

Nutrigenomics and its Role in Periodontal Health – A Review

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Abstract

Nutrigenomics is an emerging form of science involving tools that assess the benefit of diet and nutrition in various disease conditions at molecular and genetic level. Nutrigenomics investigates the relationship of nutrient regimen in maintaining health. This article reviews the role of nutrients in maintaining periodontal health and the use of nutrigenomics in understanding genotype, phenotype diet interactions on periodontal health of an individual and the effect of dietary modification on periodontal disease progression.

Key Words: Nutrigenomics, nutrition, periodontal health, periodontal disease

Introduction

Nutrigenomics is the science that utilizes genetic information together with “omics” technology for studying the inter-relation between nutrition and health.¹ Periodontal health is vital for the integrity of the tooth structure. Periodontal disease is the most common disease among various populations second only to dental decay. Fluoride Mapping (2002–2003), DCI, New Delhi, 2004, did a first ever epidemiological survey in India and the prevalence of periodontal disease was 57%, 67.7%, 89.6%, and 79.9% in the age groups 12, 15, 35–44, and 65–74 years, respectively.^{2,3} In failure of inflammatory response of the host to remove the pathogen, there is prolonged release of neutrophils, proteolytic enzymes, proinflammatory mediators and reactive oxygen species resulting in destruction of periodontal attachment.

Periodontal disease affects the supporting structures of the teeth and failure to intervene timely leads to loss of tooth. It is characterised by a dysregulated host inflammatory/immune response to plaque bacteria in susceptible individuals. A variety of risk factors have been associated of which nutrition is the one whose role would be discussed in this paper. Diets rich in saturated

fats and sugars and low in fruit, vegetables and fiber are common risk factors associated with periodontal disease.

Nutrient is a source of nourishment that can be metabolized to give energy and build up tissue. Nutrients are divided into six major classes, i.e. carbohydrates, proteins, fats, minerals, vitamins, and water. Sub dividing it further, there are two broad categories, “macronutrients” (fats, carbohydrates, and proteins) which are required in large quantities from the diet and “micronutrients” (minerals, vitamins, trace elements, amino acids, and polyunsaturated fatty acids [PUFA]) which are only required in small quantities in the diet and which are essential for many biological processes that are responsible in supporting and providing optimal health.¹⁶

History

The term “nutrigenomics” was first described in 2001 from Pelegrin (2001). On, 14th April 2003, Genomic era was launched by launching of Human Genome Project which contained the complete sequencing of Human Genome.

The ‘omics’ revolution-

· In 2004, NuGo (European Nutrigenomics

Organization) was born and funded until 2014⁴

In 2007, Nestle research centre joined the industrial platform of the Kluyver Centre for genomics of industrial fermentation, Netherland.⁴

In 2008, US Berkley scientist predicted human genome tests within five years for \$100⁴

“OMICS” Technology in Nutritional Research

It includes Genomics, Proteomics, Transcriptomics and Metabolomics. Genomics is the study of the genome, an approach of mapping, sequencing and analysis of all genes present in the genome, focusing on resolving the variation in the genome between individuals. Transcriptomics is the study of gene expression at the level of the mRNA. Using either cDNA or oligonucleotide microarray technology, it describes the approach in which gene expression (mRNA) is analysed in a biological sample under certain conditions and a given point of time.⁶ Proteomics takes forward this analysis and addresses three categories of biological interest: protein expression, structure and function. It attempts to characterize all proteins in a biological sample at the functional level.^{7,12} Metabolomics is the scientific study that involves quantitative analysis of metabolites. It tries to measure the level of all substances (other than DNA, RNA or protein) present in a sample; the metabolome comprises the complete set of metabolites synthesized by a biological system.⁸

Periodontal disease and role of Nutrition

Chronic inflammation is destructive and is central to a number of chronic diseases including periodontitis. Oxidative stress is a key driver of chronic inflammation and as a result has a central role in the pathogenesis of a wide range of chronic inflammatory diseases¹⁷ such as type 2 diabetes, cardiovascular disease and metabolic syndrome, and has been proposed as a common link between periodontitis and systemic disease.⁹ When the fine balance that exists between oxidants and antioxidants found in the body in healthy conditions is disturbed due to excess production of oxidants or depletion of local antioxidants, oxidative stress is the result which is associated with local tissue damage seen in periodontitis. The tissue damage is caused by altering proteins, lipids and DNA damaging the cells directly or

