VOLUME - 13, ISSUE - 04, APRIL - 2024 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Periodontology

FIGHT AGAINST PERIODONTITIS – ANTIOXIDANTS - THE MOST FORMIDABLE WEAPON OF ALL

K. Malathi

Hima Bindu Reddy. C

Varshini. S

Rachana Anagol

Kiruthika. A

ABSTRACT One of the prime factors in the pathogenesis of periodontitis is increased oxidative stress. Therefore, antioxidant therapy may become a promising tool in the treatment of periodontal disease. Low levels of antioxidants is a risk factor for periodontal disease and infection. The imbalance between oxygen species and antioxidant defense system may increase the oxidative burden, that leads to the damage of macromolecules. The relationship between antioxidants and their association with periodontitis are discussed here.

KEYWORDS : Periodontitis, antioxidants, reactive oxygen species

INTRODUCTION:

An antioxidant is any substance that when present at low concentrations compared to those of an oxidizable substrate significantly delays or prevents oxidation of that substrate. [1]

Biologically important compounds those have been known to have antioxidant properties are vitamin C, vitamin E, vitamin A, β-carotene, metallo-thiamine, melatonin, adenosine, coenzyme Q-10, urate, cysteine, homocysteine, reduced glutathione, glutathione peroxides, superoxide dismutase, catalase, nitric oxide synthase, haem oxygenase I, eosinophil peroxidase.[2]

Antioxidant blocks the process of oxidation by neutralizing free radicals and in doing so, the antioxidant themselves become oxidized[3]. Due to this there is a constant need to replenish our antioxidant resources.

The primary etiological agent in periodontal disease is bacteria within the subgingival biofilm.[4] Periodontal destruction is caused by periodontopathic bacteria and their products. The destruction is mainly due to imbalance between proteolytic enzymes and their inhibitors, reactive oxygen species (ROS), the antioxidant defense that protects and repairs vital tissue, cell and molecular components, is believed to be responsible.[5]

During inflammatory response oxidative stress occurs, reactive oxygen species overwhelm the endogenous antioxidant defense system. During phagocytosis, reactive oxygen species are generated by PMNs in the process of oxidative burst.[6] One of the prime factors in periodontal disease is increased oxidative stress, therefore antioxidant therapy may become a promising tool in the treatment of periodontal disease.

Diet rich in vitamins appear to be associated truly with good periodontal health and negatively with progressive periodontal diseases.[7] Exogenous antioxidants in the form of dietary supplement strengthens the body's antioxidant defense system.

Classification:

Antioxidants are categorized by [8]

1. Their mode of action:
Preventive
Scavenging
2. Their location of action:
Intracellular
Extra cellular
Membrane associated
3. By solubility:
Water soluble
Lipid soluble
4. By structures they protect:
DNA
Protein
lipid
5. By their origin:
Exogenous
Endogenous

Mechanism Of Action:

1. Chain Breaking Mechanism:
In this mechanism the primary antioxidant donates an electron to the free radical present in the system.[9]

Eg: lipid radical.
2. It involves removal of ROS/RNS initiators by quenching chain-initiating catalyst.
Electron donation, metal chelation, co-antioxidants and gene expression regulators are the different techniques involved.

Predominant Antioxidants

- VITAMIN C OR L-ASCORBIC ACID

It is water soluble and most important antioxidant in extra cellular fluid. Its activity includes scavenging water soluble peroxyl radicals, super oxides and perhydroxy radicals, hypochloric acid, singlet oxygen and hydroxy radicals and preventing damage mediated by hydroxyl radicals on uric acid.[10]

It also uses the heme breakdown and subsequent iron release thereby preventing Fenton reactions. It also protects against ROS release from cigarette smoke, retains -tocopherol from its radical. It also acts as a strong antioxidant in the plaque and presents a synergistic effect with co-antioxidant.

- α-TOCOPHEROL

This lipid soluble antioxidant is very effective and most important. By peroxy radical scavenging mechanism it maintain the cell membrane integrity against lipid peroxidation. Antioxidant behaviour is the result of a single phenolic hydroxyl group.[11]

Vitamin E possess anti-inflammatory as well as antioxidant properties by inhibition of protein kinase C, inhibition of nitric oxide production by vascular endothelium and inhibition of

super oxide production by macrophages and neutrophils and inhibition of p47 phox phosphorylation.

