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RESEARCH ARTICLE

NUTRIGENOMICS -THE DIETARY APPROACH TO PERIODONTAL DISEASES-A REVIEW

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ABSTRACT

Nutrigenomics is a branch of nutritional genomics focusing on identifying and understanding molecular- level interaction between nutrients and other dietary bio-actives with the genome. Nutrition is an important environmental factor that interacts with the genome to modulate disease risk. Genes are important in determining the function, but nutrition is able to modify the degree of gene expression. The response of an individual to dietary modification can be attributed to differences in their genetic make-up, which emphasizes the importance of exploring the role of nutrient–gene interactions in the development of chronic diseases and how diet affects the inflammatory mechanisms underlying severe periodontitis. Improved understanding of the mechanism behind periodontal tissue destruction, the potential protective role of nutrients and the advent of modern genomic measurement tools have led to an increased interest in the association between nutrition and periodontal disease. Nutrigenomics aims to reveal the relationship between nutrition and the genome and to provide the scientific basis for improved public health through dietary means. This manuscript reviews the interrelation between nutrigenomics and periodontal health.

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INTRODUCTION

Periodontitis represents a heterogeneous multifactorial group of infectious diseases with destructive inflammatory pathogenesis that lead to destruction of the supporting tissues of the teeth. If the inflammatory response fails to remove the causative pathogens, the prolonged release of neutrophils, proteolytic enzymes, proinflammatory mediators and reactive oxygen species occurs, which in turn destroy the periodontal attachment.[1] Host based risk factors such as genetic background of an individual, socio-economic status, smoking and dietary habits have all been suggested to alter the innate susceptibility of the host to periodontal disease.[2]Common dietary chemicals act on the human genome, either directly or indirectly, to alter gene expression or structure. Genes are important in determining the function, but nutrition is able to modify the degree of gene expression.

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[3]Recently, it has been suggested that nutrition may be important in redressing the balance between microbial challenge and the host response because it has been implicated in inflammatory diseases and conditions, including type II diabetes, cardiovascular disease, rheumatoid arthritis and inflammatory bowel disease, all of which have also been associated with periodontal disease.[4] Nutrigenomics is also called as nutritional genomics which refers to both the study of how diet affects genes and how genes affect diet .The response of an individual to dietary modification can be attributed to differences in their genetic make-up, which emphasizes the importance of exploring the role of nutrient–gene interactions in the development of chronic diseases and how diet affects the inflammatory mechanisms underlying severe periodontitis. Improved understanding of the mechanism behind periodontal tissue destruction, the potential protective role of nutrients and the advent of modern genomic measurement tools have led to an increased interest in the association between nutrition and periodontal disease. [5]

WHAT IS NUTRIGENOMICS?

Nutrigenomics facilitate greater understanding of how nutrition affects metabolic pathways and how this process is related to diet-related diseases. The term genomics describes the process by which all genes present in the genome of a given speciescan be mapped, sequenced and characterized. Nutrigenomics is an emerging field of science and technology unrevealing inter-relationships between nutrients and human genome using modern tools such as transcriptomics, metabolomics, epigenomics and proteomics.[6]It implies that nutrition and genetics both play asignificant role in the maintenance of human health as well as the development of lethal diseases. Nutrigenomicsaims to reveal the relationship between nutrition and the genome and to provide the scientific basis for improved public health through dietary means. It is extremely likely that interactions between genotype and diet are important in determining the risk of the most common complex diseases, including periodontal disease.[5]

HISTORY[3]

- **In 1997**, the first nutrigenomics company was launched.
- **In 1999**, the name nutritional genomics was changed to genomics by Nancy Fogg-Johnson and Alex Merolli which provides powerful means of discovering hereditary factors in disease

On April 14, 2003, it was believed that genomic era was born when Human Genome Project was launched with the participation of former US President Bill Clinton and former British PM Tony Blair, which contained thecomplete sequencing of the human genome.[7]

- **In 2004**, NuGo (European Nutrigenomics Organization) was born and funded until June 2010
- **In 2007**, Nestle Research Center joined the industrial plat form of the Kluyver Centre for Genomics of Industrial Fermentation, The Netherlands
- **In 2008**, the US Berkeley scientist predicted humangenome tests within 5 years.

