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Dental enamel defects in children with coeliac disease

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Objective. The aim of this study was to investigate whether Dutch children with proven coeliac disease show specific dental enamel defects, and to asses whether children with the same gastrointestinal complaints, but proved no-coeliac disease, lack these specific dental enamel defects.

Materials and methods. Eighty-one children (53 coeliac patients and 28 control subjects) were examined during the period 2003–2004 in the Oral Surgery Outpatient Clinic of the Academic Medical Centre in Amsterdam.

Result. Twenty-nine (55%) coeliac patients had enamel defects against 5 (18%) control subjects. In the coeliac disease group, the enamel defects were diagnosed as specific in 20 (38%) children, compared with 1 (4%) in the control group. Statistical analysis showed significantly more specific enamel defects in children with coeliac disease than in children in the control group ($\chi^2 = 12.62$, d.f. = 2, $P = 0.002$).

Conclusion. This study showed significantly more specific enamel defects in Dutch children with coeliac disease as compared with children in the control group. Dentists could play an important role in recognizing patients with coeliac disease.

Introduction

Coeliac disease is a genetically influenced immune-mediated disorder characterized by damage to the small bowel mucosa as a result of contact with gluten. Gluten is a protein found in wheat, rye, and barley. The classic form of coeliac disease occurs in children under the age of 2. Although the presentation of coeliac disease has changed over the years and monosymptomatic patients are more prevalent today, the clinical symptomatology described include chronic diarrhoea, failure to thrive, abdominal distension and bloating, steatorrhoea, vomiting, tiredness, muscle weakness, tetany, haemorrhage, and other symptoms of malabsorption. As the spectrum of clinical presentation is broad and some patients have evidence of severe malabsorption, whereas others have minimal symptoms or are even asymptomatic, diagnosing coeliac disease may be difficult. The prevalence of coeliac disease in Europe and the USA in children between 2.5 and 15 years of age is approximately 1 : 300 to 1 : 80[1].

Diagnosis is based on biopsy of the jejunal intestinal mucosa[2]. A second method to diagnose coeliac disease is a serological test. A combined IgA antiendomysium-test together with an IgA antigliadine-test results in 90–100% sensitivity and 98–100% specificity[3]. Therapy consists of a gluten-free diet. A gluten-free diet will lead to remission of all clinical symptoms in a few months and the morphology and function of the jejunum will also recover[2].

Dental enamel defects have first been reported in children with coeliac disease by Aine[4]. A classification of specific enamel defects, grades I–IV, in children with coeliac disease was designed by her and was considered unique for coeliac disease (Table 1). Specific enamel defects had to be symmetrically and chronologically detectable in all four sections of the dentition. Other enamel defects, defined as disturbances in hard tissue matrices, including enamel hypoplasias, enamel opacities, and enamel discolorations, that were not symmetrically and chronologically in all four sections of the dentition, were considered unspecific (Figs 1 and 2).

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Table 1. Classification of systematic and chronological enamel defects, according to Aine[4].

Classification	Enamel defect
Grade 0	No defect
Grade I	Defect in colour of enamel Single or multiple cream, yellow or brown opacities with clearly defined or diffuse margins; in addition a part or the entire surface of enamel is without glaze.
Grade II	Slight structural defects Enamel surface rough, filled with horizontal grooves or shallow pits; light opacities and discolorations may be found; in addition a part or the entire surface of enamel is without glaze.
Grade III	Evident structural defects A part or the entire surface of enamel rough and filled with deep horizontal grooves that vary in width or have large vertical pits; large opacities of different colours or strong discolorations may appear in combination.
Grade IV	Severe structural defects The shape of the tooth has changed: the tips of cusps are sharp-pointed and/or the incisal edges are unevenly thinned and rough; the thinning of the enamel material is easily detectable and the margins of the lesions are well defined; the lesion may be strongly discolored.

