American Journal of
Oral Medicine and Radiology

ISSN - 2394-7721

www.mcmed.us/journal/ajomr

Review Article

PERIODONTAL DISEASE - A REVIEW

Sivsankar P[1], Sabarigirinathan C[2], Vimala G[3], Vinayagavel K[4], Srinidhi L[5], Periyasamy S[6]

[1]Senior Assistant Professor, Tamilnadu Government Dental College and Hospital, Chennai, Tamil Nadu, 600003, India.
[2]Professor and Vice-Principal, Tamilnadu Government Dental College and Hospital. Chennai, Tamil Nadu, 600003, India.
[3]Professor and Principal, Tamilnadu Government Dental College and Hospital. Chennai, Tamil Nadu, 600003, India.
[4]Professor and HOD, Thiruvarur Medical College and Hospital, Tamil Nadu, India.
[5,6]Post graduate student, Tamilnadu Government Dental College and Hospital, Chennai, Tamil Nadu, 600003, India.

ABSTRACT
Periodontal diseases are infections associated with pathogenic bacteria that colonize the subgingival area, causing inflammation, which may lead to the destruction of periodontal tissues. Besides these direct host-pathogen interactions, periodontitis is exacerbated by risk factors represented by age, male gender, smoking and diabetes mellitus.

Key words:- Acute periodontitis, Inflammatory diseases, Prostaglandin E2, Cytokines.

Access this article online	
Home page: http://www.mcmed.us/journal/ajomr DOI: http://dx.doi.org/10.21276/ajomr.2020.7.2.11	**Quick Response code**

Received:25.07.20	**Revised**:28.08.20	**Accepted**:23.09.20

INTRODUCTION

Periodontal diseases are a group of inflammatory diseases mainly caused by bacteria and their products. The host response to bacteria and their products is mediated by the production and release of local factors from inflammatory cells, especially lymphocytes and monocytes, as well as cells of mesenchymal origin, such as osteoblasts and fibroblasts.[1].

Prostaglandin E_2;

It is a vasoactive eicosanoid produced by activated macrophages and fibroblasts and is found in the crevicular fluid of patients with periodontitis, and is considered the major inflammatory mediator of alveolar bone destruction.

Corresponding Author

Dr. Sabarigirinathan C
Email : - sabarigirinathandr@yahoo.co.in

Biopsies of gingival tissue from periodontitis patients showed a 15-fold increase in PGE_2 content compared with healthy patients. This finding has been confirmed in various other studies[2]

Moreover, in adult periodontitis patients, a significant increase in PGE_2 levels was found in the gingival crevicular fluid compared with healthy patients. An association between increasing levels of PGE_2 in gingival crevicular fluid and increasing severity and aggressiveness of disease has also been noted.[3] A direct correlation between the level of PGE_2 and the rate of attachment loss during periodontal disease was also found[4]. In addition, PGE_2 also potentiates production of other proinflammatory cytokines, which results in bone destruction.[5]

Cytokines

The role of cytokines in bone loss is important in the context of periodontitis, where inflammation-induced bone destruction is a major manifestation.

Numerous cytokines have been implicated as mediators of bone resorption. It has been hypothesized that the spectrum of cytokines which are produced in the surrounding microenvironment determines the development of normal bone remodeling or pathologic bone loss.[6]

Higher levels of IL-lβ, but not IL-lα, were found in the gingiva of patients with periodontal disease compared with healthy patients, suggesting that this cytokine is involved in mediating the diseases[6,] In other studies, significantly higher levels of IL-1β were found in tissue around active sites of bone loss than from inactive sites or healthy sites. In addition, there are significantly greater amounts of IL-lα and β in the gingival crevicular fluid of periodontal pockets.[7][7]

Therapeutic Approaches to Control Bone Destruction in Periodontal Diseases

NSAIDs

Various animal studies have demonstrated that systemic indomethacin therapy suppressed alveolar bone resorption.[28,] [29] Daily peroral administration of flurbiprofen (0.02 mg/kg) in beagles significantly decreased the rate of radiographic alveolar bone loss.[30] The propionic acid–derived NSAID, ibuprofen at 4.0 and 0.4 mg/kg (sustained release and standard peroral formulations) was effective in blocking alveolar bone loss in beagles with naturally occurring periodontitis.[7]

Systemic administration of flurbiprofen in humans, over a period of 2 years, resulted in depressed bone loss rates. A research group has demonstrated significant reduction in bone loss in subject taking naproxen compared with placebo group.[35] Similar results have been obtained with systemic administration of aspirin and aspirin plus indomethacin in humans. Recently, COX-2 inhibitor, etoricoxib has been shown to retard alveolar bone loss in ligature induced periodontitis models in rats[8].

