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Nutrigenomics In Periodontics "A Hype Or A Hope" - An Overview

Review Article

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Abstract

The role that diet plays in the development and progression of dental caries has been well documented, but the importance of nutrition as a predisposing factor for the development of periodontal diseases is still under research. The possible protective role of nutrients and genetics on periodontal tissue has led to an increased interest to establish the association between nutrition and periodontal disease. Nutrition influences growth, development and metabolic activities of periodontium, where as the pathogenesis of periodontitis is regulated by an imbalance between microbes and the immune system which in turn is influenced by various genetic factors. This review throws a ray of hope and summarizes the evidence of nutritional impact on periodontitis and daily nutritional regime for periodontal disease prevention.

Keywords: Nutrigenomics; Periodontitis; Metabolomics; Antioxidants.

Introduction

Periodontitis represents a multifactorial group of infectious diseases that lead to destruction of the supporting tissues of the teeth. Prolonged release of neutrophils, proteolytic enzymes, proinflammatory mediators and reactive oxygen species occurs, when inflammatory response fails to remove the causative pathogens, which in turn leads to destruction of periodontal attachment. The importance of successful management and treatment of periodontitis has gained more attention in the recent years with the recognition that periodontitis is a risk factor for a number of important systemic diseases, which include cardiovascular disease, diabetes and rheumatoid arthritis. Investigating the relation amongst nutrients and periodontal disease has been important to understand the potential role of dietary modification in the prevention and treatment of periodontal disease.

All About Nutrigenomics

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. The term "NUTRI" refers to Nutrition and "GENOMICS" is referred to as the process by which all genes present in the genome of a given species can be mapped, sequenced and characterized [1] Nutrigenomics is also called as nutritional genomics which refers to both the study of, on how diet affects genes and how genes affect diet. The term "nutrigenomics" was first described in 2001 from Pelegrin (2001). In 2004, NuGo (European Nutrigenomics Organization) was started and funded until June 2010 [2]. Nutrigenomics aims to identify the genes that influence the risk of diet-related diseases on a genome-wide scale, and to understand the mechanisms that underlie these genetic predispositions. 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.

Future Of Nutrigenomics: Transcriptomics, Proteomics Or Metabolomics?

Genomics tools can be used in two different, but complementary, strategies in molecular nutrition research: specific genes and pro-

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teins, the expression of which is influenced by nutrient are identified using genomics tools-such as transcriptomics, proteomics and metabolomics.

DNA is made up of genes and every gene contains all the information to produce a protein. Genes are read or expressed to produce function. The transcription or reading of genes to produce RNA is the first stage of gene expression. The transcriptome is the whole set of RNA transcript.

Proteomics is the study of the proteome, and it addresses three categories of biological interest: protein expression, structure and function. It attempts to characterize all proteins in a biological sample, including their relative abundance, distribution, post-translational modifications, functions, and interactions with other biological molecules.

Metabolomics is the scientific study of chemical processes involving metabolites. It tries to detect the extent of all substances (other than DNA, RNA or protein) present within a sample; the metabolome comprises the entire set of metabolites synthesized by a biological system [3].

The presence of a specific gene or mutation in most cases merely connotes a predisposition to a particular disease process. Whether that genetic potential will eventually manifest as a disease depends on an intricate inter play between the human genome and environmental and behavioural factors. Nutrigenomics and genome health are emerging as important new research areas because it's becoming increasingly evident that (a) risk for developmental and degenerative disease increases with DNA damage which successively depends on nutritional status and (b) optimal concentration of micronutrients for prevention of genome damage is additionally hooked into genetic polymorphisms that alter function of genes involved directly or indirectly in uptake and metabolism of micronutrients required for DNA repair and DNA replication. Although genes are critical for defining predilections nutrition modifies the extent to which different genes are expressed and thus prevents expression of disease in an susceptible individual [4].

Objectives:

The identification of transcription factors that function as nutrient sensors and the genes they target; the elucidation of the signalling pathways involved, and characterization of the main dietary signals.

The measurement and validation of cell and organ specific gene expression signatures of the metabolic consequences of specific micronutrients and macronutrients.

To understand the process of metabolic dysregulation that leads to diet related diseases; the identification of genotypes that are risk factors for the development of diet related human diseases (such as diabetes, hypertension or atherosclerosis) and quantification of their impact [5].

Key Nutrients That Modulate Periodontal Health

Periodontitis is initiated by the plaque biofilm, but most tissue destruction results from an abnormal inflammatory immune response in patients predisposed to the condition. The response is characterized by hyper inflammation, which fails to eradicate the causative pathogens and generates prolonged release of neutrophil proteolytic enzymes, proinflammatory mediators and reactive oxygen species (ROS), which in turn destroy the periodontal attachment.

