,9}. The treatment burden of these children will obviously vary according to the severity of the hypomineralisation and the number of teeth affected, but it is estimated that around one-quarter of children with MIH will need clinical interventions as a result of symptoms or posteruptive tissue breakdown¹. The results of new epidemiological studies, performed in different areas worldwide, are being published regularly from around the world, with survey data from the USA making a relatively recent contribution to the literature¹⁰. It is difficult to make valid comparisons between these disparate epidemiological surveys

because of poor standardisation in the research protocols, calibration methods, choice of index, number of participants and population characteristics. These methodological variables also impede assertions that MIH has become more prevalent in recent years. To address this problem, Elfrink *et al.*¹¹ have outlined standard protocols for conducting MIH prevalence studies. They suggest that the ideal age to diagnose MIH in a child is around 8 years because, at this age, all FPMs and incisors have erupted but any ‘destruction’ of hypomineralised enamel is limited.

AETIOLOGY: A PUZZLE STILL TO SOLVE

The precise aetiology of MIH remains uncertain, generating considerable debate and enquiry. To date,

knowledge has been largely drawn from observational data, with an understandable lack of controlled studies. The literature has described a wide variety of risk factors for MIH, which often involve a hypoxic or hyperpyrexia insult at a critical phase of tooth mineralisation^{8,12}.

During the prenatal period (the last gestational trimester), maternal illness, medication use and exposure to environmental pollutants seem to be associated with an increased likelihood of MIH¹³. A recent meta-analysis found that children whose mothers experienced health problems during pregnancy showed a 40% greater chance of developing MIH than children whose mothers remained healthy¹³. Perinatal complications, such as difficulties during labour and delivery, delivery by Caesarean section, premature birth and low birth weight, have also been linked to MIH⁴.

During the first 3 years of life, when calcification of FPMs and incisors occurs, episodes of acute or chronic childhood illnesses, environmental pollutants and medication also appear to pose an increased risk of MIH¹⁴. Childhood illnesses (such as otitis media), renal failure and episodes of high fever have all been implicated in disturbing the function of proteolytic enzymes, which are key in the amelogenesis process⁴. Additionally, conditions such as asthma, and other respiratory diseases (notably bronchiolitis), can cause respiratory acidosis and abnormal oxygen levels which, in turn, can affect the pH of the enamel matrix and lead to abnormal ameloblastic activity during enamel mineralisation. Asthmatic children often require therapy with corticosteroids – known suppressants of osteoblast formation and activity – which similarly may be detrimental to ameloblast function and predispose to MIH¹⁵.

Additionally, several retrospective studies have found an association between early childhood antibiotic use and MIH⁸. However, it cannot be ascertained whether the causative factor is the antibiotic itself, the disease being treated, or a synergistic relationship between these factors¹⁶. Further research, using drug combinations in animal models, with and without infections or fevers, is required to determine the exact role of antibiotics in MIH development¹⁷. Speculation also remains about the possible link between nutritional vitamin D deficiency (both pre- and postnatal) and MIH¹⁸.

Perplexingly, despite the plethora of purported causes of MIH, up to 20% of affected children appear to have no identifiable risk factors⁶. This finding, and the impression that MIH is more common amongst siblings, has led to a growing belief that variations in genes related to amelogenesis are likely to play a key role in susceptibility to MIH¹⁹. Research involving monozygotic and dizygotic twins (with and without

MIH) has provided the most compelling evidence, to date, for genetic influences²⁰. Genes such as enamelin (*ENAM*), tuftelin interacting protein 11 (*TFIP11*) and tuftelin 1 (*TUFT1*) appear to be associated with the development of MIH¹⁹. Surprisingly, no correlation has yet been identified between MIH and the amelogenin, X-linked (*AMELX*) gene, which is primarily concerned with amelogenin deposition²¹.

A correlation between MIH and hypomineralisation of the primary dentition, notably hypomineralised second primary molars (HSPMs), is also an area of ongoing enquiry. The conclusion of a 2018 systematic review was that hypomineralisation of second primary molars was a predictor of subsequent MIH²² (*Figure 1d*).

