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Review Article

Role of Reactive Oxidative Species in Periodontitis: A Review Article

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Abstract

Introduction: Common periodontitis that attacks the human population is periodontitis induced by plaque. Periodontitis begins with the ordering of plaque that adheres to the tooth surface. Dental plaque is a thin layer of multi-species biofilm containing colonization of bacteria, bacterial products, and food debrish. The dental plaque that causes periodontitis is usually located in the subgingival area, then extends apical to the tooth, causing inflammation of the periodontal tissue. The causes of periodontitis in general are bacterial species found in dental plaque, and about 10 species have been identified as pathogens in periodontal disease, especially gram-negative stem bacteria, including Porphyromonas gingivalis, Prevotella intermedia, Actinomyces viscosus, Bacteroides forsythus, Campylobacter rectus, Treponema denticola, and Fusobacterium nucleatum.Apart from plaque factors, periodontitis can also be caused by systemic factors, genetic disorders as well as environmental and risk factors. Studies show that people with diabetes mellitus and smokers suffer from periodontitis a lot. Whereas in patients with periodontitis due to genetic disorders caused by damage to the periodontal tissue by macrophages that respond to IL-1 excessively. ROS, also plays role in pathophysiology in periodontitis.

Discussion: Chronic periodontitis is a chronic infectious disease with a complex etiology. The main etiology is bacteria and is exacerbated by various other factors. In this case, excessive production of ROS and changes in state can lead to abnormal activation of apoptosis, approaches important factors involved in the production of periodontitis extensions and various clinical features of periodontitis. Several studies have demonstrated a role for ROS in the deregulation of apoptosis. Between ROS and the body can produce neo-epitopes which then stimulate a broad spectrum associated with tissue damage and breakdown of the periodontium. Studies in periodontitis patients and involves oxidative stress in disease pathogenesis. Polymorphism genes coding for superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and the gene encoding NADPH oxidase NCF2 have been identified in many ways with a risk of periodontitis. All biomolecules (lipids, proteins and DNA) can be damaged by the overproduction of ROS.

Conclusion: During infection, immune system produce reactive oxygen species (ROS) which are released into the extracellular environment. The ROS does not have a specific target that could damage tissue especially in periodontitis.

Keywords: ROS; Pathophysiology; Periodontitis

Introduction

Periodontitis is an inflammatory condition in the periodontal tissue or tooth supporting tissue that progressively decreases the alveolar bone structure (bone loss) and connective tissue around the teeth, thus forming periodontal pockets. Periodontitis is a continuation of gingivitis that has been previously suffered. The types of periodontitis that are very common in the human population are chronic periodontitis, aggressive periodontitis and acute necrotizing ulcerative periodontitis. Chronic periodontitis attacks the human population. An Australian study showed that patients with moderate and severe periodontitis made up 22.9 percent of the total population. Meanwhile in Indonesia, 10 out of 11 people suffer from periodontitis [1, 2, 3].

Common periodontitis that attacks the human population is periodontitis induced by plaque. Periodontitis begins with the ordering of plaque that adheres to the tooth surface. Dental plaque is a thin layer of multi-species biofilm containing colonization of bacteria, bacterial products, and food waste. The dental plaque that causes periodontitis is usually located in the subgingival area, then extends apical to the tooth, causing inflammation of the periodontal tissue. The causes of periodontitis in general are bacterial species found in dental plaque, and about 10 species have been identified as pathogens in periodontal disease, especially gram-negative stem bacteria, including Porphyromonas gingivalis, Prevotella intermedia, Actinomyces viscosus, Bacteroides forsythus, Campylobacter rectus, Treponema denticola, and Fusobacterium nucleatum [4].

Apart from plaque factors, periodontitis can also be caused by systemic factors, genetic disorders as well as environmental and habitual factors. Studies show that people with diabetes mellitus and smokers suffer from periodontitis a lot. Whereas in patients with periodontitis due to genetic disorders caused by damage to the periodontal tissue by macrophages that respond to IL-1 excessively [5].

