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Fundaments Of Genetics And Malocclusion

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Abstract
Etiology of malocclusion plays important role in proper diagnosis and treatment and that plays major role in success of orthodontic treatment. Growth of an individual is combined result of both genetic factor and environmental factor interaction on the development of orofacial region. Genetics plays major role in etiology of the malocclusion. Effects of genetics on etiology of dentofacial characteristics in the branch of genetics allowed the orthodontists to better understand the effects of genetics with advances. For investigation of genetically determined variables of malocclusion twin study is one of the most effective methods. This review article focuses on the fundaments of genetics and the effect of genetic factors on various malocclusions.

Keywords: Malocclusion, Genetics, Twin Study

Introduction

The malocclusion is a misalignment of teeth and jaws that may cause to deformed facial appearance, limited or restricted function of mastication, and chances of increased risk for dental trauma, and compromise quality of life[1, 2].It is important to understand the causative factors leading to the variability in dentofacial morphology associated with different type of malocclusions to develop innovative treatment modality approaches. Genetics is the discipline of biology science of heredity and the inheritance of variation and traits of living organisms. For variability in different type of the malocclusion the interactions between genetic factors and environmental factors are responsible.

The interactions of genetic and environmental factors may account for the variability in expression of malocclusion.

Horowitz et al. (1960) studied fraternal and identical adult twin pairs using only linear cephalometric measurements, and he also demonstrated highly significant hereditary variations in the anterior cranial base, mandibular body length, lower face height, and total face height[3]. Hunter (1965) did study and also used linear measurements on lateral cephalograms and concluded that there is astronger genetic component of variability for vertical measurements, rather than for measurements in the anteroposterior dimension[4].According to Fernex et al. (1967), he found that girls show less similarities to their parents than boys and boys shows more similarities. Transmissions of similarities from mothers to son were more as compare to mothers to daughters in skeletal structures of face. When comparison was made of facial features between female and male twin they concluded male twins showed lesser concordance than female twins[5]. In 1970, Litton et al. did genetic study on class III malocclusion and concluded that siblings usually show similar types of malocclusion and he also summarizes that older siblings can provide a clue to the need for interception and early treatment of malocclusion[6].

Due to various studies on genetics they found that these orofacial structures are under genetic control and are significant in craniofacial development they must be considered in the causative factor of malocclusion. Understanding the genetics will aid in progress towards effective treatment and prevention of malocclusion.

Twin Studies In Malocclusion:

When the twin method is appropriately applied it helps geneticists for diagnosis of genetic trait which is complex. To know the heredity of orofacial and dentofacial structures, another substitute method is by familial studies. In such studies heritability is revealed in terms of parents/offspring and also in siblings where twins are of special kind [7, 8]

In twins, the study of the craniofacial relationship has provided abundant information to now the heritability of the malocclusion. The procedure of the twin study observed difference between monozygotic twins, whose genotype are identical and in dizygotic twins who share about 50% of total genotype and 50% total environment [9, 10]

Class II Division 1 Malocclusion

To determine the heritability of various craniofacial patterns in class II Division 1 malocclusion there are many studies that have been carried out [11.] In the Class II patient, the cephalometric investigations have shown that, the mandible is significantly retruded more than in Class I patients. The body of the mandible is smaller and overall mandibular length reduced. These studies also concluded a and supported the concept of polygenic inheritance for Class II division 1 malocclusions which is due to higher correlation between patient and his family as compared to random pair of unrelated siblings[12, 13]

The environmental factors are also contributing factor for the cause of Class II division 1 malocclusions. Soft tissues can exert an impact on inclination or position of upper and lower incisors. The need to achieve lip and /or tongue contact for an anterior oral seal during swallowing may lead the lower lip to retrocline the lower incisors and the protruding tongue may lead proclination of the upper incisors and that will influences overjet to become severe. Even if the person has skeletal base relation class 1, digit sucking can lead to class II division 1 malocclusion. Incompetent lips also encourage upper incisor proclination by virtue of both lingual and labial pressure on teeth[14].

