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REVIEW ARTICLE

Genetic Bases of Orthodontics: A Review

Zainab Mousa Kadhom [1]

[1] Department of Orthodontic, College of Dentistry, University of Baghdad, Baghdad, Iraq.

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Corresponding author:
Zainab Mousa Kadhom
Email: schati1981@yahoo.com
Department of Orthodontic
College of Dentistry
University of Baghdad
Baghdad, Iraq

ABSTRACT

Objectives: This review aimed to show the genetic components of malocclusion and craniofacial disorders to assist in understanding the causes of the presence of a particular occlusion or dentofacial anomalies in some patients and considering genetic factors as an important element to diagnose the dentofacial disturbances and the malocclusion of genetic origin.

Conclusion: The genetics parts in orthodontics should be considered to recognize the reasons for certain occlusion in some individuals. Furthermore, detecting a genetic component's role in most dental anomalies and malocclusions is very challenging because of its polygenic nature.

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INTRODUCTION

The interaction between different genetic and environmental factors over time result in growth.[1] Malocclusion display the influence of environmental and genetic on the development of the orofacial area. The genetic factors consideration is very important in the diagnosis of dentofacial anomalies. So orthodontists may be concerned in genetics to realize the cause of particular occlusion in the patient.[2] The science that deals with the structure of all genes and their function is genetics. The "father of modern genetics" is Austrian monk, Gregor John Mendel, He put forward. The basic genetics laws had been put ahead by him: the law of segregation, law dominance law, and independent assortment law. While the "Chromosomal Theory of Inheritance" had been proposed by Sulton and Boveri in 1903.[3] Genetics has detected that any two persons share 99.9% of their DNA sequences. Thus, the remarkable variety of humans is encoded in about 0.1% of our DNA.[4] The chromosome model by Solenoid was suggested by Finch and Klung. Where Thomas Hunt Morgan studied the genes ordering along chromosomes. Moreover, Watson and Crick explained the composition of DNA molecules in 1953.[3]

In the fifth century BC in Greece, the first evidence of inheritance was improved by Hippocrates according to Stent (1971), which can be termed as 'Bricks and mortar theory was the name of Hippocrates ideas' which states that hereditary material consists of physical matter. He assumed that a human in the womb comes from all parts of the body concentrated in male semen. Aristotle criticized Hippocrates theory a century later and instead proposed that heredity included transmitting information- a blueprint model'. Aristotle rejected hippocrates' theory for several causes. He referred to that persons sometimes like remote ancestors rather than their immediate parents.[5]

The basic unit of any living body is many organelles such as cell wall cytoplasm, endoplasmic reticulum, ribosomes, mitochondria, and nucleus, which form the cell. The chromosomes are the threadlike structures present in the nucleus in different shapes and lengths. Although, a cell of an organism has a constant number of chromosomes, they changes among the species. Usually, there are 23 pairs of chromosomes as 22 pairs of autosomes, and one pair of sex chromosomes found in a human. Male contains one X- and one Y-chromosome, while two X chromosomes present in females.[3] The entire genetic content is found in the genome as a chromosomes group within a cell or an organism.

Genes act as the smallest functional and physical units of inheritance within the genome that resides in certain positions called ―loci‖ or ―locus‖ for a single location. In 1909 the gene term was coined by Wilhelm Johannsen. Initially, the gene was defined as the unit of genetic information that controls a particular aspect of the phenotype, and they specify of one polypeptide formation.[6] Also, it was regarded as the whole DNA sequence substantial in the molecule of functional polypeptide formation a (synthesis of a protein by a messenger RNA intermediate) or RNA molecule (ribosomal RNA and transfer RNA). Electively the gene has the 5′ and 3′ non-coding areas participating in organizing translation and transcription of the gene and all introns within the gene. The structural gene refers to the portion that is transcribed to produce the RNA product.[7] The alterations that promote by a particular factor in the synthesis of the DNA base pairs are known as gene mutations, leading to a change in the expression of particular traits and protein synthesis. Mutagens are certain viruses, ionizing radiation, chemicals, and rise temperature.[8]

This review aimed to show the genetic components of malocclusion and Craniofacial disorders to assist in understanding the causes of the presence of a particular occlusion or dentofacial anomalies in some patients and considering genetic factors as an important element to diagnose the dentofacial disturbances and the malocclusion of genetic origin.

