The dental age in the child with coeliac disease

ABSTRACT

The coeliac disease deprives affected individual of the main nutritive factors, which are essential to promote body development: coeliac children are often subject to weight loss and have a lower somatic growth rate compared to healthy children. In addition, it is proven that prolonged malnutrition can have irreversible effects on dental eruption: teeth development also suffers a delay or it is slowed down in coeliac children. The purpose of this study was to evaluate and quantify the persistence of a delay in the dental age in children with coeliac disease and the presence of a possible constant relationship between the estimated delay in skeletal development and that referred to the dental age.

Materials and methods

Seventy children (24 males and 46 females) were selected, all affected by coeliac disease, aged between 5.3 and 13.8 years, with a mean age of 9 years ± 2 months SD. Through teleradiography of the skull in latero-lateral projection and orthopantomography of the dental arches, the estimate of the skeletal development and dental age was carried out for each patient, applying two specific methods extensively described in the literature.

Results and conclusion

The results obtained, in agreement with the literature, show how the dental age, which is delayed in children affected by coeliac disease, may be considered as a reliable indicator of somatic growth and also of biological age. Furthermore, a gluten-free diet has considerable beneficial effects on skeletal development in relation to the dental age, in agreement with the hypothesis that dental development is controlled by different regulatory mechanisms, totally independent from those that influence skeletal development and the somatic and sexual development of the individual, even if the delay of dental development decreases progressively from the time of diagnosis of coeliac disease to introduction of a gluten-free diet.

Keywords: Dental age; Coeliac disease; Paediatric patient.

Introduction

The coeliac disease, coeliac sprue or gluten enteropathy, is an immune-mediated enteropathy due to ingestion of gluten in genetically susceptible individuals [Fasano, 2005]. It is one of the most frequent causes of malabsorption that involves Caucasian populations, especially those of European origin. During the last few years, the incidence of this pathology has remarkably increased, with a concomitant decrease in the severity of symptoms at the time of diagnosis [Murray, 1999]. In the United States, the prevalence of coeliac disease is estimated at 1/104 children in the first 5 years of life. In Italy, in children of school age, the prevalence varies from 1/230 to 1/106 [Catassi, 2004; Tommasini, 2004].

Based on symptoms and their severity, in 2005 the concept of the so-called coeliac iceberg was developed, which allowed to distinguish four typical forms: Classical Coeliac Disease and Coeliac Disease with Atypical symptoms both characterized by signs of gastrointestinal malabsorption, Silent Coeliac Disease, asymptomatic, and Latent Coeliac Disease, which is asymptomatic as well, but over time may develop symptoms such as anaemia, hypo-stature, skin alteration and skin appendages [Dewar, 2005].

With regards to the delay in somatic growth, it was observed that serious malnutrition stages affect the height and weight of the growing subject, determining developmental delays or deficits and that coeliac disease is able to deprive an individual of the main nutritive factors, essential to promote body development. If dietary instructions are followed closely, bone development—which is almost always altered at the time of diagnosis—regularises with time [Balli, 1988; Bonamico, 1992; Groll, 1980; Nemet, 2009; Nuslé, 1974].

Basically, in coeliac children there is an endocrine system dysfunction: reduced basal level of the growth hormone, a partial insensitivity to it and a persistently low level of insulin-like growth factor-1 (IGF-1), related to the poor nutritional status secondary to the active phase of the coeliac disease [Bonamico, 1992; Catassi, 2004; Giovenale, 2006; Meazza, 2009; Nemet, 2009; Salardi, 2005]. In addition to the involvement of the (GH)/insulin-like growth factor-1 (IGF-1), a pathogenic role was recently recognised also to ghrelin [Krscek, 2002], a gastrointestinal hormone secreted in the stomach and duodenum [Soriano-Guillén, 2004], which has a role in the absorption of nutrients and release of the growth hormone, and as a consequence, it influences skeletal development, somatic growth and physical development of coeliac children [Soriano-Guillén, 2004; Krscek, 2002].

It is also well-known that prolonged malnutrition can have irreversible effects on dental eruption. In this regard, it was hypothesised that, since coeliac children are often subject to weight loss and have a lower somatic growth rate compared to healthy children, teeth development is also somewhat subject to a delay or anyhow, a slower process [Aine, 1986].

