Journal of Orthodontics, Vol. 36, 2009, 277–282

CUTTING EDGE

New developments in understanding development defects of enamel: optimizing clinical outcomes

Nicky Kilpatrick
Royal Children's Hospital and Oral Health Research Unit, Murdoch Children's Research Institute, Victoria, Australia

Developmental defects of enamel appear to be presenting with increasing frequency and with this comes significant clinical challenges. Affected teeth, in particular first permanent molars, are susceptible to dental caries as they are not only more porous but also very sensitive making effective oral hygiene difficult. Affected children require more dental treatment than their unaffected peers while also suffering greater pain and anxiety. Current clinical approaches focus on the placement of contemporary adhesive restorative materials onto the compromised tooth which in turn, fail, leading to premature loss of permanent molars with associated repercussions. Incomplete understanding of the structure, composition and behaviour of affected enamel means that clinical protocols are, as yet, empiric rather than evidence based. This review summarises contemporary evidence regarding this condition and identifies potential areas for future research which would assist in improving clinical outcomes.

Key words: Developmental enamel defects, molar-incisor-hypomineralization, paediatric dentistry

Received 28th January 2008; accepted 3rd June 2009

Introduction

The prevalence of developmental defects of enamel (DDE) appears to be increasing with up to a fifth of otherwise healthy children and 80% of children with other medical or genetic disorders affected.[1,2] Clinically, such defects are seen as white-yellow or yellow-brown demarcated opacities which vary greatly in their size, colour and shape. Affected teeth pose significant clinical challenges,[3,4] with nearly half the restorations placed in affected permanent molars failing and many requiring extraction.[5] The aim of this review is to summarise the contemporary evidence surrounding the impact of developmental disruptions on the structure, function and behaviour of enamel and to make some evidence based recommendations for optimizing the clinical outcomes for young patients presenting with such defects.

Aetiology and classification

Enamel is derived from ectoderm and produced by ameloblasts which differentiate from inner enamel epithelial cells of the dental organ. Simply, enamel formation can be divided into three stages: matrix formation, initial calcification and final maturation.[6] During matrix formation enamel matrix proteins emerge and matrix is deposited. Calcification follows the enzymatic cleavage of the matrix proteins leaving a relatively heterogeneous protein solution, and subsequently the newly formed matrix becomes mineralized to approximately 30%. Final maturation occurs as the proteins are removed from the enamel matrix, the ameloblasts disintegrate and the resulting enamel is fully mineralized with little remaining matrix.[6] If ameloblast function is disrupted during the secretory phase then they may be irreversibly damaged and the teeth are characterized by a deficiency of tooth substance that ranges from minor pits and groves to total absence of enamel. This enamel defect is termed hypoplasia and is a quantitative defect.[7] If however, disruption of ameloblasts occurs during either the calcification or maturation phase then the teeth will appear mottled and the enamel will have a qualitative defect.[7] This is termed enamel hypomineralization and can present as an enamel opacity. Clinically and histologically, combinations of hypoplasia and hypomineralization may coexist with superimposed carious and non-carious tooth tissue loss.[8–10]

Basic science research suggests that ameloblasts are highly susceptible to relatively minor changes in their

Address for correspondence: Nicky Kilpatrick, Royal Children's Hospital, Flemington Road, Parkville Vic. 3052, Australia.
Email: nicky@bassdata.com.au