There are six major classes of nutrients: carbohydrates, fats, minerals, protein, vitamins, and water. These nutrient classes are often categorized as either macronutrients (needed in relatively large amounts) or micronutrients. Micronutrients are dietary compounds, such as vitamins, minerals, trace elements, amino acids, poly-unsaturated fatty acids (PUFA) that are required only in small quantities (micrograms or milligrams per day) by living organisms and are essential for optimal health, proper growth, and metabolism. Specific nutrients can modulate immune and inflammatory responses. Omega 3 polyunsaturated fatty acid metabolites may act as signals to prevent neutrophil mediated periodontal tissue damage. Many studies have investigated the genetic relationship between periodontal disease and type II diabetes. Intake of polyunsaturated fatty acids, predominantly found in oily fish, increase the tissue concentrations of eicosapentaenoic acid and docosahexaenoic acid, which are known to down regulate inflammation. Based on the pathology of periodontal disease the assumption is that these nutrients could modulate periodontal health [6].

Antioxidant Micronutrients-An Emblem In Health and Disease

The term "antioxidant" is now limited to in vitro studies and the term "micronutrient" is employed for in vivo studies, in recognition that a diverse range of bioactivities un-related to free radical scavenging may explain the health benefits of such species. Increased production of reactive oxygen species raises requirements for the antioxidant nutrients involved in defense. Antioxidants may help in reducing the severity of disease by scavenging reactive oxygen species. Essential food groups that can function as antioxidants have shown potential for improving periodontal health. Antioxidant vitamins (vitamins A, C and E) and trace elements (selenium, copper and zinc) have been known to be depleted during inflammation which then counteract reactive oxygen species damage to cellular tissues and modulate immune-cell function through the regulation of redox regulated transcription factors which eventually affect the production of cytokines and prostaglandins [7]. Moreover, selenium has further important redox functions, with selenium-dependent glutathione enzymes being involved in the reduction of damaging lipid and phospholipid hydro peroxides to harmless products. The recommended dietary allowances (RDAs) for selenium in adult males and females are 55mcg. However, the range may vary from 20-40mcg in children [8].

Zinc supplementation may alter periodontal disease progression through changes in expression of the ZnT8 transporter gene. ZnT8 mediated zinc transport is important for normal beta cell function in insulin storage and release. Increased extracellular zinc concentration has been found to have a positive effect on glucose induced insulin secretion, indicating a potential benefit of zinc supplementation to susceptible type 2 diabetes individuals carrying the risk allele [9]. RDA of zinc varies from 2mg in infants to

13mg in adults per day [10].

Meisel et al. (2005) reported the results of the population-based cross-sectional health survey from north-eastern Germany, performed to identify risk indicators or risk determinants associated with periodontal disease. The concentrations of serum magnesium and calcium were determined and associated with periodontal parameters. It was shown that a higher Ca/Mg ratio was associated with a significantly lower level of periodontitis. The possible explanation implicated was:

Neutrophils invading periodontal tissues maintain the inflammatory process and participate in tissue destruction leading to attachment loss (Deas et al 2003).

Magnesium has a strong relationship with the immune system, plays a pivotal role in modulating the immune response (Mooren et al., 2003). Activation of neutrophils has an early effect of hypomagnesemia, and high Mg concentrations inhibit free-radical generation (Bussiere et al., 2002a). Thus, reduced Mg concentrations are associated with enhanced inflammatory response to bacterial challenge (Malpuech-Brugere et al., 2000). In contrast, calcium deficiency exerts a protective effect on inflammatory events (Bussiere et al., 2002b). Therefore, a ratio of calcium to magnesium should be 2:1, since a ratio above this has been associated with increased risk of metabolic, inflammatory and CVS disorders [11].

Vitamin C is a powerful antioxidant radical scavenger with in the aqueous phase, but upon oxidation forms an ascorbyl radical, which then breaks down to DHAA (Bergendi et al. 1999). It acts as a powerful scavenger of free radical. The role of vitamin C is to promote the synthesis of a normal mature collagen network by preventing iron-dependent oxidation of lysyl and prolyl hydroxylase and protecting these enzymes against auto-inactivation (Puistola et al. 1980). The relationship between vitamin C deficiency and necrotizing ulcerative gingivitis has frequently been described (Melnick et al. 1988). Vitamin E terminates 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. (Offenbacher, 1990). Panjamurthy et al. (2005) demonstrated lower plasma levels of vitamin C, vitamin E and reducedglutathione (GSH) in periodontitis patients compared with healthy controls [12].