The heritability studies of dentoalveolar occlusal and craniofacial skeletal disorders

The twin and familial studies represent the bulk of the evidence for the heritability of different types of malocclusion. The heritability assessment methods are based on measurements and correlation of the traits among different children of person's pairs in families, which include:

1. Twins of Monozygotic
2. Twins of Dizygotic
3. Sib-Sib (Sibling Pairs)
4. Parent-Child[9]

Most studies except sib ships and twin pairs, including single or multiple treated patients (with intermediate to severe malocclusion).[10] The best evidence in the foundation of the relative contribution of environment and genes in the malocclusion development are Twin studies. Twins are either Monozygotic twins or Dizygotic twins.[11] Twin studies and pedigree studies/ familial studies are studied the heritability patterns. The genetic factors have an extreme effect on occlusal traits, as revealed through the twin studies.[3,8]

Therefore, the defect in considering general ecological influences can contribute to the rating of genetic and environmental effects. While in the Familial studies/pedigree studies the kind of inheritability of traits can be studied by the family trees building which named lineages in which the circles refer to the females and males symbolized by squares and then observing who in the family has the trait and who does not.[12] The inheritance manner of successive generations could be assessed by a particular trait observation of this generation. The consanguineous marriages (Marriage into a family), where interbreeding is permitted, are the best to study the autosomal recessive traits.[13] Many investigations that seek occlusal traits show that genetic change has more influences with phenotypic changes for jaw length and jaw width than for overbite, overjet, and molar relationship, although the decrease of heritability estimations. While the environmental change affects more than genetic variation on the arch size and shape[14] In Hawaii, the research about varied interbred ethnic groups discovered there is no increased risk of malocclusion in the children of racial crosses except what would have been anticipated from the usual parental effect. As well as that, the people who have traveled recently into an industrialized lifestyle have very fast increased in malocclusion due to genetic variation caused by gradual development healthiness pressure.[15] The isolated industrialized (urbanized) populations have less severe and less frequent malocclusion. Usually, the malocclusion occurs highly as these inhabitants are “civilized” or become more urbanized. This occurs because of the interbreeding of populations with a certain degree of variable physical characteristics, presumably resulting in a synergistic disproportion of the relationships between the arches and teeth. The crossbreeding trails that Stockard and Anderson[16] have done in inbred some of dogs races have supported this idea, where a mismatch of the jaws leads to increasing malocclusion.

Craniofacial disorders and genetic etiology of malocclusion

A. Types of malocclusion with genetic causes

1. Class III malocclusion

The genetic component of malocclusion comes from monitoring mandibular protrusion (frequently related to Angle’s Class III) discrimination in families. The House of Habsburg, is the best-known example which produced kings and emperors of Bohemia (current Czech Republic), England, Germany, Croatia, Illyria (an Austria area Hungary, the Mexican second empire, Portugal, Ireland, Spain, and many principalities and directors of Denmark and Italy.[17] Other studies, such as twin studies and Suzuki’s (1961) study on 243 Japanese families, have also proposed that mandibular prognathism has strong genetic basis. Although class III malocclusion could result from various environmental factors, such as premature loss of permanent

molars due to trauma, enlarged tonsils, nasal blockage, and posture, an autosomal dominant model is best suitable to the overall inheritance pattern.[18] There is an understanding that the mandibular prognathism follows an autosomal predominant Mendelian manner of inheritance (monogenic or isolated gene) because many of these cases aggregate in families.[19] To date, to identify the genetic mutations effectively, they are thought to cause Class III malocclusion than the association studies of Class III are DNA sequencing technologies in conjunction with family linkage analyses. Therefore, it is necessary to sub classify patients according to their form with a combination of cephalogram and/or geometric morphometric information for outlook researches of many unrelated patients who have a Class III malocclusion and to better study the genetics of the dominant subtype(s)of dental and skeletal Class III a cross families.[20]