Chronic periodontitis is an inflammatory condition that can lead to increased free radical production. The invasion of the antigen from the plaque into the tissue stimulates the inflammatory cells to leave the capillaries to phagocyte these antigens. During the phagocytosis process, PMN cells, neutrophils and macrophages produce reactive oxygen species (ROS) which are released into the extracellular environment. The ROS does not have a specific target so that it can damage tissue damage with DNA damage, lipid peroxidation, protein, oxidation of other important enzymes and stimulation of the release of proinflammatory cytokines by monocytes and macrophages [6].

Discussion

Chronic periodontitis is a chronic infectious disease with a complex etiology. The main etiology is bacteria and is exacerbated by various other factors. In this case, excessive production of ROS and changes in state can lead to abnormal activation of apoptosis, approaches important factors involved in the production of periodontitis extensions and various clinical features of periodontitis. Several studies have demonstrated a role for ROS in the deregulation of apoptosis. Between ROS and the body can produce neo-epitopes which then stimulate a broad spectrum associated with tissue damage and breakdown of the periodontium [7].

Studies in periodontitis patients and involves oxidative stress in disease pathogenesis. Polymorphism genes coding for superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and the gene encoding NADPH oxidase NCF2 have been identified in many ways with a risk of periodontitis. All biomolecules (lipids, proteins and DNA) can be damaged by the overproduction of ROS. Table 1 summarizes the oxidative stress in periodontitis [8].

Mechanisms of tissue damage

Mechanism of protein damage	Mechanism of lipid damage	Mechanism of DNA damage
The effects of ROS on proteins include	Products of lipid peroxidation include a variety of bioactive molecules	Mechanisms of DNA damage by peroxynitrite and hydroxyl radicals include
Protein folding/unfolding	Conjugated dienes	Strand breaks
Protein fragmentation	Lipid peroxides	Base pair mutations
Protease degradation of the modified protein	Aldehydes, e.g., malondialdehyde	Conversion of guanine to 8-hydroxyguanine
Formation of protein radicals, protein-bound ROS	Acrolein	Deletions
Formation of stable end products, e.g., carbonyl compounds such as oxo-acids or aldehydes (e.g., alanine to acetaldehyde)	Isoprostanes, e.g., F2-isoprostanes	Insertions
	Neuroprostanes (F4-isoprostanes)	Nicking
	Volatile hydrocarbons, e.g., pentane, ethane	Sequence amplification

DNA – Deoxy ribo nucleic acid; ROS – Reactive oxygen species

Table 1: Mechanisms of oxidative stress damage in periodontitis [8].

The main source of free radicals is the product of catabolism. Highly reactive superoxide anions are mainly produced in mitochondria, xanthine oxidase and NADPH-oxidase. Superoxide anions can react with nitric oxide to produce the strong oxidant peroxynitrite, or they can be degraded by superoxide dismutase into less reactive hydrogen peroxide species. Hydrogen peroxide can then be catabolized by glutathione peroxidase or catalase reactions, reacting with Fe2+ to form hydroxyl radicals through the Fenton reaction, or degraded by myeloperoxydase, another source of hydroxyl radicals [6].

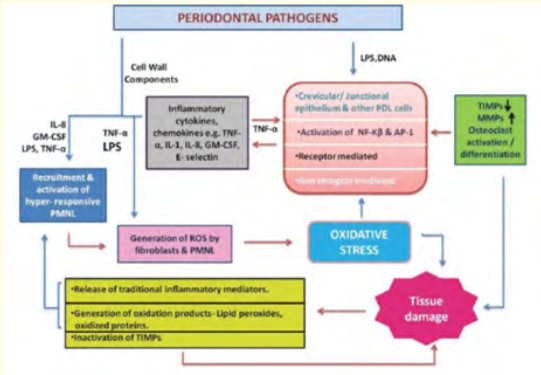

Figure 1: The mechanism for the formation of oxidative stress [6].

Role of Reactive Oxidative Species in the Pathogenesis of Periodontitis

Periodontal disease can be caused by an immune reaction between the pathogenic bacteria and the host. Sub-gingival dental plaque is the main etiologic agent for the initiation of inflammatory changes in the periodontal tissues. Lipopolysaccharide (LPS) and DNA from these bacteria cause activation of both the protein-1 pathway and the factor-kβ pathway in gingival fibroblasts via CD14 and TLR-4 (toll like receptors) and the production of inflammatory cytokines [7].

