



Oxidative stress and Antioxidant Defense Mechanisms in Dentistry: A Literature Review.

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Abstract

This review paper aimed to evaluate the effect of oxidative stress in the prevalence of some dental diseases and the role of antioxidants in dentistry. Oxidative stress is a normal phenomenon, present in healthy human body help them to produce energy that they need for their life. During that, the formation of free radicals begins, including both reactive oxygen species "ROS" & also reactive nitrogen species "RNS". These radicals have a role in a many types of signalling pathways that regulate inflammation. Antioxidants constrain the formation of free radicals. Mitochondria, a small cell organelle acts to generate energy in the form of adenosine triphosphate "ATP". It combines oxygen & glucose to form carbon dioxide, water, & ATP. Free radicals result as by-products of this metabolic process & when natural defence apparatuses be unsuccessful, the level of free radicals begins to increase to levels where the capacity of the body is unable to neutralize them entering the body into the state of high oxidative stress, which means greater risk of numerous oral & systemic diseases. Oral tissues are liable to free radical damage in a unique manner due to the presence of mucus membranes that allow rapid absorption of constituents throughout their surfaces. In oral environment, infection of gingiva can produce oxidative stress. The rise in formation of free radicals by oxidative stress results in further destruction of cellular walls and oral tissues. The study results suggested that the use of antioxidants is an adjunct approach to dental therapy may be helpful in controlling the oral health status.

الخلاصة

تهدف ورقة المراجعة هذه إلى تقييم تأثير الإجهاد التأكسدي في انتشار أمراض الأسنان ودور مضادات الأكسدة كعامل مساعد في علاج الأسنان. الإجهاد التأكسدي هو ظاهرة طبيعية، تظهر في جسم الإنسان السليم تساعده على إنتاج الطاقة التي يحتاجها في حياته خلال ذلك، يتم تكوين الجذور الحرة، بما في ذلك أنواع الأكسجين التفاعلية "ROS" وأنواع النيتروجين التفاعلي "RNS". تشارك هذه الجذور الحرة في عدد من مسارات الإشارات التي تنظم الالتهاب. تمنع مضادات الأكسدة تكوين الجذور الحرة. الميتوكوندريا، عضوية خلوية صغيرة تعمل على توليد الطاقة على شكل أدينوسين ثلاثي الفوسفات "ATP". فهو يجمع بين الأكسجين والجلوكوز لتكوين ثاني أكسيد الكربون والماء و ATP. تنتج الجذور الحرة كنتاج ثانوي لعملية التمثيل الغذائي هذه وعندما تفشل أجهزة الدفاع الطبيعي، يبدأ مستوى الجذور الحرة في الزيادة إلى مستويات لا تستطيع فيها قدرة الجسم على تحييدها وهي تدخل الجسم في حالة الإجهاد التأكسدي العالي، والذي يعني زيادة خطر الإصابة بالعديد من أمراض الفم والجهازية. أنسجة الفم هي المسؤولة بشكل فريد عن ضرر الجذور الحرة لأن الأغشية المخاطية تسمح بالامتصاص السريع للمواد في جميع أنحاء أسطحها. في أنسجة الفم، يمكن أن تؤدي إصابة اللثة إلى الإجهاد التأكسدي. تؤدي الزيادة في تكوين الجذور الحرة من الإجهاد التأكسدي إلى مزيد من الانهيار لجدران الخلايا وأنسجة الفم. أشارت نتائج الدراسة إلى أن استخدام مضادات الأكسدة هو نهج مساعد لعلاج الأسنان قد يكون مفيداً في التحكم في حالة صحة الفم.

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INTRODUCTION

In the healthy human body, oxidative stress is a normal phenomenon that helps to produce the energy necessary for their life ⁽¹⁾. Free radicals "a necessary evil" play an important role in life. They result, as byproducts, including reactive oxygen species "ROS" and reactive nitrogen species "RNS" triggering different signaling pathways inside the cell. ⁽²⁾ A small cell organelle called mitochondria acts to combine oxygen & glucose to form adenosine triphosphate "ATP", carbon dioxide and water ⁽³⁾.

