



ROLE OF ANTIOXIDANTS IN PERIODONTAL THERAPY- A REVIEW

Dental Science

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ABSTRACT

Periodontal disease comprises a group of all conditions, from inflammation to infections to tumors, that affect the well-being of the tooth-supportive apparatus that is the periodontium (gingiva, periodontal ligament, cementum, and alveolar bone). Hyperactivity of peripheral blood neutrophils is associated with periodontitis, which are considered as the main source of Reactive Oxygen Species (ROS). Biomarkers used for oxidative stress associated with periodontitis include products of lipid peroxidation, protein damage and DNA damage. Periodontitis influenced local and systemic activities of antioxidants. Nutrition plays an important role in preventing oxidative damage of periodontium. It does not only protect the periodontium from free radicals but also helps in reduction of inflammation. Herbal medicine and phytoconstituents are also important to manage pathological conditions of those diseases caused by free radicals.

KEYWORDS

Periodontitis, Antioxidants, Reactive oxygen species, Oxidative stress.

INTRODUCTION

Periodontitis is an inflammatory disorder that leads to damage to tissues and bone as a result of complex interactions between pathogenic bacteria and the host's immune response.¹ Primary etiological factor for periodontitis is predominantly gram-negative anaerobic or facultative bacteria within the sub gingival biofilm.²

Oxidation is defined as a chemical reaction that transfers electrons from a substance to an oxidizing agent. The reduction of molecular oxygen to water gives rise to energy release and Free Radicals (FR) and/or ROS which causes several chronic degenerative diseases.³

FRs have been defined as any species which are capable of independent existence and contain one or more unpaired electrons.⁴ They are very reactive and different species, capable of extracting electrons and oxidized a variety of biomolecules which are vital to cell and tissue function and they not only include oxygen free radicals, but also nitrogen and chlorine species.

"Anti-Oxidant therapy" has evoked a wide response in all medical circles as prevention of ageing, oncogenicity and much similar illness. When antioxidants are depleted, the ability of gum tissue is compromised to overcome oxidative stress, maintain normal tissue and control the bacterial damage. The mechanisms of ROS mediated tissue damage and of antioxidant defence in response to bacterial colonisation can be studied in periodontal tissues.⁵

Reactive Oxygen Species

ROS encompasses other reactive species which are not true radicals but are nevertheless capable of radical formation in the intra- and extracellular environments.

The majority of periodontal tissue destruction is caused by an alteration in host response to microorganisms and their products. Mainly, a loss of homeostatic balance between proteolytic enzymes (e.g. neutrophil elastase) and their inhibitors (e.g. a 1-anti-trypsin), ROS and the antioxidant defence systems that protect and repair vital tissue, cell, and molecular components is believed to be responsible.

Oxidative killing mechanism of neutrophils and other phagocytes involves the formation of ROS. Within the gingival crevice/pocket, a low redox potential is regarded as essential for the growth and survival of subgingival anaerobes, whereas within cells and tissues a reducing environment (low redox potential) is protective against oxidative stress. So, there is an apparent conflict in developing future therapeutic strategies for periodontitis which are based on redox biology, because

maintaining low redox status (i.e reducing environment) to protect host cells and tissues from oxidative stress is conducive to encouraging growth and survival of anaerobes.⁶

Origin and formation of ROS and free radicals

1. Exogenous sources include:⁷

- Heat, trauma, ultrasound, ultraviolet light, ozone.

2. Endogenous sources include:⁷

- By-products of metabolic pathways.
- Functional generation by host defence cells (phagocytes) and cells of the connective tissues (osteoclasts and fibroblasts).

Evidence for the presence and role of ROS in periodontal destruction

The four criteria proposed by Halliwell⁸, similar to those proposed by Robert Koch⁹ to establish a causal relationship between an organism and a disease, are:

- The cause for ROS or the oxidative damage must be present at site of injury;
- The time course of ROS formation or the oxidative damage caused should collide with tissue injury;
- Direct application of ROS to tissues at concentrations found in vivo should reproduce damage similar to that observed in the diseased tissue;
- Removal or inhibition of ROS formation should decrease tissue damage to an extent related to their antioxidant action in vivo.

Antioxidants

Antioxidants are any substance that delay or inhibits oxidative damage to a target molecule.¹⁰ At a time one antioxidant molecule can react with single free radicals and are capable to neutralize free radicals by donating one of their own electrons, and stop sharing the carbon atoms. Antioxidants act as scavenger by preventing cell and tissue damage. Cell produce defense against excessive free radicals by their preventative mechanisms, repair mechanisms, physical defenses and antioxidant defenses.¹¹

Classification of antioxidants

The antioxidants can be classified depending on several criteria like according to their nature, mode of action, location, origin, or solubility.¹² **Table 1**

Table-1: Classification of antioxidants

Classification basis	Classification	Examples
Depending on nature	a. Enzymatic antioxidants	Super oxide dismutase (SOD)

	b. Non enzymatic antioxidants	Vitamin E, Ascorbic acid
Depending on their mode of action	a. Preventive antioxidants	Catalase
	b. Scavenging antioxidants	Ascorbate (vitamin C), carotenoids
Depending on the origin	a. Endogenous	SOD
	b. Exogenous	Ascorbic acid
Depending on location of action	a. Extracellular	Haptoglobin
	b. Intracellular	SOD
	c. Membrane associated	Tocopherol
Depending on solubility	a. Water soluble	Haptoglobin
	b. Lipid soluble	Carotenoids

