UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA
DOCTORAL SCHOOL

PhD THESIS ABSTRACT

APPRECIATION OF CRANIO-FACIAL GROWTH AND DEVELOPMENT BY ANTHROPOMETRIC AND RADIOLOGICAL METHODS

PhD COORDINATOR: PROF. IOANA-ANDREEA GHEONEA

PhD STUDENT: IOANA ADINA COTOI (TECUȚA-BUȘOI)

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INTRODUCTION

The 0-6 year period represents an important interval in the development of the viscerocranium, by increasing the vertical and horizontal dimensions, due to the processes of enchondral ossification and surface accretion [1]. Also, an important factor in the growth of viscerocranium is the decisional dentition and, consequently, the development of the masticatory muscles [1]. There are studies of cranio-facial anthropometry in the literature in the field, studies we have reported in our paper [1,2]. These studies show the development of viscerocranium during childhood and we noticed notable differences compared to our group.

We considered the anthropometry to be useful in evaluating the growth and development of viscerocranium for the following reasons: it is an inexpensive, non-invasive method and the measurement methods are well standardized, and compared to cephalometry, anthropometry provides data with much lower measurement errors [3].

We present in this study the growth rates of viscerocranium in children aged 0-6 years from the southwest region of Romania, through anthropometric methods. The purpose of this study was to create a database with normal reference values for children from 0-6 years of age in our region, values applicable in pediatrics, orthodontics or forensic medicine.

Cephalometry is also used in the assessment of the morphological changes of the skull and face, besides the role that this radiographic method has in diagnosing the different pathological conditions related to the orthodontic condition, in which the dentist has a special interest.

The assessment of neuro and viscerocranium morphology by cephalometry has been studied in a small number of specialized papers, but these studies are of particular importance through their conclusions which lead to the establishment of typologies and morphological changes according to the etiology underlying these changes, at the level of the cephalic extremity [4].

In principle, in the child the facial and cranial changes occur as a result of growth hormone deficiency, small gestational age or genetic defects [4].

In our study we evaluated a group of subjects with craniofacial morphological changes of different etiologies, at the initiation of hormone replacement therapy. In fact, it discusses the effects of growth hormone deficiency on the neuro and viscerocranium known to be that in the process of growth and development the somatotropic hormone plays a primary role through its effects [5].
GENERAL PART

RECENT CONSIDERATIONS ON NORMAL SKULL DEVELOPMENT AND GROWTH

Embryonic phase - takes place in the first eight weeks of pregnancy, when the formation of the calvaria is preceded by the formation of mesenchymal cells by epithelial-mesenchymal transformation, thus beginning the development of skull bones by condensation of mesenchymal cells [6].

The neurocranium develops from the paraxial mesenchyme, from the first five somites and from non-segmental somitomers, located rostrally from the first somite and from the ectoderm, via the neural crest [7]. The viscerocranium is formed exclusively from the mesenchymal neural crest. The neural crest produces the mesenchyme that forms the frontal bone, the sphenoid, the squamous portion of the temporal bones and the bones of the face [7]. The paraxial mesoderm (somites and somitomers) plays a direct role in the skeletogenesis of the parietal bones, the petrous portion of the temporal bones and the occipital bone. However, the neural crest plays an important role in the space between the two parietal bones. Thus a small line in the neural crest originates from the mesenchyme and remains between the two parietal bones and contributes to the enlargement of the suture at the level of the sutures and to the development of meningeal leaves [7].

Fetal phase - in this phase the ossification occurs. There are two processes in normal bone formation: intramembranous ossification and endochondral ossification [7]. Intramembranous ossification, or osteogenesis, begins with the development of ossification centers from the outer layer of the ectomeninx and thus the individual bones are formed. The centers of ossification appear for the first time in the areas corresponding to the future eminences, in the week of VII and VIII post conception. The next step is calcification, which begins a few days after the storage of organic substances by osteoblasts. With the beginning of the condensation of the ossification centers, the bone spicules appear, which have a progressive increase in the radial direction from the center to the periphery. Osteoids lead to the formation of primitive trabecular bone. The embryonic primitive bone is immature and is gradually replaced by mature lamellar bone until birth [7].
PERSONAL PART

PURPOSE, OBJECTIVES AND MOTIVATION OF RESEARCH

The purpose of this paper is to determine the rates of growth and cranio-facial development in the 0-6 year old child and to evaluate the cranio-facial changes in children with different deficiencies.

