International Journal of Dentistry and Oral Science (IJDOS)
ISSN: 2377-8075

Oxidative Stress and Dental Caries - A Perspective

Research Article

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Oxidative stress occurs as a state of disturbance between free radical produced and the capability of antioxidant system to counteract such [1]. Oxidative stress is a dysbalance between the production of free radicals and antioxidant status leading to oxidative damage of macromolecules including lipids and proteins. Markers of oxidative stress were found in saliva and were related to both, systemic and local oral diseases, the latter including inflammatory diseases such as dental caries, gingivitis and periodontitis and oral cancer [2]. Free radicals can be defined as molecules or molecular fragments with an unpaired electron which imparts certain characteristics to the free radicals are able to produce chemical modifications and to damage proteins, lipids, carbohydrates and nucleotides in the tissues. There are various major routes in which free radicals can interact with neighboring components in cells to disturb their integrity and functions. One of these routes is lipid peroxidation [3, 4].

Reactive oxygen species are naturally occuring oxidants, which are products of normal cellular metabolism,involved in numerous cellular biochemical events that are essential to life but at the same time capable of causing harmful oxidative stress when overproduced. Free radicals cause damage to all essential biocompounds such as DNA, proteins, and membrane lipids, thereby causing cause cell death [5, 6].

Saliva is a biological fluid with great potential in biomedical research, especially in dentistry. It mediates the oral health of individuals through various defense mechanisms such as its flow, buffering capacity, lipids, total protein, and its antioxidant system. It is widely used as a biomarker for evaluating the oxidative damage mediated by free radicals including lipid peroxidation occurring in the oral cavity [7].

The non-invasive sampling makes saliva particularly useful in the research on children, mentally disabled people or in experiments where repeated sampling is needed. Most of the studies focusing on salivary markers of oxidative stress were conducted in adult patients [8, 9].

Saliva also provides defense against free radical (FR)-mediated oxidative stress, since most of the physiological activities such as mastication and digestion of ingested food promotes a variety of reactions including lipid peroxidation. Battino et al., 2002, stated that antioxidant property of saliva provides the first line of defense against oxidative stress [10].

Oxidative stress causes tissue destruction as well as lipid peroxidation. It occurs when there is oxidative stress in the oral cavity. Thiobarbituric acid reacting substances (TBARS) are a marker of lipid peroxidation widely used in experimental research as well as in clinical studies. Although the specificity of the spectrophotometric or spectrofluorometric assay has been questioned in the past, TBARS are still measured, especially in studies focusing on inflammatory disorders. Malondialdehyde (MDA) is the end product of lipid peroxidation [8]. The byproducts of these reactions are present in saliva and can be reliably quantified as marker of oxidative stress [11, 12].

Dental caries is a complex process of demineralization and dissolution of substance of the teeth leading to cavitation.It has been shown to have a multifactorial etiology which leads to the initiation and progression of the lesion [13]. Dental Caries has got multifactorial etiology which involves several factors like diet, host, bacteria, time and personal factors like oral hygiene. The first line of defense against DC is saliva. Oxidative stress is also evident in children with Early childhood caries (ECC). According

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Received: July 20, 2019
Accepted: August 15, 2019
Published: August 25, 2019

Citation: Deepa Gurunathan, Divya Subramanian, Lakshmi Thangavelu. Oxidative Stress and Dental Caries - A Perspective. *Int J Dentistry Oral Sci.* 2019;S8:02:0014:73-75. doi: http://dx.doi.org/10.19070/2377-8075-SI02-080014

to the American Academy of Pediatric Dentistry, early childhood caries (ECC) is defined as the presence of one or more decayed (noncavitated or cavitated), missing (due to caries), or filled tooth (DMFT) surfaces in any primary tooth in a child 71 months of age or younger.

Oral diseases are not caused by an overgrowth of a single pathogen as previously thought, such as Streptococcus mutans in dental caries, rather, they are caused by dysbiotic composition of the oral microbiome which has been revealed by comparison with healthy individuals [14]. However, despite rigorous metagenomic sequencing efforts, there is no consensus about specific pathogens which cause these oral diseases. When pathogens are being engulfed by human leukocytes, reactive oxygen species (ROS) are formed. Inflammation-related production of ROS might result in oxidative stress, which triggers structural and functional changes of proteins, lipids, and nucleic acids [15].

It is shown in the literature that lipid peroxidation reaction releasing the free radicals has been associated with the pathogenesis of several pathological disorders. Lipid peroxidation is known to cause alterations in the structure and function of the host cells by producing malondialdehyde (MDA) as the by-product [16, 17].

