British Journal of Pharmaceutical and Medical Research Vol.02, Issue 01, Pg.342-346, January-February 2017

Available Online at http://www.bjpmr.org

BRITISH JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

DOI: In-Process Volume 02, Issue 01, January-February 2017

Review Article

Role of Genetics in Dental Caries

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ARTICLE INFO

Article History:
Received on 29th November, 2016
Peer Reviewed on 24th December 2016
Revised on 19th January, 2017
Published on 02nd February, 2017

Keywords:
Genetics, Twin, heredity, Candidate Genes, Caries.

ABSTRACT

This paper highlights the influence of genetics on vulnerability of dental caries. Heredity and environmental factors has a role i.e. ("flora vs. foster") in the pathogenesis of dental caries and diseases of the periodontium has occupied clinical and basic researchers for decades. Success in the endeavor has come more easily in the case of caries; the complex interactions that occur between host-response mechanisms and mutative microbiologic pathogens in periodontal disease have made explication of genetic factors in disease susceptibility more difficult. The evidence for the influence of genetics in dental anomalies and malocclusion has also been discussed in the paper. The most important conclusion of this review is that genes have a role to play in dental caries; however, both environmental and genetic factors have been implicated in the etiology of caries. Superfluous studies will have to be conducted to replicate the findings in a different population. Identification of genetic risk factors will help screen and identify susceptible patients to better understand the contribution of genes in caries etiopathogenetic. Information derived from these diverse studies will provide new tools to target individuals and/or populations for a more efficient and effective implementation of newer preventive measures and diagnostic and novel therapeutic approaches in the management of this disease.

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INTRODUCTION:

Genetics is the study of genes at all levels from molecules to populations. In dentistry, we encounter numerous differences in the dentofacial characteristics of individuals, even among family members. Some children have large teeth; some may have high prevalence of caries, while only some have good occlusions. Is dental health inherited? Infact, Human genetics is much more than the study of mere hereditary diseases. It has emerged as a biological science for understanding the endogenous factors in health and disease and the complex interaction between nature and nurture. Owing to rapid specialization, several branches in genetics have come into being e.g. cytogenetics, biochemical genetics, clinical genetics, pharmacogenetics, immunogenetics, microbial genetics, and population genetics and so on.[1]

Genetics is not just about rare disorders anymore, and it is no longer confined to the genetic specialist; it increasingly affects every facet of healthcare- including dental practice. Of course, dentists have long recognized patients that have a genetic contribution to a dental health problem. Some of these patients have physical malformations resulting from a hereditary condition (such as osteogenesis imperfect with dentinogenesis imperfect; cleft lip/cleft palate). Dental practitioners also commonly encounter hereditary conditions associated with abnormal tooth formation or periodontal disease.[2]

Likewise, Dental caries incidence is affected by host factors that may be related to the structure of dental enamel, immunologic response to cariogenic bacteria, or the composition of saliva. Therefore, genetic variation of the host factors may contribute to increased risks for dental caries.

Establishing a basis for a genetic contribution to dental caries will provide a foundation for future studies utilizing the human genome sequence to improve understanding of the disease process. Inherited disorders of tooth development with altered enamel structure increase the incidence of dental caries. Therefore, a better knowledge of oral and dental caries is required for a general dental practitioner. With the progress of eradication of communicable diseases in the last hundred years and the improvement of socioeconomic and sanitary levels of the world population, human genetics is emerging as an area that requires further study for caries reduction. Interest in dental genetics is probably increasing due to advances in our understanding of genetic problems and better evaluation of the problems of patients and their families. Hence, the focus of this review is to provide a brief overview of genetics, its clinical implications and its relation to dental caries.[2]

GENETICS AND DENTAL CARIES

Genetics being a mature and dynamic science, clearly in its prime and recognized as the very core of modern biology. New developments in genetics are currently accumulating at the unprecedented rate and genetic engineering is now a reality. Moreover, genetic risk factors, environmental factors play a vital role in diseases such as periodontitis and peri-implantitis.[3]The three most common problems in dentistry today remain dental caries, periodontal diseases and malocclusion.[4] However, more than 90% adults of age 20years or older with permanent teeth have suffered from dental caries leading to pain, infection or even tooth loss. Although caries prevalence has decreased over the past decade, there are still about 23% of dentate adults who have untreated carious lesions.[5]

Dental caries is a complex, chronic, multifactorial disease and one of the most prevalent diseases in industrialized and developing countries[6]. Bacteria, acid, food debris and saliva combine in the mouth to form a sticky substance called plaque that adheres to the teeth. Tooth decay begins if this plaque is not removed thoroughly and routinely. These acids dissolve minerals on the surface of the tooth.[7] The disease process may involve enamel, dentin and cementum, causing decalcification of the tissues and disintegration of the organic substances. Streptococcus mutans species is the main factor that initiates caries, and the bacteria of the genus Lactobacillus species are important in further caries development, especially in the dentin. Caries can also be caused by other bacteria, including members of the mitis, anginosus and salivarius groups of streptococci, Enterococcus faecalis, Actinomyces naeslundii, A. viscosus, Rothia dentocariosa, Propionibacterium, Prevotella, Veillonella, Bifidobacterium and Scardovia etc. Untreated tooth decay also destroys the internal structure of the tooth (pulp) and ultimately causes loss of the tooth structure.[8]