A recent novel finding was the significantly increased risk of hypodontia in children with MIH; a British hospital-based study reported the overall prevalence of hypodontia to be 11% in young patients (aged 7–16 years) with MIH, twice as high as that expected in a normal population²³. This incidental finding may support a genetic contribution to the development of MIH. In view of this growing body of evidence, the aetiology of MIH must be considered to have polygenetic factors with environmental influences²⁴.

HYPOMINERALISED ENAMEL: FINDINGS FROM THE LABORATORY

Knowledge of the ultrastructural, mechanical and chemical changes in hypomineralised enamel is fundamental in furthering our understanding of MIH aetiology, as well as for informing treatment strategies. The systematic review of Elhennawy and co-authors²⁵ included 22 basic science studies which investigated the various chemical and physical characteristics of extracted human hypomineralised teeth. In summary, compared with ‘normal’ enamel, hypomineralised enamel appears to have reduced hardness and elasticity, increased porosity, a higher protein content and an altered carbon:carbonate ratio. The relative abundance of serum albumin in yellow/brown hypomineralised enamel has also been reported as a notable finding and a potential inhibitor of enamel crystal growth²⁶. Previous work has highlighted the potential for invasion of bacteria into the underlying dentine of hypomineralised teeth²⁷. Despite these laboratory investigations, questions remain about the depth and degree of defective enamel and the corresponding clinical presentation²⁸. Furthermore, the scope of this *in vitro* research is limited to extracted human molars, as anterior teeth are unlikely to be removed for clinical reasons.

MIH DIAGNOSIS: CHALLENGES AND CAVEATS

Determining a definitive diagnosis of MIH can be challenging, particularly in younger children in whom

permanent teeth are still erupting, as the full distribution of any enamel defects will not yet be evident. Furthermore, lesions similar to those seen in MIH may also involve permanent canines, premolars and second permanent molars, suggesting a continuum²⁹. Differential diagnoses must therefore be considered, including amelogenesis imperfecta and dental fluorosis. To aid the clinician and the researcher, diagnostic criteria have been proposed by several different groups. Many of these indices have now been validated for use, to inform treatment decisions and to categorise the severity (tooth and patient burden) of the condition^{30–32}. For example, Ghanim and colleagues applied their validated MIH index to determine the potential clinical needs of children with MIH and reported that 14% of affected teeth warranted treatment as a result of the presence of posteruptive breakdown³².

CLINICAL MANAGEMENT: A HOLISTIC APPROACH

The management of children with MIH must consider a host of patient/parent/clinician-related preferences as well as acknowledge the need for short- and long-term planning. It is often important to seek an orthodontic assessment to inform decision-making, especially when considering extractions. Management is further challenged by behavioural factors as younger patients may demonstrate high levels of dental anxiety, which may be exacerbated by failure to achieve adequate levels of local analgesia during treatment³³. Affected teeth are often extremely sensitive to thermal/mechanical stimuli, at greater risk of caries, susceptible to posteruptive breakdown and demonstrate bond failure to adhesive dental materials. In addition, many children report significant psychosocial impacts from having visible anterior enamel opacities³³. Management is largely informed by best-practice clinical guidelines, produced by a consensus of expert opinion amongst paediatric dentists and orthodontists^{6,35}.

Caries prevention and desensitisation

Several investigators have found that children with hypomineralised FPMs are at higher risk of caries, although there is a recognised need for more research in this field^{36,37}. It is imperative that a rigorous and evidence-based preventive strategy is established early for each child, as stressed in the European Academy of Paediatric Dentistry's clinical guidelines⁶. Additionally, interventions must aim to reduce sensitivity of hypomineralised FPMs, which can be experienced even during normal toothbrushing. Professionally applied topical fluoride preparations, home use of fluoride mouthwashes, desensitising dentifrices and casein phosphopeptide-amorphous calcium phosphate topical

preparations can all be considered, although the evidence base for their efficacy in patients with MIH is lacking^{4,35,38}. Conventional fissure sealants are reported to have a high failure rate; thus, glass ionomer-based sealants may be preferable for newly erupted and sensitive FPMs³⁵.

