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Literature Review

NUTRIGENOMICS -AN ENIGMA TO PERIODONTAL DISEASES

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Abstract

Background: Nutrigenomics is used to learn about how genes and diet together may affect an individual's health and risk of developing diseases and also to prevent and treat disease. It also helps in the interaction between nutrients with the genome at the molecular level to get insight into the role of nutrients that may affects or influences health. Periodontitis results from imbalance between host and microbial response which results in improper functioning of periodontal tissues. Although there are several novel techniques to readdress and restore the function of periodontal structures, Nutrition can act as an anti-inflammatory component and can decrease the incidence of systemic conditions such as cardiovascular diseases, diabetes mellitus, rheumatoid arthritis, and Crohn's disease which are known to be associated with periodontal diseases. Nutrigenomics is an area of nutrition and periodontics which is involved with the influence of diet and its components on the genome, proteome, and metabolites.

Materials and methods: This review was reported per the PRISMA guidelines. PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 15 articles were included for full text. This article reviews nutritional impact and impact of nutrigenomics on periodontitis.

Keywords: *Nutrigenomics, Periodontitis, Nutrition*

INTRODUCTION

Periodontitis is an inflammatory condition which is caused by particular microorganisms or their groups involving episodic, progressive loss of the dento-gingival complex and the periodontal ligament resulting in exfoliation of teeth in susceptible patients.[1] It is the 2nd most common disease globally, after dental caries with a prevalence of 30-50% with mild forms of the population in United states, but only about 10% have periodontitis in severe forms.[2] Nutrigenomics is an emerging field of science dealing with the mutual-relationships between dietary components and human genome through the use of metabolomics, transcriptomics, epigenomics

and proteomics.[3]

This field is extensively related with the impact of nutrients on genome, proteomes (total proteins in body), and metabolites (Total metabolites in the body).[4] Dietary products that decrease or eliminate the undesirable effects of pro-inflammatory genetic variations may represent excellent preventive agents for periodontal diseases that enhance and benefit large sections of the population.

Pathophysiology of periodontal diseases is complex and involves various pathways. Susceptibility to periodontitis involves the reciprocity between local, bacterial, genetic, nutritional, environmental factors. For example, loss of tooth has been associated with changes in diet preferences and nutrient deficiency.[2] Common dietary agents act either directly or in an indirect way to modify gene structure and expression, on the human genome. Degree of gene expression can be modified by nutrition which can alter the physiologic and diseased processes during lifetime through environmental (Epigenetic) influence mechanisms that are critical for gene expression. Investigating the inter-relation between dietary components and alveolar bone loss is essential to thoroughly understand the probable role of nutritional adjustments in preventing and treating periodontal disease.[3,4] Understanding the patho-physiology behind attachment apparatus destruction, protective role of dietary components and the beginning of novel genomic functional measurement tools have increased the attention in researching the correlation between periodontal disease and nutrition. This review was reported per the PRISMA guidelines (fig.1).

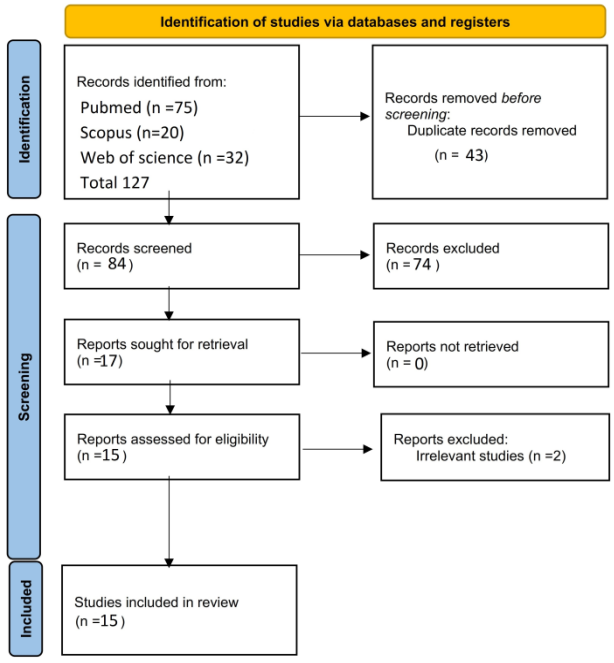

Figure 1. Prisma flow chart

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History of Nutrigenomics and its Introduction

- First nutrigenomics company was launched In 1997.
- Term "Nutrigenomics": 2001 from Pelegrin (2001).
- Human Genome Project was launched on April 14th, 2003, which had the complete sequencing of Human Genome. This project had marked the beginning of new revolution in biological and medical sciences which was named as "OMICS" revolution.

The 'omics" revolution

- 2004: European Nutrigenomics organization NuGo was born and continued till 2014.
- In 2007, Nestle research center collaborated with the (KCGIF) Kluyver Centre for genomics of industrial fermentation, Netherland.
- In 2008, US Berkley scientist forecasted human genome tests within 5 years for $100.

