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Genetic Autosomal Dominant Disorders: A Knowledge Review

Trastornos Autosómicos Dominantes: Una Revisión de los Conocimientos

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ABSTRACT: Genetic disorders occur by excess or absence of chromosomal material, and the consequence of these changes is reflected in morphological and physiological changes. Autosomal disorders, which have dominant inheritance, as cleidocranial dysostosis, Craniofacial syndrome Apert, Treacher Collins and Achondroplasia have peculiar and similar characteristics. Because of their implications in the dental field, the aim of this review is to report on dysostoses, through exposure of general clinical factors and highlighting the signs in the oral cavity. Articles were selected from Lilacs, PubMed and Bireme databases, included in the year 2007–2014, and the keywords were: cleidocranial dysplasia, craniofacial dysostosis, mandibulofacial dysostosis, dysostosis and oral. Alterations of maxillofacial bones and craniofacial are well documented in the literature, but studies reporting an association between treatment odontologic and dysostoses are scarce. In conclusion, Oral pathological manifestations developed cause difficulty in speech, chewing, breathing, social involvement, and in a general perspective, psychological impairment and physical limitations.

KEY WORDS: cleidocranial dysplasia, craniofacial dysostosis, mandibulofacial dysostosis.

INTRODUCTION

It is not uncommon to come across people who believe that the care provided by Dental Surgeons are uniquely geared to the teeth and their pathologies. However, it is necessary that the professional knows how to deal with fears, anxieties and doubts of each patient, whether these factors are relevant or not, at the time of treatment. Several doctrines based on psychology have been studied, and are increasingly gaining acceptance among dentists, in order to reduce the risk of error in their decisions regarding treatment and help deal with the physical conditions, diseases, syndromes, psychological factors previous experiments and specific for each patient (Cruz & Oliveira, 2007).

The morphological processes of humans are closely related to their genetic load. The formation and growth of bones; the hair type; eye color; tooth formation. All these processes depend on environmental, constitutional and nutritional factors. However, if an imbalance occurs in the genetic load, even if all other factors are normal, it is likely that this individual has a disorder, and therefore have their morphological processes affected. Some of these genetic abnormalities aggressively affect the formation, growth and mineralization of bones and teeth, therefore strongly influencing the development, the masticatory, respiratory and fonetic functions of the individual (Cruz & Oliveira; Corrêa *et al*., 2009).

In this context it is essential that the dentist has the knowledge and proficiency of clinical signs, that identify each of these disorders in order to adapt and improve care for patients. The knowledge about the condition of these patients also allows the dentist to plan palliative treatments that improve the patient's condition outside the office, developing and teaching techniques that help families and society deal with them (Corrêa *et al*.).

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Genetic disorders are conditions that produce specific sets of morphological and / or physiological changes in response to a change in the genetic formation of the individual (Cruz & Oliveira; Corrêa *et al*.). These genetic changes are the result of excess or lack of chromosomal material in varied groups, and depend on many factors (affected chromosome pairs, genetic combination of the parents of the individual) (Cruz & Oliveira; Corrêa *et al*.; Bezerra *et al*., 2007).

Currently, genetic disorders have no permanent cure. Many treatments for these patients are only palliative and aim to improve the condition of life of patients, without permanently curing the disorder (Bezerra *et al*.; Martins *et al*., 2014).

Different disorders are genetic alterations in the expression of different genes, and thus on different chromosomes. However, the disorders discussed here are only those that affect the 22 pairs of autosomal chromosomes, and have dominant inheritance.

We will discuss the dental dysostoses interest (cleidocranial dysostosis, Craniofacial, and Mandibulofacial and Acrocephalosyndactylia) besides Achondroplasia, which is a genetic disorder that causes skeletal malformations and therefore other tissues. Most dysostosis cause hypoplasia of the affected tissues, but there dysostoses that cause hyperplasia of the affected tissues (Bezerra *et al*.; Martins *et al*.; Trigui *et al*., 2011).

Based on the importance of knowledge of the characteristics, peculiar or not, assigned to each autosomal dominant genetic disorder by the dentist, the present review aims to discuss the dysostoses that have greater clinical significance in the dental environment, exposing the general clinical factors and stressing signals that affect the oral cavity of patients.

MATERIAL AND METHOD

The topics that follow are divided according to the disorder discussed and subdivided into clinical, oral manifestations and types of treatment; aiming a dynamic reading, as well as facilitate the understanding of each disorder reported. Articles were selected from Lilacs, PubMed and Bireme databases, included in the year 2007–2014, and the keywords were: cleidocranial dysplasia, craniofacial dysostosis, mandibulofacial dysostosis, dysostosis and oral.