2. Hypodontia

Although Hypodontia is often familial, it may happen when the household has no history of hypodontia, in addition it present as part of a syndrome, mostly in one of the many types of ectodermal dysplasia, Although it generally occurs lonely(secluded). Genetic factors are supposed to play the main part in most cases, with autosomal recessive, X-linked, autosomal dominant, and multiple agent inheritance officially described.[21] One of the most prevalent, if not the most common example of hypodontia (precluding the third molars) includes the upper lateral incisors. This may be an autosomal dominant trait with imperfect penetrance and changeable meaningfully as proofed by the phenotype at some points being a peg-shaped lateral instead of agenesis, sometimes involving both sides or the other some points "skipping" generations.[22] It was a proposal that multiple factors with polygenic influence on the teeth patterning and size, for existing hypodontia in some families, the apparent teeth may still small; however, the relatives do not have hypodontia.[23]

3. Impaction\Ectopic of maxillary canine

About15% of upper canine displacement or impaction cases are buccal/labial to the jaw and sometimes related to dental crowding. But when the impaction or displacement of canine palatally occurs (which is represent about 85%) of the cases it is not correlated with the crowding of teeth.[24] Frequent displacement of canines Palatally, but not always, are found in dentitions with several anomalies. Such as hypodontia, including other teeth, small, missing maxillary lateral incisors or peg-shaped dentitions with delayed development, and dental spacing.[25]

There is a relation between class II malocclusion and ectopic maxillary canines, as have to be seen by (Mossy, et al in 1994 and others),[26] and this has a strong basis. Commonly, the class position of maxillary canine/first premolar affected by tooth transposition and display a familial occurrence. However, there has been some discussion about the influence of genetic factors to some degree on palatally displaced canines themselves, since of different degrees of genetic effect on these anomalies. Furthermore, the displacement of the canines in the palatal sides has appeared in the general population less than within families.[27]

4. Genetic Implications on Orthodontic Tooth Movement

The genes effectiveness in directing angiogenesis, osteoblast formation, inflammation and remodeling of extracellular matrix occur due to the primary response to the thorough forces.[28] To date, various molecular paths that influence the orthodontic movement of the teeth are identified. There are two ways that effect on both external apical root resorption and orthodontic tooth movement involve the RANKL/RANK/OPG pathway of bone modelling and remodeling and the ATP/P2XR7/IL-1B inflammatory signaling pathway.

Minor studies have concentrated on determining how fundamental changes in non-syndromic genetic factors corresponded with the actual clinical results observed during OTM in humans, although this comprehension of key pathways affecting the orthodontic movement of teeth.[29] The outcome of orthodontic treatment can be forecasted by the osteopontine protein that is thought to be a strong biomarker because it plays a part in periodontal and bone remodeling.[17] Many studies have been done with genetic variation markers depend on the part of the ATP/P2RX7/ IL-1B pathway, the genes related cytokine interleukin 1 α IL-1α the genes (IL1B and IL1A, respectively), for IL-1β and another and the gene (IL1RN) for another molecular pathway (IL-1 receptor antagonist, IL-RA) that assist the regulation of their action biologically.[30] Interleukin 1 β-IL-1β is the most powerful for inhibiting the bone formation and bone resorption of these two types. Therefore, orthodontic tooth movement needs an equilibrium between IL-1β and IL-1RA formation for the bone remodeling and modelling procedures.[31]