Class II Division 2 Malocclusion:

This type of the malocclusion is a definite clinical entity which is more compatible collection of definable morphometric features occurring simultaneously i.e. it is a syndrome and is accompanied by specific morphometric dental feature with poorly developed cingulum and characteristic angulation of crown.

In 1998, Peck et al. described when teeth are measured mesiodistally they appeared smaller than average teeth [15]. In 1969, similar study was studied by Beresford and in 1965 a study by Roberston and Hilton , where they found out that these teeth are significantly thinner in the labial lingual dimension [16,17]. A further characteristic feature of the Class II division 2 ‘syndrome’ is a likelihood to a forwardly rotating mandibular development, which leads to the chin prominence, deep bite and reduced lower face height. This probable last feature has an influence in the position of the lower lip relation to the upper incisors. An increase in masticatory muscle forces has been reported by Quinn and Yoshikawa (1985)[18].

Markovic (1992) carried out a clinical and cephalometric study where he considered 114 patients of Class II division 2 malocclusions. He studied pairs of 48 twins and six sets of triplets[19]. To determine concordance/discordance rates for monozygotic twins and dizygotic twins, Intra and inter pair comparisons were made. In monozygotic twin pairs, 100 percent reveal concordance for this type of malocclusion, i.e class II division 2, while almost 90 per cent of the dizygotic twin pairs were discordant. This is strong evidence for heredity as the main causative factor in the evolution of Class II division 2 malocclusions.

Ballard (1963), Houston (1975), Mills (1982) considered that particular lip morphology and high lip line and behavior were the main contributing factors in it [20]. Graber (1972), Hotz (1974), Meskov (1988), and Markovic (1992) concluded that genetic factors play a key role in the aetiology of Class II division 2 malocclusions [21-23]. Aspects of muscle and skeletal morphology both are being genetically determined and also there is some recent experimental conclusion from a twin study

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(Lauweryns et al. 1995) that indicates strong genetic factors in behavior of masticatory muscle [24].

Class III Malocclusion:

A genetic trait is the one of the most well known example of trait that elapse in humans through several generations is the pedigree of the so-called Hapsburg jaw probably. This was the very famous mandibular prognathism which was concluded by several generations of the Austrian/Hungarian dual monarchy.

When Strohmayer (1937) did pedigree analysis of the Hapsburg family line he concluded that the prognathic mandible was passed as an autosomal dominant trait.[25] Suzuki (1961) studied 1362 persons from 243 Japanese families and summarized that, while the cases had prognathic mandible, there was a significantly higher incidence of this trait in other members of his family (34·3 per cent) in comparison to families of individuals with normal occlusion (7·5 per cent) [26].

Schulze and Weise (1965) also studied mandibular prognathism in both monozygotic and dizygotic twins. The concordance in monozygotic twins was six times higher than among dizygotic twins in conclusion to this study. Both of the above studies concluded a hypothesis which is polygenic as the predominant cause for mandibular prognathism (Litton et al., 1970) [27].

Not only genetic but also enormous number of environmental factors has also been suggested as contributing factor for the development of prognathic mandible. Among these one of them are enlarged tonsils (Angle, 1907), endocrine imbalances (Downs, 1928), posture (Gold, 1949) and trauma/disease including premature loss of the first permanent molars (Gold, 1949) then nasal blockage (Davidov et al., 1961), hormonal disturbances (Pascoe et al., 1960) congenital anatomic defects (Monteleone and Davigneaud, 1963) [28 - 33]. Litton et al. (1970) also studied and analyzed a group of probands, siblings and parents[6].

The polygenic multifactorial threshold model that was put forward by Edwards (1960). The prevalence in siblings of affected persons and in general population was presented by authors and they found out a polygenic model. Polygenic model with threshold was used to determine the familial distribution [34].

Usually soft tissue do not play a part in the of Class III malocclusion, and in fact there is a liability for tongue lip and pressure to camouflage for a skeletal Class III discrepancy by proclining upper incisor and retroclining lower incisors.

