

## Oxidative stress and periodontitis: Cause or effect

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### ABSTRACT

Periodontitis is an inflammatory disease of the tooth supporting tissues which occurs as a response to the lipopolysaccharides released by the gram negative anaerobes present in the plaque biofilm. This article summarizes the role of reactive oxygen species, antioxidants and oxidative stress in periodontitis. It is concluded that considering the confirmable involvement of excess ROS activity and associated antioxidant depletion at local and systemic levels in periodontitis, it may be reasonable to advocate the use of antioxidants in periodontitis

**Keywords:** Antioxidant, Oxidative stress, Periodontitis.

### Oxidative stress and periodontitis: Cause or effect?

Periodontitis is an inflammatory disease of the tooth supporting tissues which occurs as a response to the lipopolysaccharides released by the gram negative anaerobes present in the plaque biofilm. Though the primary etiological agent is specific, the greater part of periodontal destruction occurs as a result of an inappropriate host response to the periodontal – pathogenic microorganisms and their products.<sup>1</sup> As the periodontal diseases progress, there is a loss of attachment of the periodontal tissues to the tooth accompanied by a supporting bone loss which eventually results in tooth loss.

Chronic inflammatory conditions are generally assumed to be related to oxidative stress. Polymorphonuclear leukocytes (PMNs) are the primary inflammatory cells in the periodontal tissues. It is believed that phagocytes particularly neutrophils are involved in disease pathogenesis by causing oxidative burst during phagocytosis and killing. Initially, it was thought that reactive oxygen species (ROS) are microbicidal, but now is supposed that they create an environment within the vacuole suitable for killing and digestion by enzymes released from the cytoplasmic granules.<sup>2</sup>

Free radicals are defined as 'any species capable of independent existence that contain one or more unpaired electrons'.<sup>3</sup> It include oxygen free radicals, nitrogen and chlorine species. These are highly reactive species capable of extracting electrons and thereby oxidizing a range of bio molecules which are crucial for the cell maintenance and tissue function. In normal physiology, there is a dynamic balance or homeostasis between the oxidants and antioxidants.

Antioxidants are defined as 'those substances which when present at low concentrations, compared to those of an oxidizable substrate, will significantly delay or inhibit oxidation of that substrate'.<sup>4</sup> Whenever there is an imbalance, either by an excess production of ROS or a decreased release or activity of antioxidants, oxidative stress results.

### ROS production in periodontal diseases

As ROS have a very short half – lives, it is not easy to detect their presence directly. Most of the studies, concentrate on monitoring the products (biomarkers) which are generated as a reaction of ROS to biomolecules like proteins, lipids and DNA.

Enhanced ROS production by hyper- reactive neutrophils as a response to periodontal

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pathogens (*Fusobacterium nucleatum*, *Aggregatibacter actinomycetemcomitans*) leading to progressive tissue damage has been suggested in both chronic and aggressive periodontitis.<sup>5</sup> Further, studies have suggested that *F. nucleatum* can stimulate ROS generation in presence or absence of plasma in healthy individuals and can also induce lipid peroxidation in vitro.<sup>6,7</sup>

It has been demonstrated that patients with chronic periodontitis have higher levels of markers of lipid peroxidation, thiobarbituric acid reactive substances (TBARS) and malondialdehyde (MDA) compared to periodontally healthy individuals.<sup>8,9</sup> Both salivary and gingival crevicular fluid (GCF) MDA levels have been demonstrated to decrease after successful phase 1 periodontal therapy.<sup>9</sup>

Also, the two most important risk factors for periodontitis, smoking and diabetes have been linked to oxidative stress. Systemic and local MDA levels were found to be increased by smoking in addition to the impact of periodontitis<sup>10</sup> and were found to be deranged in diabetics in our previous study.<sup>11</sup>

A marker of oxidative damage to DNA, 8-hydroxydeoxyguanosine has been found to be significantly elevated in individuals with chronic periodontitis<sup>12</sup> and the levels correlated with the clinical attachment level.

### Antioxidants in periodontal diseases

A loss of homeostatic balance between ROS and antioxidants is believed to be partly responsible for the periodontal destruction. Various studies have suggested a decrease in total antioxidant capacity (TAOC) and individual antioxidants levels and activity in periodontitis. It is crucial to know that different compartments of body differ in their antioxidant profile and the contribution of individual antioxidant species in maintaining tissue homeostasis and balance. It was pointed out that the antioxidant profile of GCF differed from serum or saliva.<sup>13</sup> The most dominant antioxidant in GCF was reduced glutathione<sup>14</sup> while uric acid predominated in the saliva.<sup>15</sup>

Chapple et al.(2007)<sup>16</sup> concluded that the local total antioxidant capacity in chronic

periodontitis is related to the increased oxygen radical activity during periodontal inflammation and can be restored to the control subject levels by successful non-surgical therapy. Panjamurthy et al. (2005)<sup>8</sup> found lower plasma vitamin C, vitamin E and GSH in periodontitis patients, whereas antioxidant enzyme levels were found to be raised. The authors attributed this to a protective response to oxidative stress. A reduction in antioxidant capacity in saliva, serum and GCF has also been documented in various studies.<sup>9,13</sup>

In a study by our group, a significant reduction in antioxidants studied was found in periodontitis group compared to the control group. Also, a negative correlation with the clinical parameters was documented which was speculated to have a clinical relevance.<sup>17</sup>

### Antioxidant supplementation in periodontitis

It has been suggested that the oral environment offered an excellent opportunity to investigate the free radical and antioxidant biology more conveniently than the other body systems. The ability to apply antioxidants locally and the significant concentrations which can be attained by local administration provides scope for novel host modulating therapies.<sup>18</sup>

Increasing tissue concentration of certain antioxidants which are of strategic importance to the periodontium may offer protection against oxidative stress. The presence of superoxide dismutase which offers biological protection against ROS has been reported in the periodontal ligament.<sup>19</sup>

Various studies involving Vitamin C, Vitamin E, Coenzyme -Q and antioxidant enzymes have provided conflicting results. Chapple et al.<sup>20</sup> (2007), found an inverse association between carotenoids and periodontitis in the United States using data from NHANES III. A study showed that patients with periodontitis who rinsed their mouths with vitamin E daily for 21 days experienced a significant decrease in GCF flow compared with an unsupplemented control group,<sup>21</sup> while in another no noticeable benefit was obtained from a 5% vitamin E gel used as an adjunct to therapy.<sup>22</sup>

Clinical improvement in periodontal condition has been shown by supplementation of multi-vitamin phytonutrients,<sup>23</sup> Vitamin C/Vitamin E and grape seed extract<sup>24</sup> supporting the therapeutic benefit of antioxidant supplementation.

### Conclusion

Oxidative stress is an important contributing factor in periodontal diseases. However, it is not clear whether it is the cause or the result of the disease. Considering the confirmable involvement of excess ROS activity and associated antioxidant depletion at local and systemic levels in periodontitis, it may be reasonable to advocate the use of antioxidants in periodontitis. A better understanding of the basic mechanisms would help in implementing improved preventive and therapeutic strategies.

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### Author contribution:

Dr. Shilpa Trivedi: Article search, manuscript writing and editing.

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