- CAROTENOIDS

They are lipophilic. Higher plasma concentration of carotenoids have shown to protect against various inflammatory and malignant diseases.

Lycopene is an effective natural antioxidant and a quench of free radicals. It exhibits the highest physical quenching rate, atleast three fold more effective than β-carotene. One of the recent study stated that there is a positive relation between CHF and periodontitis, and high monthly tomato consumption.[12]

Lycomed, G-power lyco are commercially available lycopene. Lycopene is atleast twice as effective as -carotene in acting as a effective protectors of lymphocyte cells from nitrogen dioxide radical damage and highest protection is given by lycopene.

- POLYPHENOLS

Polyphenolic flavonoids are more in dietary intake of vegetable, red wine and tea. The cellular mechanism involved is mainly due to their antioxidant properties or to their inhibitory activity towards lipooxygenase pathway. Polyphenol function by terminating lipid peroxidation.[13] By sparing vitamin E or by restoration of vitamin C, it enhances ROS protection. Generally polyphenols functions by radical scavenging and iron chelation.

- GLUTATHIONE:

It acts as an intrinsic antioxidant, immune booster and detoxifier. It is an essential tripeptide and has 3 major roles in the body.[14]

It is one of the most vital intracellular antioxidant scavengers and plays a major role in maintaining the intracellular redox balance, thus regulating the signaling pathways which are affected by oxidative stress.

- URIC ACID

It is a weak acid distributed throughout the Extracellular fluid as sodium urate. Uric acid is produced from purines. Scavenger of singlet oxygen, hydroxyl radicals and hypochloric acid are its antioxidant activities. Apart from this its antioxidant activity include protection of α1-antitrypsin when combined with ascorbate and binding of divalent metal ions that prevents Fenton chemistry.

As a result of bacterial clearance and killing, free radicals are released and oxidative stress occurs. To overcome this oxidative stress and maintain homeostasis, antioxidants are important. Periodontal tissue depends on natural antioxidant to overcome this oxidative stress. Low levels of antioxidants are a risk factor for periodontal diseases. Because, when it is depleted, the ability of gingival tissue to overcome oxidative stress, maintain normal tissue and control the bacterial damage appears to be compromised. Increase in the risk by 13 fold is noted with low level of selenium in association with gum disease.

Apart from this, low levels of vitamin A and C, α-carotene and β-cryptoxanthine also increase the risk of periodontal disease. Protective response of oxidative stress is rapid in periodontium when antioxidant levels are increased. In epileptic cases with periodontal disease, oxidant-antioxidant distress play a important role in the patho-mechanism of periodontal disease. The systemic administration of alpha lipoic acid (ALA) and vitamin C could inhibit inflammatory bone resorption and osteoclast activation. This reveals a new possible method for preventing periodontitis and improving periodontal health.[15]

- Coenzyme Q10

It exists in two forms, oxidized and reduced form. Both has powerful antioxidant activity. It has an important role in the free radical mediated neurodegenerative diseases. Coenzyme 10 is present in gingival tissues and patients with periodontitis.[16]

Antioxidant Defense System:

The antioxidant defense system of the human body are complex enzyme like SOD enzyme, catalase, glutathione peroxidase, DNA repair enzyme are preventive antioxidants and ascorbate, carotenoids, uric acid, vitamin E, polyphenols, bilirubin, albumin and other thiols are scavenging antioxidants. The preventive antioxidants functions by enzymatic removal of superoxide and Hydrogen peroxide or by sequestration of divalent metal ions. Lactoferrin is more important than transferrin within the periodontal tissue and the recognition of higher levels of lactoferrin within the gingival crevicular fluid.[17] The chain breaking antioxidants are most important within the extracellular fluid.

Most of the antioxidants have dual and sometimes triple actions. For example ascorbate acts as a chain breaking or scavenging antioxidant as well as a preventive antioxidant. intracellular enzymes are regarded by some as preventive antioxidants. The efficacy of an antioxidant depends upon its location and the nature of the reactive oxygen species challenge and other environmental conditions.