DISCUSSION

Disorders of Autosomal Dominant Inheritance. Are syndromes in which the affected individual received from one parent (heterozygous) or both (homozygous) the disease encoding gene, and that the affected individual has an affected parent (except in cases of highly mutable gene). These syndromes spread through several generations, because the affected individual has a 50% chance of transmitting the affected gene to their children. Men and women have equal probability to pass the affected gene to their next generation (Cruz *et al*.; Corrêa *et al*.; Bezerra *et al*.).

Cleidocranial Dysostosis. It is a rare inherited condition, also known as Sainton disease characterized by hypoplasia of the bone tissue in several locations. The delayed closure of the cranial sutures and fontanelles oversized cause disorder in the organization, unity and articulation of bones (Martins *et al*.; Trigui *et al*.).

The cleidocranial dysostosis can be mistaken for other diseases related to bone malformations having several phenotypes, thus there is a high risk of misdiagnosis (Almeida Junior *et al*., 2012; Shen *et al*., 2009).

With the overall physical manifestations, there is partial or complete absence of clavicles (allowing the front against the shoulder); exaggerated size of the pubic symphysis (large bowel) and the trapezius muscle; phalangeal joint abnormalities (Almeida Junior *et al*.); well as delayed motor and mental development, generally mild (Almeida Junior *et al*.; Shen *et al*.; Roberts *et al*., 2013; Machado *et al*., 2010).

Oral Manifestations: The presence of mandibular prominence and malocclusion is common, due to poor bone formation and consequent unequal size between the bones of the head. In most cases, occurred late eruption of teeth, both by composers from deciduous and permanent dentition, and the presence of supernumerary teeth over existing teeth, and / or in paranasal sinuses (Machado *et al*.).

Affected individuals have problems in the stomatognathic system functions related to swallowing, breathing and phonation, and otologic problems (Machado *et al*.; Serratine *et al*., 2007).

The high prevalence of supernumerary teeth is attributed to the delay in the formation of the crown of

the permanent teeth, favoring the activation of remnants of tooth blades, and thus formation of supernumerary teeth (Bezerra *et al*.). Types of treatment: Surgical therapy: excision of supernumerary teeth, orthognathic surgery for correction of maxillary hypoplasia or prognatia associated with orthodontic treatment and / or prosthetic (Serratine *et al*.; Silva Junior *et al*.).

Craniofacial Dysostosis. Also called Crouzon's disease, is the expression of chromosomal genes varied. It is the most common disorder among cranial dysostoses due to their dominance of 100% (Diniz *et al*., 2011). This disorder has highly variable phenotypic expression, being mainly originating from craniofacial tissue hypoplasia (sutures and fontanelles) and, for this reason, commonly compared to the Sainton disease (Alonso *et al*., 2009).

General physical manifestations: Despite the similarity with the disease Sainton is in this factor that both differ, as in Crouzon's disease there are no manifestations on the trunk and limbs, the hypoplasia are limited to the head region (Diniz *et al*.; Alonso *et al*.).

The growth disorders that affect different sutures cause retarded growth of some, while others suffer the effect of compensatory growth giving irregular and varied ways to the skull, thus causing breakdown of bones, bone union structures and fission of sutures, which should be close, uniting the bones associated with them (Diniz *et al*.).

Oral manifestations: Also related to hypoplasia and craniosynostosis are early closings cranial sutures and compensatory growth are basically hypoplastic. Retrusion of the mandible and maxilla causes brachycephaly, giving a bulging appearance to the skull (Alonso *et al*.).

In the oral cavity there is malocclusion and "V" maxillary dental arch (upper) with anomalous spaces between teeth. Cases of bisection of the uvula and narrowing of the bony palate are also reported, acquiring ogival aspect, there may be cleft palate. Due to the small size of the jaw, tongue and jaw become overly prominent, causing malocclusion. The maxillo-mandibular dysplasias also give the nose a parrot beak-like aspect (Alonso *et al*.).

Moreover, rhino-pharyngeal narrowing is common, leading to the occurrence of a sunken jaw deviated septum, sleep apnea and snoring, due to blockage and reduced space of paranasal sinuses (Diniz *et al*.).

Types of Treatment: Surgical therapies have several steps and are recommended for patients age coincident with fontanelar period, due to bone flexibility. Such interventions aim to harmonize the face by increasing facial volume. However, surgical procedures should be accompanied by psychosocial, speech-language therapies, as well as being associated with the use of orthodontic and hearing aids. Early diagnosis is important to prevent cranial hypertension, and consequent visual and auditory disorders (Diniz *et al*.; Alonso *et al*.).

