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REVIEW ARTICLE

Antioxidant Capacity of Saliva: Effect on Onset and Progression of Dental Caries

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ABSTRACT

Introduction: In recent years, free radicals and related species have attracted a great deal of attention. They are mainly derived from oxygen [reactive oxygen species (ROS)] and nitrogen [reactive nitrogen species (RNS)], and are generated in our body by various endogenous systems, through exposure to different physicochemical conditions or pathophysiological states. Overproduction of ROS/RNS results in oxidative stress, which is a deleterious process that can be an important mediator of damage to cell structures, including lipids and membranes, proteins, and DNA. In living organisms, the levels of free radicals and other "reactive species" are controlled by a complex web of antioxidant defenses, which minimizes the oxidative damage to biomolecules.

Objectives: The total antioxidant capacity (TAC) is a biomarker often used to investigate the oxidative stress. Saliva can be collected noninvasively and be used as a diagnostic fluid for detecting biomarkers of various pathological conditions.

Materials and methods: Data was obtained and analyzed from electronic database searches of relevant published literature from PUBMED and Google Scholar.

Conclusion: Salivary composition acts like a mirror reflecting the general health, oral health, diseases, inflammation, infection, etc.

Keywords: Dental caries, Free radicals, Oxidative stress, Saliva, Total antioxidant capacity.

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INTRODUCTION

Saliva is proven to have antioxidant capacity since late 1980s by various investigators. The effect of this on dental caries has been studied since then. Contradictory views and debates have concluded the role of salivary antioxidant capacity in the onset and progression of carious activity in individuals. This article is an attempt to review various studies where the researchers have endeavored to correlate between the total antioxidant capacity (TAC) of saliva and dental caries.

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FREE RADICALS, ANTIOXIDANTS, AND OXIDATIVE STRESS: HOW ARE THEY INTERRELATED?

Free radicals are an atom or group of atoms that have one or more unpaired electrons generated in various normal physiological activities of cells. They are defined as "any molecular species capable of independent existence that contains an unpaired electron in an atomic orbit." They have either a positive, negative, or neutral charge. Their formation occurs continuously in the cells as a consequence of both enzymatic and nonenzymatic reactions. It has been estimated that an average person has around 10,000 to 20,000 free radicals attacking each body cell each day. Some free radicals are good in that; they enable our body to fight inflammation, destroy bacteria, and control the tone of smooth muscles, which in turn regulates the working of internal organs and blood vessels.[1]

Free radicals are extremely reactive and unstable. Thus, they either donate or accept an electron, thereby behaving as an oxidant or reductant. When there is an excess or overload of these free radicals, they cause cellular damage. The concept of free radicals was first explored by Denham Harman in 1956 for their role in the aging process. The byproducts of oxygen metabolism, like superoxide anion, peroxide, hydrogen peroxide, hydroxyl ion, hydroxyl radicals formed, are known as reactive oxygen species (ROS). Reactive oxygen species and reactive nitrogen species (RNS) are formed during all normal cellular activities like cell cycling and signal transduction. The harmful effect of free radicals causing potential biological damage is termed oxidative stress and nitrosative stress.[1]

Uncontrolled free radical activities combined with other factors are responsible for the cause of some diseases, such as neurodegenerative diseases, heart disease, cancers, etc. The balance between the production of

free radicals and the antioxidant defenses in the body has important health implications. Under the normal conditions, the antioxidant defense system within the body can easily handle free radicals that are produced. If there are too many free radicals produced and too few antioxidants, this may cause chronic damage. Radicals derived from oxygen represent the most important class of radical species generated in living systems.[2] Reactive oxygen species and RNS are products of normal cellular metabolism that are well recognized for playing a dual role in both deleterious and beneficial species, since they can be either harmful or beneficial to living systems.[1]

Oxidative stress is a general term used to describe a serious imbalance between the production of ROS and the antioxidant defense mechanism in favor of the former, leading to a situation of potential risk. Under these conditions, ROS may damage membrane lipids and DNA, and affect the function of cellular proteins. For these reasons, oxidative stress contributes to the general decline in optimum bodily functions and may be involved in the pathogenesis of several disorders, whether as a cause or as an effect.[3]

ROLE OF SALIVA

Saliva is a heterogeneous biological fluid that comprises enzymes, hormones, antibacterial constituents, electrolytes as well as small organic molecules and compounds transported from the blood. It also acts as a cleansing solution, a buffer, an ion reservoir, and a lubricant. Saliva constitutes as first line of defense against free radical-mediated oxidative stress, because the process of mastication and digestion of food promotes various reactions, including lipid peroxidation.[4]

Pereslegina reported that unstimulated saliva was better in the determination of antioxidant defense parameters when compared with stimulated saliva, as TAC was found to be higher in unstimulated saliva.[5] Since saliva has found application as a diagnostic aid in an increasing number of clinical situations (Mandel), including dental caries and the possible therapeutic effects of antioxidants in maintaining a balance between ROS and antioxidants, there is an increasing interest in the evaluation of antioxidant capacity of saliva and its relationship with dental caries.[4]

