THE ROLE OF DIET IN PERIODONTAL DISEASE

MR Milward, ILC Chapple

Introduction

Periodontitis is a ubiquitous chronic inflammatory disease affecting the supporting structures of the teeth and if not promptly recognised and correctly managed can ultimately lead to tooth loss resulting in reduced masticatory function and subsequent alterations in dietary intake and nutritional status.\(^1,2,3\) The importance of successful management and treatment of periodontitis has gained added press in 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.\(^4,5,6\) Periodontitis is highly prevalent in the community with data suggesting that periodontitis affects approximately 43% of UK adults overall and 83% of those >65 years of age.\(^7\) Moreover the UK population is shifting towards higher proportions of older people, with 10 million over the age of 65 years, which is projected to increase to 15 million by 2030 and nearly 20 million by 2050. This will result in more people with periodontal disease further reinforcing the need for successful management, a key public health priority.

Periodontitis is characterised by a dysregulated host inflammatory/immune response to plaque bacteria in susceptible individuals, however the host response exhibits wide heterogeneity in common with other chronic inflammatory diseases, and with relatively minor shifts in host response resulting in disease development and progression in susceptible people. A variety of risk factors have been identified that modify the host response and thereby tip the biological balance from health to disease. These factors can be characterised as genetic, environmental (e.g. stress, bacterial challenge) and lifestyle/behavioural (e.g. exercise, nutrition, smoking). Risk factors are important in the development and propagation of periodontal disease and act predominantly via modification of the host response to bacterial challenge, resulting in less effective clearing of pathogenic species and inflammation resolution which in turn increases host mediated tissue damage.\(^8\) For many years the literature has cited the importance of nutrition in a range of chronic inflammatory diseases, but in recent years there has been an increasing body of research investigating this phenomenon; however until recently the role of nutrition in periodontal disease had attracted little attention.

This article aims to discuss the role of nutrition in periodontitis, and how our patients nutritional status may impact at a biological level on this fascinating and complex disease process.

Types of nutrients

Nutrients can be divided into six major classes i.e. fats, carbohydrates, proteins, minerals, vitamins and water, these can be further subdivided into two broad categories, ‘macronutrients’ (fats, carbohydrates and proteins) which are required in large quantities from the diet and ‘micronutrients’ (minerals, vitamins, trace elements, and amino-acids) which are only required in small quantities in the diet and which are essential for a range of biological processes important in supporting optimal health.

Role of nutrition in periodontal disease

It has been acknowledged for many years that nutritional intake can impact upon the levels of inflammation seen in a number of diseases, and this is no less the case in periodontitis. 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.\(^9\) This finding has been further supported by a study investigating volunteers placed on a primitive diet which was high in fibre, anti-oxidants, 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, but unexpectedly gingival bleeding significantly reduced from 35% to 13%.\(^10\) These studies support a role for nutrition in controlling periodontal inflammation. However to date the precise mechanisms underpinning this observed dietary effect have yet to be fully elucidated. This article provides a brief overview of our current understanding of the proposed mechanisms of how diet may impact on the periodontal tissues of our patients.

Nutritional mechanisms of inflammation

Acute inflammation is protective but chronic and non-resolving inflammation is destructive and is central to a number of chronic diseases including periodontitis; in this section we will discuss the current understanding of these processes and the impact nutrition has on them.

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 diseases\(^11\) (e.g. type 2 diabetes, cardiovascular disease and metabolic syndrome) (Figure 1), indeed it has been proposed as a common link between periodontitis and systemic disease.\(^12,13\) In health a fine balance exists between, on one the hand oxidants and on the other antioxidants which are found in all tissues of the body (Figure 2). 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 (Figure 3). Oxidative stress was recently defined as “an imbalance between oxidants & antioxidants in favour of the oxidants, leading to a disruption of redox signalling & control and/or molecular damage.”\(^14\) It can cause direct tissue damage by altering molecules, such as proteins, lipids and DNA, thus damaging cells directly, or by activating redox-sensitive transcription factors within the cell that leads to downstream gene expression changes and production of pro-inflammatory molecules (cytokines - Figure 4). These cytokines or chemical messengers can further enhance and propagale the inflammatory response adding to local levels of oxidative stress.

