

Developmental enamel defects of primary incisors in preterm infants with very low and extremely low birthweight. A case-control study



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Abstract

Aim To determine the prevalence of developmental defects of enamel (DDE) in primary incisors of preterm very low birthweight (VLBW) and extremely low birthweight (ELBW) one-year-old infants and to compare the findings with fullterm one-year-old normal birthweight (NBW) infants.

Materials and methods All infants were enrolled in the case-control study at birth. Personal information and medical histories were obtained through interviews with parents and from medical hospital records. The presence of DDE in primary incisors was evaluated in 82 one-year old preterm infants delivered with VLBW, in 50 ELBW and in 58 fullterm NBW infants. The data were statistically analysed by ANOVA and chi-square tests, and a statistical significance level $p < 0.05$ was established.

Results DDE were diagnosed in 19 (23.2 %) preterm VLBW infants, in 27 (54%) ELBW infants and in 4 (6.9%) infants of the control group. The most frequent DDE found in the case group was hypoplasia in 10 (12.2%) VLBW infants and in 14 (28%) ELBW infants. The opacities were found in 6 (7.3%) VLBW infants and in 8 (16%) ELBW infants.

Conclusion The results of the study confirmed a significantly higher prevalence of DDE in the primary incisors in preterm ELBW infants than in VLBW infants and than in full term NBW infants.

birthweights $< 1,500$ g, extremely low birthweight (ELBW) infants with birthweights $< 1,000$ g and incredibly low birthweight (ILBW) infants with birthweights < 750 g. The incidence of preterm VLBW and ELBW infants in the Czech Republic is respectively 1.1% and 0.4 % of live births [Markova, 2005]. This means that annually in the Czech Republic 1,000 infants with VLBW and 350–390 infants with ELBW are born. Survival of VLBW and ELBW preterm neonates has improved with the widespread use of exogenous surfactant agents, maternal steroids, use of assisted ventilation and advancements in neonatal intensive care [Hack and Fanaroff, 1999; Saigal and Doyle, 2008]. Premature infants with VLBW and ELBW are very susceptible to all the complications of premature birth both in the immediate neonatal period and during childhood [Hack and Fanaroff, 1999]. They have a short prenatal period and are at great risk for early and late morbidity involving, for example, neonatal hypocalcemia, hyperbilirubinemia, perinatal asphyxia, respiratory, cardiovascular, gastrointestinal, neurological problems and nutritional deficiencies, as well as possible disabilities and impairments affecting physical growth and mental development. The preterm and VLBW or ELBW delivery may affect development and growth of the orofacial region, including primary and permanent teeth. The primary teeth have a long prenatal and postnatal process because the primary incisors start developing at around the 6th–7th intrauterine week and continue for a few months after birth [Avery and Chiego, 2006]. The onset of the calcification process in primary teeth starts at the 14th intrauterine week and continues up to the first year of postnatal life. The critical period of primary teeth development and growth occurs very early prenatally. Dental enamel of primary teeth in preterm infants is abnormal in surface quality and significantly thinner compared to fullterm enamel. The thinner enamel is due mainly to reduced prenatal growth and results in smaller dimensions of the primary dentition [Seow et al., 2005].

The aetiological factors associated with disturbed development of enamel can be categorised as localised or generalised; generalised factors can be further divided into environmental and hereditary, both of which affect enamel during prenatal, neonatal and postnatal development [Suckling, 1989]. The prenatal conditions that may be associated with

KEYWORDS Developmental defects of enamel; Extremely low birthweight; Very low birthweight; Preterm infants.

Introduction

A preterm infant is defined as one born before the 37th gestational week or having low birthweight [WHO, 2004]. Prematurity can be classified as mild when the infant is born between the 32nd and 36th weeks of gestation; moderate, if the birth occurs between the 31st and 28th weeks; or extreme, if the gestational age is less than or equal to 27 weeks. A low birthweight (LBW) is established as weighing less than 2,500 g, regardless of the gestational age. Low birthweight neonates are subdivided into very low birthweight (VLBW) infants with