The specific objectives proposed to be achieved are the following:

- Assessment of normal cranio-facial growth in children from 0-6 years by anthropometric methods
- Assessment of the rates of cranio-facial growth in the healthy child of 0-6 years, by sex, by anthropometric methods
- Establishing a cranio-facial morphology specific to our region
- Evaluation of cranio-facial changes by cephalometric methods in children with dental pathology of different etiologies

The approach of this study topic derives from the reality that surrounds us, human mobility being today a factor that potentiates the amalgamation of the races, and the determination and detection of the age of the children represents a challenge for specialists in all fields.

Also, the explosive development of the imaging methods and the possibility of their use in the assessment of normal and pathological cranio-facial development constitute an important starting point in establishing the cranio-facial typologies, but also in the diagnosis of the different pathological conditions that involve cranio-facial anomalies, in order the application of appropriate and specific therapies.

MATERIAL AND METHOD

Subjects

307 subjects, ranging in age from 0 to 6 years, 144 females and 163 males, were measured by anthropometric methods. The measurements were made during 30 months, in the period 2014-2016. The inclusion criteria considered healthy subjects apparently, with normal birth weight, normal weight children, with normal mental development, according to age.

The group of subjects taken in our cephalometric study included 14 children with growth hormone deficiency, 10 children with low birth weight and 7 girls with Turner syndrome. The classification of subjects in the growth hormone deficient group was made by the endocrinologist
based on hormonal dosages, with the consent of the legal representatives and the current doctor for access to the data from the medical records. For the group of children with low birth weight the personal data of the subjects were taken from the medical files having the complete history, established by the neonatologist and pediatrician. The group of girls with Turner syndrome was selected from the Endocrinology Clinic of the County Clinical Hospital of Craiova Emergency, also having the agreement of the current doctor and legal guardians regarding the use of medical data.

Anthropometric measurements

The direct measurements were performed according to the rules described in the literature and we studied the following parameters of the viscerocranium: the height of the viscerocranium (or the height of the nasion-gnation face N-Gn, the distance between the root of the nose and the lower edge of the mandible, in the center), upper face or height of the respiratory floor (nasion-stomion N-Sto the distance between the root of the nose and the middle of the lip crack), the height of the lower face or the height of the digestive floor (stomion-gnation Sto-Gn the distance between the middle of the labial fissure and the lower mandible, ), face width (zygion-zygion Zy-Zy distance between the most lateral points of the zygomatic arches), width of the mandible (gonion-gonium Go-Go distance between the angles of the mandible).

At the level of the neurocranium we measured: skull height (V-Gn), skull width or biparietal diameter (Eu-Eu), skull length or antero-posterior diameter (G-Op), neurocranium height (VN), brow width or bifrontal diameter (Ft-Ft).

Cephalometric measurements

The profile cephalometers were performed using a Carestream CS 8100SC equipment, the examination position being the standardized one, with the perpendicular orientation of the X-ray beam on the patient’s sagittal plane.

We measured the following cephalometric variables: total skull base = N-Ba, anterior skull base = NS, posterior skull base = S-Ba, total height of the anterior face = N-Gn, height of the anterior face in the upper segment = N- Sp, front face height in lower segment = Sp-Gn, jaw body length = Gn-Go, maxilla length = Sp-PNS, SBA angle, SNA angle, ANB angle, ML-NL angle, S-N-Ss angle, S-N-Sm angle.

RESULTS OBTAINED AND THEIR INTERPRETATION

The results obtained by anthropometric measurements
The values of the measurements and the standard deviation are entered in the table no. 1.

