Dentofacial characteristics of growing patients with Duchenne muscular dystrophy: a morphological study

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SUMMARY Occlusal traits and craniofacial morphology were studied in growing patients with Duchenne muscular dystrophy (DMD). Sixteen patients from 6 to 20 years of age were examined and compared with 16 healthy male individuals matched according to age. The dental arches and occlusal traits of both groups were analysed on dental casts and compared with the norms of healthy individuals from the literature. Lateral cephalograms of the patients were compared with normal individuals by using scored values based on standard deviations in order to compensate for heterogeneity in the age of the subjects. Statistical analysis was undertaken for continuous variables with a paired Student’s t-test and non-continuous variables with a chi-square test. Linear regressions were used to evaluate the influence of age.

A high prevalence of malocclusions was found, including posterior crossbites, anterior and lateral open bites, a tendency towards mesio-occlusion due to a skeletal Class III malocclusion, and dental compensations of the Class III relationship by retrusion of the lower incisors. Both upper and lower arches were widened posteriorly. The lower arches were even wider than the upper arches, resulting in frequent posterior crossbites. No significant skeletal vertical deviations were observed in this group of DMD patients, except for the maxillary plane angle (NL/NSL) that was larger than normal, while the anterior upper face height (NSp) was smaller. However, no difference was found in lower face height.

The posterior enlargement of the dental arches and the dentoalveolar development towards an Angle Class III relationship were significantly related to age and found more frequently among the older subjects.

Introduction

Progressive muscular dystrophy, or Duchenne muscular dystrophy (DMD), is a recessive neuromuscular disease affecting the short arm of the X chromosome in the p21-2 position (Jennekens et al., 1991; Onimus et al., 1999) and has a prevalence of one male newborn in 3500.

This gene codes for dystrophin, a protein which is present in the sarcolema of the muscular cell, are absent or hardly detectable in DMD.

The disease is detected clinically at an average age of 3.5 years, but in the majority of the subjects, the parents recognize an earlier delay in motor function (Fowler, 1982). From the age of 7–8 years, the progression of the disease is dramatic. The patient becomes wheelchair-bound at approximately 10–12 years of age with a subsequent loss of muscle strength in the upper limbs and the development of scoliosis (Onimus et al., 1999).

In the 1980s, life expectancy was low since most patients died of respiratory failure before 20 years of age. Nowadays, many patients reach 25 or even 30 years of age due to improved medical support (Fardeau, 2005).

During post-natal growth, bones continue their modelling process to maintain a form that is appropriate to their biomechanical function. Muscle function exerts an influence on skeletal growth and also on the facial skeleton (Kiliaridis, 1995).

In humans, vertical dentofacial aberrations have been observed in patients with reduced muscle function, as can be found in myotonic dystrophy (Kiliaridis et al., 1989). Similarly, a high prevalence of malocclusions has been noted in DMD patients, such as anterior open bites and posterior crossbites, which appear to be strongly related to the involvement of the orofacial muscles in the disease (Morimoto et al., 1981; Stenvik and Storhaug, 1986; Kulkarni and Chandran, 1995; Eckardt and Harzer, 1996; Hara et al., 2002; Matsumoto et al., 2002).

In DMD patients, the effects of the disease progress with the age of the individuals and this may also progressively influence orofacial function (Onimus et al., 1999). Thus, the hypothesis tested in this study is that in children and adolescents suffering from DMD, dentofacial aberrations may show a higher frequency and severity in older children. The aim of the investigation was to examine DMD patients of different ages, record their dentofacial characteristics and determine any relationship between age and dentofacial characteristics. Linking these factors would indirectly relate dentofacial characteristics to severity of the disease. This investigation will provide the base for a longitudinal prospective study, to record the individual changes in this group.

