World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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Aging and periodontium: Slowing aging process by improving periodontal health

Chiquita Prahasanti [1,*], Mela Karina [2], Widyawati Sutedjo [2] and Haryono Utomo [2]

[1] *Department of Periodontology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.*
[2] *Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.*

World Journal of Advanced Research and Reviews, 2024, 24(02), 756–760

Publication history: Received on 22 September 2024; revised on 05 November 2024; accepted on 07 November 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.24.2.3391

Abstract

Introduction: Aging is characterized by a progressive decline or loss of physiological functions, leading to increased susceptibility to disease or death. The periodontium, a complex structure surrounding and supporting the teeth, is composed of the gingiva, periodontal ligament, cementum, and alveolar bone. Supportive and protective roles of the periodontium are very critical to sustain life, but the periodontium undergoes morphological and physiological changes with age.

Purpose: The aim of this review is to summarize the current findings of delaye aging process by improving periodontal health.

Conclusion: Daily oral hygiene maintenance with toothbrushing, flossing, mouthrinsing and appropriate use of anti-oxidants, such as vitamin C, as well as regular visit to dentist or periodontist is mandatory to maintain healthy periodontal tissue which support general health, also slowing down aging process

Keywords: Aging process; Oxidative stress; Periodontal disease; Antioxidants; Ssystemic factors

1. Introduction

Aging is characterized by a progressive decline of the homeostasis and physiological function of multiple organs. In the course of organismal aging, tissue degeneration and alternatively, inadequate tissue regeneration, are intimately linked to weakened immune responses and inefficient wound healing. As a stable arrest of cell cycle progression, senescence was originally reported in human primary fibroblasts, which experienced consecutive passaging under culture conditions with a terminated proliferation[1]. Accelerated aging has been associated with higher vulnerability to chronic diseases and death. In addition, recent studies suggest several promising interventions, such as regulating nutrient sensing, controlling cellular senescence, and balancing the gut microbiome [2]. Accordingly, understanding the factors associated with accelerated aging is crucial for the institution of effective strategies to delay aging [3].

Age is among systemic factors that influence the occurrence of periodontal disease. The prevalence and severity of periodontal disease tends to increase with patient age. Degenerative changes in periodontal tissues are assumed to be the cause of this condition.[4]. While epidemiological data is clear that periodontitis increases significantly in prevalence and severity with aging, the fundamental biological mechanisms generating this susceptibility remain ill-defined. Furthermore, the disease demonstrates a disproportionate increase in aged minority individuals and males, various systemic diseases, and related to socioeconomic status and even geographic location [5].

Periodontitis is usually associated with activation of polymorphonuclear leukocytes, which in turn may generate reactive oxygen species (ROS) during inflammatory conditions. Oxidative stress is a complex biological process

* Corresponding author: Chiquita Prahasanti

characterized by the excessive production of ROS, which act as destroyers to the redox balance in body and induce oxidative damage [6,7]. All the metabolisms are impaired in oxidative stress and even nucleic acid balance is influenced. ROS causes oxidative damage to the tissues via multiple mechanisms, including DNA damage, protein oxidation and lipid peroxidation (LPO) damage [6,8] When inflammation happens, ROS production is drastically increased mainly due to cells of innate immune system, e.g., neutrophils and macrophages during the process of phagocytosis via the metabolic pathway of the "respiratory burst" [9].

Aging research proposed critical aging hallmarks that describe common denominators among species, including genomic instability, cellular senescence, and mitochondrial dysfunction. During aging, genetic damages are accumulated and gene expression patterns are continuously changed. These alterations are mediated by extracellular chemical/biological stimuli, as well as by intracellular replicative/oxidative stress. Therefore, the aim of this review is to summarize the current findings of delaye aging process by improving periodontal health

2. Material and methods

2.1. The oxidative stress theory of aging

Oxidative stress is an imbalance between the production of ROS and the antioxidant capacity of cells, which damages biological systems due to increased ROS production and dysfunction of the antioxidant system [6,10,11]. Under physiological conditions intracellular ROS are normal components of signal transduction cascades. And the levels of ROS are maintained by a complex antioxidants systems participating in the *in-vivo* redox homeostasis [6,12]. However, inflammatory responses can also be stimulated by ROS through protein kinases, transcription factors, and genomic expression of inflammatory factors genomic expression [6,13]. Increased ROS accumulation leads to oxidative stress, which contributes to major cellular components damage, including DNA, proteins, and lipids [6,14].

Oxidative stress is both, a pathomechanism involved in numerous inflammatory diseases causing damage to lipids, nucleic acids and proteins—oxidative distress, as well as an important physiological process that enables the immune system to cope with microorganisms and intracellular cell signaling—oxidative eustress [5,15]. The physiological functions of free radicals have been neglected for years and so, much more is known about the pathological role of oxidative stress. A variety of free radicals is produced and interacts with a variety of substrates. This leads to a palette of biomarkers that can be used for the assessment of oxidative stress-induced damage [5].