Tetracyclines

Tetracyclines and their chemically modified non-antibacterial analogues can inhibit certain host-derived tissue destructive matrix metalloproteinases such as collagenases and gelatinases, including those that help mediate bone resorption. In addition, it has also been found that these drugs, by a non-antibacterial mechanism, can also enhance osteoblast activity, collagen production and bone formation.

The use of SDD (20 mg b.i.d), over a 2-year period, was associated with statistically significantly reduced alveolar bone density loss in non-smokers, at first molar–second premolar interproximal sites and for sites with baseline probing depths ≥5 mm.[8]

Spironolactone

It is an aldosterone-inhibitor used in the treatment of hyperaldosteronism. It has also been shown to inhibit production of TNF. Moreover, many other cytokines and mediators involved in alveolar bone destruction may account for the lacking response to spironolactone. The possible effect of spironolactone treatment in humans with periodontal disease is yet to be investigated.

WP9QY peptide

It efficiently antagonizes the effects of TNF-α binding to the TNF receptor (I). It has been shown to prevent the P. gingivalis-induced reduction in the bone mineral density at the calvariae in mice.[9]

Lodoxamide

Lodoxamide ethyl and lodoxamide tromethamine are dioxamic acids which are potent inhibitors of mast cell degranulation. The precise biochemical mechanism of action has not yet been clearly established, but they apparently stabilize the mast cell's reaction to stimulation and thus block degranulation.

Daily administration of lodoxamide ethyl alone at a dose of 20 mg/kg significantly reduced the rate of bone loss by 12 months of continuous dosing compared to a pretreatment baseline period in beagles.[10]

Batimastat (BB-94)

It is a broad-spectrum MMP inhibitor with activity against, at least, MMP-1 (MMP-13 in rats) MMP-2, MMP-3, MMP-7, MMP-9 and MMP-14. Since MMPs play an important role in tissue destruction during periodontal diseases, it has been hypothesized that this agent may inhibit progression of periodontal diseases. But initial study failed to support this hypothesis and, instead, found significantly increased bone destruction in rats treated with batimastat.[4]

Immunosuppressants

Cyclosporin A and FK506 are known to inhibit the Ca^{2+} Calcineurin pathway and to suppress RANKL expression by activated T cells. Cyclosporin A appears to inhibit periodontal bone loss induced in a ligature-model of rat periodontitis, whereas CsA alone causes only mild alveolar bone loss in control rats.

Systemic administration of CsA leads to unwanted side-effects such as renal dysfunction and hypertension, which clearly limits the therapeutic use of CsA in the amelioration of bone resorption. However, administration of CsA in combination with TGF-β or citrate, blocked the deleterious effects of cyclosporin A, and increased the percentage of mineralizing surface and the bone formation rate [4].

Potassium (K^+) channel pathway inhibitors

Several reports have demonstrated that two K^+ channels, Kv1.3 and IKCa1, play crucial roles in T-cell activation, inflammation and progression of autoimmune diseases. Kv1.3 expression appears to be up-regulated in the chronic periodontitis patients, which play an important role in the expression of RANKL by T cells. Blockade of Kv1.3 with its inhibitor, *kaliotoxin* (scorpion venom), suppressed the expression of RANKL in activated T cells.

Osteoprotegerin-Fc

It is a chimeric protein made up of OPG and the Fc portion of human IgG. In a rat model of periodontal disease using adoptive T cell transfer, systemic administration of OPG-Fc significantly reduced periodontal bone loss by about 90% compared to the control group injected with the control protein L6-Fc (Han et al. 2007). Other rodent models of periodontal disease also showed that bone resorption can be inhibited by the administration of OPG-Fc.

Denosumab

It is monoclonal antibody that inhibits nuclear factor-κB ligand and thus neutralizes RANKL. It has been shown to effectively increase bone mineral density in postmenopausal women and to decrease bone resorption. It is conceivable that, when locally applied judiciously, such an antibody may be sufficiently effective in the management of alveolar bone resorption in periodontitis, without showing side effects.

Bisphosphonates

Bisphosphonates have been successfully used to treat osteoporosis, Paget's disease, metastatic and osteolytic bone diseases. It inhibits proliferation and differentiation of osteoclasts as well as induces apoptosis in mature osteoclasts. In addition, it also decreases RANKL expression by osteoblasts. Various animal and human studies[9] have confirmed anti-bone resorptive effect of bisphosphonates.