An accurate review of the literature shows the existence of some old systematic studies on the topic of dental eruption and development in children affected by coeliac disease [Brauer, 1942; Hotz, 1959; Prati, 1987; Balli, 1988; Aine, 1994] reporting discordant results with respect to more recent studies [Mina, 2008]. Aine L, in particular, studied a sample of 85 coeliac children, aged between 3 and 12 years, in whom the evaluation of the clinical
eruption of permanent teeth shows that the overall dental age is delayed, if compared to the age indicated in the graphic series proposed by Demirjian referred to healthy children (61 cases, 71.76%). It is indeed obvious that during the first period of eruption, between 6 and 8 years of age, there is a delay in the eruption in both males and females; in the second eruptive period, between 10 and 12 years of age, the delay only concerns females [Aine, 1994].

Despite the period of eruption is considered a constant process, not easily affected, in children with coeliac disease, however, it is altered in speed, and therefore delayed [Brauer, 1942].

Aine has also observed that the systemic treatment, consisting in the introduction of a gluten-free diet, is able to positively influence the delay in dental age: it decreases proportionally with time, starting from the time of diagnosis, but nevertheless the dental age of coeliac children never reaches the typical values of the test group, even after 5 years from the introduction of the gluten-free diet [Aine, 1994].

The purpose of this study was to evaluate and quantify the persistence of a delay in the dental age of children with coeliac disease and the presence of a possible constant relationship between the delay in skeletal development and delay in the dental age.

Materials and methods

Seventy children (24 males and 46 females) were selected at the Paediatric Dentistry division of the Policlinico Tor Vergata of Rome, all affected by coeliac disease, of age ranging between 5.3 and 13.8 years, with an average age of 9 years old ± 22 months (standard deviation). For all patients, the diagnosis of coeliac disease had been previously made in specialised centres after the onset of symptoms, based on the presence of anti-endomysial antibodies (EMA), anti-gliadin (AGA) and tissular anti-transglutaminase (anti-tTG). The diagnosis was then confirmed through gastroscopy and biopsy of the intestinal villi, according to the diagnostic criteria proposed by the European Society of Paediatric Gastroenterology and Nutrition [Walker-Smith, 1990].

Each child was then subject to a gluten-free diet.

It was also required the written consent by parents and through an anamnestic test the following parameters were recorded:

- time of onset and diagnosis of the disease;
- type and timing of the systemic therapy.

The sample was divided according to the time of CD diagnosis, in:

- Group 1 (early diagnosis ≤ 3 years): 25 subjects: 9 males, 16 females (mean age 8.0±1.1)
- Group 2 (late diagnosis ≥ 3 years): 45 subjects: 15 males, 30 females (mean age 9.6±1.3)

Later on, with two routine diagnostic exams such as teleradiography of the skull in latero-lateral projection and orthopantomography of the dental arches, the estimate of the skeletal development and dental age was carried out for each patient, by two trained operators, applying two specific methods extensively described in the international literature [Demirjian, 1973; Franchi, 2000; Baccetti, 2002; Caldas, 2007]. In particular, the skeletal development was determined using the Baccetti-Franchi’s method [2000] which allows to evaluate from the teleradiography of the skull in latero-lateral projection the development of the single cervical vertebrae, dividing the development in 6 stages (CVMS). This method allows only a subjective evaluation, obtained by simply comparing the radiographic image with graphic diagrams, and so it is essentially linked to the ability of the operator and the quality of the instrumental exams; in order to also obtain an objective or numeric quantification, Caldas [Caldas, 2007] developed a mathematical formula on a sample of 238 subjects (110 males and 128 females), between 7.0 and 15.9 years of age (average 11.4 years of age) (Table I). Therefore, Caldas’ formula was also used.

The estimate of the dental age was obtained using the Demirjian’s method [1973], which allows to simply and immediately identify, on the orthopantomography of dental arches, the most similar radiographic image of the tooth in object; parameters are different for the two sexes. This method takes into consideration only the development of the seven teeth belonging to the left lower quadrant. A value is obtained for each tooth, by comparing the development stage (from A to H) with the graphic diagrams proposed by the author. The sum of the values of each tooth gives the score relative to the dental development. In conclusion, the score was converted into dental age using the conversion table distinguished by sex (Fig. 1).

As for the reliability and reproducibility of the assessment of cervical vertebral maturation and dental age, the percentage of inter-intra operator agreement was 98.5% and 100%, respectively.

With regards to the quantitative variables, all data were analysed using the Student’s T test and the SPSS software (version 11.01; SPSS Inc., Chicago, IL, USA).

The differences associated to a P value < 0.05 were taken into consideration as statistically significant in the analysis.

Results

Table 2 shows the age of the sample at the time of diagnosis of the coeliac disease.