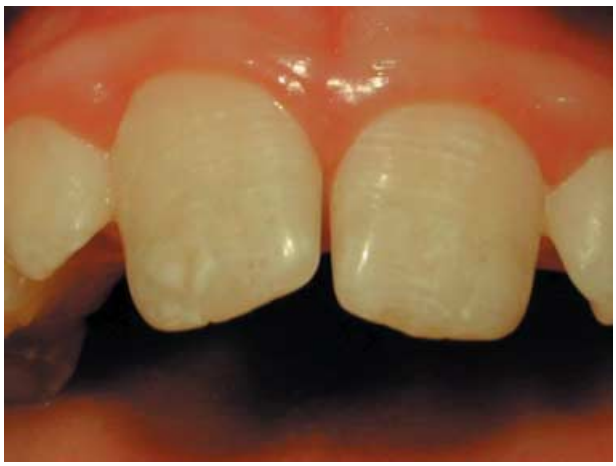

Fig. 1. Specific enamel defect, grade II.

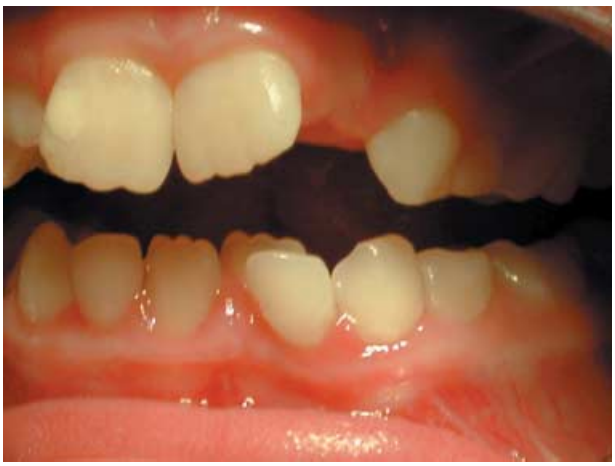

Fig. 2. Unspecific enamel defect 11.

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition included the presence of (specific) dental enamel defects as a risk factor for coeliac disease[1]. The prevalence of specific enamel defects in different European countries varies from 38% to 96% in children with coeliac disease and from 0.6% to 17% in control subjects[4–7]. In Sweden, however, no significant difference in the prevalence of specific enamel defects was found[8,9]. The prevalence of dental enamel defects in children with coeliac disease in the Netherlands has not been studied before.

None of the above mentioned studies included a control group with typical coeliac-like gastrointestinal symptoms but with negative biopsies. If the specific dental enamel defects are indeed specific for coeliac disease, only children with proved coeliac disease would be expected to have them. Children with a clinical picture of malabsorption but no coeliac disease are expected not to show coeliac-specific dental enamel defects, but only unspecific enamel defects caused by malabsorption. The awareness of the presence or absence of specific dental enamel defects in the last group could provide more insight in the pathogenesis of the enamel defects in coeliac patients.

The cause of the dental enamel defects is unknown. Speculations have been made about hypocalcaemia caused by malabsorption[10], a gluten-induced immunological process between

the ages of 6 months up to 7 years, damaging the enamel-producing organ[11–13], or a genetic cause[14].

The objectives of this study were to investigate whether Dutch children with proved coeliac disease show specific dental enamel defects as described by Aine[4]; and to asses whether children with the same gastrointestinal complaints, but proved no-coeliac disease, lack these specific dental enamel defects.

Materials and methods

Two-hundred and forty-three children (born 1985–1996), clinically suspected of having coeliac disease, underwent a biopsy of the jejunal intestinal mucosa at the Emma Children's Hospital, Academic Medical Centre (AMC) in Amsterdam during the period of 1998–2004. In 126 subjects, coeliac disease was diagnosed, based on the intestinal biopsy and the patient's response to a gluten-free diet. Coeliac disease was excluded in the other 117 subjects. Alternative explanations for their symptoms were viral infections, bacterial infections or immunological reactions. All children were approached to participate in this study, but ultimately only 54 coeliac patients and 31 control subjects were available. The study was approved by the medical ethical committee of the AMC.

All children, assisted by their parents, completed a questionnaire about their medical and dental history. Questions about use of medication, fluoride, other contributing factors for dental enamel defects (comorbidities)[15], and clinical symptoms related to malabsorption were included. Coeliac patients were asked for their age of diagnosis with coeliac disease and the time of starting a gluten-free diet. Children with an uncertain diagnosis concerning coeliac disease ($n = 2$), children without permanent first incisors and first molars ($n = 1$), and children with fixed orthodontic appliances covering the teeth surfaces ($n = 1$) were excluded from the study. The children were examined during the months July 2003–May 2004 in the Oral Surgery Outpatient Clinic of the AMC in Amsterdam.