However, it has been reported to cause osteonecrosis of jaws as a result of localized vascular insufficiency of bone. To reduce such side effects by bisphosphonates,

NO synthase inhibitors

Nitric oxide (NO) is a free radical associated with a multitude of physiological functions which include modulation of cardiovascular tone and integrity, regulation of platelet aggregation, and strong oxidative activity that contributes to the killing of microorganisms. NO is synthesized from L-arginine by a group of isoenzymes collectively termed NO synthases. NOS inhibitors, such as L-NAME (L-arginine methyl ester) and aminoguanidine, have been shown to prevent inflammatory bone resorption in experimental periodontitis.

Matrix metalloproteinase inhibitors (MMPIs)

Excessive production and/or activity of MMPs are widely recognized as a potential site of pharmacologic intervention in disorders such as periodontal disease, rheumatoid arthritis, cancer, and many others. Excessive collagenase activity is a hallmark of both experimental naturally-occurring human periodontal disease, leading to loss of gingival collagen and destruction of alveolar bone. CH1766 and CH6631 are low molecular weight MMPIs which have been shown to reduce active and/or total MMP activity as well as alveolar bone loss in experimental periodontal disease.

IL-1 & TNF antagonists

In periodontal research, the effects of soluble receptors and receptor antagonists of IL-1 and TNF-a have been studied during experimentally induced periodontitis in a non-human primate model (e.g. Macaca fascicularis). Collectively, the clinical, radio graphic and biochemical findings of these experiments showed that IL-1 and TNF-a antagonists blocked (i) the progression of the inflammatory cell infiltrate towards the alveolar crest, (ii) the recruitment of osteoclasts and (iii) periodontal attachment and bone loss [5].

Bone Destruction in Periodontal Diseases

The development and homeostasis of the skeletal system depends on a dynamic balancing of the activities of bone-forming osteoblasts and bone-resorbing osteoclasts. This balance must be tightly controlled by various local and systemic factors. Tipping this balance in favor of osteoclasts leads to pathological bone resorption, as seen in a variety of diseases, including periodontitis.

Bone Destruction Caused By Extension of Gingival Inflammation

The most common cause of bone destruction in periodontal disease is the extension of inflammation from the marginal gingiva into the supporting periodontal tissues. The factors that are responsible for the extension of inflammation to the supporting structures and that initiate the conversion of gingivitis to periodontitis are not known at this time.

The transition from gingivitis to periodontitis is associated with changes in the composition of bacterial plaque. In advanced stages of disease, the number of motile organisms and spirochetes increases whereas the number of coccoid rods and straight rods decreases.

Radius of Action

The locally produced bone resorption factors may have to be present in the proximity of bone surface

to be able to exert their action. Bacterial plaque can induce bone loss within 1.5 to 2.5 mm. Beyond 2.5 mm there is no effect; interproximal angular defects can appear only in spaces that are wider than 2.5 mm because narrower spaces would be destroyed entirely.

Large defects far exceeding a distance of 2.5 mm from the tooth surface (as found in aggressive types of periodontitis) may be caused by the presence of bacteria in the tissues.

Rate of Bone Loss

The patients with periodontal disease can be grouped into 3 categories based on interproximal loss of attachment and tooth mortality:

1. Approximately 8% of persons had rapid progression of periodontal disease, characterized by a yearly loss of attachment of 0.1 to 1 mm.
2. Approximately 81% of individuals had moderately progressive periodontal disease, with a yearly loss of attachment of 0.05 to 0.5 mm.
3. The remaining 11% of persons had minimal or no progression of destructive disease (0.05 to 0.09 mm yearly).

Periods of Destruction

Periodontal destruction occurs in an episodic, intermittent fashion, with periods of inactivity or quiescence. The destructive periods result in loss of collagen and alveolar bone with deepening of the periodontal pocket. The reasons for the onset of destructive periods have not been totally elucidated, although the following theories have been offered:

1. Bursts of destructive activity are associated with subgingival ulceration and an acute inflammatory reaction, resulting in rapid loss of alveolar bone.
2. Burst of destructive activity coincide with the conversion of predominantly T-lymphocyte lesion to one with a predominance of B-lymphocyte-plasma cell infiltrate.
3. Periods of exacerbations are associated with an increase of the loose, unattached, motile, gram-negative, anaerobic pocket flora, and periods of remission coincide with the formation of a dense, unattached, nonmotile, gram-positive flora with a tendency to mineralize.
4. Tissue invasion by one or several bacterial species is followed by an advanced local host defense that controls the attack.