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mechanisms fail to work efficiently, a viscous cycle is established and results in a transition from acute to chronic inflammatory lesions as found in periodontitis.

Increased levels of oxidative stress can result from cellular metabolism mainly due to electron leakage from mitochondria or via the host’s response to a range of stressful stimuli e.g. periodontal pathogenic bacteria such as Porphyromonas gingivalis, one of a number of bacteria strongly associated with periodontitis. Host cells have receptors on the cell surface (Pattern recognition receptors e.g. Toll-like receptors) that allow cells to recognise key bacterial components (e.g. lipopolysaccharide), resulting in activation of nuclear factor kappa-B, a pro-inflammatory gene transcription factor that is also sensitive to the redox state of the cell, and which generates downstream pro-inflammatory sequelae. In the periodontal tissues the lining epithelium of the periodontal pocket or crevice is intimately associated with the plaque biofilm and has been shown to produce a robust inflammatory response when exposed to key periodontal pathogenic bacteria (Figure 4). In susceptible patients the resulting inflammatory response is abnormally high and results in collateral tissue damage.

Increases in oxidative stress is antagonised by a complex system of antioxidants which include antioxidant vitamins, however it has been demonstrated that the most important small molecule antioxidant species is glutathione. Glutathione exists in both oxidised (GSSG) and reduced (GSH) forms and the ratio of GSH to GSSG normally favours GSH which maintains a reduced state inside the cell. GSH has a number of key characteristics that underpin its importance in antioxidant defence; it is a potent scavenger of free radicals and plays a key role in a number of other protective antioxidant systems. Other important functions of GSH include roles in cell metabolism and DNA synthesis and repair. The scientific literature identifies several studies that show that depletion of glutathione is associated with increased levels of periodontal disease.

**How can diet cause oxidative stress?**

It is already established that increased oxidative stress triggers a wide range of damaging cellular and molecular events and that increases in oxidative stress can result from normal cellular metabolism. If dietary levels of simple sugars are increased this further enhances oxidative stress levels via the generation of mitochondrial superoxide radicals, as a side effect of ATP synthesis, which can overwhelm cellular antioxidant defence mechanisms. Increased dietary intake of simple sugars or saturated fat can also increase oxidative stress by receptor binding of neutrophils. Firstly, excess glucose in the blood (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 (called the “respiratory burst”) to generate oxygen radicals. Secondly, metabolism of excess saturated fats generates elevated low density lipoprotein (LDL) cholesterol, which when oxidised forms oxidised LDL, this in turn binds to complementary receptors found on the cell membrane of neutrophils (Toll-like receptors), activating NADPH-oxidase and oxygen radical formation, further adding to the oxidative stress burden (Figure 5). These dietary – cellular interactions that increase oxidative stress are further complicated by the presence of periodontal pathogens such as Porphyromonas gingivalis, one of the key bacteria strongly associated with periodontal disease. This shows how bacteria present in the plaque biofilm stimulate a pro-inflammatory cellular response. Bacteria are recognised by cell surface receptors (Pattern recognition receptors) which results in activation of pro-inflammatory transcription factors (e.g. Nuclear factor kB) in the cytoplasm of the cell. The activated transcription factor migrates into the nucleus binds to DNA and causes changes in gene expression resulting in pro-inflammatory cytokine production in mitochondria. These cytokines are transported out of the cell and cause an inflammatory response and increases in local levels of oxidative stress.
are enhanced following a meal containing high levels of simple sugars and saturated fats generate inflammation, recently termed “meal induced inflammation”\(^\text{18}\), and are associated with increases in glucose and lipid in the blood stream, oxidative stress and downstream pro-inflammatory sequelae.

Smoking is a well-known risk factor for the development of periodontitis; it has been shown that smoking can increase levels of oxidative stress as well as reducing levels of vitamin C, and potentially more importantly the key antioxidant glutathione (GSH).\(^\text{19}\) This suggests one mechanism by which smoking increases the risk of periodontitis.