DOI 10.1179/14653120723310

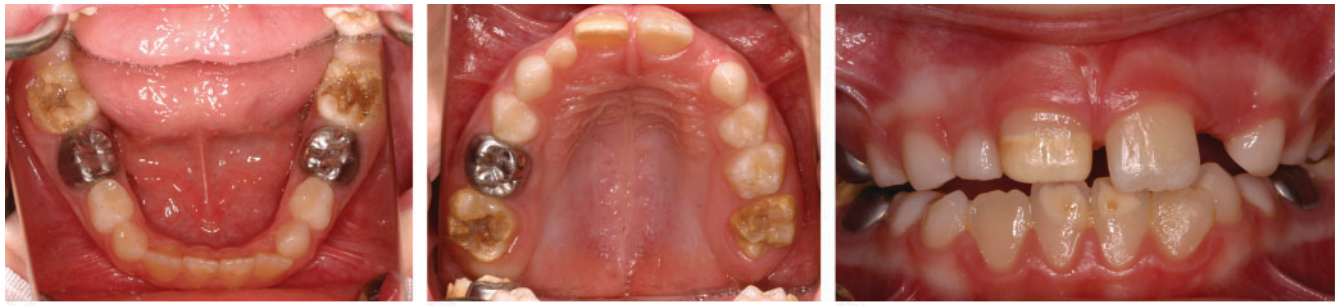


Figure 1 A typical case of molar-incisor-hypomineralization in the mixed dentition with affected teeth showing significant variation in the degree of severity of defect

environment; for example increases in temperature,[11] hypocalcaemia,[12] and pH levels[13,14] can all disrupt the normal process of amelogenesis. Any maternal or childhood illness or exposure to medications, environmental contaminants that may change the environment in which the ameloblasts are functioning can putatively contribute to the development of defective enamel. The strength of the evidence regarding causal relationships in the aetiology of enamel defects is very mixed due to differences in clinical criteria and study methodology.[15] However, there is moderate evidence that exposure to PCB/dioxins (via breast milk) is associated with an increased prevalence of developmental enamel defects[16] although very recently even this has been questioned.[17] Other potential factors include respiratory diseases, brain hypoxia and childhood illnesses particularly those associated with fevers, malnutrition, calcium deficiencies and the use of amoxycillin.[2,18–21] It is also likely that, in addition to specific environmental exposures, genetic susceptibility may play a role in this disorder but the mechanisms involved have yet to be identified.

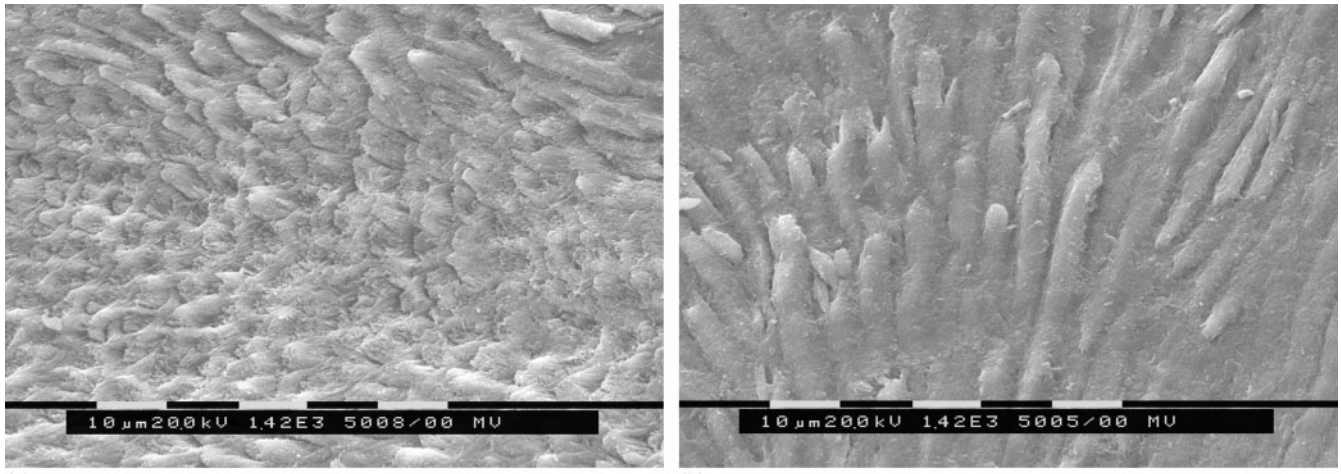
Recently a specific form of DDE has been described; molar-incisor-hypomineralization or MIH. This term is used to refer to hypomineralizion of one or more of the first permanent molars, often also involving incisor teeth, and not necessarily involving a macroscopic defect of tooth tissue.[22] Clinically, MIH may present as discrete, opaque lesions, distinct from the more diffuse linear opacities usually associated with fluorosis, and may be associated with post-eruptive enamel loss making it potentially difficult to distinguish from enamel hypoplasia. The distribution of the condition is often asymmetric, commonly with marked variation in severity within an individual (Figure 1a–c). The prevalence of MIH specifically is unclear due to differences in diagnostic criteria across studies; however, figures of between 5 and 31% have been reported.[23–26]