With regards to the determination of the skeletal age,

<table>
<thead>
<tr>
<th>Age at diagnosis</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 year</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2-5 years</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>6-9 years</td>
<td>8</td>
<td>16</td>
</tr>
</tbody>
</table>

**TABLE 2** - Age of the sample at the time of diagnosis of coeliac disease.
using the Baccetti-Franchi’s method, the CVMS stages obtained from the analysis of the skull teleradiography in latero-lateral projection showed that 67.14% of the sample falls in stage 1 (47 subjects: 19 males, 28 females; mean age 7.5±1.2), 25.71% in stage 2 (18 subjects: 5 males, 13 females; mean age 10.1±1.4) and 7.14% in stage 3 (5 subjects: 5 females; mean age 11.3 ±1.1).

In 65.71% of the cases (46 subjects: 17 males, 29 females) the bone age, obtained by applying the Caldas’ formula [2007], had a delay of 2 months compared to the chronological age. Instead, in 34.29% of the cases (24 subjects: 7 males, 17 females) there was a correlation between the chronological age and the bone age, obtained by applying the Caldas’ formula [2007].

The effect of the gluten-free diet on bone development was evaluated by comparing Group 1 and Group 2: one with early diagnosis and one with late diagnosis (Table 3).

Those subjects in whom the diagnosis was made in the first 3 years of life, the difference between mean chronological age and mean skeletal age showed a minimal delay (mean 1 month), while the difference between mean chronological age and dental age remains delayed (mean 3 months). Those subjects in whom the diagnosis was made after 3 years of life, showed a delay (mean 3 months) in mean skeletal-dental age with respect to mean chronological age.

The comparison between chronological age and skeletal age does not show statistically significant differences in the total sample as well as in Group 1 (p=0.061, p=0.894 respectively), while there is a statistically significant difference in Group 2 (p=0.018) (Table 4). Instead, the comparison between chronological and dental age shows statistically significant differences in the total sample as well as in Groups 1 and 2 (p=0.006, p=0.030, p=0.001 respectively) (Table 4).

The overall data, derived from the evaluation of the dental age using the Demirjian’s method showed that the dental age is delayed in 70% of the examined children (p-value: 0.006) (49 subjects: 17 males, 16 females). The delay in dental age is similar for both sexes and is of 3 months compared to the chronological age.

Figure 2 shows the results on the skeletal development and dental age of the sample.

**Figure 1** - Demirjian’s method for dental age estimation.

**Figure 2** - Skeletal development and dental age of the sample.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Male</th>
<th>Female</th>
<th>Mean age</th>
<th>Mean dental age</th>
<th>Mean Skeletal age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 early ≤3 years</td>
<td>9</td>
<td>16</td>
<td>8.0 yrs ±1.1 m</td>
<td>7 yrs 9 m</td>
<td>7 yrs 11 m</td>
</tr>
<tr>
<td>Group 2 late ≥3 years</td>
<td>15</td>
<td>30</td>
<td>9.6 yrs ±1.3 m</td>
<td>9 yrs 4 m</td>
<td>9 yrs 4 m</td>
</tr>
</tbody>
</table>

**Table 3** - Average of the chronological, skeletal and dental age of children with early and late diagnosis of celiac disease.

<table>
<thead>
<tr>
<th>Paired data</th>
<th>Groups</th>
<th>N. cases</th>
<th>t</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronological Age/Skeletal Age</td>
<td>Total sample</td>
<td>70</td>
<td>1,902</td>
<td>69</td>
<td>0.061</td>
</tr>
<tr>
<td>Chronological Age/Dental Age</td>
<td>Total sample</td>
<td>70</td>
<td>2,855</td>
<td>69</td>
<td>0.006</td>
</tr>
<tr>
<td>Chronological Age/Skeletal Age</td>
<td>Group 1</td>
<td>25</td>
<td>0.134</td>
<td>24</td>
<td>0.894</td>
</tr>
<tr>
<td>Chronological Age/Dental Age</td>
<td>Group 1</td>
<td>25</td>
<td>2,309</td>
<td>24</td>
<td>0.030</td>
</tr>
<tr>
<td>Chronological Age/Skeletal Age</td>
<td>Group 2</td>
<td>45</td>
<td>2,447</td>
<td>44</td>
<td>0.018</td>
</tr>
<tr>
<td>Chronological Age/Dental Age</td>
<td>Group 2</td>
<td>45</td>
<td>16,312</td>
<td>44</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Table 4** - Statistic values of Student’s T test for matched data.

Discussion

The increasing incidence of coeliac disease in its subclinical forms encourages the study of variables that...
could be used to diagnose this disease and to monitor its trends, in particular in groups at risk. In this regard, the study of oral disorders in patients affected by coeliac disease can be helpful for an early diagnosis [Mina, 2008].

