

Peripartum events and molar-incisor hypomineralisation (MIH) amongst young patients in southwest France

E. Garot^{1,2} · D. Manton³ · P. Rouas^{1,2}

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Abstract

Aim This was to investigate the association of peripartum events with the occurrence of MIH.

Methods This study, carried out between 2010 and 2011, was based on objective information noted in child health booklets on putative risk factors for MIH during the Peripartum period, aged between 6 to 28 years. The target population consisted of patients with MIH and a control group. Among the 849 patients examined by two calibrated paediatric dentists, 75 patients with MIH were recorded. These patients attended for consultation either at the teaching dental hospital of Bordeaux (France) or at a private dental practice (Bordeaux, France). Pearson's Chi-squared test was used and Odds ratios (OR) with 95 % test-based confidence intervals (CI) were calculated.

Results Correlations were observed between hypoxia during delivery and occurrence of MIH (OR = 6.1; CI = 1.7–21.85), and also between birth by caesarean section and MIH (OR = 2.9; CI = 1.2–6.9). There was no association between prematurity and MIH.

Conclusions Peripartum events such as hypoxia during birth or delivery by caesarean section are suggested to be risk factors for the occurrence of MIH in this population.

Keywords Molar-incisor hypomineralisation · Peripartum events · Hypoxia · Caesarean section

Introduction

The term molar-incisor hypomineralisation (*MIH*) was termed by Weerheijm et al. (2001). It defines a pattern of presentation of a structural anomaly in the quality of tooth enamel, systemic in origin, affecting one or more of the first permanent molars (FPM), and also commonly affecting the permanent incisors. In histological terms, MIH results from an alteration in the action of the ameloblasts during the maturation phase which lasts until approximately 3 years of age in FPM and incisors (Jälevik et al. 2005). The most vulnerable period is from around birth until 6–7 months of age (Fagrell et al. 2013; Jedeon et al. 2013). International prevalence rates are between 3 and 40 % (Soviero et al. 2009; Jälevik 2010), with an average of 15 %, which, given the possible aesthetic and functional consequences of this anomaly, means that it is a major public health problem.

To date, the aetiology of this condition is still unclear, but authors agree that this is multifactorial (Weerheijm 2004; Jasulaityte et al. 2008; Alaluusua 2010). Given the difficulties involved in treating MIH affected teeth (hypersensitivity, anxiety, difficulties with anaesthesia, poor aesthetics, carious lesions with fast progression, failure of restorations) (Jälevik and Klingberg 2002; da Costa-Silva et al. 2010; Ghanim et al. 2011), it is essential that the aetiological factors are investigated to enable identification

✉ E. Garot
elsa.garot@u-bordeaux.fr

¹ Univ. de Bordeaux, UFR des Sciences Odontologiques,
16-20 Cours de la Marne, 33082 Bordeaux Cedex, France

² Univ. de Bordeaux, PACEA, UMR 5199, Pessac, France

³ Melbourne Dental School, University of Melbourne,
Melbourne, Australia

of those at risk and, if possible, to act early to allow prevention. Prospective studies are most likely to determine the aetiology, however, due to the extended nature of the trial to record risk factors from birth to eruption of the teeth at around 6 years of age, there are issues of the large sample size required due to the potential for subjects to be lost to a study (Elfrink et al. 2015). 30 aetiological hypotheses have been cited in the literature and these can be grouped into pre-, peri-, and post-partum factors (Alaluusua 2010). Some researchers have hypothesised that a genetic predisposition exists with MIH (Crombie et al. 2008; Whatling and Fearn 2008). Aetiological hypotheses are based either on experimental or retrospective clinical studies (Laisi et al. 2009; Alaluusua 2010; Kuscu et al. 2013). To date, there has only been one prospective study focusing on risk factors (Fagrell et al. 2011). In that Swedish study, no association between hypomineralised FPM and pre-, peri- and neonatal data was determined. Only breastfeeding for more than 6 months, late introduction of gruel (cereal and water) and late introduction of infant formula were significantly associated with MIH, and it would appear that due to the nature of the identified risk factors, that these are associated factors, not causative (Fagrell et al. 2011).

The present study focused on the events that occur during birth which were recorded by an obstetrician or midwife at the time of the birth in each patient's health record. The aim was to determine if a link could be established between Peripartum factors and occurrence of MIH amongst a sample of patients from southwestern France. Peripartum risk factors included prematurity, hypoxia during delivery, delivery by caesarean section and twin pregnancy. This retrospective study focused on the determination of links between a health condition present (MIH) and a past event (Peripartum factors). However, it is based on documentation whose reliability can be ensured by the recording of data on the day of the birth.