The levels of free radicals begin to increase where the body becomes unable to neutralize them, when an equilibrium is lost & when natural defense apparatuses failed. Certain people have insufficient micronutrient, and/or conditions that may increase the need "e.g., infection, stress, and pollution" will cause an additional reduction in their stores. ⁽¹⁾ So bodies will enter into the state of high oxidative stress, which means higher risk of oral & systemic diseases. ^(4,5,6) In order to scavenge the harmful effects of these free radicals, the body introduces variable mechanisms that will neutralize the elevated levels of free radicals and keep the cells safe against their toxic effects and help in prevention of diseases. ⁽²⁾ Substances that are able to neutralize free radicals are called antioxidants. They do that by means of donating an electron. The destructive effects of oxidative stress are usually coming from free radicals of oxygen which can be altered by enzymatic and/or non-enzymatic antioxidants. Very well-known examples of these antioxidants are vitamins ^(7, 8).

Salivary Antioxidants System:

The antioxidant guard consists of cellular protective enzymes and non-enzymatic antioxidant agents. Cells have an antioxidant defensive system for avoiding the excessive production of free radicals, besides establishing repair of injury caused by free radicals. ⁽⁹⁾ Salivary protective mechanisms consist of the damage prevention, repair and removal of the damaged biomolecules before their accumulation and a new damage induction. The usefulness of the antioxidant system of saliva depends on the intake of vitamins and micronutrients as well as the regulation of antioxidant enzyme synthesis by physical activity, nutritional condition and/or aging. ^(10, 11) Also the levels of salivary antioxidants can be altered in response to diseases. ⁽¹²⁾ Enzymatic elements of antioxidants include GSH peroxidase, superoxide dismutase (SOD), myeloperoxidase and catalase while non-enzymatic elements include minerals, vitamins, thiols, polyphenols, uric acid (UA), and albumin ^(13,14). According to their function, salivary antioxidants are classified into three groups, the first group includes preventive antioxidants, those which slow down free radical formation, such as albumin, catalase, transferrin, carotenoids, GSH peroxidase, and haptoglobin. Second group includes scavenger antioxidants, such as vitamins, which eliminate free radicals to slow down the cellular injury. The last are enzymes "lipases, proteases, transrase" that repair the destruction caused in the body. ⁽¹⁵⁾ In the last few years, antioxidant

salivary protection has been an interesting subject of several medical research. Many of these researches have proved that oxidative stress has a vital role in the pathogenesis of many inflammatory diseases ⁽¹⁶⁾. In dentistry, periodontal diseases are common in the oral cavity, the activity of stress and antioxidant defence of this disease is gradually more stated. For a better understanding of periodontal diseases pathogenesis, salivary analysis for oxidant and antioxidant types is essential for new preventive approaches ⁽¹⁷⁾.

The oxidative stress with dental and oral diseases:

Oxidative stress that results in an imbalance between the ROS activity and the ability of the body to detoxify them by antioxidants, can lead to microdamage of the cell membrane, DNA damage, and protein deactivation. ⁽¹⁸⁾

Oral tissues are liable to free radical damage in a unique manner because the ability of mucus membranes to permit fast absorption. The oral tissues infections can induce oxidative stress causing an increase in formation of free radicals which further increase breakdown of cell walls and oral tissues. ^(19, 20) In a meta-analysis of 16 studies from different countries found that both serum total antioxidant levels and oxidative stress biomarkers, were lower in patients suffering from periodontal disease compared with healthy persons, indicating that such inflammatory condition may provoke systemic oxidative stress.⁽²¹⁾ Numerous researches were reported that periodontal tissue inflammation can create ROS that go to blood,

and gradually induce distress to other organs mostly due to cells of innate immunity neutrophils. ^(22,23) A conventional hypothesis is that inflammation can cause oxidative stress and vice versa. ^(24, 25)

The presence of periodontopathic bacteria in saliva has been proved. It activates the host responses and neutrophils infiltration, a main source of ROS in periodontal tissue during inflammation. ^(26, 27) They considered as an important mechanism of bacteria killing and removal ⁽¹⁶⁾. At the same time, these ROS might result in host tissues destructions when they are not defused by the antioxidant system. ⁽²⁸⁾. So that, a good balance between ROS and TAC of the host tissue is necessary for the proper tissue homeostasis that prevents tissue damage. ⁽²⁹⁾

Recently, many articles concerning the roles of free radicals and antioxidants in dental healthiness were published. They have a lot of signaling ways that control inflammation. The free radical formation was inhibited by modulation of antioxidant mechanisms which control their transfer to the area of excessive free radicals. ⁽³⁰⁾

Mechanisms of reactive oxygen species that cause tissue damage include: ⁽³¹⁾

- a. Pro- inflammatory cytokines stimulation (e.g. **IL-1, IL-6, and TNF- α**)
- b. Protein damage (e.g muscles)
- c. DNA damage and mutations X Lipid peroxidation
- d. Oxidation of important enzymes like Antiprotease.