Aging is the progressive loss of tissue and organ function over time. The free radical theory of aging, later termed as oxidative stress theory of aging, is based on the structural damage-based hypothesis that age-associated functional losses are due to the accumulation of oxidative damage to macromolecules (lipids, DNA, and proteins) by RONS. The exact mechanism of oxidative stress-induced aging is still not clear, but probably increased RONS levels lead to cellular senescence, a physiological mechanism that stops cellular proliferation in response to damages that occur during replication.

According to the oxidative stress theory of aging, accumulation of oxidative damage by reactive oxygen and nitrogen species (RONS) contributes to the process of normal aging as well as the development of pathological conditions. At a molecular level, excessive levels of exogenous or endogenous RONS result in oxidation of intracellular components, such as DNA, RNA, protein, and lipid. Oxidative modification to these macromolecules causes disturbance of normal cellular physiological activities and impairment of homeostatic maintenance including mitochondrial integrity and proteostasis, which can ultimately lead to cell dysfunction or even cell death. RONS induce cellular senescence acting on various components of SASP:

- Regulation of mammalian target of rapamycin complexes' functions;[16,17]
- Production of IL-1α leading to a proinflammatory state, which increases nuclear factor kappa-B (nfκb) activity and epithelial–mesenchymal transition and tumor metastatic progression; [16,17]
- Induction of mmps expression, which is associated with age-related and chronic diseases such as cancer, Alzheimer's, atherosclerosis, osteoarthritis, and lung emphysema;[16,17]
- Inhibition of FOXO (Forkhead box) proteins activity, which is involved in insulin/insulin-like growth factor-1-mediated protection from oxidative stress;[16,17]
- Reduction of sarco/endoplasmic reticulum Ca2+-atpase activity leading to cardiac senescence;
- Inhibition of sirtuins activity leading to an increased production of RONS by SOD inhibition, a proinflammatory state by preventing their inhibition of tumor necrosis factor alpha (tnfα) and nfκb, and tumorigenic effect by preventing their inhibitory effect on c-Jun and c-Myc;

- Regulation of p16ink4a/prb and p53/p21 pathways leading to senescence.[16,17]

ROS cause tissue damage by a variety of mechanisms, which include DNA damage, lipid peroxidation (through activation of cyclooxygenases and lipooxygenases), protein damage including gingival hyaluronic acid and proteoglycans, and oxidation of important enzymes (e.g., antiproteases, α-antitrypsin, stimulation of proinflammatory cytokine release by monocytes and macrophages by depleting intracellular thiol compounds and activating nuclear factor). Oxidative stress generally appears after exposure to a relatively high concentration of ROS and/or a decrease in antioxidant defense system against ROS. It has been implicated as a major contributor to more than 100 disorders and more recently periodontitis [18].

A major challenge in clinical periodontics is to find a reliable molecular marker of periodontal tissue destruction with high sensitivity, specificity, and utility [18,19]. The level of oxidative stress can be measured by assessing the production of malondialdehyde (MDA) levels. Earlier studies have demonstrated that it is used as marker in carcinoma [18,20]. Considering the previous facts, this study is designed as a single-centered, randomized controlled clinical trial to analyze the level of salivary MDA in periodontally healthy subjects and patients with gingivitis and chronic periodontitis [18].

2.2. Aging and Periodontal Microbiota

Since periodontal tissue damage accumulates over time, it should be possible to demonstrate shifts in the composition of the sub-gingival microbiota with increasing age . Nevertheless, as these differences can be attributed largely to differences in ecological conditions prevailing in shallow or deep pockets, the specific role of particular microorganisms at different periods of life cannot be established using such a simple approach.[21]

Slow continuous attachment loss, on the other hand, may have considerable consequences over the long run, although it is undetectable in studies limited to a few months' duration. Given the inaccuracy of periodontal probing, the detection of a continuous disease process leading to 6 mm of attachment loss over 60 years would require a minimal study period of 20 years (subsequent measurements must yield a difference of at least 2 mm in order to distinguish tissue destruction from measurement error with suficient conidence). None of the longitudinal studies conducted with the purpose of risk assessment have covered such a longperiod. Thus, in addition to microorganisms recognized as important periodontal pathogens because of their association with active phases of disease, bacteria with low pathogenic potential may also contribute signiicantly to periodontal tissue destruction if present over protracted periods of apparent "health'. The impact of these organisms would probably increase with age and should be taken into consideration in any discussion of periodontal disease among older adults.[21]