Subjects and methods

From a group of 24 DMD patients registered at the university hospitals of Geneva and Lausanne, the patients were selected based on two criteria: (1) they had to be between 6 and 20 years of age and (2) they had to give their informed consent according to the requirements of ethical committees.
of both universities. Sixteen patients with a mean age of 11.7 years [standard deviation (SD) 3.7, range 6–20] fulfilled the inclusion criteria and agreed to participate in the study. Of these 16 patients, nine used a wheelchair and stopped walking at an average age of 8.3 years. The other seven subjects who were still able to walk were among the youngest of the group and all were being treated with prednisolone (Kinali et al., 2002).

A control group of 16 healthy male children, selected consecutively and matched for age to the DMD patients were set up within the consultation of the annual school dental examination in Geneva. These controls presented no immediate need for orthodontic treatment.

These control children also gave their informed consent and had the same examinations as DMD patients, except for the radiographs, so as to meet the requirements of the ethical committees. The mean age of the control group was 11.9 years (SD 4.0, range 6–20).

To counterbalance the disadvantages of the limited size of the control group, comparisons were undertaken with the norms of cast measurements found in the literature (Moyers et al., 1976).

Impressions and occlusal wax bites were taken in order to construct dental casts for analysis of the occlusal traits. Sagitally, overjet and Angle classification, which were evaluated on the first permanent molars when applicable and converted to a continuous value from −100 per cent (full Class III) to +100 per cent (full Class II), by steps of 25 per cent were measured. Vertically, the overbite and the height of the palatal vault in the first permanent molar region were evaluated.

Evaluation of space conditions was performed using the values of Droschl et al. (1977), whenever patients were still in the mixed dentition. The depth and width of the dental arches were measured using calibrated photocopies of the casts (Figures 1 and 2). To determine the geometric centre of the crown, the centroids were used (McLean and Nelson, 1988). Width measurements were performed between the first molars, first primary molars or first premolars, and canines, both in the upper and in the lower arches.

Depth was determined by first drawing a line between the distal contact points of both canines and both first premolars in the same arch. Then, the length of the segment perpendicular to these lines and passing through the contact point of the central incisors was measured and recorded. Palatal height was determined by placing an elastic band joining the mesio-palatal cusps of the first permanent molars (when present) and measuring the distance to the midpalate perpendicular to the occlusal plane.

In order to limit the measurement errors, two operators (CMV and SB) performed all measurements separately on the casts on two occasions with an interval of at least 2 weeks. The average between these two measurements was used unless the values differed significantly in which case both examiners repeated the measurement until a consensus was found. A digital calliper (accurate to 0.01 mm) was used for all linear measurements.

Lateral cephalograms were taken of the DMD patients to study craniofacial morphology using a cephalometric method based on the Bergen analysis (Figure 3; Hasund, 1977). The cephalometric results were compared with a sample of healthy individuals of different ages (Riolo et al., 1974).
The measurements obtained from the dental casts and cephalometric analysis of the DMD patients were also compared with the dental casts of controls from a sample of healthy individuals recorded at different ages when applicable. Data from Riolo and Moyers were collected in the University of Michigan on a yearly basis starting in 1953 on children between their sixth and 16th birthday. Their ethnic background was not stated. The values used in the present study are the ones for male subjects (Riolo et al., 1974; Moyers et al., 1976). Due to the range of ages, the absolute measurements of each individual were transformed to a score of SDs, based on normal values of a group of healthy individuals of the same age (Moyers et al., 1976).

This was carried out for the linear and angular measurements of the cephalometric analysis, and linear measurements of the casts. All the scored values \( Y \) were evaluated computing the score as a number of SDs, using the formula:

\[
Y = \frac{Y_{\text{Pat}} - X_N}{SD_N},
\]

where \( Y_{\text{Pat}} \) is the measurement of the patient, and \( X_N \) and \( SD_N \) the mean value and the SD of the ‘norms’ corresponding to the age of the patient.

**Statistical analysis**

For each measurement of a continuous variable, due to the small size of the samples, a paired Student’s \( t \)-test was performed to evaluate the differences between the DMD patients and their healthy matched controls, when applicable (Campbell and Machin, 1999).