All children received a toothbrush and brushed their teeth before examination. Subsequently, all subjects were placed in a conventional dental chair. Their teeth were dried and examined with the help of artificial light, a small mirror, and probe. All enamel defects, specific and unspecific, were noted and photographed. Specific enamel defects were classified, grades I–IV, according to Aine[4] (Table 1). Two different investigators took part in the study. The investigators examined the photographs of all subjects and decided mutually on the classification of the enamel defects.

Statistical analysis

Differences between the coeliac patients and the control group were tested using χ^2-tests and independent sample *t*-tests. A significance level of 5% was used.

Results

Eighty-one children (53 coeliac patients, 28 control subjects) were examined. The male : female ratio was 27 : 26 in the group of coeliac patients and 19 : 9 in the control group. The mean age was, respectively, 9.7 (range: 6.2–18.2) and 10.0 (range: 6.5–18.8). There is no statistically significant difference in age ($t = -1.16$, d.f. = 79, $P = 0.250$) and gender ($\chi^2 = 2.14$, d.f. = 1, $P = 0.144$) between the group of coeliac patients and the control group. All coeliac patients started with a gluten-free diet from the moment their coeliac disease was diagnosed, 81% of them before the age of 7. Neither patients nor control subjects used medication with a known effect on the development of enamel. There was no difference in the use of fluoride pills (none/sometimes versus daily) between the two groups ($\chi^2 = 1.37$, d.f. = 1, $P = 0.711$). No significant difference was found in the occurrence of comorbidities between the groups ($\chi^2 = 2.14$, d.f. = 1, $P = 0.144$) (Table 2).

Twenty-nine coeliac patients had enamel defects against five control subjects. In the coeliac disease group, enamel defects were diagnosed as specific in 20 children, as compared with one in the control group (Table 3). Statistical analysis showed significantly more specific enamel defects in children with coeliac disease than in children in the control group ($\chi^2 = 12.62$, d.f. = 2, $P = 0.002$). Dental enamel defects Grade II appeared most frequently (14 coeliac patients, one control subject). Grade I was found in three children, Grade III in two

Table 2. Comorbidities and the presence or absence of (specific) enamel defects in coeliac patients and control subjects.

	No dental enamel defects		Specific dental enamel defects		Unspecific dental enamel defects		Total	
Comorbidities	**Coeliac**	**Control**	**Coeliac**	**Control**	**Coeliac**	**Control**	**Coeliac**	**Control**
No	12	6	8	1	6	2	26	9
Premature birth	0	1	2	0	0	1	2	2
Icterus	2	0	1	0	1	0	4	0
Long period of high fever	1	1	0	0	0	1	1	2
Diabetes mellitus of the gravida	2	0	0	0	0	0	2	0
Fall on the front teeth	1	1	4	0	0	0	5	1
Antibiotic use	5	4	0	0	0	0	5	4
Combinations of comorbidities	1	10	5	0	2	0	8	10
Total	24	23	20	1	9	4	53	28

Table 3. Dental enamel defects in both groups.

	Coeliac patients *N* = 53	**Control subjects *N* = 28**
No enamel defects	24 (45%)	23 (82%)
Specific enamel defects	20 (38%)	1 (4%)
Unspecific enamel defects	9 (17%)	4 (14%)

Table 4. Gastrointestinal symptoms in both groups.

	Coeliac patients *N* = 53	**Control subjects *N* = 28**
Symptoms related to malabsorption	34 (64%)	13 (46%)
Other symptoms	17 (32%)	14 (50%)
No symptoms	2 (4%)	1 (4%)

children, Grade IV in one child (all coeliac patients). Enamel defects were found mainly in the incisors.

In the group of coeliac patients, 34 of 53 patients suffered from clinical symptoms that might cause malabsorption, including diarrhoea and vomiting, 13 of them showed a specific enamel defect. In the control group, 13 of 28 subjects had clinical symptoms that might cause malabsorption processes, whereas only one of them had a specific enamel defect (Table 4).

Discussion

Dutch children with coeliac disease in this study did show specific enamel defects (38%) as described by Aine[4]. Only one subject with an identical clinical picture, but proved no-coeliac disease showed the same specific dental enamel defects (4%).