2.3. Oxidative stress and periodontitis

Reports from different studies reveal increased levels of markers of oxidative stress in saliva, gingival crevicular fluid, and plasma from patients with periodontitis, further strengthening the association between oxidative stress and periodontal inflammation. It has been shown that the levels of oxidant-induced DNA damage, as measured by the biomarker 8-hydroxy-2′-deoxyguanosine, are higher in patients with chronic periodontitis than in healthy controls. These findings agree with previous reports.Similarly, when 58 patients with periodontal disease were compared with 234 healthy controls it was demonstrated (using ELISA) that there were significantly higher levels of total protein carbonyls in the patients with periodontal disease and that this correlated with increased loss of periodontal attachment. Along similar lines, the levels of malondialdehyde were found to be increased in serum, saliva, and gingival crevicular fluid samples from patients presenting chronic periodontitis in comparisson with their periodontally healthy counterparts. In the same experiment, nonsurgical therapy significantly modified the levels of malondialdehyde to levels that were comparable with those found in periodontally healthy patients, highlighting the interplay between the expression of oxidative biomarkers and periodontitis. Others have demonstrated that nonsurgical therapy for periodontitis reduces salivary levels of the antioxidant glutathione peroxidase [22].

3. Discussion

The theoretical basis supporting a possible relationship between antioxidant supplementation and longevity are mainly from the evidence showing a relationship of the latter with the rate of mitochondrial oxygen radical generation and the degree of unsaturation of membrane fatty acids. Consuming varied antioxidant supplements including vitamin C, vitamin E (particularly mixed tocopherols and tocotrienols including more than just the alpha tocopherol form found in most multivitamins), quercetin, resveratrol, carnitine, alpha lipoic acid, N-acetylcysteine (NAC), CoQ10 (preferably the ubiquinol form), idebenone, lycopene, lutein, and many others may help further lower the level of oxidative damage throughout the body. However, the concept of antioxidant supplementation for antiaging is not the only solution.

Oxidative stress is induced by an imbalance between excessive ROS production and anti-oxidant mechanisms. Increased levels of ROS leading to a state of Oxidative Stress have been implicated in the pathogenesis of a large number of diseases, including cardiovascular diseases and diabetes. Nevertheless, more recently, evidence has also emerged for a crucial role of ROS in periodontal tissue destruction. Therefore, individuals suffering from periodontitis might be at higher risk of developing other chronic systemic inflammatory diseases, like cardiovascular diseases and diabetes.

Antioxidants present a strong defense function against ROS; therefore, numerous studies tried to examine the application of antioxidants in the treatment of periodontitis. It has been shown that supplemental periodontal treatments with antioxidants like vitamin E, taurine and lycopene result in improved clinical periodontal parameters, higher activities of local and systemic antioxidants, and lower levels of local and systemic ROS compared with conventional periodontal treatment. A recent review concluded a useful effect of vitamin C on maintaining periodontal health for elderly people . Another recent review focused on the effects of the complimentary use of lycopene, vitamin C, vitamin E, capsules with fruits/vegetables/berry and dietary interventions to periodontal therapy . It confirmed that only the use of lycopene and vitamin E is associated with improved clinical parameters. These results indicate a promising use of antioxidants for periodontitis treatment, which could be beneficial for both periodontal status and systemic oxidative status [9].

The aging process clearly contributes to the incidence and severity of periodontitis and has been related to altered physiologic and pathophysiologic changes enabling a dysregulation of normal development, maturation, replenishment, and response patterns of the immune system to the noxious challenge of the disease-associated oral microbiome [23]. Aging effects on the immune system include distinct alterations in both innate and adaptive immune cell functions and effector biomolecules contributing to processes of immunosenescence, immunoactivation, and inflammaging. Furthermore, aging-associated in vivo microenvironments, such as a chronically inflamed periodontium, likely also contribute to the complexity of these aging defects. The heightened inflammation observed in the periodontium of aged individuals reflecting an ineffective immunity leads to chronic persistence of these pathogens and unresolved destructive inflammation with contributions from both arms of immunity. Nevertheless, there is clearly an array of systemic health conditions related to bacterial translocation through damaged periodontal tissues and the resulting chronic elevation in systemic inflammatory responses that leverage with other risk factors for general disease processes[23].

Therefore, daily oral hygiene maintenance with toothbrushing, flossing, mouthrinsing and appropriate use of anti-oxidants, such as vitamin C, as well as regular visit to dentist or periodontist is mandatory to maintain healthy periodontal tissue which support general health, also slowing down aging process.

4. Conclusion

Aging-related intrinsic factors, including replicative stress, oxidative damages, genetic alteration, mitochondrial decline, and cellular senescence, and extrinsic factors, including changes in oral flora and medication-driven pathologies, synergistically weaken the performance of the periodontium. Therefore, understanding the effect of aging on homeostasis in the periodontium would be important to keep the oral environment and further life quality in a good condition. Nevertheless, further researches should be done to explore other factors that are involved in periodontal disease which also accelerate the aging process.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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