Management of anterior opacities

Incisor (and canine) opacities are not always present in children with hypomineralised FPMs (and vice versa) but are reportedly more common with increasing severity of molar hypomineralisation³⁹. These well-demarcated areas of enamel hypomineralisation appear to 'randomly' affect one or more maxillary/mandibular permanent anterior teeth and vary in colour, ranging from chalky white or cream, to yellow and brown. However, the areas of enamel hypomineralisation tend to be limited to the labial surfaces and are located more towards the incisal third, sparing the cervical enamel. Sensitivity and posteruptive enamel breakdown are not common features unless the areas of hypomineralisation have a yellow/brown appearance and often involve the incisal edge³⁰. Clinical management is therefore largely driven by patient (and parent) psychosocial concerns relating to dental appearance, rather than functional limitations (*Figure 1e*).

A range of minimally invasive techniques can be employed to try to improve the appearance of anterior opacities whilst attempting to preserve tooth tissue. One of the greatest challenges, however, is predicting the likely success of any intervention. The most common options include tooth whitening, microabrasion, resin infiltration and direct/indirect composite resin restorations, or various combinations of these treatments^{38,40,41}. Tooth whitening is usually undertaken by the patient at home, over a few weeks, using a laboratory-made soft acrylic bleaching tray filled with a 10%–16% carbamide peroxide preparation⁴¹. Another minimally invasive option is microabrasion; this involves removing approximately 40–100 µm of enamel by concurrent abrasion and erosion of the tooth surface, using a proprietary preparation of acid and abrasive particles^{41,42}. A more recent treatment is the use of a resin infiltrant⁴³. Following application, this low-viscosity resin is capable of penetrating the porous subsurface enamel to a depth of up to 700 µm⁴⁴ (*Figure 1f*). The widely used resin infiltrant system, Icon™ (DMG, Hamburg, Germany), includes pretreatment with 15% HCl to dissolve the relatively intact enamel surface layer and facilitate access into the subsurface porous lesion. A series of case reports, published by DMG, illustrate the use of Icon™ for improving the appearance of a variety of smooth surface enamel lesions, including those seen in children

with MIH⁴⁵. Resin infiltration appears to be most effective in improving the appearance of white/chalky enamel opacities, but further well-conducted trials are needed to substantiate clinical observations⁴³. Conventional restorative treatment with resin composite materials may be indicated when these minimally invasive approaches fail to reduce the visibility of the enamel opacity. However, it is well recognised that shear bond strengths may be compromised when bonding resin composite to hypomineralised enamel⁴⁶.

Undoubtedly, clinical interventions for visible developmental enamel defects are likely to undergo continued development, driven by increasing patient and professional expectations for dental 'perfection'.

Management of FPMs

Management of hypomineralised FPMs can be challenging, and treatment approaches may vary widely in different countries and in specialist and non-specialist services^{12,24}. The choice of approach – essentially restoration or extraction (with/without orthodontic space closure) – has considerable economic implications, which may also influence decision-making²⁴. In the absence of definitive high-quality research, the European Academy of Paediatric Dentistry provides guidelines on best clinical practice, which outline a host of patient- and clinical-related factors to be considered for each patient's personalised treatment plan⁶.

Following an early clinical diagnosis of hypomineralised FPMs, a panoramic radiograph should be taken to confirm the presence of the permanent dentition (including third permanent molars). The child and parents must be informed about the likely prognosis of the affected teeth and the various treatment options available to them. A definitive plan may not be appropriate at the initial assessment because the clinician needs to ascertain child/parent compliance with treatment as well as the need for future orthodontic treatment. Having established a rigorous preventive foundation, the broad decisions relate to short- or long-term restorations or extraction⁶.