The main sources of free radical formation are internal factors including normal

cellular metabolisms, and different enzymatic activities. The second one is the external factors including radiation, cigarette smoke and oxygen itself.⁽³²⁾

Categorization of Antioxidants:

There are three classes of antioxidants: The primary one which control prevention of oxidants development; secondary antioxidants which act as scavengers of reactive oxygen species, and tertiary one which act as oxidized molecules renewal agents. They can also be divided as:⁽³³⁾

1-Enzymatic antioxidants: The system of enzymes like glutathione, Catalase, peroxidase, and superoxide dismutase participates either in direct or indirect manner in defence against the ROS.

2- Nonenzymatic antioxidants: like vitamins and minerals.⁽³⁴⁾

3-Hydrophilic antioxidants

4-Hydrophobic antioxidants

5-Endogenous antioxidants: they can be classified into primary and secondary. They dissociate and inactivate ROS.⁽³³⁾

Periodontal Diseases and oxidative stress:

Reactive oxygen species have major action in the initiation and progression of inflammatory response. Oral bacteria are responsible of the instigation and the progression of some oral diseases like gingivitis. Gingival bacteria can aggravate ROS synthesis and may result in periodontal tissue injuries.^(35,36)

Clinical studies showed that diseases of periodontium are associated with high lipid

peroxidation in saliva⁽³⁷⁾. ROS formed by inflammation like gingivitis or periodontitis go to the blood during progression of these diseases, resulting in oxidation of different blood molecules leading to progressive harm of circulating oxidative stress to many parts of the body.

Therefore, the changes in the level of circulating antioxidant are mandatory to study the relation between oral inflammations and circulatory oxidative stress. A study found that antioxidant levels of blood in individuals having gingival inflammations were less than individuals having normal gingival.⁽³⁸⁾ At the present, many methods are available to measure the antioxidant level in blood and saliva. An earlier study showed that enzymes, like "glutathione peroxide, superoxide dismutase and catalases", were higher, while the levels of nonenzymatic one, like vitamins were lower in gingivitis compared to control groups. Saliva with it is highly effective antioxidative properties has an essential role in the preservation of oral health providing the gastrointestinal tract with a primary defensive line of antioxidant against ROS.⁽³⁹⁾ Other oxidative stress impact of saliva still needs to be studied. A study carried out on salivary peroxidase, uric acid, superoxide dismutase, salivary flow rate, and products of oxidative damage were predicted in saliva. It was established that they may be helpful in the disease investigations, that oxidative stress has a major role in its aetiology.⁽⁴⁰⁾

Oxidative Stress and dental caries:

Dental caries is widely distributed worldwide. Reviews concern with the aetiology,

pathology, and treatment of dental caries were available before. ⁽⁴¹⁾ Recently, the concept of oxidative stress is strongly connected with an inflammatory response in dentin, leading to teeth destruction. The action of oxygen free radicals and antioxidants on parotid gland was suggested in the theory of dental caries ⁽⁴²⁾. The relation between oxidative stress and dental caries is less obvious. Researches were mostly study the salivary oxidative stress in relation to caries of teeth were examining the antioxidant salivary biomarkers ⁽⁴³⁻⁴⁵⁾ but not the caries itself.

In a study analysed saliva collected from patients with active caries, a higher lipid peroxidation was identified in those patients compared to the control group. ⁽⁴⁶⁾

The association between caries and total antioxidant capacity was confirmed by some researchers. ⁽⁴⁷⁾ The levels of acute antioxidant effect might be elevated in response to inflammation and dental caries, but chronic effects might be related to use of antioxidants. A panel connection between antioxidant markers and oxidative stress is apparently required to understand the action of oxidative stress in pathogenicity and development of oral disease. ⁽⁴⁸⁻⁵⁰⁾ Although studies have a clear outcome, the destructive mechanisms of oxidation in saliva with regard to dental caries were still lacking. So, to explain the association between them in saliva; more studies dealing with the underlying mechanisms of their association appears to be necessary.

Studies have been conducted to found a relationship between dental restorations and antioxidant enzymes. The presence of Hg in the amalgam filling material can induce oxidative

stress in patients who had dental amalgam restorations for long time's periods ⁽⁵²⁾.

CONCLUSION

Oxidative stress compromises the body's ability to fight infection and inflammation in dental disease. Dental materials as well as diet and environment are among the many sources of oxidative stress. Antioxidants can inhibit and/or stop the production of ROS and it may be therapeutically useful in reducing the risk for many dental diseases.

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