For non-continuous variables and small samples, the chi-square test was used to evaluate the significance of differences in frequency between the groups (Campbell and Machin, 1999).

Linear regressions were used to evaluate the influence of age where DMD patient characteristics diverged from the control group or the data of Riolo et al. (1974). In these regressions, \( \alpha \) denotes the slope and \( \beta \) is the ordinate at the origin of the age axis (as in \( Y = \alpha X + \beta \)).

The significance of these regressions was evaluated by computing the \( P \) value on the slope \( \alpha \), as well as regression coefficients \( R^2 \), for DMD patients and control group.

\( X_0 \) denotes the age at which both regressions intersect, and is computed by:

\[
X_0 = \frac{\beta_N - \beta_{DMD}}{\alpha_N - \alpha_{DMD}}.
\]

When the intersection \( X_0 \) between the two regression lines was in the range of 5–20 years of age, it was considered as significant; otherwise, since both regressions were almost parallel, it was noted as non-significant.

Paired \( t \)-tests were systematically performed to evaluate the significance of the results.

**Error of the methods**

The error of the measurements in the dental analysis of the stone casts and the cephalometric analysis was computed after duplicate determinations, based on recordings of 10 randomly chosen subjects, using the following formula:

\[
\text{SE} = \sqrt{\frac{\sum d^2}{2N}},
\]

where \( d \) is the difference between the first and second recordings and \( N \) is the number of double determinations. The error was computed for each operator in the DMD and control groups for the cast measurements and the radiographs of the DMD patients. The error of measurements did not exceed 0.6 mm for linear measurements or 1.0 degrees for the angular measurements of the cephalometric analysis, and 0.3 mm for the linear measurements of the casts.

**Results**

The analysis of the dental casts revealed a higher frequency of malocclusions in the DMD patients than in the control group.

A significantly higher number of Class III malocclusions were observed (31 per cent, \( P = 0.015 \)) in the DMD subjects, with a tendency to a smaller overjet ( \( P = 0.069 \)). This anteroposterior dental relationship, expressed as a continuous
Figure 4  Angle classification of the first molars in the Duchenne muscular dystrophy (DMD) patients and the control group, as expressed by a continuous value from −100 (%) for a full Class III to +100 (%) for a full Class II. Linear regression lines depict the sagittal molar relationship associated with the age of the subject, based on the average between left and sides.

Figure 5  Overjet (a) and arch widths at the lower (b) and upper (c) first molar in the Duchenne muscular dystrophy (DMD) patients and control group and their linear regression lines.

Figure 5  Overjet (a) and arch widths at the lower (b) and upper (c) first molar in the Duchenne muscular dystrophy (DMD) patients and control group and their linear regression lines.

Table 1 Occurrence of malocclusions in Duchenne muscular dystrophy (DMD) patients and a matched control group expressed as a percentage and numbers and their significance, based on a chi-square test. A chi-square test was performed for Angle Class III separately and then a global chi-square test by pooling Angle Class I, II, and III prevalences together.