When restoring hypomineralised FPMs, the extent and site of the hypomineralised enamel, degree of any posteruptive breakdown, caries involvement, sensitivity and patient compliance, will influence the choice of material employed. Options broadly include resin-modified glass ionomer cements, direct or indirect resin composite restorations, preformed metal crowns or laboratory-made ceramic/metal onlays and crowns. Elhennawy and Schwendicke's systematic review³⁵ found no strong evidence for superiority of any one restorative approach but suggested that resin composite restorations, preformed metal crowns or laboratory-fabricated crowns were appropriate choices when

the FPMs demonstrated moderate-to-severe degrees of hypomineralisation. A more recent addition to the evidence base for survival of restorations placed in hypomineralised FPMs in children comes from a retrospectively designed cohort study, in which four different non-invasive and conventional restorative procedures in children with MIH were analysed⁴⁷. Following tooth preparation, conventional resin composite restorations and computer-aided design/computer-aided manufacturing (CAD/CAM) ceramic restorations were found to have moderate-to-high survival rates after 36 months. Although glass ionomer restorations that were placed without tooth preparation showed poor survival rates, they were felt to have a place as a temporary solution in young children. A fundamental limiting factor to the success of resin composite restorations in MIH is the weaker bond strength⁴⁸. A number of strategies have been explored to improve adhesion of resin composite, including different etch systems, deproteinisation and use of resin infiltrant, but studies remain largely inconclusive⁴⁸.

When one or more FPMs is deemed to have an extremely poor prognosis, the option of extraction must be considered, especially if the child is at an appropriate stage of dental development (around 8–10 years of age)^{49,50}. It is important to assess the child's overall orthodontic status to confirm the timing of any extractions and the need for any compensating extractions or pre-extraction orthodontic intervention. Removal of one or more FPMs at the optimal stage of dental development, especially with the presence of third molars, is more likely to result in optimal spontaneous space closure⁵¹. However, extraction of FPMs prior to eruption of premolars and second permanent molars carries the risk of not knowing if these teeth will also be similarly affected. The decision to extract a FPM does not sit lightly with all clinicians and there may be significant differences in cultural attitudes/practices when making a choice between extraction and extensive restorative treatment. However, it is important to consider that oral health outcomes for children who receive restorative treatment for severely hypomineralised FPMs may be poor in the longer term, presenting them with a lifetime treatment burden⁵². It is clearly important to involve children and parents in this decision-making process, considering not only the risks and benefits of extraction, but also the need for any behavioural or pharmacological adjuncts (e.g., sedation or general anaesthesia) to support the child during treatment.

PSYCHOSOCIAL ASPECTS: CHILDREN'S PERSPECTIVES

The psychosocial impact of enamel defects on children is not a new concept, and there is a growing body of

literature on this subject from both clinical and social science researchers⁵³. However, the oral health-related quality of life (OHRQoL) and well-being of children with MIH, as a specific entity, is a relatively recent area of enquiry. In the main, studies have shown that young children (8–10 years of age) with moderate/severe MIH may experience significantly poorer OHRQoL than their peers, which is attributed to the functional limitations (symptoms) of their FPMs^{54–56}. Negative impacts relating to the social and emotional effects of having visible incisor opacities have also been highlighted as children may be embarrassed to show their teeth in normal social encounters⁵⁷. In order to address children's concerns about their dental appearance, Hasmun and coworkers³⁴ carried out a prospective study in which aesthetic treatment was provided to 93 children with MIH who were reportedly upset by the appearance of their anterior opacities. One month following minimally invasive intervention, children reported significantly improved OHRQoL and self-esteem. This was the first study to explore the impact of aesthetic treatment on children with MIH, but further research is clearly needed to investigate how the management of FPMs may also affect children's OHRQoL.

CONCLUSIONS

Molar incisor hypomineralisation is a common childhood condition that presents a unique set of clinical challenges to dental health professionals. It is important that basic and clinical research continues to inform an evidence-based approach for these children in both the short- and long-term.

Conflict of Interest

The authors have no conflict of interest in relation to this work.

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