Acrocephalosyndactylia. Better known as Apert syndrome is the most differentiated between genetic syndromes, which cause craniosynostosis giving a cuneiform aspect to the skull. During pregnancy a mutation of this one on the long arm of chromosome 10 (10q) gene occurs, characterizing this disorder. The high frequency of mutation of the gene encoding generates large amount of sporadic affected generations. Increased paternal age, especially after 35 years significantly increases the chance of a mutation (Iieri & Goyenc, 2012).

General Physical Manifestations: The differential diagnosis between disorders that cause craniosynostosis is that Acrocephalosyndactylia presents as clinical signs the syndactyly. The merger of the webbing of the hands and feet can be formed by bone or just the skin, as well as partial or total. There are also recurring eye and hearing problems, as in other craniofacial syndromes, due to delayed closure of the cranial sutures (Iieri *et al*.; Almeida *et al*.).

Oral Manifestations: Premature fusion of specific cranial sutures causes maxillo-mandibular hypoplasia, creating the cuneiform appearance. The maxillary hypoplasia also causes malocclusion, irregular placement of teeth, opening of bone formation or palatal cleft palate shaped warhead, due to poor connections between the jaws (a result of misshapen hypoplasia) (Almeida *et al*.).

Regarding the pharyngeal tract, the presence of a decrease of pharyngeal cavity resulting from premature closure of the spheno-occipital suture is common. Limitations are also observed in the transverse growth of the palate-pharyngeal arch (Iieri *et al*.).

Nasal cavities and paranasal sinuses are also affected causing a limitation in respiratory capacity, as well as decreased taste. Such changes cause difficulties in speaking and breathing, as in chewing and swallowing process (Vadiati Saberi *et al*., 2012).

Types of Treatment: Basically, the treatment is surgery, especially when the disease is diagnosed early, in order to correct the orthognathic problems and facial matching. Orthodontic treatment with the aid of an intra-oral device is recommended for patients beyond the growth period and, therefore, already having a slightly stable stomatognathic system (Vadiati Saberi *et al*).

Mandibulofacial Dysostosis. Also known as Treacher Collins syndrome is a craniofacial disorder characterized by symmetrical abnormalities of structures originating from the 1st and 2nd arches of head development. The mutant gene that causes the disease possibly found on the long arm of chromosome 5 (5q). It is believed that the manifestation of the characteristics of this mutant gene happens during the seventh week of gestation, the period of formation of cephalic bones (Chang & Steinbacher, 2012; Chung *et al*., 2012).

Prevalence is variable, and is considered a very rare disorder, and highly variable expressivity in relation to the signs. The probability of an offspring inheriting the gene encoding the disorder is 50%, if one of their parents is affected (Masoti *et al*., 2009).

General Physical Manifestations: The main manifestations are related to the skull and adjacent systems. The neurocranium, or skull itself, suffers a reduction in anteroposterior and lateral-lateral sides and may be extended until the end of puberty. Hypoplasia of the zygomatic bone creates a lack of volume in the malar region, with or without cleft zygomatic. The visual defects are caused by inclination of the palpebral fissures, and consequent reduction of ocular orbital space. Audio systems are also affected, atresia of the external pinna may occur, as well as partial or total deafness. Ocular colobomas that reach all parts of the structures that comprise the visual system can cause blindness and give the subject the appearance of cat eyes (Trainor *et al*. 2009; Trainor, 2012; Silva *et al*., 2008).

Oral Manifestations: Includes mandibular and pharyngeal hypoplasia with impairment of masticatory, phonetic and respiratory functions. Respiratory impairment is related to the decrease of the space of choanal. Cleft palate, high arched palate, absence or retraction of the soft palate generate abnormal spacing of the teeth, and therefore malocclusion. The damage to function of the temporomandibular joint and mastication muscles differ between patients, and are evident in most cases. Retraction of the lingual position occurs less frequently due to micrognathia. Micrognathia is also responsible for excess divergence angles of the mandibular and mental. There is variation in the size of oropharyngeal resonance boxes, featuring an incongruous aspect causing defects in the voice (Chang & Steinbacher; Chung *et al*.; Trainor; Trainor *et al*.; Silva *et al*.).