<table>
<thead>
<tr>
<th>Classification</th>
<th>DMD (n=16)</th>
<th>Controls (n=16)</th>
<th>χ²</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td>Angle classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8</td>
<td>50</td>
<td>14</td>
<td>88</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>19</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>31</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Global angle classification</td>
<td>16</td>
<td>100</td>
<td>16</td>
<td>100</td>
</tr>
<tr>
<td>Anterior open bite</td>
<td>6</td>
<td>37.5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Lateral open bite</td>
<td>7</td>
<td>44</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Posterior crossbite</td>
<td>14</td>
<td>88</td>
<td>3</td>
<td>19</td>
</tr>
</tbody>
</table>
Table 2
Interarch relationship, space conditions, and upper arch dimensions measured on dental casts. The molar relationship is expressed as a percentage, from –100 (%) for a full Class III to +100 (%) for a full Class II. The average and standard deviation (SD) for Duchenne muscular distrophy (DMD) patients and controls are provided. Significance was evaluated using paired t-tests.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>DMD</th>
<th>Controls</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\bar{x}$</td>
<td>SD</td>
<td>$\bar{x}$</td>
</tr>
<tr>
<td>Molar relationship (%)</td>
<td>16</td>
<td>−13.4</td>
<td>61.0</td>
<td>13.7</td>
</tr>
<tr>
<td>Overjet (mm)</td>
<td>16</td>
<td>1.5</td>
<td>4.1</td>
<td>3.5</td>
</tr>
<tr>
<td>Overbite (mm)</td>
<td>15</td>
<td>0.29</td>
<td>3.2</td>
<td>2.7</td>
</tr>
<tr>
<td>Space upper arch (mm)</td>
<td>14</td>
<td>−0.93</td>
<td>6.2</td>
<td>0.61</td>
</tr>
<tr>
<td>Space lower arch (mm)</td>
<td>14</td>
<td>3.1</td>
<td>5.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Palatal width (mm)</td>
<td>14</td>
<td>42.8</td>
<td>5.5</td>
<td>40.3</td>
</tr>
<tr>
<td>Palatal height (mm)</td>
<td>13</td>
<td>17.8</td>
<td>3.9</td>
<td>17.5</td>
</tr>
</tbody>
</table>

Table 3
Upper and lower arch width and depth in the Duchenne muscular dystrophy (DMD) patients and control group as per Figures 1 and 2, measured according to Riolo et al. (1974) on photocopies of occlusal surface of the dental casts. The average $\bar{x}$ and standard deviation (SD) are provided. Significance was evaluated using paired t-tests.

<table>
<thead>
<tr>
<th>Arch width (W)</th>
<th>DMD</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\bar{x}$</td>
<td>SD</td>
<td>$\bar{x}$</td>
</tr>
<tr>
<td>Upper arch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W6 (mm)</td>
<td>52.8</td>
<td>6.3</td>
<td>47.7</td>
</tr>
<tr>
<td>W4 (mm)</td>
<td>38.7</td>
<td>4.1</td>
<td>35.6</td>
</tr>
<tr>
<td>W3 (mm)</td>
<td>32.5</td>
<td>4.1</td>
<td>30.5</td>
</tr>
<tr>
<td>D4 (mm)</td>
<td>19.5</td>
<td>3.0</td>
<td>20.4</td>
</tr>
<tr>
<td>D3 (mm)</td>
<td>12.1</td>
<td>2.0</td>
<td>13.4</td>
</tr>
<tr>
<td>Lower arch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W6 (mm)</td>
<td>52.9</td>
<td>7.8</td>
<td>42.7</td>
</tr>
<tr>
<td>W4 (mm)</td>
<td>36.6</td>
<td>5.2</td>
<td>30.5</td>
</tr>
<tr>
<td>W3 (mm)</td>
<td>26.9</td>
<td>3.6</td>
<td>24.4</td>
</tr>
<tr>
<td>D4 (mm)</td>
<td>13.7</td>
<td>2.6</td>
<td>16.0</td>
</tr>
<tr>
<td>D3 (mm)</td>
<td>7.1</td>
<td>1.7</td>
<td>9.4</td>
</tr>
</tbody>
</table>

healthy controls ($\alpha = -0.046$, $R^2 = 0.01$, $P = 0.173$). The two regression lines for the lower arch of the DMD and the healthy control group intersected at 6.7 years of age. The corresponding line for the upper arch was 9 years. This indicates that from those ages, the DMD patients had progressively larger dental arches (Figure 5b,c).

ANB angle was significantly smaller ($P = 0.008$) in DMD patients when compared with the sample of Riolo et al. (1974; Table 4). Furthermore, the inclinations of the lower incisors (ii/NB) and lower arch depth were smaller in DMD patients ($P = 0.037$; Tables 3 and 4).

The upper part of the anterior face, NSp, was smaller ($P = 0.001$), while the inclination of the maxilla in relation to the anterior cranial base (NL/NSL, $P = 0.010$) and the cranial base angle (NSBa, $P = 0.048$) was larger in the DMD patients when compared with the norms. It should be noted that other values, including the vertical relationship between the mandible and the cranial base and the intermaxillary angle, did not show any statistically significant difference from the norms.