developmental defects of enamel (DDE) include maternal vitamin D deficiency, hypertension, urinary tract infection, smoking and use of antibiotics or medicaments during pregnancy [Velló et al., 2010]. However, some authors [Franco et al., 2007; Johnsen, 1984] have found no relationship between maternal general health and the occurrence of DDE in primary dentition. The perinatal and postnatal aetiological factors of mineralisation disturbances of enamel can be birth complications, postnatal infections, metabolic disorders, congenital cardiac diseases, gastrointestinal malabsorption, respiratory distress syndrome, nephritic syndrome, nutritional disturbances and intake of some medications [Franco et al., 2007; Johnsen, 1984]. The disturbed calcium metabolism during the first days of life may also be an important etiological factor of DDE in the primary teeth, as well as the fact that the major accumulation of calcium and phosphate takes place during the last trimester of pregnancy [Seow et al., 1984b]. In addition to systemic factors, trauma caused by a laryngoscope and endotracheal intubation can be associated with DDE in primary upper incisors [Seow et al., 1984a; de Oliveira Melo, 2014].

The aim of the present study was to determine the prevalence of DDE in primary incisors of preterm infants delivered with VLBW and ELBW and to compare the findings with one-year old fullterm infants delivered with NBW. We hypothesised significant differences in prevalence of DDE in primary incisors between case and control groups of infants.

Materials and methods

Study design and subjects

All infants were enrolled in the present case-control study at birth by the Department of Obstetrics, Faculty Hospital in Pilsen, Czech Republic. Preterm VLBW, ELBW and full term NBW Caucasian infants of both genders were recruited during a two-year study period (2014–2015). Follow-up visits were conducted at 12 months of chronological or corrected age. For preterm infants, the corrected age was considered, i. e. chronological age reduced by the number of weeks before 40 weeks of gestation. Personal information including gestational age, birthweight, general health status, antibiotic use and self-reported socio-economic status of the family were obtained through interviews with parents and from medical hospital records. The gestational age was estimated from the reported date of the mother's last menstruation.

Infants were eligible for the study if they met the following inclusion criteria for case group: (1) gestational age <37 weeks; (2) birthweight <1,500 g; (3) corrected age 12 months; (4) the presence of all primary incisors in the oral cavity; (4) self-reported middle class socioeconomic status of family. During the neonatal period, all preterm infants received antibiotic treatment consisting of intravenous ampicillin and gentamicin. Infants with genetic syndromes and malformations diagnosed in the neonatal period were excluded from the study. Of the 160 examined preterm infants, 132 were selected based on the inclusion and exclusion criteria. The selected preterm infants were divided into two groups according their birthweight: very low birthweight and extremely low birthweight.

The control group was comprised of one-year old fullterm infants. The inclusion criteria for control group were: (1) gestational age >37 weeks; (2) birthweight >2,500g; (3) the presence of all primary incisors in the oral cavity; (4) self-reported middle class socio-economic status of the family. Infants with systemic diseases, immunological deficiencies,

genetic syndromes, congenital malformations, antibiotic treatment and morbidity in neonatal period were excluded. Of the 70 one-year old full-term infants, 58 were selected for the control group.

All participants of the study were residents of communities with low natural fluorid content (<0.3 ppm).

Dental examination

Dental examination of VLBW, ELBW and NBW infants was performed by one previously trained calibrated examiner at the Paediatric Dentistry Department of the Medical Faculty and Faculty Hospital in Pilsen, Czech Republic. The dental examiner was blinded to the groups of infants. The infants were examined under ideal condition using a sterile dental mirror, dental probe and artificial light. The teeth were dried with gauze, then dental mirror and probe were used to detect developmental defects of enamel (DDE). DDE were recorded on the labial surface of each tooth. The defects measuring less than 1 mm were excluded and where any doubt existed concerning the presence of DDE, the tooth was scored as without enamel defects. The number and type of teeth with enamel defects was registered. The alteration of enamel was classified according to the Modified developmental defects of enamel index, suggested by the Commission on Oral Health, Research and Epidemiology [FDI Commission on Oral Health, Research and Epidemiology, 1992]. Qualitative changes in enamel translucency without loss of enamel surface were categorised as demarcated or diffuse opacities. The demarcated opacities were described when enamel with normal thickness and intact surface displayed alteration in enamel translucency of variable degree. It is demarcated from the adjacent normal enamel with clear boundaries, and may present a white, creamy, yellow, or brown colour. The diffuse opacities comprise alteration in enamel translucency of variable degree and white colour. There is no clear demarcation between the adjacent normal enamel and the opacity. Hypoplasia is a defect affecting the enamel surface, presenting reduction in enamel thickness and can manifest itself in the form of pits, grooves or other quantitative surface loss (Fig. 1). When an enamel defect presents both opacity and hypoplasia, it was classified as a combined defect. The colour photographs showing typical examples of different types of DDE were used as a guide in scoring the teeth for the enamel defects. The opacities were differentiated from white spot carious lesions based on colour, texture, demarcation and relationship to gingival margin [Merglova et al., 2020].