Levels of vitamin A, vitamin C and alpha carotene and beta cryptoxanthin are also important. Beta carotene and lycopene are effective protectors of lymphocyte cells from nitrogen oxide radical damage and lycopene is atleast as twice effective as beta carotene.

A study of Tinkler et al, showed that beta carotene, astaxanthin, lycopene and canthaxanthin bound to the surface of lymphoid cells and found that they protect the cells against the photodynamic reaction sensitized by rose bengal or meso-tetra-porphine.[18] The protective response in oxidative stress is increased when the antioxidant levels are increased. Study on epileptic patient with periodontal disease showed oxidant and anti-oxidant disturbance. It plays an important role in the patho- mechanism of periodontal disease. Systemic administration of ALA (alpha lipoic acid) and ALA +vitamin C could inhibit inflammatory bone resorption and osteoclast activation, that reveals a new and possible method_for preventing periodontal bone resorption and improving periodontal health.

Antioxidant In Periodontal Health:

Antioxidants are the powerful new weapons in the fight against periodontal disease. The imbalance between oxygen species and antioxidant defense system may increase the oxidative burden, that leads to the damage of macromolecules. It blocks the process of oxidation by neutralizing free radicals and in doing so, the antioxidant themselves become oxidized. decreased levels of most antioxidants are a risk factor for periodontal disease and infection to overcome the oxidative stress and maintain periodontal homeostasis. Decreased level of antioxidants results in inability of gingival tissue to overcome oxidative stress, maintaining the normal tissue and controlling the bacterial damage appears to be compromised and as a result bacterial clearance and killing free radicals are reduced.[19] Study on serum levels of antioxidant nutrients and their relationship to Periodontal disease showed that selenium had the strongest association with gum disease, low levels of which increased the risk of periodontal disease by 13 fold.

Antioxidants Etiology:

The primary etiological factors causing periodontal disease is periodontal pathogens, yet multiple factors are involved in its

pathogenesis, oxidative stress is one of them and is supported by scientific literature that demonstrated high levels of oxidative damage products of DNA, lipids and proteins and minimal levels of antioxidant enzymes in chronic periodontal inflammation.

There is a positive correlation between periodontal health and adjunctive antioxidant supplementation with Non Surgical Periodontal Therapy.[20]

The etiological role of free radical injury in periodontitis with diabetes showed that the compensatory mechanism of the body is partially collapsed due to excessive production of free radicals during periodontitis and is not able to cope up with increased free radical generation due to diabetes, thereby worsening the situation.

Total Antioxidant Capacity (taoc):

The measurement of total antioxidant capacity (TAOC) was developed as a cost effective instrument to assess the activity of the whole antioxidant system and most of the studies says that the periodontitis is associated with compromised local total antioxidant capacity (TAOC). [21] TAOC in plasma and saliva was shown to correlate with periodontal parameter and some studies suggested that the periodontitis could influence the circulating TAOC. Systemic conditions like gender, smoking, pregnancy and systemic diseases can affect the TAOC associated periodontitis. Men have higher serum TAOC than women and same in saliva also. In pregnancy, especially in the last trimester lower TAOC in serum and GCF was noted and it correlates with periodontal status. Lower TAOC was also noted among smokers and diabetes mellitus patient was also associated with periodontal status.

An assay based on the oxidation of ferrous ion to ferric ion in the presence of various oxidant species in acidic medium was introduced to measure the total oxidant status and this could be used as a stable and convenient measurement of the whole oxidant status. Oxidative stress index (OSI) is another parameter to calculate TOS/TAOC and these two parameters have been widely used to measure whole oxidative stress associated periodontitis.[22] Higher value of TOS and OSI in GCF and serum can be reduced by periodontal management. Stage III periodontitis is associated with significantly higher values of TOS and OSI compared to chronic periodontitis. Studies had proposed OSI as a new biomarker for periodontitis.[23]

CONCLUSION:

Periodontitis is an inflammatory disease initiated by bacterial infection and progressed by aberrant host response. Under normal conditions, there is a balance between reactive oxygen species (ROS) and antioxidants. Local and systemic activities of antioxidant can also be influenced by periodontitis, total antioxidant capacity, total oxidant status and oxidative stress index are used to evaluate the oxidative stress associated periodontitis. Uric acid is a major antioxidant in saliva that can be used as a marker to assess the total antioxidant capacity. Different antioxidants are applied as supplement to the conventional periodontal therapy and optimal results are obtained.