Caries is a major public health concern worldwide, affecting more than 80% of the population in the world. The etiology of dental caries has been studied for many years. Multiple factors contribute to a person's risk for caries. Some of them are illustrated below:

1. *Environmental Factors*: Diet, oral hygiene, fluoride exposure and the cariogenic bacteria.
2. *Host Factors*: Salivary flow, salivary buffering capacity, position of teeth relative to each other, composition of tooth enamel and host immune response.[7]

HOW WE COME TO KNOW THAT GENETICS PLAYS A ROLE IN THE ETIOLOGY OF CARIES

Twin studies are used to estimate the influence of genetic factors on dental caries. The role of twins in the analysis of human behavioral and physical development was first described by Galton.[9] Twin studies were carried out in the beginning of 20th century in order to investigate the role of genetics in the etiology of caries. In case of multifactorial diseases where genetic and environmental factors play important role in the causation of disease, twin studies can be

used as useful tools to evaluate the roles of genetic component of the disease. Presence or absence of the trait or disease in a large number of the two types of twins (mono and dizygotic varieties) is calculated in percentage.[10]

Diseases in which the percentage of twin pairs, where both the twins of the pairs are affected, is greater in the monozygotic group as compared to the dizygotic group, the disease can be confirmed to have a definite genetic etiology.[10] Genetic contribution to dental caries and monozygous (MZ) twin pairs show smaller intrapair variances for caries than dizygous (DZ) pairs.[9]

Several studies on twins indicated toward the genetic component of dental caries. Bretz et al. suggested that variation in dental caries surface traits has a significant genetic contribution and microbial acid production is modulated by the environment in their study. Environmental contribution has been proposed by Liu.[9]

Bertz et al. stated in their study that 70% of the variation in frequency and severity of dental caries could be explained by a genetic contribution to dental caries traits. Heredity plays a significant role in lesion progression and site-specific incidence rate.

The classic Vipeholm study clearly showed that greater exposure to foods rich in sugar increased the severity of caries, but although the individuals in the study consumed caramels four times a day in between meals, therefore, 20% of them had not developed any caries lesions after one year. The result suggests that individual susceptibility also modulates caries experience.

Several variables related to caries experience (i.e. number of teeth present, percentage of teeth restored, percentage of surfaces restored, percentage of teeth affected by caries, percentage of surfaces affected by caries) show statistically significant concordance rates in monozygotic twins, but not in dizygotic twins.[11] It has been suggested that loci in chromosomes 1, 2, 7, 8, and 17 contribute to caries susceptibility.[12-14]

CANDIDATE GENES FOR DENTAL CARIES

A **candidate gene** is a gene known to be located in a region of interest in the genome. Products of the candidate gene has biochemical or other properties the presence or absence of which can be directly related to a disease. Some of the findings that form the different significant studies are as under:

1. A study on the mice indicated that major genes responsible for the regulation of susceptibility of dental caries or resistance are located on chromosomes number 1, 2, 7 & 8.[15]
2. Genome wide genotype data and DMFT scores in a large number of families were evaluated. Low caries susceptibility loci were found on chromosomes number 5(5q13.3), 14(14q11.2) and X (Xq27.1). The high caries susceptibility genes were identified on chromosome number 13(13q31.1) and 14(14q24.3). the presence of genes for caries on X chromosome may account for the sex differences observed in the incidence of caries. This study was the first of genome wide scans introduced for dental caries.[16]
3. In a recently concluded study, single nucleotide polymorphism (SNP) assays were performed for 6 candidate genes. The candidate genes selected for the study were the amelogenin(AMELX), ameloblastin(AMBN), tuftelin(TUFT1), enamelin(ENAM), tuftelin-interacting protein(TFIP11) and kallikrein 4 (KLK4) genes. There were no significant associations concluded between single candidate genes and caries susceptibility. However, a significant interaction between tuftelin and S.mutans was observed.[17]
4. The osteopontin (OPN) gene plays an important role in mineralization. In a recently conducted study OPN was chosen as candidate gene with respect to caries susceptibility as OPN gene was found to be associated with incidences of enamel hypoplasia in primary dentition. Results indicated an association between the OPN gene and caries in the primary dentition.[18]
5. A new study applied scanning of single nucleotide polymorphism (SNP) markers with relation to selected candidate genes (ameloblastin, amelogenin, enamelin, tuftelin-1 and tuftelin interacting protein 11) that influence enamel formation. One copy of a rare amelogenin allele was found to be associated with caries experience. This result suggested that variations in amelogenin may contribute to caries susceptibility.[19]

FUTURE OF GENETICS IN DENTISTRY

As we move into the post-genomic era, clinicians will increasingly be called upon to apply molecular based diagnostic and treatment approaches in their practices. Even today more than 800 single nucleotide polymorphisms (SNPs) have been identified within the 75 genes thought to be candidates for hypertension. A similar number of candidates SNPs probably exists for the periodontal diseases.[20]Genetic tests of the future will include measurement of other patient characteristics that influence dental care, such as response to medications. This is an emerging discipline known as pharmacogenomics. Assessment of pain response at the molecular level may provide improved options for future pain management, which is an example of pharmacogenomics being used to individualize patient care.