**How can diet reduce oxidative stress?**

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 reduces activation of a diverse range of pathways (some of which are discussed in the previous section) thereby reducing oxidative stress. As previously discussed, research has shown the importance of total amounts of simple sugars, carbohydrates and fat intake entering the blood stream\(^\text{20}\), but it also indicates that frequency of intake is also a key factor in generating oxidative stress, the more frequent the intake the greater the inflammation recorded in blood vessels.\(^\text{21}\)

Foods rich in antioxidants may help reduce oxidative stress, for example green leafy vegetables (broccoli, spinach etc.), berries (e.g. blueberries, blackberries, cranberries, strawberries etc.), red beans, red wine, and dark chocolate with greater than 70% cocoa are all rich in key antioxidant micronutrients (Figure 6). Other ways include diets that slow down gastric emptying (digestion) resulting in less pronounced spikes in blood glucose, examples of which include nuts, olive and fish oils which also have antioxidant properties, further adding to their effectiveness.\(^\text{12}\)

Research over recent years investigating a range of chronic diseases indicates that dietary supplementation with a single vitamin or antioxidant often fails to demonstrate the expected benefits and it is now recognised that such supplementation fails to account for the complex interactions present in a natural food source. Moreover, overloading with a single vitamin may destabilise antioxidant networks and generate vitamin radicals, which may be more detrimental to health than the oxygen radicals they remove. It has been demonstrated that the interaction and range of actions of a natural food source provides a number of additional benefits over and above that of the single component, and is the preferred route until we better understand the complex interactions between antioxidant micronutrients.

The physiological impact of nutrients on the host depends upon many factors including bioavailability following transit through the digestive system, absorption from the gut into the circulation, conversion to a bioactive form and transport to target cells. A dietary supplement may show excellent antioxidant/anti-inflammatory properties in the laboratory, but have no clinical efficacy if it fails to reach the target tissues in an active form. It is also becoming clear that individual differences in genetic makeup account for a diverse array of responses to dietary supplementation, something that needs to be taken into account when a new dietary intervention is proposed, i.e. “one size may not fit all”.

**Diet and Periodontal Disease**

The current literature on the relationship between diet and periodontal disease is largely inconclusive; this is most likely due to a lack of clarity in assessment of nutritional status. Over the last few years improved understanding of ways to assess and investigate nutritional status has emerged along with the recognition of the importance of assessing nutritional intake, body composition and biochemical measures of nutrition. Measuring serum levels of various micronutrients alleviates issues surrounding self-reporting of dietary intake (poor compliance) and inadequate absorption of the dietary supplement.

However, the literature suggests periodontitis is associated with reduced serum micronutrient levels\(^\text{22-24}\) this may be due to a number of reasons including poor diet, lifestyle factors (e.g. smoking) and/or genetic factors which impact on absorption, distribution, bioavailability and synthesis of micronutrients.

A recent randomised double-blind clinical trial by our group investigated potential clinical benefits of a powdered fruit and vegetable juice concentrate on the treatment of patients with chronic periodontitis. The study assessed dietary intake and biochemical nutritional status.
(plasma β-carotene). It concluded that supplementation with the fruit and vegetable concentrate resulted in increased pocket depth reduction following standard non-surgical therapy when compared to a placebo control. A second multi-centre follow up study is currently in progress aiming to determine the effects of supplementation upon periodontal inflammation prior to periodontal treatment, we eagerly await the outcome.

**Dietary recommendations for periodontal disease management**

The recommendations of the 2011 European workshop on Periodontology suggest that the dental team should consider including advice to all patients on increasing levels of fish oils, fibre, fruit and vegetables and to reduce levels of refined sugars as part of a periodontal prevention/treatment regime and a general health benefit message.

**Conclusions**

Periodontitis is a highly prevalent disease which affects a large proportion of the UK population, and as the population demographic shifts towards higher proportion of older people and disease prevalence increases with age, the already considerable demands placed on health care provision in managing periodontitis are set to further increase. The relatively recent finding that periodontitis is associated with a range of systemic chronic inflammatory diseases further emphasises the importance of successful periodontal disease management, and not just for tooth retention, but also for general health.

Our current management strategies focus on reduction in the microbial biofilm as a way of reducing inflammatory load; this approach has remained unchanged over the last 50 years and has limitations in treatment outcome. New treatment modalities need to place more emphasis on host inflammatory response which is dysregulated in periodontitis and is recognised as the most important factor in disease pathogenesis.

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.