These results correspond with the investigations of Martelossi *et al.*, Aguirre *et al.*, and Priovolou *et al.*[5–7]. They found, respectively, 53, 38, and 44% specific dental enamel defects in their coeliac patients and 0.6, 17, and 11% specific enamel defects in their control subjects. None of these control groups consisted of children who had had gastrointestinal complaints in the past. Before the clinical examination, no biopsy procedures had been performed, so all control subjects were considered healthy. In the study of Martelossi *et al.*, all control subjects with specific dental enamel defects were tested for coeliac disease[5]. In four subjects, coeliac disease was diagnosed. It is not excluded that there might also have been (asymptomatic) coeliac patients in the other control groups. The great difference in the size of the control groups might, however, offer an explanation for the very small number of specific dental enamel defects in the study of Martelossi *et al.*

The mechanism of the development of dental enamel hypoplasia caused by gluten in patients with coeliac disease is still unknown. There are three hypotheses. Nikiforuk and Fraser suggested that a low serum calcium concentration during enamel formation is a specific determinant of enamel hypoplasia[10]. Aine *et al.*[11,13] and Maki *et al.*[12] explained the damage of the enamel organ by an autoimmune response. The study of Mariani *et al.*[14] showed that the HLA-DR3 antigen significantly increased the risk of dental lesions, suggesting a genetic cause. The results of this study suggest that specific dental enamel defects do not develop due to malabsorption processes causing a low serum calcium concentration, because almost half of the control subjects had malabsorption symptoms and only one of them had specific dental enamel defects. The presence of proved coeliac disease seems to predict specific enamel defects better than the presence of malabsorption does. The second hypothesis: an autoimmune response, described by Maki *et al.*[12] might be the cause of the enamel defects. A specific antigen, described by Mariani *et al.*[14] might be an explanation for the fact that not all coeliac patients suffer from enamel defects. More research in this field will be necessary.

Remarkable is the location of the enamel defects. Like Aquirre *et al.*[5], this study found enamel defects mainly in the incisors, whereas the enamel development of incisors and first molars takes place at the same time[16]. Enamel defects through calcium deficiency caused by malabsorption or by an autoimmune episode would affect incisors as well as first molars. No explanation has been put forward for this finding yet.

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition formulated a clinical practice guideline for the diagnosis and treatment of coeliac disease in children[1]. Dental enamel defects were mentioned as a symptom of coeliac disease. This guideline urgently advises the following procedure when dental enamel defects are noticed. Serological testing is recommended. Children with a positive serologic test are referred to a paediatric gastroenterologist for small intestinal biopsy. Those with histological features of coeliac disease on biopsy are treated with a strict gluten-free diet. Treatment with a gluten-free diet is also recommended for asymptomatic children who have characteristic histological findings on small intestinal biopsy.

This study obviously has some limitations. Only a few patients were available for this study, especially the patients with a negative biopsy result were difficult to motivate to participate in this study. It is possible that the small number of control subjects influenced the results. Because of the small number of available subjects, controls were not matched with coeliac patients. Statistical analyses, however, did not show significant differences regarding age and gender between the groups. The results of this small study are an encouragement for further investigation.

In conclusion, this study showed significantly more specific enamel defects in Dutch children with coeliac disease as compared with Dutch children in the control group. Dentists could play an important role in recognizing patients with coeliac disease. The dentist will have to be alert for specific dental enamel defects, especially when there are symptoms suspect for coeliac disease in the medical history of a child. If there are specific dental enamel defects, corresponding to the classification of Aine[4], referral to the family doctor to be tested for coeliac disease should be considered.

What this paper adds

- Dutch children with coeliac disease show specific enamel defects.
- This is by our knowledge the first study that compares dental enamel of children with coeliac disease, with dental enamel of children with the same clinical picture but proved no-coeliac disease.
- This study provides more information about the possible causes of the specific enamel defects. An autoimmune response would seem to offer a better explanation for the existence of specific enamel defects than malabsorption processes do.

Why this paper is important to paediatric dentists

- Early recognition of children with specific dental enamel defects and referral to the family doctor might help in early diagnosing coeliac disease and preventing complications.

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