Table 2 shows that the percentage of coeliac disease diagnosed after the first year of life, in agreement with the data reported in the literature, is high: 63 cases, which account for 90% of the sample [Ansaldi, 1989]. The data reported in this study confirm that there is a delay in dental development in children affected by coeliac disease. Overall 70% of the examined children exhibited a delayed dental age, in agreement with the data obtained by Aine [1986] on a sample of 85 children, in which 71.76% presented a delay in the dental age using Demirjian’s method.

However, the results obtained in this study are in contrast with those recently reported by Mina et al. [2008], who identified a delay in the eruption of permanent teeth only in 23.7% of patients with coeliac disease. The accurate analysis of the results obtained in this study shows that, despite the fact that a delay in dental development frequently occurs in coeliac children, this must not be considered as a constant phenomenon. In fact, 16 children included in the sample exhibited a normal dental age (4.29%) or even greater (18.57%) if compared to the chronological age. This is strictly linked to the early diagnosis of the coeliac disease and the strict compliance with the gluten-free diet.

The evaluation of the skeletal age through the Baccetti-Franchi’s method showed that 67.14% of the examined children fall in CVMS stage 1, even if this is due to the young age of the population included in the sample. An average chronological age of 9 years ± 22 months SD, is indeed still far from the growth peak registered during the pubertal age which, according to Franchi and Baccetti, occurs between CVMS stages 3 and 4. An objective evaluation of the skeletal age was obtained using Caldas’ formula. The data obtained, in agreement with the works of the 1980s by Aine [1986], Prati [1987] and Balli [1988], confirm the presence of a delay in the skeletal age of children with coeliac disease, in particular in those with a late diagnosis. Compared to the chronological age, the skeletal age appeared to be the most reliable parameter in the evaluation of the biological and somatic development of the growing individual, in particular in case of a constitutional delay [Tanner, 1983]. The delay in bone development recorded in this study is certainly linked to the coeliac disease, which as a chronic disease related to malnutrition is responsible for the progressive delay during the entire somatic development and growth cycle of the child, therefore also influencing the skeletal development [Tanner, 1983]. This work shows that the beneficial effects derived from the gluten-free diet are greater in patients whose pathology was discovered in the early stages (Table 3, 4). However, these effects mainly act on the skeletal development rather than on the dental age. This is in agreement with the hypothesis that dental development is controlled by different regulatory mechanisms, totally independent from those that influence skeletal growth and the somatic and sexual development of the individual [Demirjian, 1985]. The delay of the linear growth is mainly due to the malabsorption of nutrients, and the strict compliance with a gluten-free diet, especially during the first year of life, may determine a significant growth resumption [Nemet, 2009]. On the contrary, in cases in which the diagnosis is late (≥ 3 years), bone development and dental age show a similar trend and a parallel course, as already described by Balli et al. [1998]. These results confirm therefore the thesis that there is a close relationship between coeliac disease in the active phase, growth and dental eruption delay [Prati, 1987].

Conclusion

Coeliac disease is a relatively frequent pathology, with an estimated prevalence between 1/230 and 1/106 children. The spectrum of the clinical presentations is wide and the extraintestinal disorders, as those identified in the oral cavity, are more common than the typical symptomatology of malabsorption. The “Coeliac Iceberg” concept shows how subjects with typical disorders, easily identified, are only the tip of the iceberg [Catassi, 2004]. The visit of the paediatric dentist can be a diagnostic tool to intercept the coeliac disease in its subclinical form, thus preventing possible complications [Costacurta, 2010]. Among the disorders found in the oral cavity of the patient with gluten enteropathy, we focused on the study of the delay in dental age.

The results obtained in this work, in agreement with the literature, show how the dental age, which is delayed in children affected by coeliac disease, may be considered as a reliable indicator of somatic growth and of the biological age in children affected. For this reason, the dental age can be considered a diagnostic parameter easy to evaluate through simple instrumental tests such as orthopantomography and skull teleradiography, which are routine exams for the young paediatric patients. This parameter, associated to an accurate anamnesis and an objective exam that evaluates the presence and persistence of alterations of the enamel structure and recurrent aphthous stomatitis, may be useful to study the trend of the pathology in the coeliac patient in-depth and to obtain an early diagnosis, with the help of a multidisciplinary collaboration.

Clarification

The authors declare that dental age, when delayed, is a diagnostic parameter of coeliac disease only associated with the presence and persistence of alterations of enamel structure and recurrent aphthous stomatitis. The delay of dental age is common synthon of many diseases.

References


Ansaldi N, Morabito A, Balocco P, Galleano E. Dental changes in children...