To evaluate the reproducibility of the examination used, 19 (10%) of the infants were randomly selected for re-examination. Kappa values were calculated 0.6 for enamel opacities and 0.9 for hypoplasia.



FIG. 1 Developmental enamel defects of teeth 51, 61 and 62 in preterm ELBW infants.

Statistical methods

The obtained data were statistically analysed using Statgraphics software distributed by Stat Point Technologies, Inc. of Warrenton, Virginia, USA. ANOVA and chi-square tests were used in order to compare mean birthweight, mean gestational age and prevalence of DDE in case and control group of infants. A statistical significance level of $p < 0.05$ was established.

Ethical considerations

Ethical approval for the investigation was obtained from the Research Ethics Committee Faculty of Medicine in Pilsen, Charles University in Prague, Czech Republic. The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983. All infants were recruited from the Department of Neonatology of the Faculty Hospital in Pilsen, Czech Republic. Before the study, the legal guardians of all infants provided informed consent for their children to participate in the study.

Results

Characteristics of subjects

A definitive case group was composed of 82 one-year-old infants delivered with VLBW (39 boys i.e. 47.6% and 43 girls i.e. 52.4%) and of 50 one-year-old preterm infants delivered with ELBW (27 boys i.e. 54% and 23 girls i.e. 46%). A control cohort comprised 58 one-year-old full term infants with NBW (34 boys i.e. 65.5% and 24 girls i.e. 34.5%). Table 1 presents the characteristics of the groups of infants concerning gestational age, birthweight and correlations between these groups. In preterm infants, the most frequent perinatal and neonatal complications were respiratory distress syndrome, bronchopulmonary dysplasia, neonatal sepsis and perinatal asphyxia. Preterm infants received various drug therapy, ventilatory assistance, parenteral nutrition, iron and calcium supplements. The need for this treatment was directly related to the seriousness of the general health status of the neonates.

Prevalence of DDE

DDE (hypoplasia and opacities) of primary incisors was diagnosed in 19 (23.2%) of preterm VLBW infants, in 27 (54.0%) of the preterm ELBW infants and in 4 (6.9%) of the full term NBW infants. The difference between the case and

control cohorts was statistically significant (chi-square test, $p < 0.05$). In the current study, the main defect found was enamel hypoplasia. The hypoplastic changes of primary incisors were present in 10 (12.2%) of VLBW infants, in 14 (28.0%) of ELBW infants and in 2 (3.45%) of the control group. The difference concerning prevalence of enamel hypoplasia between case and control groups was statistically significant (chi-square test, $p < 0.05$). The diffuse or demarcated opacities of enamel in primary incisors was found in 6 (7.3%) of VLBW infants, in 8 (16.0%) of ELBW infants and in 2 (3.45%) of control group. The higher prevalence of opacities in the case groups was statistically significant (chi-square test, $p < 0.05$). The combined defect of enamel was detected in 3 (3.7%) of VLBW infants and in 5 (10.0%) of ELBW infants. The combined defect was not present in infants of the control cohort (Table 2).

DDE were found in 51 (7.8%) of 656 examined teeth in VLBW infants and in 45 (11.25 %) of 400 teeth presented in ELBW infants, while in the control group only in 8 (1.7%) of 464 teeth. The hypoplasias of enamel were detected in 24 teeth (3.7%) of VLBW cohort, in 20 teeth (5%) of ELBW group and in 4 teeth (0.9%) of control cohort. The opacities of enamel were found in 23 teeth (3.5%) of VLBW cohort, in 18 teeth (4.5 %) of ELBW group and in 4 teeth (0.8 %) of control infants (Table 3). The distribution of DDE in primary incisors of premature VLBW and ELBW infants is shown in Table 3. Most of the teeth with DDE in the VLBW case group were situated in the upper jaw (38 i.e. 74.5%) compared to 13 teeth (25.5%) in the mandible. The situation in the ELBW infants was similar. Forty-one teeth (91.1%) were in maxilla and only 4 teeth (8.9 %) in the lower jaw. In the control group of infants all teeth with DDE were localised in the upper jaw.