APPLICATIONS OF NUTRIGENOMICS[8]

- Genes and proteins expressed differentially in health and disease that are modifiable by nutrients are identified.
- Genes, proteins, and metabolites are influenced by specific nutrients that are known to be beneficial or harmful are identified.
- To identify genes, proteins, and metabolites that are altered by dietary fats associated with cardiovascular disease.
- To identify genes, proteins, and metabolites that is altered by omega 3 fatty acids.
- Genetic variations that alter the nutrient– gene interactions in applications 1 and 2 areidentified

NUTRIENTS

Nutrient is defined as a source of nourishment, such as food, that can be metabolized by an organism to give energy and build tissue whereas nutrition is the organic process by which an organism assimilates food and uses it for growth and maintenance. Nutrients can be divided into six majorclasses, i.e., fats, carbohydrates, proteins, minerals, vitamins,and water; these can be further subdivided into two broadcategories, "macronutrients" (fats, carbohydrates, andproteins) which are required in large quantities from the dietand "micronutrients" (minerals, vitamins, trace elements, amino acids, and polyunsaturated fatty acids [PUFA]) whichare only required in small quantities in the diet and whichare essential for a range of biological processes importantin supporting optimal health.[9]

Mechanisms Revealing Nutritional Modulation Of Periodontal Inflammation: Periodontitis is initiated by the plaque biofilm, but most tissue destruction results from an abnormal inflammatory immune response in patients predisposed to the condition.[10]Oxidativestress is a key driver of chronic inflammation and as aresult has a central role in the pathogenesis of a widerange of chronic inflammatory diseases.[11]In health a fine balance exists betweenoxidants and antioxidants ,If this fine balance is disturbed by excess production of oxidants and/or depletion of local antioxidants the resulting oxidant excess causes oxidative stress and is associated with the local tissue damage seen in periodontitis.[12]Elevated glucose andlipid levels generate ROS at a rate that exceeds endogenous AO defenses and oxidative stress results. Investigators have noted that this "postprandial dysmetabolism" playsa role in the genesis of inflammation. [13] Diet-induced hyperlipidemia induces oxidative stress and downstream inflammation, and lipoproteinsformed by liver hepatocytes can be converted to freefatty acids within the circulation and taken up byadipocytes, thus acting as a basis of proinflammatoryadipokines. Furthermore, in states ofoxidative stress, lipid peroxidation (a chain reactioninduced by ROS attack on the polyunsaturated fattyacid [PUFA] sidechains of lipid membranes) arises,lowdensity lipoproteins are oxidized (oxLDL) and theoxLDLs bind to a group of pattern recognition receptorscalled "toll-like receptors" (TLR-2/4) on inflammatorycell membranes, triggering NF-κ βactivation via theprotein-kinase-C enzyme and other related pathways.NF-Kβ transcribes several proinflammatorycytokines.[14]

DISCUSSION

NUTRITION AND PERIODONTAL DISEASES: Diets high in saturated fats and sugars and low in fruit, vegetables and fiber are common risk factors associated with these chronic diseases.[15] Specific nutrients can modulate immune and inflammatory responses.[16]Nutrients influence intracellular signalling pathways, and the secretion of hormones or metabolites Glucose cannot directly regulate gene expression but its metabolitesact as signalling molecules that in turn activate the transcription factor.[17] Research studies using an experimental gingivitis model have shown increased levels of bleeding on probing when participants were fed with a diet high in carbohydrates when compared to those on a low sugar diet.[18] This finding was further supported by another study investigating volunteers placed on a primitive diet which was high in fiber, antioxidants (AOs), and fish oils but low in refined sugars and with no oral hygiene measures. As would be expected, plaque levels increased significantly and classic periodontal pathogens emerged within the biofilm; however, unexpectedly, gingival bleeding significantly reduced from 35% to 13%.[19] **S**pecific nutrients (antioxidant vitamins A, C, E) and trace element selenium, copper, zinc can modulate the immune and inflammatory responses that maintain epithelial cell integrity and structure. The nutrients get depleted during inflammation with generation of Reactive Oxygen Species

(ROS) causing damage to the cellular tissues.[20]Moreover, selenium has further important redox functions, with selenium-dependent glutathione enzymes being involved in the reduction of damaging lipid and phospholipid hydroperoxides to harmless products. Vitamin C acts as a powerful scavenger of free radical. The association between low intake of vitamin C and occurrence of periodontitis has been demonstrated, in a study by Nissada 2010.[21]Furthermore, expression of genes encoding inflammatory peptides, including interleukin 1α and interleukin 1β, was more than two fold downregulated by vitamin C intake. Role of vitamin D in periodontal health is supported by studies of polymorphisms in the VDR gene, which are reported in many studies to be associated with periodontitis[22.]