Evidence Of Nutrional Benefits In Periodontics

Chapple et al. (2010) conducted a randomized controlled double blind intervention to elucidate the adjunctive effects of ingesting whole fruit, vegetable, and berry concentrates in a powdered capsular form during non-surgical periodontal therapy in 60 non-smokers with mild-moderate periodontitis. The result showed reductions in pocket depth and GCF volume post therapy in the phytonutrient supplement verses the placebo group Non-surgical periodontal therapy restored certain antioxidant components in a process attributed to reducing levels of oxidative stress secondary to the resolution of periodontal inflammation (Chapple et al. 2007b). Munoz et al. (2001) studied the effect of a nutritional supplement in a randomized, placebo controlled trial of 63 patients with early periodontitis. Subjects took the assigned tablet at breakfast and at dinner after brushing their teeth twice daily. The nutritional supplement consisted of seven ingredients i.e. folic acid, vitamin B12, vitamin C, Echinacea angustifolia, Vitis vinifera seed, ubiquinone and Piper nigrum extract. After 60 days a significant reduction in gingival index, bleeding index, and pocket depth could shown for the experimental group. The hydro-alcoholic extract from pomegranate fruit has shown to decrease the Colony Forming Unit (CFU) per millilitres of dental plaque by 84% [13]. Variety of treatment strategies has been developed to target the host response to periodontal infection like antimicrobial peptides, probiotics, anti-inflammatory lipid mediators and micronutrients. Use of live probiotic cultures for propagation of healthy microflora is a relatively new concept. There is evidence that probiotics can influence the composition of microflora and to a lesser degree the outcome of periodontal therapy. Local action and topical

Table 1. Summarizes Fda Recommended Daily Intake Of Various Nutrients.

NUTRIENTS	SOURCES	DAILY RECOMMENDED VALUES
Vitamin A	Cantaloupe • Carrots • Dairy products • Eggs • Fortified cereals • Green leafy vegetables (e.g., spinach and broccoli) • Pumpkin • Red peppers • Sweet potatoes	900 Mcg
Vitamin C	Fruit (e.g., cantaloupe, citrus fruits, kiwifruit, and strawberries) • Juices (e.g., oranges, grapefruit, and tomato) • Vegetables (e.g., broccoli, Brussels sprouts, peppers, and tomatoes)	90 mg
Vitamin E	Fortified cereals and juices • Green vegetables (e.g., spinach and broccoli) • Nuts and seeds • Peanuts and peanut butter • Vegetable oils	15 mg
Zinc	Beans and peas • Beef • Dairy products • Fortified cereals • Nuts • Poultry • Shellfish • Whole grains	11 mg
Magnesium	Avocados • Beans and peas • Dairy products • Fruits • Green leafy vegetables (e.g. Spinach) • Nuts and pumpkin seeds • Potatoes • Whole grains	420 mg
Calcium	Canned seafood with bones (e.g., salmon and sardines) • Dairy products • Fortified orange juice • Fortified plant-based beverages (e.g., soy, rice, and almond) • Fortified ready-to-eat cereals • Green vegetables	1,300 mg

effects of antioxidant agents from pomegranate on the oral tissues are hypothesized to possess preventive effect against diseases of the mouth. One minute rinsing with a mouthwash containing pomegranate extract successfully reduced the amount of microorganisms cultured from dental plaque [14].

A Road Map To Future

To highlight on nutrigenomics in periodontics as "HYPE OR HOPE", then definitely, nutrigenomics is a potential goldmine for the discovery of genes that are important as dietary targets.. The future of nutrigenomic research promises to supply additional knowledge of biological function and individual response to diet. The question still tarries; will nutrigenomics stay exciting enough over the next several years to sustain development of an extensive research foundation? It is clear that this will be the case because it is very well appreciated that further developments in nutrition and food development are impossible without exploring the mechanisms underlying nutrition and genomics. It should also have an important role in elucidating nutrient signalling pathways that might contribute to certain diet-related diseases including periodontal diseases [15]. However; the main challenge is that the heterogeneity in periodontitis cases is still one of the major problems in the interpretation of the various studies available in the literature in relation to genetic risk factors for periodontitis. The challenge is to identify nutrient-influenced molecular pathways and determine the down-stream effects of specific nutrients. Nutrigenomics can assist in this identification because it allows the genome-wide characterization of genes, the expression of which is influenced by nutrients. To apply these new discoveries for an improvised management of the periodontal disease, we must understand host response pattern and understand that our ultimate aim is to develop strategies to improve health management and to prevent periodontal diseases [16].

Conclusion

It has been shown that inadequate nutrition is a major lifestyle risk factor for a number of inflammatory diseases and conditions including cardiovascular diseases, type 2 diabetes, rheumatoid arthritis and inflammatory bowel disease, all of which are related to periodontitis. Therefore appropriate amount of nutrition may also play an important role in periodontitis pathogenesis and management. The available evidence would support the recommendation of an adequate daily intake of foods comprising natural sources of antioxidants, and supplements of vitamin D and calcium in deficient patients. Therefore, the medical history should include detailed information regarding the daily dietary in take of the various micronutrients as well as related life style characteristics.

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