"OMICS" Technology

It includes

Genomics: It focusses on resolving inter genome variations. It is the study of genome that involves an approach to gene mapping, sequencing, and analysis present in the genome.

Proteomics: It helps in expression of protein structure and physiology. This helps to differentiate the sum of proteins in a genetic (biologic) sample at the functional level. The sample can be from cell, organ, tissue or biofluid.

Metabolomics: Scientific study that involves quantitative analysis of metabolites. It also measures the level of substances (other than DNA, RNA, or protein) present in a sample.

Transcriptomics: This involves study m-RNA expression levels. It describes the approach in which m-RNA expression is evaluated in a sample using either oligonucleotide or cDNA microarray technology.

Goals of Nutrigenomics

1. Identify transcription factors which are sensors for nutrient recognition and the target genes for the interpretation of the signaling pathways associated with representation of main Dietary signals.

2. Cell and tissue specific gene representation (expression) signatures measurement and validation; Metabolic outcomes of specific micro-nutrients and macro-nutrients are also measured.
3. Regulatory pathways associated with various nutrients and Pathway interaction prior to inflammatory stress.
4. To recognize the process of dysregulation of metabolic pathways that lead to diet related diseases.
5. Detection of risk factors (Genotypes) to attain improvement of diet related systemic conditions such as myocardial infarction, diabetes, and hypertension.
5. Development of biomarkers (early metabolic dysregulation and susceptibility) using nutritional systems biology.

Practical Applications of Nutrigenomics [3,5,6]

1. Nutrients which can modify the genes and particular proteins which are expressed differentially in wellbeing and illness are identified.
2. Specific nutrients that influence proteins, genes and metabolites and are known to be advantageous or detrimental are identified.
   - ✓ To detect the variation by dietary fats associated with CVD's (cardiovascular diseases).
   - ✓ To detect that are altered by ω-3 fatty acids.

3. Nutrient-gene interactions can be identified.

Secret behind the concept of Nutrigenomics

The plaque biofilm initiates mechanisms uncovering Nutritional Modulation of Periodontitis. Tissue destruction is a result of abnormal inflammatory immune response represented by hyper inflammation.[5]

This inflammation fails to exterminate the causative pathogens and generates the continued release of pro-inflammatory mediators, reactive oxygen species (ROS), neutrophil proteolytic enzymes which terminate the tooth attachment apparatus. [6]

Many studies have found out that macro and micronutrients regulate the inflammatory process and can modify the pro-inflammatory and anti-inflammatory cascades, influencing one's own inflammatory status.

Besides providing energy and co factors for body functioning, nutrient's play a very important role in acting as a molecular signal which can modulate molecular gene and protein expression leading to alteration of inflammation.[7]

Oxidative stress and its role

Oxidative stress is caused by diet-induced hyperlipidemia leading to down streaming of inflammation.

The basis for pro-inflammatory adipokines include the hepatocytes which form lipoproteins which are converted to FFA (free fatty acids) and taken up by adipocytes. In oxidative stress, a process known as lipid peroxidation arises where low-density lipoproteins are oxidized (oxLDL) and bind to "toll-like receptors" (TLR-2/4) which are a group of PRR'S (pattern recognition receptors) on membranes of inflammatory cells, triggering Nuclear Factor - kappa β activation (fig.2). [5,6,7]

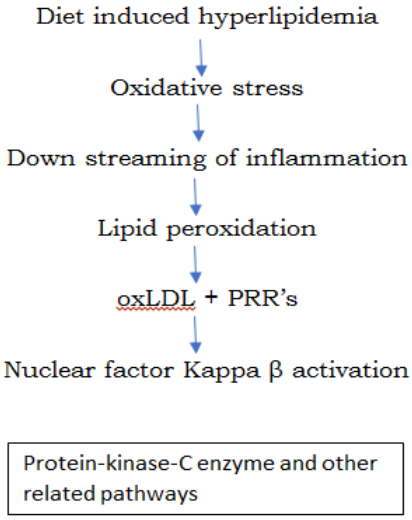

Figure 2. Oxidative stress and its role in Periodontitis

It has also been reported that Periodontitis patients have higher levels of serum n-6 PUFA, suggesting that a discrepancy between ω-6 and 3 fatty acids may lead to susceptibility to peridontitis.[6]

Role of Nutrients in inflammation reduction

Evidence suggests that periodontitis is associated to some extent with reduced serum micronutrient levels which may include insufficient diet, lifestyle factors like smoking. Genetic factors also impact on some of the metabolic and physiological processes such as bioavailability, absorption, distribution, and synthesis of micronutrients.