Genes Responsible For Malocclusion:

Class II Division 1 Malocclusion

With mandibular hypoplasia a small study of Colombian families has suggested a gene candidate of this jaw size discrepancy. The human NOGGIN genes are one of the modulator of bone morphogenic protein and are essential for various late events in mandibular development. This study which was conducted has shown that all individuals affected with mandibular hypoplasia were homozygous for the rare allele of the polymorphism rs1348322 within the NOG gene.[35] The SNAIL family of zinc-finger transcription factors is the another group of genes that merits attention . These genes are important in epithelial to mesenchymal transitions and are contributing factor for the formation of the mesoderm and the neural crest [36.] The neural crest-specific deletion of Snai on a Snai2-/- background has been in view to cause craniofacial defects in mice, such as cleft palate and mandibular deficiency, indicating that these SNAIL genes may regulate the upper and lower jaw growth[37.] Da Fontoura et al. genotyped individuals with skeletal Class II for 198 single-nucleotide polymorphisms in 71 craniofacial genes and loci. They found out that FGFR2 was associated with increased risk for Class II malocclusion when compared to the control group (Class I), while EDN1 was correlated with reduced risk[38.]

Moreno Uribe et al. identified seven principal components of Class II that accounted for 81% of the variation, representing a variation on mandibular rotation, maxillary incisor angulation, and mandibular length and by cluster analyses they identified, five distinct types of Class II phenotypes[39]. Although this study is descriptive, it gives an important evidence of the different variation of Class II traits, which indicates a significant participation of the interaction of genotype and environment on the regulation of skeletal Class II malocclusions.

Skeletal Class II Division 2

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The skeletal Class II, division 2 malocclusion is characterized by a distinct and consistent clinical phenotype, which includes a combination of retroinclined incisors, deep overbite, and high lip line with a lower lip trap, and high activity of the mentalis muscle which is also known to be syndrome. These skeletal class II patients often present a counterclockwise rotation of mandibular development, prominence of the chin, and reduced lower face height [40, 41.]

All the genes for the mandibular retrognathism in those candidates and deep-bite traits described in the anterior sections are associated as well with this type of division of Class II. While some studies have concluded the mode of inheritance of this type of malocclusion as autosomal dominant with incomplete penetrance and variable expressivity; a polygenic model with expression of a number of genetically determined morphological traits has also been correlated to the Class II, division 2.[42] This malocclusion has also been associated with higher incidence of numerous congenital tooth anomalies, such as missing teeth, peg-shaped laterals, transpositions, supernumerary teeth, and canine impactions, suggesting that genetic factors related to dental development may also play a key role in the maxillomandibular size discrepancies.[43]

Skeletal Class III

Among all the types of sagittal skeletal discrepancies seen, the skeletal Class III is the malocclusion the most studied genetically. Class III malocclusion is mainly caused by a deficiency of the either maxilla growth, excessive mandibular growth, or a combination of both.[42, 44, 45]

The Class III malocclusion is been associated with mandibular height and prognathism and has described with the genes ADAMTS1, ARHGAP21, GHR, Matrilin-1, EPB41, TGFB3, LTBP2, MYO1H, and KAT6B, implying that molecular pathways involved in the development of bone (TGFB3, LTBP, KAT6B) and cartilage (GHR, Matrilin-1) may be implicated in mandibular size discrepancy.[41, 46-53] Other class of genes, IGF1, HOXC,COL2A1, and DUSP6 have been associated not only for with mandibular prognathism, but also with maxillary deficiency.[54-56]

for skeletal Class III malocclusion, Da Fontoura et al. described the single-nucleotide polymorphisms in FGFR2 and COL1A1 as having a higher risk, and the TBX5 gene as a reduced risk for this malocclusion.[38]

Conclusion

There are multiple factors which are responsible for development the malocclusion. Heredity and environmental factors are also one of the factors which are responsible for the cause of the malocclusion. However, the challenge remains on how to determine the contribution of environmental factors and genetic factors in a specific type of skeletal malocclusion. Early detection of the consequences of abnormal craniofacial development and assessment of orthodontic practices will validate the treatments used, establish practice parameters. With the advent of diagnostic techniques in the field of molecular genetics, the orthodontic treatment may take on a completely new direction to treat the cases. Various technological advances may open doors for the development of molecular approach to develop better strategies for the diagnostic, prevention and facilitate treatment modalities

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