Structure and properties

Ultra micro indentation studies have shown a striking reduction (up to 90%) in the mechanical properties; hardness and elastic modulus, of hypomineralized enamel.[27,28] Hardness is often correlated with mineral content however, despite this dramatic reduction in the mechanical properties there appears to be only a 5–10% reduction in the total mineral content of these enamel lesions.[8,27,28] SEM and TEM studies of the enamel of affected teeth suggest that the crystalline structure of the hypomineralized lesions is more porous and disorganized than otherwise normal enamel.[9,27,28] The borders of the enamel rods appear indistinct, the inter rod spaces are wider and the sheath structures around the prisms thicker.[29] However, whilst the increased porosity and disorganization of the crystalline structure may contribute to the deterioration, it cannot fully explain the catastrophic nature of the reduction in the mechanical properties. An alteration in the calcium mineral phases, may contribute to the poor mechanical properties with higher carbon levels reported in hypoplastic enamel with a simultaneous reduction in the Ca/P ratio.[10] The higher carbon content in the defective enamel may reflect a higher content of carbonated apatite resulting from incomplete maturation. An alternative explanation is that the raised carbon content represents an increase in protein in the defective enamel, the aetiology of which may be intrinsic (i.e. residual enamel matrix protein) or extrinsic (i.e. salivary or pellicle proteins).

Clinical behaviour

Affected teeth, particularly first permanent molars, present significant clinical challenges as the enamel is consistently soft and chips away easily under



(a) (b)

Figure 2 (a) Characteristic appearance of healthy enamel following 60 s acid etching. (b) Appearance of hypomineralized enamel following 60 s acid etching with the notable absence of the characteristic etch pattern

masticatory forces as soon as the teeth erupt into the oral cavity thus exposing dentine. The presence of such defects significantly increases dental treatment need as the teeth are more susceptible to plaque accumulation and dental caries.[5,20,30] Children with affected molars may receive up to 10 times more dental treatment than those without and are likely to be more fearful in the dental environment.[31] Furthermore, these teeth are often extremely sensitive and require robust local analgesia which adds to the complexity of their treatment.[30–32] The aetiology of this sensitivity has, until recently, remained obscure; however, an increase in the expression of transient reception potential ion channel (TRPV1) in hypomineralized teeth has been reported which may reflect underlying pulpal inflammation.[33] Given the rapid post-eruptive tissue loss associated with these teeth and the increased porosity of residual enamel, pulpal inflammation is unsurprising as oral microbes and fluid have easy access to the pulp via the dentinal tubules.

From an orthodontic perspective, there are well recognized issues related to the management and potential early loss of compromised first permanent molars.[34] However, there is also evidence that differences in the structure of affected enamel leads to sub-optimal adhesion which may impact on orthodontic bracket retention.[5,9,35] The mode of adhesive failure is more likely to be cohesive within the defective tissue reflecting its weakened structure.[35] It has been demonstrated that hypomineralized enamel is resistant to conventional acid etching,[28] the etched surface failing to demonstrate the characteristic well defined etch pattern (Figure 2a–b). This in turn may contribute to poor micro-tag formation at the interface between hypomineralized enamel and adhesive.[35]

Management strategies

Caries prevention

Affected teeth are at significant risk of developing dental caries[20] and as such early identification is important to optimize outcomes. Regular dental reviews around the time the first permanent molars and incisors erupt will allow proactive preventive strategies to be introduced. It is particularly important that parents of children with a co-existing chronic medical condition or disability are informed of the increased risk of MIH and its consequent impact on caries risk. When incisors erupt prior to the molars, the presence of an opacity on the labial surface of a newly erupted incisor is a strong indicator of MIH and additional caries preventive strategies should be promoted. Such strategies should include; optimization of fluoride exposure, parental assisted oral hygiene and reducing the frequency of exposure to cariogenic substrates. The use of warm water when brushing the teeth may minimize sensitivity in these teeth which, in turn, is a disincentive to effective oral hygiene.