Discussion

Although the size of the control group was small due to the difficulty in gathering a larger cohort from the annual scholar dental examination, many of the results are in line with the literature and are significant.

This study has shown that DMD patients present mainly dentoalveolar deviations, and these are more frequent and severe in post-pubertal individuals. No significant skeletal vertical deviations were observed in these DMD patients. From a dentoalveolar point of view, the frequency of an anterior open bite, lateral open bite, and lateral crossbite was very high, which confirms the observations of many previous studies (Morinushi and Matsumoto, 1986; Stenvik and Storhaug, 1986; Ghafari et al., 1988; Ertük and Dogan, 1991; Matsumoto et al., 2002; Symons et al., 2002). The findings, which were based on comparison with a healthy matched control group, were comparable with those found in the literature.

For the antero-posterior dimension, the results are in agreement with those of Eckardt and Harzer (1996) who found a small overjet in patients with DMD, and other studies that found a dental Class III tendency (Ertük and Dogan, 1991; Matsumoto et al., 2002). In the present study, DMD patients also showed a tendency towards a skeletal Class III relationship with dental compensation, as expressed by a smaller angle of the lower incisor to the NB line (ii/NB). Similar results confirming a clear skeletal Class III

Table 4
Absolute and scored cephalometric variables and number of standard deviations (SD) in Duchenne muscular dystrophy (DMD) patients and the control group based on the values of Riolo et al. (1974). The $\bar{x}$ and SD for DMD patients and controls are provided. Significance was evaluated using paired t-tests.

<table>
<thead>
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<td></td>
<td>$\bar{x}$</td>
<td>SD</td>
<td>$\bar{x}$</td>
</tr>
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</table>

SNA (°) 79.4 5.69 −0.482 1.63 0.258
SNB (°) 77.9 6.35 0.254 2.24 0.525
ANB (°) 1.5 3.49 −1.171 1.53 0.008
ML/NSL (°) 36.6 6.14 0.517 1.30 0.123
NL/NSL (°) 3.6 3.36 0.956 1.35 0.010
ML/NL (°) 27.2 5.65 −0.063 1.25 0.827
NSBa (°) 132.8 6.62 0.694 1.36 0.048
Gn-tgo-Ar (°) 128.5 6.48 0.380 1.11 0.206
I/I (°) 133.0 9.85 0.470 0.99 0.063
Is-NA (°) 23.1 4.83 0.105 0.86 0.499
ii/NB (°) 20.3 9.47 −0.820 1.45 0.037
Sp-Gn (mm) 66.1 9.41 −1.059 1.47 0.148
N-Sp (mm) 48.8 4.37 −1.500 1.07 0.001

For the antero-posterior dimension, the results are in agreement with those of Eckardt and Harzer (1996) who found a small overjet in patients with DMD, and other studies that found a dental Class III tendency (Ertük and Dogan, 1991; Matsumoto et al., 2002). The findings, which were based on comparison with a healthy matched control group, were comparable with those found in the literature.

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relationship were found in DMD patients in the permanent
dentition, in contrast to DMD patients who were in the
mixed dentition and showed only a tendency to a Class III
skeletal relationship (Matsumoto et al., 2002).

In the vertical dimension, the high frequency of anterior
and lateral open bites is characteristic of DMD patients. In
this study, anterior and lateral open bites were more frequent
in the older than in the younger patients. Skeletally, no
significant vertical discrepancies were observed, except for
a larger inclination of the maxilla in relation to the anterior
cranial base and a small upper anterior face height (NSp);
the latter finding is in agreement with the observations of
Eckardt and Harzer (1996). The large inclination of the
maxilla may be attributed to specific palatal remodelling
due to the increased tongue volume influencing mainly the
posterior part of the maxilla. Contrary to the findings of a
recent longitudinal study where a posterior rotation of the
mandible was found (Matsuyuki et al., 2006), no statistically
significant differences in the vertical skeletal dimension in
relation to the norms of healthy individuals were observed.
This may be explained by the fact that the power of a
cross-sectional cephalometric evaluation has limitations in
detecting the fine changes that can be identified by a
longitudinal follow-up. It is intended to follow these patients
longitudinally to observe the skeletal and dentoalveolar
changes that may take place within this group.