by production of pro-inflammatory cytokines.¹⁸

Elevated dietary levels of glucose and lipids increases oxidative stress levels by receptor binding of neutrophils. Hyperglycaemia results in the formation of Advanced Glycation End products (AGE) when glucose binds to proteins in tissues and the bloodstream. Neutrophils have receptors for AGE called RAGE and their ligation by AGEs activates the NADPH-oxidase enzyme complex to generate oxygen radicals. Metabolism of excess saturated fats generates elevated Low Density Lipoprotein (LDL) cholesterol and on its oxidation forms oxidised LDL. This binds to the complementary receptors found on the cell membrane of neutrophils (Toll-like receptors), triggering NF- κ B activation through the protein-kinase-C enzyme and other related pathways. NF- κ B transcribes several pro-inflammatory cytokines.⁹ In addition, researchers have proposed reduced glutathione (GSH), the key intracellular AO redox regulator of NF- κ B as a novel approach to down regulation of hyper inflammatory events.¹⁹

Literature reviews suggest periodontitis to be associated with reduced serum micronutrient levels which may be due to poor diet, lifestyle factors (e.g. smoking) and/or genetic factors which impact on absorption, distribution, bioavailability and synthesis of micronutrients.²⁰ Studies have shown irrefutable evidence that macronutrients and micronutrients modulate pro-inflammatory and anti-inflammatory cascades. Control of dietary sugar and fat intake can help reduce levels of oxidative stress and downstream inflammatory sequelae. Reductions in simple sugars, refined carbohydrates and saturated fats reduce activation of a diverse range of pathways thereby reducing oxidative stress. Foods rich in antioxidants such as green leafy vegetables (broccoli, spinach etc.), berries (e.g. blueberries, blackberries, cranberries, strawberries etc.), red beans and dark chocolate with greater than 70% cocoa are all rich in key antioxidant micronutrients and would help reduce oxidative stress. On the other hand, diets which includes nuts, olive and fish oils having antioxidant properties can also work to slow down gastric emptying (digestion) resulting in less pronounced spikes in blood glucose.⁹

Nutrients for Periodontal Health

Vitamin C is the most powerful anti oxidant.

Genes encoding inflammatory peptides, including interleukin 1 α and interleukin 1 β , was more than two fold down regulated by vitamin C intake. It was found that smokers with the lowest intake of vitamin C were likely to have the worst periodontal condition.¹⁰ Plasma vitamin C levels of 56.8 μ mol/l may be regarded as the optimum vitamin C plasma level. In order to achieve this level, at least 200 mg vitamin C per day should be ingested and this is to be suitably advised to periodontitis patients.

- Vitamin D plays an important role by influencing the action of monocytes, macrophages and dendritic cells which express the vitamin D receptor (VDR), which when up regulated by activated Toll-like receptors -2/1, results in the intracellular production of 1,25(OH)₂ D₃ which in turn induces the release of LL-37 cathelicidin, a potent anti-microbial peptide.¹¹

- Low serum Calcium levels causes alveolar bone resorption and is a risk factor for periodontal disease.¹

- Vitamin E terminates free radical chain reaction and stabilizes the membrane structure. It is shown to have mitigatory effects on inflammation and collagen breakdown. Low levels of vitamin E in gingival tissues of periodontitis patients has been reported in many studies.²¹

- Magnesium is related to calcium and a higher Mg/Ca ratio is associated with a significantly lower level of periodontitis.¹

- Supplementation of Zinc may alter periodontal disease progression through changes in expression of the ZnT8 transporter gene.¹²

- Isabgol extract has shown effective antibiotic and weak inflammatory effect by effective action against periodontal pathogens and Matrix metalloproteins.¹³

- Omega 3 from polyunsaturated fatty acid act as a signal to prevent neutrophils mediated periodontal tissue damage.¹⁴

- The hydro-alcoholic extract from pomegranate has shown to decrease the Colony Forming Units (CFU'S) per millimeters of dental plaque by 84 % by one minute rinse.¹⁵

- 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.⁵

Future of Nutrigenomics

Nutrigenomics aim to reveal the relationship between nutrition and the genome to provide a scientific basis for improved periodontal health through dietary means. It will increase the understanding of genotype, phenotype diet interactions on periodontal health of an individual and the effect of dietary modification on periodontal disease progression. The concept of "Personalized/ Individualized Diet" would soon revolutionize the food industry. The identification of molecular biomarkers or natural bioactive molecules for control and prevention of periodontal diseases through timely dietary interventions seems promising.