Materials and methods

Setting and study population

The present study was carried out amongst a subsample of the south-west French population chosen from a teaching dental hospital of Bordeaux and a private dental practice. The study began in May 2010 and finished in October 2011. The examination of 849 patients aged between 6 and 28 years was carried out by one of the two calibrated examiners (EG and PR). Increasing patient age may worsen the severity of the MIH defects due to post-

eruptive deterioration and may constitute a bias, however, the present study was exclusively focused on the diagnosis and not on the severity of MIH. Only subjects who possessed their Child Health Record, a booklet where parents can keep track of all of their children's health information, were included. The case group consisted of a convenience sample of 75 patients with MIH in accordance with EAPD criteria (Weerheijm et al. 2003). The control group was chosen randomly (from 6 to 27 years of age, from the same facilities) and included 53 subjects.

The research protocol (DC2012/08) was approved by the "Comité de Protection des Personnes Sud-Ouest et Outre Mer III". Data were anonymized. Oral consent by the patient (or parent in the case of minors) was obtained.

Exclusion criteria

Exclusion criteria included dental anomalies such as fluorosis, amelogenesis imperfecta and dentinogenesis imperfecta. Patients whose FPM had not completely erupted were excluded. Patients who did not possess their personal health record or if notes for the period of interest were not recorded were also excluded from this study. If subjects or their legal guardian did not agree to participate in the study, they were excluded, and this had no effect on their current or future oral health care.

Clinical examinations

An inter-observer reproducibility test for the diagnosis of MIH defects was carried out using 30 photographed cases presenting with different presentations of MIH and various dental anomalies between the two paediatric dentist examiners (EG and PR). The scoring of MIH with photographs was validated by Elfrink and colleagues (2009). This test consisted of a mix of 15 cases of MIH and 15 cases of different anomalies or enamel defects (fluorosis, caries, amelogenesis imperfecta, traumatic origin colour, dentinogenesis imperfecta). Analysis of the inter-observer test gave a kappa coefficient of 1 for diagnoses of the 30 preliminary clinical cases. The examination of 849 patients was carried out by one of the two calibrated examiners. The teeth were air-dried with a triple syringe before being examined under a scalytic (shadow free) light. Defects smaller than 1 mm were excluded. Each patient was given a score of "0" for absence or "1" for presence of MIH according to the definition and the diagnostic criteria of MIH (demarcated opacity, post-eruptive enamel breakdown, atypical restoration and atypical extraction of molars due to MIH) established by Weerheijm et al. (2001, 2003).

Data collection

Data were collected by the examiner using each patient’s health record. At birth, the child health record was completed just after the delivery by an obstetrician or midwife. It included information about the delivery and each child’s health status (Table 1). Information recorded was based on the risk factors described in the literature which occur during the Peripartum period (prematurity, hypoxia during delivery, delivery by caesarean section and twin pregnancy) (Dietrich et al. 2003; Muratbegovic and Markovic 2007; Lygidakis et al. 2008; Whatling and Fearn 2008). A preterm birth was defined as birth before 37 weeks of gestation (ACOG 2013). Hypoxia included a long labour (>24 h), respiratory distress of the newborn requiring assisted breathing techniques, the necessity to resuscitate the child, a complicated delivery and an APGAR score lower than 7. Due to the evidence of hypoxia associated with caesarean section, a grouping of hypoxia and/or caesarean section was created (Inanc et al. 2005; Cyna et al. 2006; Hansen et al. 2008; Guergolette et al. 2009). The Apgar score (named after its developer anaesthetist Virginia Apgar) is a method to quickly summarise the health of newborn children with a range of zero to ten (Apgar 1953). The five criteria are summarised using words chosen to form an acronym (Appearance, Pulse, Grimace, Activity, Respiration). Scores 7 and above are generally normal, 4–6 fairly low, with 3 and below generally regarded as critically low (Casey et al. 2001; Finster and Wood 2005).

For each the number of brothers and sisters, order of birth (dichotomised as first born or not first born), year of birth, sex, age and whether or not the siblings were also affected by this anomaly were recorded. Each of the criteria was given a dichotomous score: ‘0’ for absence or ‘1’ for presence.

Table 1 Information recorded by an the obstetrician or midwife in each subject’s health record

Delivery	Child state at birth
Date	Weight
Hour	Height
Place	Apgar score
	1st minute
Term:... weeks of gestation	5th minute
Performed by (name and title)	Resuscitation required? Yes or no
Spontaneous delivery: yes or no	Self-contained breathing after... minutes
Specification	Anomalies and malformations
	Transfer service
	Other information

The data were analysed using the Statistica® software package version 7.1 (Statsoft®, Dell Corporation, USA), and the open source R® programming environment (R Foundation, USA). Comparison of variables was performed with non-parametric statistical tests: Pearson’s Chi-squared test and logistic regression modelling were used to analyse data. A *p* value <0.05 was considered statistically significant.