Bacterial cell components and inflammatory cytokines cause responsive recruitment and activation of PMNs and thereby accelerate the production of ROS. On the other hand, activation of NF-kβ and AP-1 causes osteoclast activation and increases MMP (matrix metalloproteinase) concentration, which ultimately results in tissue damage. Periodontal tissue damage results in the production of excess

lipid peroxide, inflammatory mediators, and oxidized proteins. These products further activate macrophages, neutrophils and fibroblasts to produce more ROS. In short, we can say that periodontal pathogens, ROS and tissue damage form a related circle [8]. ROS can directly damage gingival cells. ROS generated using neutrophil myeloperoxidase, chloride, glucose, and glucose oxidase causes lysis of epithelial targets that can be inhibited by azide and catalase. Neutrophils in periodontitis show a hyperactive / reactive phenotype with respect to ROS production [9].

Certain ROS (superoxide and hydrogen peroxide) activate osteoclasts and cause proliferation of osteoclast formation. Osteoclasts themselves produce ROS when ruffle bony borders, suggesting a more direct role in resorption. Hydroxyl radicals and hydrogen peroxide can be degraded by proteoglycans of alveolar bone in vitro [10].

Other effects of ROS on glycosaminoglycans and proteoglycans can damage soft tissue and periodontium. This causes degradation of the core protein and glycosaminoglycan chains. Evidence suggests that low levels of ROS can selectively destroy proteoglycans with periodontal soft tissue and alveolar bone. This extracellular matrix component is degraded and is supported by data from a large number of studies based on gingival analysis in crevicular fluid and tissue extracts for their degradation products [8].

The collagen structure, with its high proline / hydroxyproline content, is highly susceptible to damage by ROS. Superoxide anions and hydroxyl radicals are able to rotate collagen into small peptides in proline and hydroxyproline residues, thus freeing peptides containing hydroxyproline. Indirect modification of collagen and serum proteins by ROS, through interaction with lipid peroxidation. Products such as malondialdehyde, can significantly alter fibroblast function such as adhesion, proliferation, and longevity. Changes such as in vivo fibroblast function occur in periodontal disease due to increased lipid peroxidation in the gingival tissue [9].

Oxidative changes in collagen in the periodontal connective tissue can inhibit the migration of neutrophils through the tissue and increase the potential to produce ROS. Superoxide can modify chloroform factor bound to serum plasma albumin. Metalloproteinase imbalance also occurs in the fluid of the gingival groove and in the periodontal tissue [10].

The α1-antitrypsin enzyme has the role of neutralizing the lysosomal collagenase and elastase enzymes in phagocytosis. The oxidation of α1-antitrypsin causes a loss of inhibitory role in protease and proteolytic fermentation of chymotrypsin, renin, kallikrein, plasmin, urokinase, thrombin, elastase, and collagenase [10]. Activation of the transcription factor NF-Kb ROS is induced by the release of bacterial lipopolysaccharides, IL-1, and TNF-α. NF-kB (I-kB), the cytoplasmic part of, by liberating NF-kB. NF-kB diffuses from the cytoplasm and binds to the promoter so that it can stimulate structural mRNA transcription genes for proinflammatory cytokines [9].

Matrixmetaloproteinase (MMP) is the neutrophil MMP-8 (collagenase-2) and MMP-9 (gelatinase-B). MMP-8 decreases in collagen, while MMP-9 is a gelatinolytic enzyme that degrades extracellular matrix proteins, including collagen type IV, and membrane proteins. Both matrix metalloproteinases are present in the gingival and salivary fluids that reduce collagen, especially during the inflammatory process in patients with gingivitis and periodontitis. This enzyme stimulates fibroblasts and macrophages to produce neutral metalloprotease procollagenase. Fibroblasts mainly produce MMP-1 (collagenase-1), MMP-13 (collagenase-13), MMP-2 (gelatinase-2), MMP-3 and MMP-14 [8].

Conclusion

During infection, immune system produces reactive oxygen species (ROS) which are released into the extracellular environment. The ROS does not have a specific target that could damage tissue especially in periodontitis.

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