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Short Communication

Statins- as Potential Host Modulating Agents

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Abstract

Bone resorption, through a destructive host immune response, is the ultimate consequences of periodontitis. Various therapies have been introduced to decrease the destruction. Statins besides having lipid lowering abilities also have been found to moderate or counteract the bone loss and to have beneficial effects on alveolar bone recovery. This short communication reviews the effects of statin and its potential role as a host modulating agent in periodontal therapy.

Keywords: Periodontitis; Statins; Anti-Inflammatory; Bone Formation

Introduction

Periodontal disease is a multifactorial complex disease and is characterized by an inflammatory breakdown of the tooth supporting structures seen as tissue destruction, bone resorption, attachment loss and in some cases tooth loss. Over the years, various treatment modalities have been tried at arresting these breakdowns and resorting periodontal tissues to their original structure and function. Conventional approaches were initially mechanical in nature while adjunctive therapies were solely antimicrobial. Therapies targeting immune response to periodontal ligament pathogens give promising results.

Various agents introduced for host modulation have short term effects. SDD (Subantimicrobial dose doxycycline) has positive short term effects on surrogate markers of chronic periodontitis and is thought to be mediated by inhibition of Matrix metalloproteinases (MMP-9) synthesis [1]. Bisphosphonates are group of drugs that inhibits bone resorption by disrupting osteoclast activity interfering with osteoblast metabolism and secretion of lysosomal enzymes. But bisphosphonates do not stimulate new bone formation and inhibit bone calcification [2]. However achieving greater predictability with regenerative therapy requires the introduction of an agent which not only hampers tissue destruction but also enhances the regenerative capabilities of the periodontal tissues.

Statins were introduced as agents used to lower cholesterol as they block the enzyme in the liver (HMG-CoA reductase) [3] the first committed enzyme of HMG-CoA reductase pathway that eventually produces cholesterol, as well as a number of other compound.

Recently, interest has been focused on non-cholesterol dependent, pleiotropic effect of statins, which includes antioxidants, antithrombotic, immunomodulatory, osteomodulatory, anti-inflammatory, vascular cytoprotection properties. Inhibition of the enzyme HMG-CoA reductase and subsequent blockage of the mevalonate pathway [4] is probably the most important mechanism of inhibition of bone resorption by statins. It occurs by interference with generation of isoprenoids, leading to disruption of vesicular fusion and ruffled border formation of osteoclasts, which are essential for bone resorption to occur. They are believed to increase the bone formation by stimulating the production of BMP-2 which may play an important role in periodontal and bone healing [5]. BMP induced osteoblast differentiation occur through antagonizing tumor necrosis factor (TNF- ∝- to –Ras/Rho/nitrogen activated protein kinase and also augmenting BMP-S mad signaling [2,3].

Some statins like simvastatin, cerivastatin and atorvastatin [6,7] markedly enhance gene expression for vascular endothelial growth factor (VEGF) which is involved in the process of endochondral bone formation and osteoclastic differentiation. Thus leading to new bone formation. SMV are believed to have significant antioxidant, reduces plasma levels of inflammatory markers such as CRP

(C-reactive protein), inhibits IL-6 productions by macrophages and also inhibits production of nicotinamide adenine dinucleotide phosphate oxidase, a major source oxidant production and anti-inflammatory effects. Effect of statins on immune system is mediated by building of statins to leukocyte and preventing its binding to ICAM-1 (Inter cellular adhesion molecule 1) leading to inhibition of leukocyte adhesion and extravasation [8].

An increasing number of observation studies reported benefits of statins on tooth preservation or periodontal health benefits [9-11].

Various studies have found that statins administration decreases GCF levels of TNF-α, IL-1β and MMP's in periodontal patients and thus modulates host response. These proinflammatory mediators are responsible for much of the host tissue destruction seen in periodontitis [1,5,6].

Cunha-Cruz., *et al.* [9] showed that systemic administration of simvastatin (SMV) was associated with decreased risk of tooth loss in chronic periodontitis patient's. It is administered in the prodrug form, which is lipophilic and can effectively cross cellular membrane barrier by passive diffusion. Local application of SMV [12] have proved its efficacy as potential inhibitor of bone resorption and shown to stimulate bone formation in rodents and periodontal ligaments cells in vitro and in vivo. Statins have been suggested to have potential benefit for osteoporotic women. Both topical statin gel application and local statin injections have been shown to improve fracture healing.

Therefore, Statins could play a significant role as a potential host modulating agent in the periodontal diseases.

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