Vitamin E terminates free radical chain reaction, stabilizes membrane structure. It is shown to have mitigatory effects on inflammation and collagen breakdown. A low level of vitamin E in gingival tissues of periodontitis patients has been reported.[23]It has been shown that a higher Mg/Ca ratio is associated with a significantly lower level of periodontitis [24.] Omega 3 fatty acids such as n-3 PUFA (oily fish), increase the tissue concentration of eicosapentaenoic acid, docosahexaenoicacid and down-regulate inflammation and in-hibit bone loss in vitro. **(**Sun et al 2003). It has also been reported that the n-6 PUFA levelsin the serum are higher in periodontitis patients, suggesting that an imbalance between n-6 and n-3 fatty acids may contribute to susceptibility to oral boneloss.[25] GSH levels appear depleted in periodontitisand methods of enhancing intracellular GSH may provebeneficial. [26]PUFAs of the omega-3 form (ω-3 PUFAs)found in fish oils lower postprandial triglyceride levels andfindings observed by Yokoyama M *et al.* in their randomizedcontrol study observed that it has anti-inflammatoryand cardiovascular protective effects.[27]

A recent randomized double blind clinical trial investigated the potential clinical benefits of a powdered fruit and vegetable juice concentrate on the treatment of patients with chronic periodontitis and showed that there was increased pocket depth reduction following standard non surgical therapy compared to a placebo group.[4] For inhibition and management of periodontitis, daily nutrition should include sufficient AOs, Vitamin D, and calcium. Insufficient AO levels may be managed by higher intake of vegetables, berries, and fruits (e.g., kiwi fruit) or by phytonutrient supplementation. Probiotics are live microorganisms administered in adequate amounts with beneficial health effects on the host. They repopulate the beneficial bacteria which can help kill pathogenic bacteria and fight against infection which in turn lowers the risk of developing periodontitis.[28] The main functional value of pomegranate in oral health is its polyphenolic flavonoid content. The components of pomegranate juice were found to significantly inhibit cytokine IL-8, PGE_2, nitric oxide, human salivary α-amylase, α-glucosidase activity and found to reduce aspartate ami-notransferase activity in saliva. The hydro-alcoholic extract from pomegranate fruit has shown to decrease the Colony Forming Unit (CFU) per milliliters of dental plaque by 84%.[29] Results from a prospective, observational study carried out over 14 years revealed that men with high consumption of wholegrain were 23% less likely to develop periodontitis.[30]
The seeds of Garcinia mangostana are reported to contain vitamin C. A composition in the form of abiodegradable gel, chip or ointment is provided for the treatment of periodontitis, comprising an antimicrobialor antibacterial activity against periodontal pathogen and forms a liquid crystal structure on contactinggingival fluid, which releases active ingredientsgradually, to provide a sustained release dosage form.The effect of Morinda citrifolia L. fruit juicesignificantly mitigated the gingival inflammation. Thecombination of good oral hygiene and administration ofthis juice was a promising treatment for gingivitis andperiodontitis because of its strong anti-inflammatoryeffects.[6] Recent genome-wideassociation studies have identified a geneticsusceptibilitylocus for type 2 diabetes comprising anonsynonymous single nucleotide polymorphism (C ⁄ T;rs13266634) in a β cell-specific zinc-transporter gene.[31]In light of this new finding, the existing knowledge that zinc has a specific role in beta cell function takes on new significance with respect to potential strategies to prevent or treat type-2 diabetes and potentially periodontal disease. The recommendations of 2011 European Workshop on Periodontology suggested that the dental team should consider including fish oils, fibre, fruits and vegetables and to reduce levels of refined sugars as part of a periodontal prevention / treatment regime and a general health benefit message.[32]

Future: Nutrigenomics research will increase our understanding andknowledge of phenotype, genotype diet interactions in a holistic way with an ultimate aim of developing strategies to improve health management and to prevent diseases .The application of nutrigenomic tools provided numerous leads on biomarkers of nutrient intake,undernutrition,metabolic syndrome and its complication.importantly nutrigenomic studies also led to the discovery of the associationof multiple genetic polymorphism in relation to the variability of micronutrient absorption, and metabolism, providing a potential opportunity for further research toward setting personalized dietary recommendation for individuals and population subgroups.[33]Nutrigenomics is surely expected to be the next wave for food industry, even though only a few practical ideas have emerged. The goal is to obtain more efficient individual dietary intervention strategiesaimed atpreventing diseases, improving quality of life and achieving healthy aging.From the public health point of view,the understanding of really important gene-diet modulations could help to profile the general dietary recommendations for each population.[34]

Conclusion

Nutrigenomics is a branch of nutritional genomics focusing on identifying and understanding molecular- level interaction between nutrients and other dietary bioactives with the genome. Diet is an important environmental factor that interacts with the genome to modulate disease risk.Diet modifications have the potential to influence periodontal disease management improving clinical outcomes, however further research will be required in order to fully elucidate mechanisms and potential benefits for our patients.There is now overwhelming evidence of the importance of diet in a wide range of systemic diseases with diet modification, increasing physical activity and reducing levels of obesity a key public health message. So we need to consider dietary intake when managing our periodontitis patients not only for the potential benefits in terms of their periodontal health but also the systemic benefits that it undoubtedly provides. "Let food be thy medicine and medicine by the food".

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