Discussion

DDE in primary and permanent dentition, delayed tooth eruption and oral defects associated with orotracheal intubation are a well-researched complication of prematurity and low birthweight [Eastman, 2003; Al-Sayagh et al., 2008; Aine et al., 2000; Bodh et al., 2015]. Other oral disturbances in preterm infants include notching of the alveolar ridge, palatal grooving, high arch palate, crossbite, palatal asymmetry and smaller

	VLBW group (No = 82)				ELBW group (No = 50)				NBW group (No = 58)				Test ANOVA
	mean	Min.	Max.	SD	mean	Min.	Max.	SD	mean	Min.	Max.	SD	
BW (g)	1329.49	1075.0	1499.0	130.8	775.74	570.0	995.0	117.98	3418.62	2500.0	4540.0	457.5	$p < 0.05^*$
GA (wks)	30.61	27.14	35.43	2.0	26.95	24.00	32.27	2.3	39.6	37.0	41.0	1.08	$p < 0.05^*$

*statistical significance - VLBW – very low birthweight - ELBW – extremely low birthweight - NBW . normal birthweight
No - number - BW – birthweight - g - gram - GA – gestational age - wks - weeks

TABLE 1 Neonatal data of the case and control group of infants.

	VLBW group (No=82)		ELBW group (No=50)		NBW group (No=58)		Chi-square test
	No	%	No	%	No	%	
DDE							
Hypoplasia	10	12.2	14	28.0	2	3.45	$p < 0.05^*$
Opacities	6	7.3	8	16.0	2	3.45	$p < 0.05^*$
Combined defect	3	3.7	5	10.0	0	0	$p < 0.05^*$
Total DDE	19	23.2	27	54.0	4	6.9	$p < 0.05^*$

*statistical significance - DDE – developmental defect of enamel - LBW – very low birthweight
ELBW – extremely low birthweight - BW – normal birthweight - No - number

TABLE 2 Prevalence of DDE in the case and control group of infants.

Tooth	NBW						VLBW						ELBW					
	Hypoplasia		Opacities		Combined defect		Hypoplasia		Opacities		Combined defect		Hypoplasia		Opacities		Combined defect	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
51	3	75	2	50	-	-	4	16.7	5	21.7	2	50.0	5	25.0	6	33.3	2	28.6
52	-	-	-	--	-	-	3	12.5	2	8.7	-	-	3	15.0	4	22.2	1	14.3
61	1	25	2	50	-	-	5	20.8	5	21.7	2	50.0	5	25.0	5	27.8	2	28.6
62	-	-	-	-	-	-	8	33.3	2	8.7	-	-	6	30.0	-	-	2	28.6
71	-	-	-	-	-	-	2	8.3	2	8.7	-	-	-	-	-	-	-	-
72	-	-	-	-	-	-	-	-	2	8.7	-	-	-	-	1	5.6	-	-
81	-	-	-	--	-	-	2	8.3	3	13.0	-	-	1	5.0	1	5.6	-	-
82	-	-	-	-	-	-	-	-	2	8.7	-	-	-	-	1	5.6	-	-
Total	4	100.0	4	100.0	-	-	24	100.0	23	100.0	4	100.0	20	100.0	18	100.0	7	100.0

NBW – normal birthweight - VLBW – very low birthweight - ELBW – extremely low birthweight - NO - number

TABLE 3 Distribution and frequency of the affected primary incisors in the case and control group of infants.

dimensions of primary and permanent clinical crowns [Angelos et al., 1989]. The best studied and most noticeable complications of prematurity and low birthweight are developmental disturbances of primary teeth enamel [Zaidi et al., 2015].

