INTERNATIONAL JOURNAL OF
INTEGRATIVE AND
MODERN MEDICINE

Genetic Change during Orthodontic Treatment on the Upper and Lower Jaw

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Abstract: The development of craniofacial complex and dental structures is a complex and delicate process guided by specific genetic mechanisms. Genetic and environmental factors can influence the execution of these mechanisms and result in abnormalities. An insight into the mechanisms and genes involved in the development of orofacial and dental structures has gradually gained by pedigree analysis of families and twin studies as well as experimental studies on vertebrate models. The development of novel treatment techniques depends on in-depth knowledge of the various molecular or cellular processes and genes involved in the development of the orofacial complex. This review article thus aims to explore the link between role of genes in the development of dentofacial abnormalities and malocclusions.

Keywords: Genetics, malocclusion, orthodontics, dentofacial anomalies, craniofacial malocclusion.

Introduction. Many authors have noticed, that in children with Central Asia , flattening and falling of tissues in the zygomatic region on the side of the lesion are expressed due to underdevelopment of the upper jaw and zygomatic bone. However, the underdevelopment of the cheekbone on the side of the lesion, manifested by in their asymmetry, it indicates the severity of a congenital anomaly, which in this variant also affects other bones of the facial skeleton, as well as the base of the skull [3].

The underdevelopment of the upper jaw and zygomatic bone on the non-fusion side [1, 2] is also confirmed by changes in the parameters on the TRG of the head in the lateral and direct projections: narrowing at the level of the zygomatic bones (Z-Z), shortening of the anterior part of the base of the skull (N-S), shortening of the posterior upper height of the face (NSL-PNS), retroposition of the apical basis of the upper jaw (<SNA). In patients with upper micro- and retrognathia, it is found retroposition of the mandible (<SNB< norm), as well as the displacement of the chin point in the direction of non-fusion.

Materials and methods of research. Mandibular prognathismis caused by a deficiency of the maxillary growth, excessive mandibular growth, or a combination of both. Familial studies of mandibular prognathism are suggestive of heredity in the etiology of this condition. Various models have been suggested, such as autosomal dominant with incomplete penetrance, simple recessive, variable both in expressivity and penetrance with differences in different racial populations. The familial nature of mandibular prognathismwas first reported by Strohmayer as noted by Wolff et al. in their analysis of the pedigree of the Habsburg family. The Habsburg jaw is seen in European royalty in which mandibular prognathism recurred over multiple generations. The genetic factors appear to be heterogeneous with monogenic influence (usually autosomal dominant with incomplete penetrance and variable expressivity) in some families and multifactorial (polygenic complex) influence in others.The clinical study was conducted in 22 children with Central Asia aged 9 to 12 years, including 17 patients who were treated after surgical correction of the position of the segments of the upper jaw, and 5 patients in the control group. The main group included patients with different genetic determinations. Out of 17 children, 5 were determined by distal occlusion (genetic similarity with a parent who had distal occlusion, according to photo-, bio- and ephalometry). 3 patients with OSNGN without genetic determination of sagittal abnormalities, but the parents had violations in the transversal and vertical

planes. The remaining 9 patients were a group of the most pronounced degree of mesial occlusion of the gnaticform, since there was a genetic determination of mesial occlusion. The control group consisted of patients with OSNGN from 9 to 12 years old, who underwent cheilo- and uranoplasty by various methods and in different regions of Russia in a timely manner, but after 6 years the most comprehensive treatment was not carried out due to pronounced general somatic disorders, change of residence, socialfactors, remoteness of specializedmedical institutions, disorganization,etc.

Biometric diagnostics was performed in all patients when studying jaw models, X–ray diagnostics - when studying op topantomograms, lateral cephalograms (TRG) and computed tomograms. Lateral cephalometrywas performed using CT images. Patients undergoing treatment, latralcephalometry of the head was performed according to CT scans 4 times: before treatment, after treatment (protraction on the face mask), after 1 and after 3 years. Patients of control groups – twice.

Results and discussion. Dental agenesis, which is the most common developmental anomaly seen in humans, is genetically and phenotypically a heterogeneous condition. Based on the current knowledge of genes and the factors involved in the tooth development and morphogenesis, it is assumed that different phenotypic forms are caused by different genes involving different interacting molecular pathways, providing an explanation not only for the wide variety in agenesis patterns but also for associations of dental agenesis with other oral anomalies. More than 200 genes have so far been identified, which are expressed during tooth development, and mutations in several of these genes are known to cause arrested tooth development in mice.

Population studies have shown that tooth agenesis can be manifested as an isolated trait or part of a syndrome. Isolated forms may be either sporadic or familial. Familial tooth agenesis can be the result of a single dominant gene defect or recessive or X-linked. Third molar agenesis cannot be explained in most of the cases with a simple model of autosomal dominant transmission. Besides, a polygenic mode of inheritance has also been reported in the literature. Grahnen stated that tooth agenesis is typically transmitted as an autosomal dominant trait with incomplete penetrance and variable expressivity. Twin studies have been widely used to show the importance of the genetic component involved during tooth development to control both tooth size and form. There are numerous case reports, suggesting concordance for tooth agenesis in monozygotic twins, and case reports where variation in the expressivity is observed.