Results

Among the 849 patients who were examined, 75 MIH patients and 53 ‘not affected’ patients participated in this study. The mean age ± SD (Standard Deviation) of these 128 patients (MIH and control groups) was 14.3 ± 6.1 years old with a similar distribution between male and female individuals (Table 2).

A statistically significant association (*p* = 0.002) between having an episode of hypoxia at birth and developing MIH was determined (Table 3). An hypoxic episode at birth increased the risk of MIH by more than 6 times (OR = 6.1; CI = 1.7–21.85). Of the MIH group, 30 % had hypoxia at birth compared to 6 % within the control group (Table 3).

A statistically significant association (*p* = 0.01) existed between birth by caesarean section and developing MIH (Table 3). Being born by caesarean section increased the risk of presence of MIH by 2.9 times (OR = 2.9; CI = 1.2–6.9). Of patients with MIH, 38 % were born by caesarean section compared to 17 % of the controls (Table 3).

Hypoxia at birth and/or being born by caesarean delivery had a statistically significant association (*p* = 0.0005) with the presence of MIH (Table 3). More than half of the patients with MIH had at least one of these factors, multiplying the risk of the occurrence of MIH by more than 4 times (OR = 4.08; CI = 1.8–9.2; Table 3).

Being born prematurely was not a significant risk factor for MIH (*p* = 0.3; Table 3). Amongst the MIH group,

Table 2 Characteristics of the population studied on MIH aetiology

	MIH group <i>N</i> (%)	Control group <i>N</i> (%)
Male	34 (45 %)	30 (57 %)
Female	41 (55 %)	23 (43 %)
CHU	56 (75 %)	40 (75 %)
Private practise	19 (25 %)	13 (25 %)
>15-year-old	18 (24 %)	12 (23 %)
≤15-year-old	57 (76 %)	41 (77 %)

CHU teaching dental hospital

Table 3 Odds ratios (95 % confidence interval) and Chi-squared test of MIH occurrence within perinatal variables

	MIH group <i>N</i> (%)	Control group <i>N</i> (%)	Adjusted Odds ratio	95 % confidence interval	<i>p</i> value
Hypoxia	19/63 (30 %)	3/50 (6 %)	6.1	1.7–21.9	0.002*
Caesarean section	26/68 (38 %)	9/53 (17 %)	2.9	1.2–6.9	0.01*
Hypoxia and/or caesarean section	37/70 (53 %)	11/52 (21 %)	4.1	1.8–9.2	0.0005*
Premature birth	12/75 (16 %)	5/50 (10 %)	1.7	0.6–5.2	0.3
Birth order (1st)	37/73 (51 %)	22/52 (42 %)	1.4	0.7–2.9	0.2

N number of patients

* Statistically significant difference between test and control groups ($p < 0.05$)

16 % were born prematurely compared with 10 % of the healthy patients (Table 3).

Six pairs of twins were included, and both twins were affected by MIH in only one pair. No additional analysis was carried out in these cases because the sample size was considered too small. No significant association was found between birth order and occurrence of MIH.

Discussion

For retrospective studies, the reliability must be questioned of the responses given by the parents of the affected children, and also the responses of the patients themselves in the case of older patients. MIH cannot be diagnosed with any certainty until the eruption of the four FPM at the age of 6 years. It would therefore, seem rather difficult to guarantee the reliability of responses concerning events that took place many years before, as a memory of certain events may be unreliable. During childhood, treatment and disease is noted by a paediatrician in each patient's health records, however, it may not always have been completed fully, so care must be taken when considering this information. Varying levels of objectivity of the aetiological hypotheses described in the literature was considered, and a decision made to focus only on events during childbirth, which in France are required to be recorded in a structured manner in the health record by any obstetrician or midwife at birth. Peripartum events such as mode of delivery, premature birth, twin birth or the use of assisted breathing techniques are systematically noted in each child's health record. In addition Peripartum episodes are relatively objective, compared with studies based on recollection of maternal interviews, unlike most of the existing aetiological hypotheses (antibiotics, upper respiratory tract infections, illnesses in children between 0 and 4 years of age, episodes of high fever, duration of breastfeeding, etc.). Results based on this peripartum data can therefore provide information that should, in principle, be reliable. The result is that some aetiological hypotheses appear to be based

upon more objective than others. A person might forget that a specific antibiotic was used, but it would be unusual to forget that a birth was difficult. For other criteria there is no doubt at all, such as delivery by caesarean section.