Bone Destruction Caused By Trauma from Occlusion

Trauma from occlusion can produce bone destruction in the absence or presence of inflammation. In the absence of inflammation, the changes caused by trauma from occlusion vary from increased compression and tension of the PDL and increased osteoclasis of alveolar bone to necrosis of the PDL and bone and resorption of bone and tooth structure.

These changes are reversible in that they can be repaired if the offending forces are removed.[9] However, persistent trauma from occlusion results in funnel shaped widening of the crestal portion of the PDL, with resorption of the adjacent bone.

These changes, which may cause the bony crest to have an angular shape, represent adaptation of periodontal tissues aimed at “cushioning” increased occlusal forces, but the modified bone shape may weaken tooth support and cause tooth mobility.

Bone Destruction Caused By Systemic Disorders

Local and systemic factors regulate the physiologic equilibrium of bone. When a generalized tendency toward bone resorption exists, bone loss initiated by local inflammatory processes may be magnified. This systemic influence on the response of alveolar bone has been termed the bone factor in periodontal disease.

Although the term bone factor is not in current use, the concept of a role played by systemic defense mechanisms has bee validated, particularly by studies of immune deficiencies in severely destructive types of periodontitis, such as the juvenile forms of the disease.

In recent years, interest has increased in the possible relationship between periodontal bone loss and osteoporosis. Few studies on the relationship between periodontitis and osteopororsis are available, and some show relationships between skeletal bone density and oral bone density and between crestal height and residual ridge resorption.[6]

Periodontal bone loss may also occur in generalized skeletal disturbances (e.g., hyperparathyroidism, leukemia, Langerhans cell histiocytosis) by mechanisms that may be totally unrelated to the usual periodontal problem.

CONCLUSION

Periodontal osseous defects are a frequent sequela of periodontitis. Sites with infrabony defects have been shown to be at higher risk of disease progression in subjects who did not receive systematic periodontal therapy. Several lines of evidence indicate that teeth with furcation involvements are at higher risk for periodontal disease progression and tooth loss during periodontal recall.

REFERENCES

1. Dewhirst FE, Moss DE, Offenbacher S, Goodson JM. Levels of PGE_2, thromboxane, and prostacyclin in periodontal tissue. *J Periodont Res 1983: 18: 156-163.*

2. Offenbacher *S*, Farr DH, Goodson JM. Measurement of prostaglandin E in crevicular fluid. *J Clin Periodontol 1981: 8: 359-367.*
3. Offenbacher S, Odle BM, Gray RC, Van Dyke TE. Crevicular fluid prostaglandin E levels as a measure of the periodontal disease status of adult and juvenile periodontitis patients. *J Periodont Res 1984: 19: 1-13.*
4. Offenbacher S, Odle BM, Van Dyke TE. The use of crevicular fluid PGE, levels as a predictor of periodontal attachment loss. *J Periodont Res 1986: 21: 101-112.*
5. Czuszak CA, Sutherland DE, Billman MA, Stein SH. Prostaglandin E_2 potentiates interleukin-1β induced interleukin-6 production by human gingival fibroblasts. *J Clin Periodontol 1996; 23: 635-640.*
6. Stashenko P, Jandinski JJ, Fujiyoshi P, Rynar J, Socransky SS. Tissue levels of bone resorptive cytokines in periodontal disease. *J Periodontol 1991; 62(8): 504-509.*
7. Crotti T, Smith MD, Hirsch R, Soukoulis S, Weedon H, Capone M, Ahern MJ, Haynes D. Receptor activator NF kappaB ligand (RANKL) and osteoprotegerin (OPG) protein expression in periodontitis. *J Periodont Res 2003; 38: 380–387.*
8. Mogi M, Otogoto J, Ota N, Togari A. Differential expression of RANKL and osteoprotegerin in gingival crevicular fluid of patients with periodontitis. *J Dent Res 2004; 83: 166–169.*
9. Williams RC, Jeffcoat MK, Wechter WJ, Johnson HG, Kaplan ML, Goldhaber P. Non-steroidal anti-inflammatory drug treatment of periodontitis in beagles. *J Periodont Res 1984; 19: 633–637.*
10. Williams RC, Jeffcoat MK, Howell TH, Reddy MS, Johnson HG, Hall CM, Goldhaber P. Ibuprofen: an inhibitor of alveolar bone resorption in beagles. *J Periodont Res 1988; 23: 225–229.*

Cite this article:
Sivsankar P, Sabarigirinathan C, Vimala G, Vinayagavel K, Srinidhi L, Periyasamy S. Periodontal Disease - A Review. *American Journal of Oral Medicine and Radiology*, 7(2), 2020, 57-61.
DOI: **http://dx.doi.org/10.21276/ajomr.2020.7.2.11**