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Review

The impact of antioxidant agents complimentary to periodontal therapy on oxidative stress and periodontal outcomes: A systematic review

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ABSTRACT

There is significant evidence linking chronic periodontitis (CP) and oxidative stress (OS). CP is a multifactorial infecto-inflammatory disease caused by the interaction of microbial agents present in the biofilm associated with host susceptibility and environmental factors. OS is a condition that arises when there is an imbalance between the levels of free radicals (FR) and its antioxidant defences. Antioxidants, defined as substances that are able to delay or prevent the oxidation of a substrate, exist in all bodily tissues and fluids, and their function is to protect against FR. This systematic review assessed the effects of the complimentary use of antioxidant agents to periodontal therapy in terms of oxidative stress/antioxidants. Only randomised, controlled, double-blind or blind studies were included. The majority of the included studies were performed in chronic periodontitis patients. Lycopene, vitamin C, vitamin E, capsules with fruits/vegetables/berry and dietary interventions were the antioxidant approaches employed. Only the studies that used lycopene and vitamin E demonstrated statistically significant improvement when compared to a control group in terms of periodontal parameters. However, oxidative

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Abbreviations: CP, chronic periodontitis; OS, oxidative stress; FR, free radicals; ROS, reactive oxygen species; SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase; SRP, scaling and root planning; 8-OHdG, 8-hydroxydeoxyguanosine; TAOC, total antioxidant capacity; ELISA, enzyme linked immunosorbent assay.

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stress outcomes did not follow the same pattern throughout the studies. It may be concluded that the use of some antioxidants has the potential to improve periodontal clinical parameters. The role of antioxidant/oxidative stress parameters needs further investigations.

Contents

1. Introduction

Periodontitis is a chronic infecto-inflammatory disease presenting inflammation of the periodontal tissues that cause alveolar bone loss and, in some severe cases, tooth exfoliation.[1] Progression of periodontal disease is dependent on the host immune response and susceptibility.[2,3] Recently, studies have pointed to oxidative stress as being part of the pathogenesis of periodontal diseases.[4] Oxidative stress is a condition caused by a harmful increase in the production of reactive oxygen species (ROS),[5] which are important signalling molecules in the regulation of several cellular processes,[6] emerging when there is an imbalance between ROS levels and the host antioxidant defences. Consequences of the oxidative stress include adaptation, damage or cell death[7] through a variety of mechanisms, such as DNA, lipid and protein damage.[8]

Regarding the prevention of ROS formation, enzymatic and non-enzymatic antioxidant mechanisms have been studied and reported in the literature. Enzymatic mechanisms are responsible for direct ROS neutralisation,[4,9,10] and these mechanisms are constituted by primary enzymes involved in human organism protection in attempt to maintain the ROS levels in a normal range. Examples of these enzymes are superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx).

Superoxide dismutase (SOD) is one of the most abundant antioxidant enzymes in the human body.[11,12] One of its mechanisms of action is the conversion of superoxide anions into hydrogen peroxide (H_2O_2), which operates as a preventive antioxidant because it avoids the formation of the hydroxyl radical (OH^-).[13] The SOD levels are reduced in chronic periodontitis patients when compared with controls,[12] and it has been shown that, after scaling and root planing (SRP), its serum and salivary levels were increased significantly.[14] CAT is mainly located in the peroxisomes, and it is capable of removing intracellular H_2O_2 and superoxide radicals with great efficacy.[4,10,15] Salivary levels of CAT were reduced in chronic periodontitis patients when compared to periodontally healthy subjects.[16] GPx is a selenium-containing peroxidase responsible for the protection of mammalian cells against oxidative damages by reducting a variety of hydroperoxides, such as ROOH and H_2O_2 extracellularly and in the mitochondria.[4,17] Additionally, one study showed that gingival crevicular fluid from periodontitis patients contained significantly lower amounts of reduced and oxidised glutathione than matched periodontally healthy subjects.[17]

Furthermore, non-enzymatic antioxidants are secondary mechanisms to neutralise ROS.[4,9,18,19] Generally, these types of antioxidants are obtained exogenously, mainly through a balanced diet, which included a variety of fruits and vegetables, such as blueberries, strawberries, grapes,[20] avocado,[21] tomatoes,[22] spinach,[23] and carrots.[19] The non-enzymatic antioxidants are represented by fat-soluble vitamins (vitamin A, vitamin E-tocoferol and β-carotene), water-soluble vitamins (vitamin C and vitamin B complex), trace elements (zinc and magnesium), and bioflavonoids (plant derived).

Studies have demonstrated that, in patients with periodontitis, oxidative levels are increased when compared to periodontally healthy subjects.[24,25] However, the antioxidant levels are significantly lower in chronic periodontitis patients when compared to periodontally healthy individuals.[17,26–28]

It is well established that most types of periodontitis can be successfully treated by removing the supra- and subgingival biofilm by scaling and root planing combined with adequate periodontal support maintenance.[29] Scaling and root planing is also capable of decreasing the total oxidant status in the gingival crevicular fluid and improving the antioxidant levels in patients with chronic periodontitis.[26,30]

Therefore, periodontal diseases and reduced antioxidant levels seem to be associated with one another, leading to increased oxidative damages in the oral environment. This systematic review assessed the effect of antioxidant agents as complimentary to periodontal therapy in terms of oxidative stress/antioxidants.

2. Methodology

The focused question for this systematic review was: is there a benefit of antioxidant agents complimentarily to periodontal