Reactive free radicals have the capacity to modify the reactions occurring in the cells and cause deterioration of lipids, proteins, and nucleotides present in the tissue. Saliva has a role in controlling the pathogenesis of plaque formation leading to reduced susceptibility of dental caries by production of certain chemical reactions. The goal of antioxidants is to prevent the free radical-mediated oxidative damage to the host cell membrane [18, 19]. The dynamic interactions between the immune system and the composition of the microbiome in an apparently healthy oral cavity is reflected in temporal variability of the oxidative stress marker levels in otherwise healthy subjects.

It has been shown that good oral hygiene and toothbrushing decrease salivary oxidative stresses [20, 21]. Inflammatory and infectious sites show increased MDA levels, which can reveal higher levels of oxidative stress in periodontitis and dental caries. MDA levels can reflect the extent of infection, dental plaque, and microbial counts.

Previous studies have shown that MDA has deleterious effects on dental caries performance and progression [8, 22].

Oxidative stress-decreasing factors in dental diseases involve good oral hygiene which may affect the composition of saliva [21].

The balance of oxidant antioxidant system of saliva determines the overall health of the oral cavity. Impairment of oxidant-antioxidant balance in saliva may lead to various oral pathologic conditions [10].

Antioxidants, with many health benefits, are classified in 3 groups as chain-breaking, preventative and enzymes, and control ROS [23]. Antioxidant defense systems remove free radicals for healthy aerobic life. Some antioxidants are vitamins E, C, A, urate, bilirubin, substances containing SH groups, peroxidase, catalase, superoxide dismutase, and glutathione peroxidase [24].

Several research has been carried out to analyse the relationship between Total antioxidant capacity (TAC) and dental caries. Most studieshave shown that TAC levels are elevated in children with dental caries. There have been a few studies that have shown that children with dental caries have lower TAC levels than caries-free children [25].

It was observed that studies used different methods to measure salivary TAC. While spectrophotometryand ferric-reducing antioxidant power, were the most commonly used methods, some studies also utilized the 2,2'-azino-bis 3-ethylbenzthiazoline-6-sulfonic acidor the enzyme-linked immunosorbent assay [25].

Subramanyam D et al., 2018 evaluated the levels of MDA in children with ECC. The salivary MDA concentration in saliva was found to be comparatively higher in ECC group than that of the control group, but there was no significant difference between them, indicating some role of lipid degradation in the pathogenesis of dental caries [26].

Rahmani et al reported that TAC of saliva in those with dental caries was significantly lower compared with those without dental caries [27]. Rai et al. studied the relation between lipid peroxidation and dental caries and found that there was no difference in salivary MDA levels in children with or without ECC.[28]Findings of a study performed by Uberos et al. reported that TAC of saliva was higher in primary teeth of children with dental caries [29]. Oztürk et al., compared the association between DMFT and salivary MDA levels in the dental caries, but they did not find any significant difference in salivary MDA levels among the groups studied [30].

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 [31].

Tulonoglu et al., studied the relation between caries and TAC, and showed that there was an opposite linear relation between the two, i.e., an increase in TAC is associated with an increased caries experience among the healthy children. In our study, contradicting the above, even though the TAC value increased in healthy children, dental caries did not increase in these children. In fact, there was a minimal decrease in caries experience among these children. These observations clearly show that dental caries prevalence is not directly related to only one factor like TAC but can be modified by various other factors such as good oral hygiene practice and good diet [32]. Further clinical studies are required to find the association between oxidative stress induced lipid peroxidation reaction and other salivary biomarkers, to analyse the dietary practices and to determine the distinctive role of lipid peroxidation in ECC. And also, future researches should be conducted to determine the role of antioxidants such as Vitamin C and Vitamin E in reducing the oxidative stress-induced lipid peroxidation.

Since Dental caries and Early childhood caries is a common hurdle faced by dentists, there is a paradigm shift over the recent years where the current scenario is to prevent the dental caries

by identifying the risk factors early to reduce the initiation of the disease process. Although it is a time-consuming and complicated process, the evaluation of oxidative stress through lipid peroxidation as a risk factor for dental caries may be essential to diagnose and perform the treatment at the earliest. Antioxidants can be prescribed, which are capable of neutralizing the free radicals induced by oxidative stress, thereby preventing lipid peroxidation process in the oral cavity, which minimizes the bacterial infection [28, 33].

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