Types of Treatment: If the diagnosis of the disorder is intrauterine, even during the prenatal period it is advisable to begin family orientation, about the care to be taken from birth. In the first months of life, the intubation may be complicated due to the small size of the nasal passages. Therefore, tracheostomy is usually well suited in these cases, and also for its efficiency. In the presence of cleft palate, surgical procedures are usually indicated only when the affected individual reaches the age of literacy. Associated with the use of orthodontic therapy, surgical procedures are effective to prevent jaws and dentofacial biggest problems. Bone grafts and plastic surgeries are quite suitable for reconstruction and matching face (Chung *et al*.; Trainor; Trainor *et al*.; Silva *et al*.).

Achondroplasia. Is a disorder which expresses the encoding of the mutation of a gene, which is still unknown. It is believed that a problem with the fibroblasts receptor type 3 of the endochondral growth of long bones plate affects the cartilage plate, so as to always keep it active, and thus affecting the growth of these bones. It is one of the oldest known disorders, reported in several distinct historical periods and representing an endemic disease in specific regions of the planet. Despite being a genetic disorder with autosomal dominant inheritance, currently about 80% of new cases arose due to the existing high mutability of the disorder gene encoding (Arishima *et al*., 2013).

General Physical Manifestations: Short stature is the result of hypoplasia of endochondral bone plate of long bones, characterized disproportionately lower members in relation to the size of the stem, which is normal. The fingers are arranged with extra spacing, giving a tridente aspect. Mainly the separation between the third and fourth finger are observed. The skull is hypertrophied (macrocephaly) and disproportionate to

face. The abdomen is prominent, due to vertebro-columnar problems, in the first years of life (Kaissi *et al*., 2013).

Oral Manifestations: The main manifestations are related to mandibular prognathism. The prognathism observed is relative, since the problem is hypoplasia of the maxilla and other facial bones. The pseudo-prognathism, or anomalous disparity between the sizes of the mandible and maxilla generates malocclusion, spacing issues and organization of teeth, and in most cases the presence of problems with the central incisors and the molars (Saito *et al*, 2013).

The dental growth is normal, but is hampered by the delay in bone growth related to the sphenoid-occipital craniosynostosis, moreover, in some cases, the presence of supernumerary teeth with taurodontia and deterioration of tooth root is emphasized. Due to abnormal spacing between the teeth, the presence of diastema is inevitably observed, especially in the teeth of the lower arch. Tooth agenesis, chronic gingivitis and bone loss function are also observed (Saito *et al*, 2013; Shinde *et al*., 2013).

Types of Treatment: Surgical procedures are formed as the main alternative for patients with hypoplastic genetic disorders. Surgery is indicated for increasing the size of the members as to harmonize the face. Surgery for localproblems, such as abnormal dentition, twisting ankles, narrowing of the vertebral canals in thoracic and lumbar regions. Such procedures, however, should be associated with orthodontic therapy and physiotherapy to improve dental and postural reeducation conditions, reaching maximum effectiveness in treating (Kaissi *et al*., 2013; Saito *et al*.; Shinde *et al*.).

Through this study the importance of the study of genetic syndromes was noted, highlighting oral pathological manifestations, which are of fundamental importance to the dentist. Among the manifestations of the above anomalies, the most common in most disorders are malocclusion, delayed bone growth, presence of supernumerary teeth and mandibular hypoplasia. Usually, treatment is based on psychological treatment combined with surgery. However, there is no cure for such chromosomal events, so patients are only offered palliative treatments.

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RESUMEN: Las enfermedades genéticas se producen debido a un exceso o ausencia de material cromosómico, y la consecuencia de estos cambios se refleja en los cambios morfológicos y fisiológicos. Trastornos autosómicos dominantes que tienen herencia dominante, como la disostosis cleidocraneal, el síndrome craneofacial de Apert, Treacher Collins y acondroplasia tiene características peculiares y similares. Debido a sus implicaciones en el campo de la odontología, el objetivo de esta revisión es hablar, a través de la exposición de los factores clínicos y generales, destacando los signos en la cavidad oral. Se seleccionaron los artículos de las bases de datos Lilacs, PubMed y BIREME, incluyendo los años 2007-2014, y las palabras clave fueron: displasia cleidocraneal, craneofacial mandibulofacial disostosis, disostosis y oral. Los cambios de huesos maxilofaciales y craneofaciales están bien documentados en la literatura, pero los estudios que informaron una asociación entre el tratamiento dental y disostosis son escasos. En conclusion, las manifestaciones orales son causas de dificultades del habla, masticación, respiración y la participación social.

PALABRAS CLAVE: dysplasia cleidocraneal, disostosis craniofacial, disostosis mandibulofacial.

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