Numerous mutations in transcription factor and growth factor-related genes involved in dental development have been shown to play a role in human dental agenesis, including paired box 9 (PAX9), a transcription factor, and muscle segment homeobox 1 (MSX1). MSX1 gene mutations can lead to hypodontia or oligodontia as well as variations in the downstream signaling gene bone morphogenetic protein 4 (BMP4). In humans, a point mutation in MSX1 homeobox results in agenesis of second premolars and third molars in affected individuals.

Mutations in PAX9 typically show a nonsyndromic autosomal dominant mode of inheritance for oligodontia, with variable expressivity within families. The characteristic pattern of dental agenesis caused by PAX9 mutations primarily affects molars in both dental arches and second premolars most often in the maxillary arch than the mandibular arch, occasionally presenting with missing or peg-shaped mandibular central incisors and maxillary lateral incisors. Agenesis of maxillary first premolars or canines can occur with a low frequency among PAX9 mutations. In contrast, the PAX9 Ala240Pro mutation may be unique, in that it leads uniquely to third molar agenesis with or without affected incisors. Mutations in the axis inhibitor 2 gene (AXIN2) have also been linked to oligodontia, often exhibiting a similar pattern of affected teeth as PAX9 mutations. From this, it is clear that the functions of PAX9 and MSX1 are essential for the establishment of the odontogenic potential of the mesenchyme through the maintenance of mesenchymal Bmp4 expression. However, the relationship between these three genes on the molecular level remains unknown.

Primary failure of eruption (PFE), which was described initially by Profitt and Vig, is characterized by nonsyndromic eruption failure of permanent teeth in the absence of mechanical obstruction. Many studies have stated the heritable basis of this dental phenotype, and recently, mutations in parathyroid

hormone receptor 1 (PTH1R) have been identified. It functions in signaling in mesenchymal progenitors, alveolar bone formation, and periodontal ligament development during eruption physiology. The recent report of PTH1R mutations associated with primary failure of eruption makes this a high-priority candidate gene for confirming the diagnosis of a nonsyndromic PFE phenotype.

Crowding of teeth is a complex dental anomaly that affects esthetics and quality of life. Crowding is usually caused by insufficient arch space that cannot accommodate all erupting permanent teeth. Genetics is suggested to contribute to the etiology of crowding. A study conducted by Ting et al suggested a significant association for the genes ectodysplasin A (EDA) and X-linked ectodermal dysplasia receptor (XEDAR), which are important in the signaling pathway that plays a role in the development of dental crowding among the Hong Kong Chinese population. Since this association study was done in the Hong Kong Chinese population, the results might not apply to other ethnic groups. Further replication studies in other ethnic groups with a larger sample size are vital for confirmation of these findings.

A genetic tendency for ectopic maxillary canines has also been reported in various association studies. Peck et al concluded that palatally ectopic canines, as an inherited trait, is one of the anomalies in a complex of genetically related dental disturbances, often occurring in combination with missing teeth, tooth size reduction, supernumerary teeth, and other ectopically positioned teeth. Previous studies have also shown an association between ectopic maxillary canines and class II division 2 malocclusion, a genetically inherited trait.

Genetic variation showing a significant effect on arch width and length was confirmed in various studies on monozygotic and dizygotic twins. A genetic contribution to arch shape was found by Richards et al after comparing the intraclass correlations between monozygotic and dizygotic South Australian twins.

A study was conducted by Corruccini et al on the occlusal characteristics in 32 pairs of monozygotic twins and 28 pairs of dizygotic twins using dental stone casts. They studied arch shape, size, and symmetry, overjet, overbite, posterior crossbite, buccal segment relation, rotation, and displacements. They concluded that arch size variation, tooth displacement, and crossbite showed significant genetic variance and also found an increased environmental component of variance in occlusion. A study on north-west Indian twins revealed significant genetic variance for dental arch and palate dimensions, but environmental influences seemed important for occlusal traits.

Conclusion. The knowledge of the role of genetics is essential for the orthodontist which helps to understand why a patient has a particular occlusion, because malocclusion is a manifestation of genetic and environmental interaction on the development of the orofacial complex. Awareness regarding the genetic expression of the dentofacialmal development is an essential aid in the correction of malocclusion, as it helps to segregate the inherited malocclusions from those due to the effect of environmental factors and thereby helps to diagnose, treat, and possibly even prevent a malocclusion from occurring in the next generation.

There has been immense progress in the field of genetically supported orthodontics to date. Although it is very challenging to reveal the genetic component of most malocclusions and dental anomalies because of its polygenic nature, data developed and provided by the human genome project have made it feasible to map inherited conditions related to the dentofacial development. However, further genetic studies are required to determine all the specific genes leading to a particular skeletal variability. Genome-wide association studies are necessary to evaluate further as well as provide a database for evidence-based practice.

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