**Table no. 1 The mean and DS values of anthropometric variables at the viscerocranium level**

<table>
<thead>
<tr>
<th>Age</th>
<th>Face height (mm)</th>
<th>Upper face height (mm)</th>
<th>Lower face height (mm)</th>
<th>Face width (mm)</th>
<th>Mandible width (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M±</td>
</tr>
<tr>
<td>Newborn</td>
<td>46±3.6</td>
<td>45±3.7</td>
<td>29±4.2</td>
<td>17±4.6</td>
<td>79±4.4</td>
</tr>
<tr>
<td>4 months</td>
<td>50±2.5</td>
<td>49±2.2</td>
<td>33±3.3</td>
<td>17±3.6</td>
<td>84±3.4</td>
</tr>
<tr>
<td>6 months</td>
<td>56±3.5</td>
<td>54±3.7</td>
<td>36±4.3</td>
<td>20±3.7</td>
<td>84±3.2</td>
</tr>
<tr>
<td>8 months</td>
<td>60±5.4</td>
<td>58±5.2</td>
<td>38±3.6</td>
<td>22±3.4</td>
<td>85±4.2</td>
</tr>
<tr>
<td>12 months</td>
<td>69±4.2</td>
<td>62±4.6</td>
<td>47±5.3</td>
<td>21±4.6</td>
<td>92±5.2</td>
</tr>
<tr>
<td>18 months</td>
<td>79±3.2</td>
<td>78±3.5</td>
<td>50±4.2</td>
<td>28±3.7</td>
<td>97±3.4</td>
</tr>
<tr>
<td>24 months</td>
<td>83±4.5</td>
<td>81±4.3</td>
<td>51±3.4</td>
<td>32±3.4</td>
<td>100±4.6</td>
</tr>
<tr>
<td>30 months</td>
<td>84±4.3</td>
<td>83±4.5</td>
<td>52±3.5</td>
<td>32±4.3</td>
<td>102±3.6</td>
</tr>
<tr>
<td>3 years</td>
<td>87±4.4</td>
<td>85±4.6</td>
<td>52±5.4</td>
<td>34±4.6</td>
<td>106±4.7</td>
</tr>
<tr>
<td>4 years</td>
<td>88±5.2</td>
<td>88±5.4</td>
<td>53±4.4</td>
<td>34±4.7</td>
<td>107±5.2</td>
</tr>
<tr>
<td>5 years</td>
<td>89±3.2</td>
<td>89±3.6</td>
<td>53±4.2</td>
<td>36±4.7</td>
<td>111±4.6</td>
</tr>
<tr>
<td>6 years</td>
<td>91±3.4</td>
<td>90±3.2</td>
<td>55±3.7</td>
<td>36±4.6</td>
<td>112±4.3</td>
</tr>
</tbody>
</table>

The results obtained by cephalometric methods

The results of the measurements are presented in the following table according to the present pathology (table no. 2).
Table no. 2 Mean and Standard Deviation values of cephalometric variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Lot with growth hormone deficiency</th>
<th>Lot with small gestational weight</th>
<th>Lot with Turner syndrom</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean values</td>
<td>Standard Deviation</td>
<td>Mean values</td>
</tr>
<tr>
<td>N-Ba (mm)</td>
<td>85.72</td>
<td>2.46</td>
<td>84.82</td>
</tr>
<tr>
<td>N-S(mm)</td>
<td>60.23</td>
<td>2.32</td>
<td>60.57</td>
</tr>
<tr>
<td>S-Ba(mm)</td>
<td>36.27</td>
<td>3.18</td>
<td>37.24</td>
</tr>
<tr>
<td>N-Gn(mm)</td>
<td>101.42</td>
<td>5.82</td>
<td>102.58</td>
</tr>
<tr>
<td>N-Sp(mm)</td>
<td>45.67</td>
<td>4.28</td>
<td>46.24</td>
</tr>
<tr>
<td>Sp-Gn(mm)</td>
<td>54.23</td>
<td>5.17</td>
<td>54.18</td>
</tr>
<tr>
<td>Gn-Go(mm)</td>
<td>61.38</td>
<td>5.62</td>
<td>62.33</td>
</tr>
<tr>
<td>Sp-PNS (mm)</td>
<td>46.41</td>
<td>4.12</td>
<td>46.18</td>
</tr>
<tr>
<td>SNB (°)</td>
<td>76.32</td>
<td>4.27</td>
<td>74.62</td>
</tr>
<tr>
<td>SNA (°)</td>
<td>75.83</td>
<td>3.67</td>
<td>80.24</td>
</tr>
<tr>
<td>ANB(°)</td>
<td>3.72</td>
<td>2.46</td>
<td>2.82</td>
</tr>
<tr>
<td>ML-NL(°)</td>
<td>25.87</td>
<td>5.37</td>
<td>27.36</td>
</tr>
<tr>
<td>S-N-Sst(°)</td>
<td>78.53</td>
<td>2.68</td>
<td>78.28</td>
</tr>
<tr>
<td>S-N-Sm(°)</td>
<td>75.26</td>
<td>3.83</td>
<td>73.64</td>
</tr>
</tbody>
</table>

**DISCUSSIONS**

Analysis of the results obtained by anthropometric methods

Height of viscerocranium (N-Gn)

From the analysis of the graph of annual growth rates of the height of the face we find that these with very small differences are similar in both sexes (at 1 year the growth rate of boys is 23 mm,
for girls 17 mm). The highest growth rate of this period, the first year of life is due to the development of the respiratory stage and especially the digestive floor.