Information on the molecular control of bone, periodontal, salivary gland and tooth development will lead to new and novel treatment approaches well beyond those of our current surgical-based techniques. Tissue engineering approaches are already making significant strides in cell manipulation and

developing tissues such as skin, bone and cartilage. Similarly, in drug delivery, gene therapy and biopharmaceuticals will present new therapeutic opportunities. The post genomic era will present many opportunities for improvement in oral health care and a multitude of challenges. The dental profession will be faced with determining how best to incorporate this knowledge and the resulting new technologies into our health care system and how to effectively educate oral health care providers and keep them abreast of the rapidly changing field of molecular biology.[21]

ROLE OF GENETICS IN PUBLIC HEALTH DENTISTRY

From the era of eugenics to the present era, this area has seen many turns in which geneticists have put through their effort to tie together the strings of both molecular genetics and public health. Though still the dark clouds of eugenics, the predictive power of genes, genetic reductionism, non-modifiable risk factors, individuals or populations, resource allocation, commercial imperative, discrimination and understanding and education are hanging above. Therefore, the mission of health professionals is to "fulfill society's interest in assuring conditions in which people can be healthy". Requirements of the mission is to respond towards the ever changing priorities and advancements in the scientific world. From the past few decades major technological advances have been witnessed. Breakthroughs in human genetics provide great promise for improving the health of the public. Discoveries in genetics are already impacting society's health in numerous ways. Every day, health professionals and general public are provided information about exciting discoveries in areas such as cancer, heart disease and birth defects, creating expectations for better health services.

But, it was not that before, earlier, the science of human genetics was focused only on micro-level health influences and clinical genetics on rare, single gene disorders, providing diagnosis, risk estimation, reproductive organs and some newborn screening . Moreover, in the decades to come, insights and techniques of molecular genetics will have great influence on prevention and health care. Community-based genetics epidemiology has become a basic science in understanding the human genome. In the 19th century when public health and the eugenics movement shared common ground values and ideas, programs and personnel, a historic association between public health and genetics has begun. In 1939, high profile geneticists were promoting improvement of the genetic constitution of the population through voluntary eugenics, facilitated by changing social conditions and human attitudes. Simultaneously, public health was focused on preventing disease primarily through the control of infection and malnutrition. In the year 1940, many people, including those who were involved with public health, withdrew their support for eugenics, as the ethics behind these practices were increasingly questioned. By the 1950s, human genetics had extricated itself from eugenics and the practice of non-directive genetic counselling was introduced. This divergence was maintained throughout the second half of the 20th century with public health shifting focus from infectious diseases to complex, chronic diseases and geneticists concentrated on mapping the human genome.

However, Professor Leo ten Kate rejects the term "public health genetics" and proposed to use "community genetics" because the latter refers to values that are not safe with the first. The term "Public health genetics" has been introduced to donate the interface between genetics and public health and is mainly used in titles of training courses and names of research groups. It attempts of the public health profession to cope with and make best use of the rapid advances in genetics.

TEN ESSENTIAL PUBLIC HEALTH SERVICES AND GENETICS

1. Monitor health status to identify community health problems
2. Diagnosis and investigation of health problems as well as hazards occurring in the community
3. Inform, educate and empower people about health issues
4. Mobilize community partnerships at the state and local levels to identify and solve health problems
5. Development of different policies and practices that support individual as well as community health efforts
6. Enforce laws and regulations that protect health and ensure safety
7. Connect people to health services, including genetic services and assure the law of health care when it found unavailable
8. Assure a public health and personal health care workforce competent in genetics
9. Evaluate effectiveness, accessibility and quality of personal and population based health services including genetics
10. Research for new insights and innovative solutions to health problems[12]

CONCLUSION

Genetic diseases are caused due to genetic mutations that are inherited from one or both parent's. certain genetic diseases can cause abnormalities in teeth, affecting the rate of development of primary and secondary teeth or their physical characteristics. Genes have a role to play in dental caries; however, both environmental and genetic factors have been implicated in the etiology of caries. The identification of major genes and knowledge of their functions, their regulations by local, systemic and environmental factors should provide clearest understanding of clinical manifestations. Therefore, Oral health professional should understand the advances in dental health research and genetic studies, thus identifying the etiologic mechanisms of craniofacial anomalies. With the new available technologies and the fast growing body of related knowledge, the prospects are very auspicious. The genetic

basis of dental caries is moving from experimental evidence to a more consistent translation effect on diagnosis and development of new strategies to modulate the host.

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