This is the first study comparing the Peripartum factors with occurrence of MIH in a French population. In the present study, Peripartum problems such as hypoxia at birth and caesarean section were significantly associated with occurrence of MIH; in agreement with previous studies (Lygidakis et al. 2008; Ahmadi et al. 2012; Ghanim et al. 2013; Pitiphat et al. 2014). Thus a retrospective Greek study covered the largest sample of patients with MIH ($n = 360$) (Lygidakis et al. 2008). They reported that the medical problems encountered most frequently during Peripartum period were: a long/complicated birth (9.4 %), delivery by caesarean section (25.5 %), premature birth (8 %), twin birth (16.6 %), and haemorrhage with detachment during delivery (0.5 %) (Lygidakis et al. 2008). Some authors did not determine an association between perinatal problems and occurrence of MIH (Dietrich et al. 2003; Whatling and Fearn 2008). Brogardh-Roth et al. 2011 reported that there was no association between delivery by caesarean section and occurrence of MIH. However, that study looked at premature children only, incorporating a putative bias since selecting a specific type of delivery will affect the rate of caesarean sections. A German study ($n = 31$ MIH patients) determined no significant difference between the rate of complications during birth and MIH, but the criteria for perinatal complications were not clarified (Dietrich et al. 2003). Information on this subject is therefore variable. In the only prospective study published to date, Fagrell et al. 2011 found no correlation between neonatal complications (from birth to 1 month) or type of delivery and the occurrence of MIH. The criteria used to define the neonatal complications in this present study did not include criteria such as a long labour (>24 h), assisted breathing techniques and complicated vaginal delivery as used in others studies (Lygidakis et al. 2008; Ghanim et al. 2013; Pitiphat et al. 2014). These different results may be explained by a multifactorial aetiology and factors may

vary according to the differing health systems of different countries.

The possibility of an association between birth by caesarean section and hypoxia at birth must be considered. Maternal hypotension is the most frequent complication from spinal anaesthesia for caesarean delivery. It may be accompanied by severe nausea or vomiting which may have serious consequences for the mother (unconsciousness, pulmonary problems) and also for the unborn child (hypoxia, acidosis and neural issues) (Cyna et al. 2006). Children born by elective caesarean section (before labour or rupture of the membranes) have an increased risk of respiratory morbidity (OR = 1.9; CI 1.2–3) compared with children born by vaginal delivery or by emergency caesarean (Hansen et al. 2008). In 2011, Labour can be associated with an increase in placental oxidative stress and has an influence on resultant maternal stress (Guergolette et al. 2009). In contrast, however, others concluded that oxidative stress in the foetal circulation did not depend on the type of delivery (Fogel et al. 2005). Another study showed that newborn babies are exposed to more oxidative stress when they are born by vaginal delivery (Inanc et al. 2005). However, there is scientific consensus amongst most authors regarding the link between hypoxia and caesarean delivery (Inanc et al. 2005; Cyna et al. 2006; Hansen et al. 2008; Guergolette et al. 2009). In the majority of all types of caesarean section, with the exception of those in an emergency Caesarian section during labour, spinal anaesthesia is used. In future studies, it is clearly important that the reason for the caesarean delivery should be determined, whether it is associated with foetal distress (cord prolapse, retro-placental haematoma, eclampsia, etc.), or with a maternal problem (narrow pelvis, possible serious maternal disorders during a normal delivery, maternal disorders that may affect the foetus, after-effects from a procedure on the perineum for previous trauma, malformations, tumours, abnormal or scarred uterus, multiple pregnancy (i.e. twins, triplets, etc.). A distinction should be made between children born by caesarean section with or without labour, and the type of anaesthesia used before the caesarean will also be noted to make a differential diagnosis between the presence or absence of hypoxia, when the latter can be a decisive factor in choosing the type of delivery (e.g. caesarean), but can also be caused by caesarean section. Is there some correlation with the increasingly high caesarean section rate or a lower caries experience in many children? The WHO (World Health Organization) has highlighted the ever-increasing numbers of caesarean births over the last 30 years and in particular the problem of the over-medicalisation of childbirth in wealthy countries (Gibbons et al. 2010). Moreover, Brazil has the highest caesarean section rates

in the world (45.9 % of deliveries) and this country also shows the highest reported MIH prevalence (40 %) (Soviero et al. 2009). This possible link should be investigated by a prospective study (Elfrink et al. 2015). The present study was retrospective in nature, however, it was based on reliable recording of risk factors at a similar time to their occurrence. Prospective studies are long and difficult to carry out as MIH diagnosis can only be completed when are erupted. Whilst we wait for the results of any new prospective studies, retrospective research based on reliable data can still provide valuable information.

Conclusions

Hypoxia during delivery is a possible causative factor of MIH. Researchers are currently inclined nevertheless more towards a multifactorial aetiology. The prevention of risk factors remains the key issue and the most important route to explore.

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Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this retrospective study, oral informed consent was obtained from all individual participants included in the study.

Conflict of interest Authors declare that they have no conflict of interest.

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