In the second year the growth rates are still high (of 14 mm in boys and 19 mm in girls), but this time due to the development of the digestive floor, due to the appearance of an important number of teeth, the development of the mandible through the process of mastication, as a result of food diversification.

Between 3 years and 6 years the growth rates of the facial mass decrease greatly; at 6 years the growth rate for boys is 2mm, for girls 1mm. From the age of 2 years 6 months the boys of the two groups have an almost identical evolution up to 6 years. In girls, the evolution is a little special; the girls of the lot increase much in the height of the facial mass up to 2 years, the peak of the graph being at 1 year 6 months.

After 2 years, there is also an almost identical evolution between the two lots. Thus, the increase in size of the face height from the studied lot, is obtained mainly by an accelerated development in the first 2 years of life. According to the classification of the skulls, according to the cranial index, in the group studied we observe ultradolicoskull at 1 year of age in boys, hyperdolicoskull at 2 years and 3 years in both sexes and mesocranes at 6 years and 5 years, both in girls and in boys.

Analysis of the results obtained by cephalometry

The analysis of skull base values is very important for patients with Turner syndrome, because it is known that in this pathology there is a reduction of the skull base compared to healthy subjects. Shortening of the skull base in Turner syndrome occurs by shortening the posterior base of the skull, as a consequence of the influence of X chromosome deficiency on craniofacial development in intrauterine life and early childhood [8]. Anterior skull base may present with normal development in Turner syndrome, considering that this segment increases with pneumatization of the frontal bone and thickening of the anterior portion of the frontal bone around the age of 6 years, after the closure of spheno-ethmoidal synchondrosis [8,9].

The importance of cranio-facial anthropometric methods

The technique of anthropometric measurements is relatively simple, however, implying strict and precise measurement rules, but does not require highly qualified personnel; also, the instrumentation used is simple, with low costs. The cranio-facial anthropometric measurements give the first information regarding the normal development of the cephalic extremity, the final
aim being the monitoring of the normal cranio-facial growth. Therefore, the establishment of reference values is very important then any deviation from the reference norms can lead to the establishment of diagnoses regarding cranio-facial anomalies, orthodontic anomalies, diseases and syndromes with facial asymmetries [2]. The quality of the relationships between the measurements of the cranio-facial complex must also be evaluated quantitatively in order to detect the early signs of cranio-facial disproportionality in children [10].

The importance of cephalometric methods

There are multiple pathological dental conditions secondary to growth hormone deficiency, these conditions need to be well documented and diagnosed, as early as possible then correction therapy is best chosen, appropriate for the purpose of correcting the various pathological changes, some specific to the deficiency of growth hormone. This is why cephalometry is the best method for diagnosing and monitoring deficiencies in craniofacial growth and development in children with growth hormone deficiency. But the anomalies that occurred during the process of growth and cranio-facial development are not only of hormonal etiology, here also register the genetic defects, but also the small gestational weight [4, 11,12].

Therefore, in our study, we performed cephalometric measurements in subjects with cranio-facial changes in genetic etiology (Turner syndrome), hormonal etiology (growth hormone deficiency), and also analyzed a lot of small gestational weight.

CONCLUSIONS

The anthropometric variables measured at the viscerocranium show accelerated growth rates in both sexes, especially between 1-2 years.

The width of the mandible is the only anthropometric parameter that presents higher average values in our group, in all age groups compared to the specialized studies.

The height of the skull, the width of the skull, the length of the skull, the height of the neurocranium are the anthropometric variables measured in our group, which have much higher values compared to studies in the field, this difference being greater than about 25 mm for the height of the neurocranium.

The group of subjects with Turner syndrome presents as pathognomonic pathological changes the reduction of the posterior base of the skull, the retrieval of the mandible, the rearrangement of the maxilla, there being a functional connection between the base of the skull and the tooth-facial complex.
The group of subjects with growth hormone deficiency shows the reduction of cranio-facial dimensions compared to subjects with the same pathology reported in other studies, the differences being greater than about 7 mm, at the expense of our group.

In children with growth hormone deficiency we observed a reduction in the size of the mandible and the posterior base of the skull, but the retraction of the maxilla and mandible.

REFERENCES