The aetiology of DDE is not yet fully understood. Defects in the enamel structure can only occur during formation of this hard dental tissue. The etiology of enamel hypoplasia is probably a disturbance of short duration in the ameloblasts in the secretion phase, associated with trauma or a systemic disease [Crombie et al., 2009]. Prolonged disturbances play an important role in the etiology of enamel hypomineralization. Excessive intake of fluorides, effect of antibiotics, malnutrition or chronic diseases may be responsible for diffuse opacities. The demarcated opacities may be connected with trauma or general diseases over a longer period [Suckling, 1989; Crombie et al., 2009; Salanitri and Seow, 2013]. The DDE may cause aesthetic problems, enamel hypoplasia may predispose to plaque accumulation and early childhood caries, and in severe cases even space loss and malocclusion [Seow et al., 1987; Nelson et al., 2013]. DDE may increase tooth sensitivity and risk of attrition [Suckling, 1989]. Hypoplastic porous enamel constitutes a pathway for bacteria and other stimuli that may affect the pulp [Sabel et al., 2010; Rythén et al., 2008].

The best time for diagnosis of DDE is soon after tooth eruption because DDE in primary or permanent teeth can be lost by traumatic dental injuries, attrition or caries [Seow, 1997]. Therefore, the infants in the present study were only 12-month-old in terms of chronological or corrected age at the moment of dental examination. On the other hand, the examination of very young uncooperative infants is difficult, especially so as regards the diagnosis of diffuse opacities.

The prevalence of DDE in primary dentition has not been well reported [Salanitri and Seow, 2013]. DDE in primary dentition in healthy children of various age groups has been evaluated to occur at rates ranging between 10–49% [Casanova-Rosado et al., 2011; Corrêa-Faria et al., 2013; Masumo et al., 2013]. The prevalence of DDE in primary dentition described by Corrêa-Faria P. et al. [2013] has been 29.9% and demarcated opacities were the most frequent type of enamel defects. In contrast, in some studies diffuse opacities were the most common defect of primary teeth enamel [Masumo et al., 2013; Lunardelli and Peres, 2005]. The reported prevalence of DDE in primary incisors in the control group of the present study was 6.9%. The prevalence of DDE in primary dentition has been reported to be higher in preterm infants delivered with LBW or VLBW and may vary between studies

from 16% of cases to as many as 96% [Velló et al., 2010; Seow et al., 1987; Corrêa-Faria et al., 2013; Lai et al., 1997; Cruvinel et al., 2012; Funakoshi et al., 1981]. In our study the prevalence of DDE in one-year-old ELBW infants was 54% and in the control group 6.9%. In the literature [Franco et al., 2007; Cruvinel et al., 2012; Johnsen, 1984] the prevalence of opacities in the primary dentition of preterm children is higher than the prevalence of hypoplasia. In the present study the prevalence of opacities was only 10.6% and prevalence of hypoplasia 18.2%. An explanation of these differences could be considerable methodological differences between studies focusing on preterm children, e.g. design, choice of outcomes, study size and diagnostic criteria [Jacobsen et al., 2014]. In agreement with other authors [Ferrini et al., 2007; Schüller et al., 2018] data of a recent study indicate that VLBW and ELBW are indicators of DDE. The reason for the differences in the prevalence of DDE in fullterm NBW infants and premature ELBW infants is most likely related to both systemic and local factors. Infants with the most premature birth and lowest birthweight have the highest tendency to suffer from systemic diseases, which can affect dental development [Seow et al., 1987]. Merheb R. et al. [2016] assessed the relationship between neonatal nutrition factors in VLBW infants and DDE and reported that lower neonatal phosphorus levels were significantly associated with enamel hypoplasia.

In accordance with other studies [Aine et al., 2000; Pimlott et al., 1985; Lin et al., 2011], the occurrence of DDE in our case group was more frequent in the upper than in the lower primary incisors. This situation can be related to trauma from laryngoscopy and endotracheal intubation at the critical period of amelogenesis and may be complicated by derangement of calcium metabolism and other systemic factors [Seow et al., 1984a; de Oliveira Melo et al., 2014].

The authors are aware of certain limitations of the present study. The prevalence of DDE was determined only in upper and lower primary incisors in very young uncooperative infants.

Conclusion

One-year-old preterm VLBW and ELBW infants presented a significantly higher prevalence of DDE in the primary incisors than fullterm NBW infants. Enamel hypoplasia was the most frequent disturbance in one-year old preterm infants delivered with VLBW and ELBW. Most of the primary teeth with DDE were situated in the upper jaw.

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Conflict of interest

The authors declare no conflict of interest.

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