Effect of Locally Delivered Antioxidants as An Adjunct to Non-surgical Periodontal Therapy on GCF Level of Oxidative Stress Marker; Protein Carbonyl

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INTRODUCTION AND REVIEW OF LITERATURE

Oxygen is a double edged weapon. It is vital to life, however it may have potential toxic effect. Because of its highly reactive nature it is capable of participating in the production of potentially damaging molecules known as free radicals. Free radicals can be defined as being any species have the ability to exist independently while having one or more unpaired electrons as a result they are highly reactive by nature **(Chapple et al., 1997) (Pendyala G et al., 2008).**

Reactive oxygen species (ROS) are a subgroup of a larger "free radicals group" that includes reactive oxygen species, reactive chlorine species, reactive nitrogen species (RNS). However, ROS have become more popular than the term free radicals **(Chapple et al., 1997)**. ROS can be defined as intermediate oxygen carrying metabolites with or without an unpaired electron, which have the capability of oxidizing other components and converting them into free radicals **(Rammal H et al., 2010),(Bouayed J et al., 2010)**.

Body cells produce free radicals (oxidants) when they are exposed to substances that induce their production (pro-oxidants). **Dahiya et al, (2013)** classified sources of pro-oxidants into 2 main categories, endogenous and exogenous sources. Endogenous sources were further classified into two mechanisms. The first mechanism includes their production as being by-products of metabolic pathways.

This process occurs within the mitochondria during cellular metabolism by the action of electron transport systems resulting in electron leakage (Free radicals production). Second mechanism is called functional generation in which free radicals are produced by the action of host defense cells (phagocytes) and connective tissues cells. Exogenous sources include heat, smoking, infection, trauma, ultrasound, infection, ultraviolet light, ozone, radiation, exhaust fumes, and therapeutic drugs.

Free radicals play a dual role. They are essential for many biologic processes in mammalian cells, yet they can have a toxic effect **(Chapple IL et al., 2007)**. The sensitive balance between their beneficial and injurious effect is an important aspect of life. At low or moderate ROS levels, they have beneficial effects on cells function and immune system function. At high concentrations, they result in generation of deleterious types of stresses called "Oxidative stresses" that can damage all cell structures **(Valko et al., et al 2007)**.

Oxidative stress is a general term first defined by **Sies et al. (1991)** as disturbance in balance between production of reactive oxygen species (ROS) and a biological system's capability of detoxifying these reactive intermediates or repairing the resulting damage. There is an ascending body of evidence in literature to illustrate the role of oxidative stresses in the pathogenesis of different types of inflammatory diseases, including periodontal disease **(Masi S et al., 2011).**

In normal physiology, there is a continuously active equilibrium between activity of ROS and the capacity of antioxidant defense system. When the shift occurs in favor of ROS, either by impairment of anti-oxidant defenses or an elevation in ROS production level or activity, oxidative stress results **(Waddington R et al., 2000)**. Antioxidants are defined as substances which when available at low concentrations, in comparison to an oxidisable substrate like DNA, proteins or lipids, will significantly retard or prevent oxidation of that substrate **(Wanasundara and F. Shahidi, 2005).**

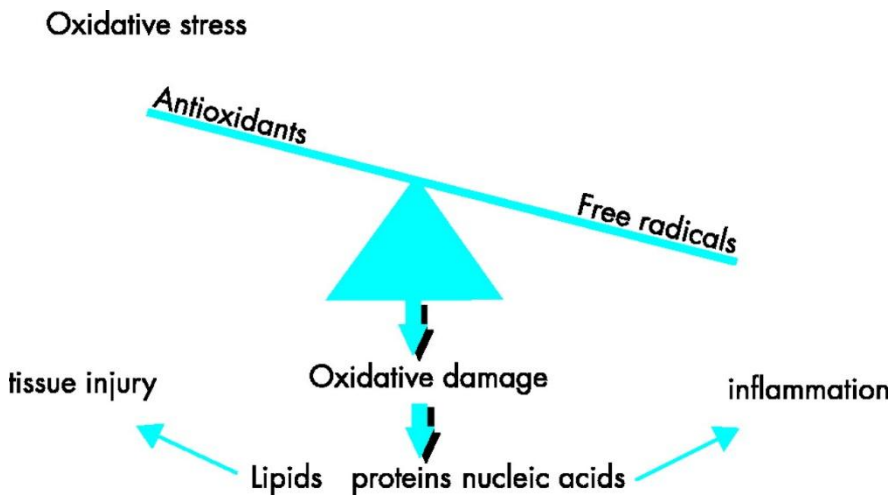

Figure 1. A digramatic represention shows oxidative stresses generation and their effect on different cell structures (Kelly F. et al., 2003).

Body cells have different mechanisms to elevate antioxidants level, which can be naturally produced in situ (Endogenous antioxidants) like superoxide dismutase (SOD) and catalase (CAT) or supplied from an external source through diet and/or dietary

supplements (Exogenous antioxidants) like vitamin C and carotenoids **(Chatterjee M et al., 2007)**.

Reactive oxygen species (Oxidants):

During normal cellular metabolism, ROS are generated from molecular oxygen. ROS can be divided into two distinct groups, true radicals and non-radicals. Non-radicals have the ability to produce radicals in the intra-cellular and the extra-cellular environments. True free radicals group involves superoxide ($O_2^{\circ-}$), Hydroxyl (OH°), hydroperoxyl (HOO°) and perhydroxyl ($HO_2^{\circ-}$) (where '$^{\circ}$' denotes an unpaired electron) while non-radicals ROS group involves hydrogen peroxide (H_2O_2), singlet oxygen ($^1O_2$) hypochlorous acid (HOCl),, and ozone (O_3) **(Dahiya et al., 2013)**.

The most common reactive oxygen species of physiological importance are superoxide anion ($O_2^{\circ-}$), hydroxyl radical (OH°), and hydrogen peroxide (H_2O_2). Superoxide anion is generated by addition of one electron to molecular oxygen **(Miller DM et al., 1990)**. The process which is mediated by the action of nicotine adenine dinucleotide phosphate [NAD(P)H] oxidase and xanthine oxidase or by electron transport system within the mitochondria.

NAD(P)H oxidase is an enzyme found in neutrophils (PMNs), monocytes, and macrophages. After phagocytosis, these cells have the ability to produce a burst of superoxides "Respiratory burst" that leads