REFERENCES

1) Halliwell B. How to characterize an antioxidant: an update. Biochem Soc Symp. 1995;61:73-101. doi: 10.1042/bss0610073. PMID: 8660405
2) Ndhlala AR, Moyo M, Van Staden J. Natural antioxidants: fascinating or mythical biomolecules? Molecules. 2010 Oct 8;15(10):6905-30. doi: 10.3390/molecules15106905. PMID: 20938402; PMCID: PMC6259562.
3) Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev. 2010 Jul;4(8):118-26. doi: 10.4103/0973-7847.70902. PMID: 22228951; PMCID: PMC324991.
4) Abdulkareem AA, Al-Taweel FB, Al-Sharqi AJB, Gul SS, Sha A, Chapple ILC. Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. J Oral Microbiol. 2023 Apr 2;15(1):2197779. doi: 10.1080/20002297.2023.2197779. PMID: 37025387; PMCID: PMC10071981.
5) Dahiya P, Kamal R, Gupta R, Bhardwaj R, Chaudhary K, Kaur S. Reactive oxygen species in periodontitis. J Indian Soc Periodontol. 2013 Jul;17(4):411-6. doi: 10.4103/0972-124X.118306. PMID: 24174716; PMCID: PMC3800399.
6) Nguyen GT, Green ER, Mecsas J. Neutrophils to the ROScue: Mechanisms of NADPH Oxidase Activation and Bacterial Resistance. Front Cell Infect Microbiol. 2017 Aug 25;7:373. doi: 10.3389/fcimb.2017.00373. PMID: 28890882; PMCID: PMC5574878.
7) Kaur G, Kathariya R, Bansal S, Singh A, Shahakar D. Dietary antioxidants and their indispensable role in periodontal health. J Food Drug Anal. 2016 Apr;24(2):239-246. doi: 10.1016/j.jfda.2015.11.003. Epub 2016 Jan 8. PMID: 28911576; PMCID: PMC9339570.
8) Mehla, N., Kothari Chhajer, A., Kumar, K., Dahiya, S., Mohindroo, V. (2021). Applications of Antioxidants: A Review. In: Ekiert, H.M., Ramawat, K.G., Arora, J. (eds) Plant Antioxidants and Health. Reference Series in Phytochemistry. Springer, Cham. https://doi.org/10.1007/978-3-030-45299-5_28-1
9) Chaudhary P, Janmeda P, Docea AO, Yeskaliyeva B, Abdull Razis AF, Modu B, Calina D and Sharifi-Rad J (2023) Oxidative stress, free radicals and antioxidants: potential crosstalk in the pathophysiology of human diseases. Front. Chem. 11:1158198. doi: 10.3389/fchem.2023.1158198
10) Agwu E, Ezihe C, Kaigama G. Antioxidant Roles/Functions of Ascorbic Acid (Vitamin C) [Internet]. Ascorbic Acid - Biochemistry and Functions. IntechOpen; 2024. Available from: http://dx.doi.org/ 10.5772/ intechopen.110589
11) Niki E. Role of vitamin E as a lipid-soluble peroxyl radical scavenger: in vitro and in vivo evidence. Free Radic Biol Med. 2014 Jan;66:3-12. doi: 10.1016/j.freeradbiomed.2013.03.022. Epub 2013 Apr 2. PMID: 23557727.
12) Imran M, Ghorat F, Ul-Haq I, Ur-Rehman H, Aslam F, Heydari M, Shariati MA, Okuskhanova E, Yessimbekov Z, Thiruvengadam M, Hashempur MH, Rebezov M. Lycopene as a Natural Antioxidant Used to Prevent Human Health Disorders. Antioxidants (Basel). 2020 Aug 4;9(8):706. doi: 10.3390/antiox9080706. PMID: 32759751; PMCID: PMC7464847.
13) Rudrapal M, Khairnar SJ, Khan J, Dukhyil AB, Ansari MA, Alomary MN, Alshabrmi FM, Palai S, Deb PK, Devi R. Dietary Polyphenols and Their Role in Oxidative Stress-Induced Human Diseases: Insights Into Protective Effects, Antioxidant Potentials and Mechanism(s) of Action. Front Pharmacol. 2022 Feb 14;13:806470. doi: 10.3389/fphar.2022.806470. PMID: 35237163; PMCID: PMC8882865.