Promoting mineralization of affected enamel through the uptake of calcium and phosphate may potentially enhance the mechanical properties and reduce susceptibility to further breakdown. The development of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) technology provides a way of delivering calcium and phosphate to the tooth surface in a supersaturated

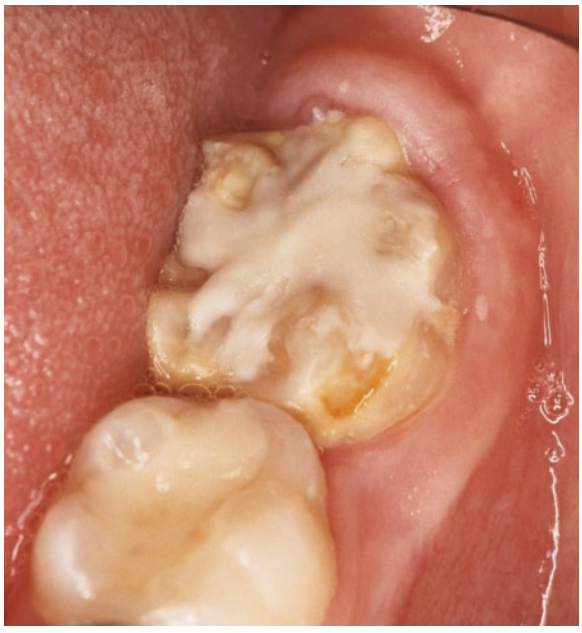


Figure 3 A hypomineralized lower first permanent molar being temporarily and asymptomatically maintained using Fuji VII glass ionomer cement

medium stabilized by the casein phosophopeptide.[36] In addition to promoting mineralization, CPP-ACP will further inhibit carious demineralization. Products incorporating this technology include Tooth Mousse (GC Corporation, 76-1 Hasunuma-cho, Itabashi-ku. Tokyo 174-8586, Japan) and Recaldent Chewing Gum (Cadbury Adams USA LLC, Parsippany, NJ 07054, USA). Whilst clinical trial data on these products are, to date, limited the application of Tooth Mousse directly on to affected teeth is associated anecdotally with a reduction in sensitivity in affected children which, in turn, optimizes oral hygiene.

Maintenance of existing tooth structure

The restoration of MIH affected molars poses significant challenges. The success of conventional restorative techniques is compromised in these teeth. Amalgam, being non-adhesive, requires the removal of excessive tooth tissue for mechanical retention leaving the residual tooth vulnerable to further tissue loss and fracture. Temporary restoration and maintenance of existing tooth structure can be achieved, often in sub-optimal clinical conditions, through the use of glass ionomer cements and in particular the low viscosity Fuji VII (GC Corporation, 76-1 Hasunuma-cho, Itabashi-ku. Tokyo 174-8586, Japan). This approach allows the compromised molar tooth to be preserved asymptomatically for many years if regularly maintained (Figure 3). Similarly

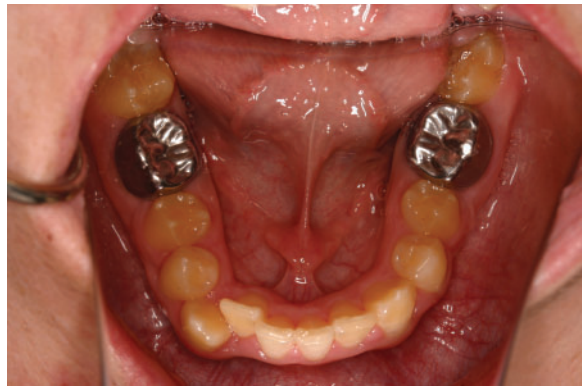


Figure 4 5-year-old preformed metal crowns on compromised first permanent molars in an adolescent with molar-incisor-hypomineralization

directly placed composite resin restorations have been shown to be successful up to 4 years after placement in young children[32] but should be monitored carefully for marginal breakdown.

