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The role of nuclear factor kappa B in periodontal diseases

Abstract

Periodontal (gum) diseases are inflammatory conditions caused by microbial dental biofilm. Chronic periodontitis is the most common form of the periodontal diseases result in loss of connective tissue attachment and supporting bone that may eventually result in loss of teeth. Nuclear factor kappa B (NF-kB) is a key regulator during inflammatory process involving the gingiva and alveolar bone of teeth. In this paper, we explain the role of NF-kB in the destructive process of teeth supporting tissues.

Keywords: periodontal diseases, NF-kb, gingiva, alveolar bone

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Introduction

Severe periodontitis and caries incidence are increasing since two decades,[1] and they are most prevalent diseases globally; where the oral conditions all ranked among the top 100 detailed causes of DALYs (disability-adjusted life-years) metric. Dental biofilm causes periodontal diseases and dental caries, affecting wide range human being and negatively affecting the quality of life (QOL) of the middle-aged and older populations.[2–5] Denitrification is a process of nitrate reduction performed by facultatively anaerobic or microaerophilic organisms, but aerobic denitrification also occurs.[6] Denitrification results in the formation of dinitrogen (N_2) from nitrate (NO_3) via nitrite (NO_2), nitric oxide (NO) and nitrous oxide (N_2O) intermediates. In the oral cavity, nitrate reduction is conducted by nitrate reducing bacteria which are residing dental biofilm on the teeth surfaces and surrounding gum.[7] Nitrate from dietary sources is absorbed by the intestine and then re-absorbed from the bloodstream to be secreted into the oral cavity as a component of saliva.[8] Nitrate-reducing bacteria in the dental biofilm reduce salivary nitrate to nitrite,[6–11] which is further reduced to nitric oxide (NO) by nitrite reducing bacteria.[12,13] Nitrate secretion in saliva would enhance the survival and growth of bacteria that possess the ability to respire nitrate. Hence, this creates a symbiotic relationship between the host and microbiota; the host providing environment and nutrients in return for nitrite production.[6]

Denitrification effect on the progression of periodontal disease

Periodontitis is an inflammatory disease resulting in the destruction of the supporting structures of the teeth (the periodontal ligament and the alveolar bone). It results in the formation of pockets between soft tissue of the gingiva and the tooth, can eventually cause tooth loss.[14] Nitrogen oxides are the denitrification important products aggravating the damage of tooth supporting tissues during periodontitis.[15] The amount Nitrogen oxides accumulated in the dental biofilm depends on the amount of nitrate in the food consumed. Nitric oxide oxidation would be another source for nitrogen oxides production in saliva.[16] In case the plaque pH level remains low for ling time, this would lead to the accumulation of high percentage of nitrogen oxide in dental biofilm. If the byproducts scavenging process is delayed or suppressed, the nitrogen oxides diffuse into the surrounding gum tissues that would aggravate nitrogen oxide-induced damage to the gingival tissues.[7] Previous studies proposed that over production of nitric oxide (NO) was implicated in the pathogenesis of periodontal disease.[17,18] NO, at normal concentrations, is a messenger molecule organizes functions of immune system cells that are part of the inflammation.[19] Lipopolysaccharides of the plaque bacteria can stimulate production of proinflammatory cytokines, which induce the immune cells to release high amount of NO. Subsequently, neutrophils would be induced to produce matrix metalloproteinases which causes further damage to the tooth surrounding tissues.[20] Using selective inducible nitric oxide synthase inhibitor or scavenger was shown to be protective against the progression of alveolar bone loss. Furthermore, subgingival local delivery of NO inhibitors might be useful in the treatment of periodontal tissue inflammation, whereas systemic NO inhibitor delivery was shown to decrease bone resorption in an animal model of periodontitis.[17]

Denitrification effect on dental caries formation

Salivary nitrate reduction by the oral bacteria contributes to the major nitrite exposure in the human body.[21] In the oral cavity, salivary nitrate will be utilized by bacteria that are capable of rapidly reducing nitrate to nitrite as part of their respiration. Mature dental biofilm is relatively thick and gelatinous which limits the diffusion of oxygen to deeper layers. Therefore, the microbes that survive in the deeper parts of the biofilm are facultative anaerobes. This would be the reason why nitrogen oxides are significantly higher in poor oral hygiene individuals than those with good oral hygiene who have thinner dental biofilm.[22] Many anaerobic facultative bacteria synthesize nitrate reductase in low oxygen tension,[9–24] hence, reduction can take place in the thick biofilm or deep tongue crypts.[23] In thick cariogenic plaque, the low pH level allows the production of acidified nitrite. It was reported that pH below 7 would promote the conversion of *L*-arginine to NO and its compounds.[25] NO is one of the byproducts and it is recognized for its antibacterial effect that inhibit the acidogenic bacteria which are

responsible for caries formation.[22,26] Nitric oxide antibacterial effects are thought to include DNA modifications and interactions with other reactive species; for example, reaction with superoxide produces the highly reactive molecule peroxynitrite.[27] Therefore, nitrate recycling and the availability of large amounts of nitrite in the oral cavity would result in bacteriostatic and possibly bacteriocidal effects which subsequently limit the survival of acidogenic bacteria and decrease caries formation.[11–26]

Conclusion

Human dental biofilm host many types of bacteria of which the nitrate reducing bacteria. These bacteria are utilizing the salivary nitrate for their respiration. Salivary nitrate is a reservoir from which a variety of nitrogen oxides are formed, most notably nitric oxide. Denitrification would have a dual effect either detrimental, by aggravating the damage of tooth supporting structure; or, beneficial by relatively limiting the dental caries formation.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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