In the transverse dimension, the posterior crossbite in the
DMD group was mainly due to the increase in lower arch
width. It was observed that the lower arch was wider in the
older than in the younger patients (Figure 6), and this may
be related to buccal tipping of the lower molar and premolar.
This is in agreement with the findings of Matsumoto et al.
(2002) and has possibly been caused by the increased
volume of the tongue.

Recent studies on DMD patients, based on ultrasound
measurements, have shown that muscular changes occur
through an increase of muscle volume and a disruption of
the muscular architecture with disappearing aponevrosis
and septums (Pillen et al., 2003; Scholten et al., 2003). This
is due to muscle cell replacement with fat and connective
tissue (Heckmatt et al., 1982; Reimers et al., 1993), and
explains the classical observations of increased lingual
volume. Matsumoto et al. (2002) assumed that a posterior
crossbite was more frequent than an anterior crossbite,
because the enlargement of the tongue progresses over time from the root of the tongue to its apex; as a result, a posterior crossbite is more prominent in older subjects.

Although DMD and myotonic dystrophy both affect the muscles in and around the oral cavity, their effect is different since muscle imbalance produces different skeletal and dental growing processes. In myotonic dystrophy, a high prevalence of malocclusion has also been found, including anterior open bites and lateral crossbites, associated with a vertical skeletal aberration (Kiliaridis et al., 1989). Malocclusions in these patients seem to be related to a vertical aberration in craniofacial growth due to the involvement of masticatory muscles, with a possibly less affected suprahypoid musculature. The lowered mandible and tongue cannot counterbalance the forces developed by the stretched facial musculature and this situation may affect the teeth transversely, decreasing the width of the palate and causing a posterior crossbite; the lowering of the mandible may permit overeruption of the posterior teeth and development of an anterior open bite (Kiliaridis and Katsaros, 1998).

By contrast, DMD patients show a high prevalence of anterior and lateral open bites without vertical skeletal aberration. DMD affects muscles at various stages of the evolution of the disease. A good example is the weakening of the masseters, which occurs at an earlier stage compared with the labial muscles (Eckardt and Harzer, 1996). Due to the imbalance between lateral and anterior forces combined with the increased lingual volume, lateral dentoalveolar effects are more significant than frontal effects and take the form of an increased transverse diameter; in turn, this causes buccal tipping of the teeth, as well as a lateral open bite and crossbite (Stenvik and Storhaug, 1986; Willig et al., 1994; Matsumoto et al., 2002; Symons et al., 2002).

An interesting observation in the present study was that many measurements start to diverge significantly from normal values at 7–10 years of age, as shown by the computation of the intersection between linear regression lines of the patient group and the healthy controls. This singular point in the clinical evolution can be related to the fact that the physical capacity of these boys significantly decreases with age; in this group, the patients stopped walking at a mean age of 8.3 years.

Therapeutic exercises on a submaximal level seem to be an interesting way to limit the loss of function (De Lateur and Giaconi, 1979; Kawazoe et al., 1982; Kilmer et al., 1994; Grimby, 2004). In addition, progress has been made in new therapeutic protocols by means of gene therapy (Goyenvalle et al., 2004; Denti et al., 2006), which in turn may lead to less frequent and severe malocclusions.

Conclusions

In patients with DMD, a high prevalence of posterior and anterior open bites with a decreased overjet, as well as posterior crossbites due to enlargement of the posterior lower arches were observed. The dentoalveolar deviations were related to the age of the patients since they showed a higher prevalence in older adolescents than in younger children.

No obvious vertical skeletal deviations were found in this patient group.

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