A more definitive, albeit still temporary, solution is the preformed metal crown (PMC). Placement of a PMC does require excellent analgesia and patient co-operation which may not be forthcoming; however, there is no doubt that PMCs placed on first permanent molars provide an excellent medium term restorative solution.[37,38] Nevertheless, consideration needs to be given to the long term management of teeth restored in this fashion (Figure 4). If the tooth is maintained using a PMC in to adulthood it can present significant restorative challenges to the prosthodontist and may still require extraction.

Individually fabricated indirect cast, composite or ceramic restorations are a potential definitive restorative option for the management of young permanent molars with developmental defects. The generally very minimal tooth preparation required in the construction and placement of these types of restoration has significant advantages in terms of preserving the often already rather limited pre-existing tooth tissue. Whilst the evidence is limited, the use of both tooth coloured and metal crowns on such teeth is associated with relatively low failure rates over the short to medium term.[37–39]

Orthodontic considerations

The removal of compromised first permanent molars is rarely the favoured option from an occlusal perspective; however at times it is either the only option or, given the limited restorative options, it may be the preferred option. The considerations associated with the timing of such extractions, which should form part of a

comprehensive treatment strategy, are well recognized and have been discussed elsewhere but should include an orthodontic opinion.[40] Given the differences in structure and etching behaviours of hypomineralized enamel there are potential problems for retention of orthodontic appliances. In addition to the preferred use of molars bands over brackets, glass ionomer cement based adhesives may not only improve appliance retention but help to reduce the risk of enamel demineralization during orthodontic treatment; however at this time there is no evidence available to support any particular bonding technique over another. It has been suggested that pre-treatment of affected enamel with sodium hypochlorite will remove the excess protein encasing the enamel crystals, optimize the quality of etch and improve the adhesive interface. Again the evidence is weak and at the moment has been limited to treatment of teeth affected by amelogenesis imperfecta rather than more general DDE which may behave differently.[41,42]

Conclusions

At a time when there has been a worldwide reduction in dental caries, developmental defects of enamel are presenting increasing challenges to the dental profession. The aetiology of these defects remains unclear, although a combination of both environmental and genetic factors is implicated. The resultant defects vary in appearance, severity and distribution but are generally limited to the first permanent molars with or without incisor involvement. Restorative management of these teeth is challenging and remains relatively ineffective. Investigation of the structure and composition of these teeth has revealed a catastrophic reduction in mechanical properties with affected enamel being up to 90% softer and more porous than normal enamel. The explanation for this reduction remains unclear at this time, but is probably related to the incomplete removal of enamel matrix proteins during amelogenesis thereby disrupting the final maturation phase. Further research is required to identify these residual proteins and establish their impact on the adhesive behaviours of enamel. In particular, strategies to improve or modify the etching behaviours of this enamel coupled with a better understanding of the tooth/adhesive interface would assist with long term retention of both restorations and orthodontic appliances. To further optimize clinical outcomes strategies to re-establish mechanical properties approaching those of an intact tooth are required. Increasing the mineral content of enamel through up-take of calcium and phosphate could enhance its mechanical properties and potentially its susceptibility to further demineralization; however the mechanism by which this can be achieved is not established and further work in this area is needed in order that these teeth can be retained in the oral cavity long term without sensitivity or breakdown.

Acknowledgements

This review is based upon a paper presented at the British Orthodontic Society Annual meeting in Harrogate in 2007. The author wishes to acknowledge the contribution of her collaborators; Professor Mike Swain, Dr Erin Mahoney, Dr Felicity Crombie and Dr John Winters in providing data, feedback and images for Figures 1 and 4 during the preparation of this manuscript.