Dentofacial disturbances of genetic origin

1. Cleidocranial dysplasia

Cleidocranial dysplasia (CCD) is an autosomal dominant bony dysplasia identified by a defect in both endochondral and intramembranous bones ossification, with severe dental anomalies been identified as the cause of The CCD caused by the RUNX2 (formerly CBFA1) gene mutations which located on chromosome 6p12-21.[32] It is autosomal dominant mode and also known as cleidocranial or mutational dysostosis. Missing of clavicles, maxillary hypoplasia with pragmatic mandible, supernumerary teeth, eruption failure of the permanent dentition, fontanels closure retarded, the underdevelopment of bones and jaws, bulging of the forehead, and delayed ossification of midline structures, are the Clinical features of CCD [33].

2. Cleft Lip and Cleft Palate

The most common congenital anomalies to affect the craniofacial region in man are clefts involving the lip and/or palate (CLP) or secluded clefts of the palate (CP).[34]

It is separated or related to syndromes, and it occurs when the body's natural structures did not fuse before birth. The cleft

palate caused by the non-fusion of median palatine processes, while non-fusion of lateral nasal and maxillary process cause Cleft of the Lip. The mutations in MSX2, MSX1, FGFR1, FGFR2, and BMP4. MSX1 and MSX2 genes caused Cleft Lip and Cleft Palate in both syndromic and non-syndromic clefts. The Cleft Lip and Palate patient clinically appears with delayed tooth eruption and development, hypodontia or hyperdontia, feeding, speech, socialization problems, and smaller facial dimensions.[35]

3. Hemifacial Microsomia

In around 1:5600 of children occurs Hemifacial microsomia (HFM) and is usually infrequent, even though autosomal dominant familial cases have been determined, it is commonly associated primarily with unilateral developmental defects in the orofacial region HFM

The patient with Hemifacial microsomia has Skeletal asymmetry of the facial region, associated with unilateral aplasia or hypoplasia of the mandibular condyle and ramus; with flattening of the facial bones and reducing size, and a marked retrognathia, associated with canting of the occlusal plane and mandibular asymmetry.[36]

In this condition, the first branchial arch tissues are deficient. Hemifacial microsomia induces by gene OTX2 duplication. Around the 6th week of intrauterine development, a hemorrhage from the stapedial artery may be founded. This hemorrhage led to damage and reorganization of tissues subsequently, so there was a complete failure of the tissue development or they may become smaller.[3]

4. Treacher Collins syndrome

Treacher Collins syndrome or mandibulofacial dysostosis (TCS) exists in about 1: 50 000 live childbirths, so it is an uncommon autosomal dominant defect of facial development. The tissues derived from 1 and 2 pharyngeal arches are the most affected facial regions, but even amongst persons within the same origin, there can be a significant change in the intensity of clinical manifestation. The Down-slanting palpebral fissures, Isolated cleft palate, present in around one-third of cases; Zygomatic, supraorbital, and mandibular hypoplasia and Usually a severely class II skeletal malocclusion with increased vertical dimension due to deficiency of the mandible and growth rotation of the mandible posteriorly. Are regarded as a common characteristic of facial appearance.[36]

It shows autosomal dominant transmission with a wide speed deficient mesenchymal tissue. The specific genes - TCOF1 (POLR1C and POLR1D).mutations give rise that. The migration of neural crest cell are controlled by treacle protein TCOF1 gene codes during craniofacial development.[37]

CONCLUSIONS

The genetics parts in orthodontics should be considered to recognize the reasons for certain occlusion in some individuals. The interaction between different genetic and environmental factors over time may affect the manner of growth and development. Also, the malocclusion treatment depends on the understanding of the genetic expression of the dentofacial maldevelopment, and this assist in differentiate inherited malocclusions from those caused by environmental factors.

Moreover, the detection of genetic components' role in most dental anomalies and malocclusions is very challenging because of its polygenic nature. Therefore, further evaluation of the genome studies is very important to provide a database for evidence-based practice.

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