Conclusion

A much comprehensive understanding of nutritional gene interactions and their impact on phenotype is required to identify and plan strategies for dietary intervention. A large body of data relating to nutritional genetic studies on periodontal disease is the need of the hour. Further research needs to be done to relate patient's signs and symptoms with their genetic profile and dietary habits.

Ethical Clearance – Not required since it is a review article

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Conflict of Interest – nil

References

1. SG Balaji, Sugumar K. Nutrigenomics: A new direction in periodontics. *Int J of Applied Dental Sciences* 2020;6(1):146-149.
2. Eke P, Barker L. Prevalence of Periodontal Disease in the United States: NHANES 1999-2004. Abstr. #1843. IADR, 2007. Available at: http://iadr.confex.com/iadr/2007orleans/techprogram/abstract_93679.htm.
3. Shaju JP, Zade RM, Das M. Prevalence of periodontitis in the Indian population: A literature

- review. *J Indian Soc Periodontol* 2011;15:29-34.
4. Priyadharshini RS, Vijayalakshmi R, Ambalavanan N, Ramakrishnan T, Logaranjani A. Nutrigenomics in periodontics – An overview. *Int J Curr Res Rev.* 2016; 8:31-5.
 5. Chapple ILC, Milward MR, Ling-Mountford N, Weston P, Carter K, Askey K et al. Adjunctive daily supplementation with encapsulated fruit, vegetable and berry juice powder concentrates and clinical periodontal outcomes: a double blind RCT. *J ClinPeriodontol* 2012;39(1):62-72.
 6. Torronen R, Kolehmainen M, Poutanen K. Nutrigenomics – new approaches for nutrition, food and health research. *Duodecim.*2005;121:213-941.
 7. Kussmann M, Raymond F, Affolter M. OMICS driven biomarker discovery in nutrition and health. *J Biotechnol.*2006;124(4):758-787.
 8. Gibney MJ, Walsh M, Brennan L, Roche HM, German B, van Ommen B. Metabolomics in human nutrition: opportunities and challenge. *Am J ClinNutr.*2005;82(3):497-503.
 9. Chapple IL. Potential mechanisms underpinning the nutritional modulation of periodontal inflammation. *J Am Dent Assoc*2009;140:178-84.
 10. Tomofuji T, Ekuni D, Sanbe T, Irie K, Azuma T, Maruyama T *et al.* Effects of vitamin C intake on gingival oxidative stress in rat periodontitis. *Free RadicBiol Med.* 2009; 46(2):163-168.
 11. Philip T Liu. Toll like receptor triggering of a vitamin D mediated human antimicrobial response. *Science.* 2006; 311(5768):1770-1773.
 12. Dang TS, Walker M, Ford D, Valentine RA. Nutrigenomics: the role of nutrients in gene expression. *Periodontol.* 2000, 2014; 64:154-160.
 13. Reddy PRT, Vandana KV, Prakash S. Antibacterial and anti-inflammatory properties of *Plantagoovata* Forssk. leaves and seeds against periodontal pathogens: An in vitro study. *Ayu.* Oct-Dec 2018;39(4):226-229. doi: 10.4103/ayu. AYU_176_16.
 14. Park Y, Harris WS. Omega-3 fatty acid supplementation accelerates chylomicron triglyceride clearance. *J Lipid Res.*2003;44:455-63.
 15. DiSilvestro RA, DiSilvestro DJ, DiSilvestro DJ. Pomegranate extract mouth rinsing effects on saliva measures relevant to gingivitis risk. *Phytother Res.* 2009;23(8):1123-1127.
 16. Van der Velden U, Kuzmanova D, Chapple IL. Micronutritional approaches to periodontal therapy. *J ClinPeriodontol* 2011;38 Suppl 11:142-58.
 17. Hensley K, Robinson KA, Gabbita SP, et al. Reactive oxygen species, cell signalling, and cell injury. *Free RadicBiol Med* 2000;28(10):1456-62.
 18. Sies H, Jones DP. Oxidative stress. *Encyclopedia of stress.* San Diego: *Elsevier*;2007.
 19. Chapple IL. Reactive oxygen species and antioxidants in inflammatory diseases. *J ClinPeriodontol* 1997;24:287-96.
 20. Ceriello A, Esposito K, Piconi L, Ihnat MA, et al. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. *Diabet*2008;57: 349-1354.
 21. Slade EW, Bartuska D, Cohen DW, Rose LF. Vitamin E and periodontal disease. *J Periodontol* 1976;47(6):352-354.