References

1. Brook AH, Smith JM. The aetiology of developmental defects of enamel: a prevalence and family study in East London, U.K. *Connect Tissue Res* 1998; **39**: 151–56; discussion 187–94.
2. Hall RK. Prevalence of developmental defects of tooth enamel (DDE) in a pediatric hospital department of dentistry population (1). *Adv Dent Res* 1989; **3**: 114–19.
3. Crombie F, Manton D, Weerheijm KL, Kilpatrick N. Molar incisor hypomineralisation: a survey of members of the Australian and New Zealand Society of Paediatric Dentistry. *Aust Dent J* 2008; **53:** 160–66.
4. Weerheijm KL, Mejare I. Molar incisor hypomineralization: a questionnaire inventory of its occurrence in member countries of the European Academy of Paediatric Dentistry (EAPD). *Int J Paediatr Dent* 2003; **13**: 411–16.
5. Mejare I, Bergman E, Grindefjord M. Hypomineralized molars and incisors of unknown origin: treatment outcome at age 18 years. *Int J Paediatr Dent* 2005; **15**: 20–28.
6. Suga S. Enamel hypomineralization viewed from the pattern of progressive mineralization of human and monkey developing enamel. *Adv Dent Res* 1989; **3**: 188–98.
7. Suckling GW. Developmental defects of enamel–historical and present-day perspectives of their pathogenesis. *Adv Dent Res* 1989; **3**: 87–94.
8. Fearne J, Anderson P, Davis GR. 3D X-ray microscopic study of the extent of variations in enamel density in first permanent molars with idiopathic enamel hypomineralisation. *Br Dent J* 2004; **196**: 634–38; discussion 625.
9. Jalevik B, Dietz W, Noren JG. Scanning electron micrograph analysis of hypomineralized enamel in permanent first molars. *Int J Paediatr Dent* 2005; **15**: 233–40.
10. Jalevik B, Odelius H, Dietz W, Noren J. Secondary ion mass spectrometry and X-ray microanalysis of hypomineralized enamel in human permanent first molars. *Arch Oral Biol* 2001; **46**: 239–47.