14) Lushchak VI. Glutathione homeostasis and functions: potential targets for medical interventions. J Amino Acids. 2012;2012:736837. doi: 10.1155/2012/736837. Epub 2012 Feb 28. PMID: 22500213; PMCID: PMC3 303626.
15) Akman S, Canakci V, Kara A, Tozoglu U, Arabaci T, Dagsuyu IM. Therapeutic effects of alpha lipoic acid and vitamin C on alveolar bone resorption after experimental periodontitis in rats: a biochemical, histochemical, and stereologic study. J Periodontol. 2013 May;84(5):666-74. doi: 10.1902/jop.2012.120252. Epub 2012 Jun 15. PMID: 22702517.
16) Ghasemi S, Torab Z, Shirmohammadi A, Babaloo A, Johari R, Farhadi F, Mobasseri M, Mohammadi H. Evaluation of the effect of coenzyme Q10 supplementation along with scaling and root planing (SRP) on periodontal and gingival indices in controlled diabetic patients. J Adv Periodontol Implant Dent. 2022 Mar 13;14(1):32-37. doi: 10.34172/japid.2022.003. PMID: 35919443; PMCID: PMC9339722.
17) Kivadasannavar AV, Pudakalakatti PS, Hattarki SA, Kambali SS. Estimation of lactoferrin levels in gingival crevicular fluid before and after periodontal therapy in patients with chronic periodontitis. Contemp Clin Dent. 2014 Jan;5(1):25-30. doi: 10.4103/0976-237X.128657. PMID: 24808691; PMCID: PMC4012112.
18) Patrizia Riso, Andrew Pinder, Alessandra Santangelo, Marisa Porrini,Does tomato consumption effectively increase the resistance of lymphocyte DNA to oxidative damage?2,The American Journal of Clinical Nutrition,Volume 69, Issue 4,1999,Pages 712-718,ISSN 0002-9165,https://doi.org/10. 1093/ajcn/69.4.712
19) Pendyala G, Thomas B, Kumari S. The challenge of antioxidants to free radicals in periodontitis. J Indian Soc Periodontol. 2008 Sep;12(3):79-83. doi: 10.4103/0972-124X.44100. PMID: 20142950; PMCID: PMC2813562.
20) Araújo EG, Oliveira DMSL, Martins CC, Stefani CM. Efficacy of Antioxidant Supplementation to Non-Surgical Periodontal Therapy on Metabolic Control in Type 2 Diabetes Patients: A Network Meta-Analysis. Antioxidants (Basel). 2022 Mar 24;11(4):621. doi: 10.3390/antiox11040621. PMID: 35453306; PMCID: PMC9031448.
21) Baser U, Gamsiz-Isik H, Cifcibasi E, Ademoglu E, Yalcin F. Plasma and salivary total antioxidant capacity in healthy controls compared with aggressive and chronic periodontitis patients. Saudi Med J. 2015 Jul;36(7):856-61. doi: 10.15537/smj.2015.7.11954. PMID: 26108592; PMCID: PMC4503907.
22) Dursun E, Akalin FA, Genc T, Cinar N, Erel O, Yildiz BO. Oxidative Stress and Periodontal Disease in Obesity. Medicine (Baltimore). 2016 Mar;95(12):e3136. doi: 10.1097/MD.0000000000003136. PMID: 27015191; PMCID: PMC4998386.
23) Wang Y, Andrukhov O, Rausch-Fan X. Oxidative Stress and Antioxidant System in Periodontitis. Front Physiol. 2017 Nov 13;8:910. doi: 10.3389/fphys.2017.00910. PMID: 29180965; PMCID: PMC5693842.