- Macro and micro-nutrients can modulate pro- and anti-inflammatory cascades in the body and can reduce the inflammatory pathway.
- Restriction in Sugars and fats can decrease the levels of oxidative stress.
- Reductions in simple sugars, saturated fats and refined carbohydrates reduce activation of a diverse range of pathways thereby reducing oxidative stress.
- Foods's rich in antioxidants such as green leafy vegetables such as broccoli, spinach, Amaranthus etc., all types of berries (Blueberries, blackberries, strawberries, cranberries) etc. red beans, green tea, turmeric, dark chocolate (>70% cocoa) are rich in key antioxidant micronutrients and would help reduce oxidative stress.

- Diets which include nuts, olive and fish oils having antioxidant properties can help in slowing down digestion resulting in less evident increase in blood glucose levels.

Micro-Nutrients

As suggested by Vander Velden in 2011, nutrition is crucial in addressing the balance between human microbe interactions because it is implicated in several inflammatory conditions.[8]

Nutrients	Function
vitamins A, C, E and selenium, copper, zinc, Antioxidants	Participate in Immune and inflammatory responses, maintain epithelial cell structure and integrity.
Selenium	Help to decrease the harmful lipids such as LDL and phospholipid hydroperoxides to safe products.
Vitamin C	Powerful free radical scavengers
Vitamin E	Stabilizes membrane structure, terminates free radical chain reaction, Mitigatory effects on inflammation and collagen breakdown.
Vitamin D	Influences the action of monocytes, macrophages and dendritic cells which express the vitamin D receptor (VDR)
ω-3 fatty acids Eg: n-3 PUFA	Increase the tissue concentration of n-3 fatty acids such as eico-sapentaenoic acid, docosahexaenoic acid and down-regulate inflammation directly inhibiting bone loss
Isabgol extract	Effective antibiotic and weak inflammatory effect [9]

Pomeogranate

Polyphenolic flavonoid content is the primary functional value of pomegranate in oral health.[9]

Pomegranate juice: The hydro-alcoholic extract in pomegranate juice, showed to decrease the Colony Forming Unit CFU/ per ml's of dental plaque by 84%. It was found to inhibit (PG) Prostaglandins (E2), human salivary α-amylase, cytokine Interleukin-8, nitric oxide, α- glucosidase function and found to decrease enzyme aspartate aminotransferase activity in saliva.[10]

Garciania magostana

Researchers demonstrated an inverse relationship between antioxidant depletion locally in the periodontium and within the plasma and periodontitis.[11]

Garcinia mangostana seeds are reported to be a rich source of vitamin C. Component delivery in the form of a biodegradable chip, gel, or ointment with antimicrobial or antibacterial activity is provided to treat periodontitis against periodontal pathogens. On contacting gingival fluid, the component forms a liquid crystal structure to provide a sustained release dosage and releases active ingredients progressively. [12]

Morinda citrifolia

Gingival inflammation was significantly improved by the effect of Morinda citrifolia L. fruit juice by its anti-inflammatory effects. Good oral hygiene maintenance along with the fruit juice had significant influence on gingivitis and periodontitis. [12]

Animal studies (Rodents) have shown that zinc deficiency has been associated with increased plaque and higher gingival index measurements and finally increased vulnerability to periodontal disease progression. One study investigated the potential role of zinc (micronutrient essential mineral), a zinc transporter gene and nutrigenomics tool for assessing role of nutrition in the risk of developing type 2 diabetes and in developing associated periodontal diseases. [13]

A locus for genetic susceptibility to diabetes and alveolar bone loss comprising a single nucleotide polymorphism (C/T; rs13266634) (non-synonymous) in a β cell-specific zinc-transporter gene has been identified through genome wide association study.[14]

Insulin storage and release is controlled by this SLC30A8, a zinc transporter gene which is coding for ZnT8. The recommendations of the 2011 EWP (European Workshop on Periodontology) suggested that the dental clinicians should consider including diet of fish oils, fiber, fruits, and vegetables and reduce refined sugar levels as part of a alveolar bone and tooth loss prevention and treatment regime with a note on general health benefits [13,14]

Nutrigenomics in Future

Nutrigenomics provides a scientific basis for better outcomes in periodontal treatment through dietary means. It aims to focus on the inter relationship between nutrition with genome and addresses the terms like genotype, phenotype diet interactions on periodontal health. Future personalized diet modifications or designed individual diets will revolutionize the future of food industry. The concept of nutrigenomics for the prevention or management of periodontal diseases seems promising.

Conclusion

Periodontitis is a destructive disease. Nutrigenomics is the mixture of nutrition and gene modification through structured diet. A much comprehensive understanding of nutritional gene interactions and their impact on physical characteristics of gene is required to identify and plan strategies for dietary intervention. During last decades, enhanced understanding of tools to assess and structure the

status of nutrition, has developed along with the importance of assessing nutritional intake.

The current evidence on the inter-relationship between nutrition and alveolar bone loss, tooth mobility, gum diseases is mostly questionable and further studies with large sample size are to be conducted to prove the effect of nutrition on periodontal diseases.

DECLARATIONS

Conflicts of interest and financial disclosures

None declared

Ethical approval

Not applicable

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