11. Tung K, Fujita H, Yamashita Y, Takagi Y. Effect of turpentine-induced fever during the enamel formation of rat incisor. *Arch Oral Biol* 2006; **51**: 464–70.
12. Yamaguti PM, Arana-Chavez VE, Acevedo AC. Changes in amelogenesis in the rat incisor following short-term hypocalcaemia. *Arch Oral Biol* 2005; **50**: 185–88.
13. Robinson C, Connell S, Brookes SJ, Kirkham J, Shore RC, Smith DAM. Surface chemistry of enamel apatite during maturation in relation to pH: implications for protein removal and crystal growth. *Arch Oral Biol* 2005; **50**: 267.
14. Sui W, Boyd C, Wright JT. Altered pH regulation during enamel development in the cystic fibrosis mouse incisor. *J Dent Res* 2003; **82**: 388–92.
15. Crombie F, Manton DJ, Kilpatrick N. Aetiology of molar-incisor-hypomineralisation: a critical review. *Int J Paediatr Dent* 2009; **19**: 73–83.
16. Gao Y, Sahlberg C, Kiukkonen A, *et al*. Lactational exposure of Han/Wistar rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin interferes with enamel maturation and retards dentin mineralization. *J Dent Res* 2004; **83**: 139–44.
17. Laisi S, Kiviranta H, Lukinmaa PL, Vartiainen T, Alaluusua S. Molar-incisor-hypomineralisation and dioxins: new findings. *Eur Arch Paed Dent* 2008; **9**: 224–27.
18. Laisi S, Ess A, Sahlberg C, Arvio P, Lukinmaa PL, Alaluusua S. Amoxicillin may cause molar incisor hypomineralization. *J Dent Res* 2009; **88**: 132–36.
19. Jalevik B, Noren JG, Klingberg G, Barregard L. Etiologic factors influencing the prevalence of demarcated opacities in permanent first molars in a group of Swedish children. *Eur J Oral Sci* 2001; **109**: 230–34.
20. Lai PY, Seow WK, Tudehope DI, Rogers Y. Enamel hypoplasia and dental caries in very-low birthweight children: a case-controlled, longitudinal study. *Pediatr Dent* 1997; **19**: 42–49.
21. Whatling R, Fearne JM. Molar incisor hypomineralization: a study of aetiological factors in a group of UK children. *Int J Paediatr Dent* 2008; **18**: 155–62.
22. Weerheijm KL, Jalevik B, Alaluusua S. Molar-incisor hypomineralisation. *Caries Res* 2001; **35**: 390–91.
23. Calderara PC, Gerthoux PM, Mocarelli P, Lukinmaa PL, Tramacere PL, Alaluusua S. The prevalence of molar incisor hypomineralisation (MIH) in a group of Italian school children. *Eur Arch Paed Dent* 2005; **6**: 79–83.
24. Fteita D, Ali A, Alaluusua S. Molar-incisor hypomineralization (MIH) in a group of school-aged children in Benghazi, Libya. *Eur Arch Paed Dent* 2006; **7**: 92–95.
25. Jasulaityte L, Veerkamp JS, Weerheijm KL. Molar incisor hypomineralisation: a review and prevalence data from a study of primary school children in Kaunas (Lithuania). *Eur Arch Paed Dent* 2007; **8**: 87–94.
26. Muratbegovic A, Markovic M, Ganibegovic Selimovic M. Molar incisor hypomineralisation in Bosnia and Herzogovina: prevalence, aetiology and clinical consequences in medium caries activity population. *Eur Arch Paed Dent* 2007; **8**: 189–94.
27. Mahoney EK, Rohanizadeh R, Ismail FS, Kilpatrick NM, Swain MV. Mechanical properties and microstructure of hypomineralised enamel of permanent teeth. *Biomaterials* 2004; **25**: 5091–100.
28. Mahoney E, Ismail FS, Kilpatrick N, Swain M. Mechanical properties across hypomineralized/hypoplastic enamel of first permanent molar teeth. *Eur J Oral Sci* 2004; **112**: 497–502.
29. Xie Z, Mahoney E, Kilpatrick N, Swain M, Hoffman M. On the structure – property relationship of sound and hypomineralised enamel. *Acta Biomaterialia* 2007; **3**: 865–72.
30. Leppaniemi A, Lukinmaa PL, Alaluusua S. Nonfluoride hypomineralizations in the permanent first molars and their impact on the treatment need. *Caries Res* 2001; **35**: 36–40.
31. Jalevik B, Klingberg GA. Dental treatment, dental fear and behaviour management problems in children with severe enamel hypomineralization of their permanent first molars. *Int J Paediatr Dent* 2002; **12**: 24–32.
32. Lygidakis NA, Chaliasou A, Siounas G. Evaluation of composite restorations in hypomineralised permanent molars: a four year clinical study. *Eur J Paed Dent* 2003; **4**: 143–48.
33. Rodd HD, Morgan CR, Day PF, Boissonade FM. Pulpal expression of TRPV1 in molar incisor hypomineralisation. *Eur Arch Paed Dent* 2007; **8**: 184–88.
34. Williams JK, Gowans AJ. Hypomineralised first permanent molars and the orthodontist. *Eur J Paed Dent* 2003; **4**: 129–32.
35. William V, Burrow MF, Palamara JE, Messer LB. Microshear bond strength of resin composite to teeth affected by molar hypomineralization using 2 adhesive systems. *Pediatr Dent* 2006; **28**: 233–41.
36. Reynolds EC. Remineralisation of enamel subsurface lesions by casein phosphopeptides-stabilised calcium phosphate solutions. *J Dent Res* 1997; **76**: 1587–95.
37. Kotsanos N, Kaklamanos EG, Arapostathis K. Treatment management of first permanent molars in children with molar-incisor hypomineralisation. *Eur J Paed Dent* 2005; **6**: 179–84.
38. Zagdwon AM, Fayle SA, Pollard MA. A prospective clinical trial comparing preformed metal crowns and cast restorations for defective first permanent molars. *Eur J Paed Dent* 2003; **4**: 138–42.
39. Koch MJ, Garcia-Godoy F. The clinical performance of laboratory-fabricated crowns placed on first permanent molars with developmental defects. *J Am Dent Assoc* 2000; **131**: 1285–90.
40. Shargill I, Hutton A. The management of hypomineralized first permanent molar teeth. *Dent Update* 2007; **34**: 636–38.
41. Venezie RD, Vadiakas G, Christensen JR, Wright JT. Enamel pretreatment with sodium hypochlorite to enhance bonding in hypocalcified amelogenesis imperfecta: case report and SEM analysis. *Pediatr Dent* 1994; **16**: 433–36.
42. Saroglu I, Aras S, Oztas D. Effect of deproteinization on composite bond strength in hypocalcified amelogenesis imperfecta. *Oral Dis* 2006; **12**: 305–08.