REVIEW

In 1999, it was claimed that the imbalances in levels of free radicals and ROS with antioxidants may play an important role in the onset and development of several inflammatory oral pathologies.[6] Most of the studies on saliva report its physicochemical properties like flow rate, buffer capacity, and pH or the concentration of components of saliva with antimicrobial activity. But there are only few studies on the antioxidant defense systems of saliva and their relation with oral diseases, especially dental caries.[5]

In 1994, Moore et al compared the antioxidant activity of saliva of apparently healthy and periodontally diseased subjects. The authors reported that the antioxidant potential of saliva was not found to be compromised in patients with periodontal disease but that may relate to the antioxidant flow from the gingival crevicular fluid.[7]

One of the earliest studies done to evaluate the relation between the physicochemical properties of saliva, such as flow rate, buffering capacity, pH, calcium level, total protein, and total antioxidant status with dental caries, age, and gender in children was by Tulunoglu et al in 2006. The authors concluded that the total protein and total antioxidant in saliva were increased with caries activity and that the higher total antioxidant values in caries active children may be attributed to elevated protein levels.[8]

Similar study by Prabhakar et al and Pandey et al also found that the flow rate, pH, and buffering capacity were slightly reduced in caries active children, but the total protein and TAC of saliva increased significantly in caries active children and the total calcium decreased significantly in caries active children.[9,10] The major antioxidant in saliva was reported to be urate; however, if there is a relatively low concentration of ascorbate, it may make an essential contribution to the salivary antioxidant activity since scavenging of free radical by urate in the absence of ascorbate can lead to further macromolecular damage, if the urate radicals formed are not recycled.[8]

Hegde et al compared the TAC of saliva in children with early childhood caries (ECC) and rampant caries, and the results suggested an increase in the TAC of saliva in children with caries irrespective of whether it is ECC or rampant caries. The authors concluded that the presence of an infectious challenge in the form of caries or poor oral hygiene could be one of the factors for the comparatively increased levels of TAC of saliva. They also observed that the TAC of saliva increases with age. This may be due to the differences in the nutritional requirements and also the change of food pattern from softer and semisolid foods to harder and more solid foods which may contain larger volumes of antioxidants in the form of micronutrients.[11]

Another reason could be that the immune status of a child improves with age, owing to optimal immunity and the corresponding TAC levels of saliva that could also be increased.[12] Dodwad et al and Kumar et al reported that TAC was higher in children and teenagers with dental caries in comparison to those without dental caries.[13,14] Kumar et al and Sneha Muchandi et al also reported that in children aged between 3 and 5 years, severe early

childhood caries (SECC) was associated with higher TAC level of saliva.[15,16]

Ahmadi-Motamayel et al reported that TAC of saliva in caries active males was higher when compared with caries active females, suggesting hormonal changes and difference in diet as a possible reason.[17] Another study done by Gunjalli et al has shown an increase in total salivary antioxidant levels in obese children when compared with nonobese children. A probable reason for this could be the high socioeconomic stratum and a diet i.e., rich in phytonutrients and antioxidants.[18]

In contrast to the similar findings of the above studies, Rahmani et al reported that TAC of saliva in those with dental caries was significantly lower compared with those without dental caries. Similarly, Krawczyk (2014) reported that, with the increase in number of caries, stimulated and unstimulated salivary antioxidant level significantly decreased. In another study, Krawczyk reported a decrease in TAC of saliva in subjects with dental caries. The reduction of salivary TAC in subjects with dental caries may be related to increased activity of neutrophils and monocytes in the oral cavity which produces ROS in the presence of bacteria, i.e., enhanced production of ROS leads to decreased salivary TAC.[19-21]

The controversy seen in all these studies could be attributed to many factors like different methods of measuring TAC, age discrepancy, the severity of dental caries, and type of dentition. According to the study of Uberos et al in 2008, type of dentition is an important factor that affects the relationship between TAC and dental caries. They observed that TAC of saliva in patients with deciduous teeth caries was significantly higher than those without dental caries. But in case of patients with permanent teeth, no significant relationship was detected between dental caries and TAC of saliva.[22]

Moore et al[8] correlated higher TAC level of saliva in patients with dental caries to their diet. Mahjoub et al[23] claimed that higher TAC level in children with S-ECC could be a compensatory mechanism against oxidative stress. These researchers stated that salivary TAC is a combination of endogenous and food-derived antioxidants. Uric acid, being the major antioxidant of the saliva, comprises more than 85% of salivary TAC and is mainly derived from sugars. Therefore, consumption of sugars not only increases the risk of dental caries, but also contributes to higher TAC level.[20,23] Ilaria Peluso and Anna Raguzzini[24] suggested that the relationship with infection and TAC depends on the type and site of infection.[24]

CONCLUSION

There is no doubt that antioxidants are necessary components for our health and that the antioxidants and free radicals production should be in balance. There is evidence that production of excessive free radicals and ROS may be substantially elevated in certain inflammatory diseases, including dental caries, and it is the antioxidant defense system that maintains the balance between them.

Because of the many confounding factors, such as age factor, gender, dietary habits, immunity, severity of dental caries, type of dentition, site of infection, and method of measuring TAC, it is difficult to evaluate and correlate the increase or decrease in salivary antioxidant capacity with the onset and progression of dental caries. More researches must be conducted in order to understand the mechanism behind the fluctuating level of total antioxidants in the presence of dental caries.

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