Oxidative Stress

Oxidative stress as defined by Sies as "A disturbance in the pro-oxidant – antioxidant balance in favour of the former leading to potential damage".¹³ It is basically an imbalance amongst the ROS and host's ability to repair the subsequent damage. Antioxidants provides a defence system against these ROS. A continuous state of balance is maintained by the body between the ROS and the antioxidants. Whenever this balance is disturbed, the ratio of ROS to AO increases, resulting in 'Oxidative Stress'.¹⁴ Nutrition plays an important role in preventing oxidative damage of periodontium. It does not only protect the periodontium from free radicals but also helps in reduction of inflammation.¹³

Antioxidant defense systems

The preventative antioxidants function by enzymatic removal of superoxide and hydrogen peroxide or by sequestration of divalent metal ions and prevents hydroxyl radical formation and Fenton reactions. Lactoferrin is probably more important than transferrin within the periodontal tissues, given the dominance of the neutrophil infiltrate and the recognition of high levels of lactoferrin within gingival crevicular fluid.¹⁵

It is important to recognize however, that several antioxidants have dual and sometimes triple actions.¹⁶ For example, ascorbate acts as a chain breaking or scavenging antioxidant as well as a preventative antioxidant by virtue of its ability to recycle α -tocopherol (vitamin E) from its oxidized form and by its ability to bind metal ions, respectively.¹⁷

Plasma Antioxidant Status in Periodontal Diseases

In periodontal literature, early studies of individual antioxidant micronutrients were not found to be convincing in their associations between dietary antioxidant intake and periodontitis. Few studies that have explored individual antioxidant scavengers in serum or plasma have shown only mildly compromised levels in periodontitis subjects relative to healthy controls, except where smoking is a co-factor.¹⁸⁻²⁰

An inverse relationship was found between serum vitamin C concentrations and antibody levels to *P. gingivalis*. Panjamurthy et al²¹ observed lower plasma vitamin C, vitamin E and reduced glutathione in periodontitis subjects. However, antioxidant enzyme levels were raised and this is a protective response to oxidative stress.

Total antioxidant capacity (TAOC) concentration was found to be less in serum and plasma of periodontitis patients.

Salivary Antioxidant Status in Periodontal Diseases

The use of saliva as a diagnostic fluid is a relatively good trend. Saliva is a mixed oral fluid that is secreted from major and minor salivary glands. Oral fluid, often considered as the mirror of the body's health, is a best medium to be explored for health and disease surveillance. Saliva is considered to be the first line of defence against oxidative stress (OS), the main cause for many systemic and oral diseases. Important sources of oral free radicals and reactive oxygen species (ROS) are tobacco, smoke, periodontitis and other oral diseases in oral cavity. Saliva contains good amount of antioxidants: uric acid, albumin, ascorbate and enzymes which constitute the antioxidant potential of saliva.²²

GCF Antioxidant Status in Periodontal Diseases

GCF continuously flows through the epithelium and enters the gingival sulcus at a very slow rate (0.24–1.56 ml/minute at non-

inflamed sites). Similarly, neutrophils migrate into the sulcus by the same route. GCF is the most appropriate fluid to sample when investigating biomarkers of tissue events in periodontium.

Spontaneous generation of superoxide in the GCF of periodontitis subjects, with no differences in antioxidant scavenging capacity between cases and controls. However, no disparity was reported in the SOD activity in GCF of periodontitis subjects.

Inter relationship of Periodontal and Systemic Conditions:

Periodontal diseases may have wide spread systemic effects, while these effects may be less in some individuals. Periodontal infections may significantly affect systemic health in others and may serve as major risk indicators for certain systemic diseases or conditions.²³ With regard to diabetes, advanced glycation end products (AGEs) present in diabetic gingiva may be associated with a state of enhanced oxidative stress, a potential mechanism for accelerated tissue injury that frequently observe clinically. This implies that the diabetic has an even greater requirement for antioxidants.²⁴ A decrease in systemic and local antioxidant defense was observed owing to both menopause and periodontitis.

Recommendation for the periodontal therapy:

1. Control bacteria with improved oral hygiene
2. Remove etiologic factors with scaling and root planing
3. Strengthen the host defence response with appropriate supplementation and track baseline and subsequent antioxidant status using non-invasive measurement of skin carotenoids.

4. Surgical objectives when surgery is necessary:

- i. soft tissue regeneration
- ii. pocket reduction
- iii. bone regeneration
- iv. periodontal plastic surgery procedures

CONCLUSION

It has been confirmed that periodontitis is associated with a hyperactivity of peripheral blood neutrophils, which are supposed to be the predominant source of ROS Products of lipid peroxidation, protein damage and DNA damage which can be used as the biomarkers of oxidative stress associated with periodontitis local and systemic activities of antioxidants can also be influenced by periodontitis.

Nutrition plays an important role in preventing oxidative damage of periodontium. It does not only protect the periodontium from free radicals but also helps in reduction of inflammation.

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