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Smoking and its Effects on Periodontium - A Review

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Abstract

Tobacco smoking has been considered an independent environmental risk factor for the development and progression of periodontal disease along with other negative consequences on multiple physiological systems. It impairs the environment and ecology of the oral cavity as well as the vasculature, inflammatory-immune responses, and periodontal tissue healing ability. Studies revealed that quitting smoking improves the health of the periodontium. The objective of this report is to draw attention to the harmful effects of tobacco smoking on the periodontium.

Keywords: Immune-Inflammatory Response, Microbiology, Periodontium, Physiology, Periodontal Therapy, Smoking

1. Introduction

In the late 15th century, dried tobacco leaves were presented before Christopher Columbus when he encountered the American Indians and thereafter, he introduced it to Europe. Thus, the spread of tobacco consumption started. It originates from the Nicotiana plant genus which belongs to the potato tribe[1].

Tobacco use is widespread and can be seen as an epidemic all over the world[2]. Tobacco smoke contains thousands of noxious chemicals that are toxic to almost every organ in the body, reducing life expectancy and quality of life. It is found that there are over 5 million deaths worldwide per year.[2] Its use has been linked to cancer, chronic pulmonary and heart disease[3].

Periodontitis is linked to smoking which is a known risk factor with higher levels of tooth mobility, loss of a tooth, clinical loss of alveolar bone, and probing pocket width influencing the frequency, duration, and seriousness of the disease[4]. When compared to non-smokers, periodontitis is four times as likely in smokers[5].

Tobacco uses also cause abrasions, teeth stains, smoker's melanosis, keratotic spots, Acute Necrotizing Ulcerative Gingivitis (ANUG), palatal erosions, black hairy tongue, oral carcinoma, and nicotinic stomatitis[6].

Tobacco cessation is critical for lowering tobacco-related mortality and morbidity. It is well known that quitting smoking is linked to lower mortality, a lower risk of contracting diseases, and a longer life expectancy[7].

2. Impact of Tobacco Smoking on Oral Microbiota

The subgingival microbiota of smokers and non-smokers was studied by Tijhof and Winkelhoff who found that the presence of *Peptostreptococcus micros*, *Campylobacter rectus, Bacteroides forsythus,* and *Fusobacterium nucleatum* in the absence of *Actinobacillus* tended to be the most pronounced microbiological characteristics of smokers[8]. Furthermore, these pathogenic bacteria were found in greater numbers in the maxilla when compared to the mandible[9].

According to Umeda *et al.,* a periodontal pocket of current smokers have a greater risk of harboring *T. denticola* and the presence of *F. nucleatum, E. corrodens,*

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A. actinomycetemcomitans, P. intermedia, P. gingivalis, or *P. gingivalis*. Moreover, Smoking enhanced the chances of having a (3.5 mm) deep pocket[10].

On the contrary, Apatzidou *et al.* and Bostrom *et al.* concluded that there were no considerable changes in the identification of potential periodontal microorganisms among smokers and non-smokers[11,12].

3. Effect of Smoking on Immune-Inflammatory Response

Periodontitis is linked to a shift in the bacterial balance of the host which can be triggered by alterations in the immune system and alterations in the bacterial makeup of subgingival plaque or a combination of both[13].

Smoking has an impact on the humoral immune system as well. Macrophages are immune cells that play a role in both cellular and humoral immunity. Mancini *et al.* discovered that alveolar macrophages of smokers express lesser Class II MHC[14].

In a dose-response fashion, smoking raises the number of CD3+ and CD4+ cells. Immunoglobulins, notably IgG2, have been found to be a key antibody against periodontal infections caused by gram-negative organisms, and their levels were observed to be lesser in smokers versus non-smokers[15].

3.1 Effect on Polymorphonuclear Neutrophils

It has been found that the expression of nicotinic receptors by neutrophils increases in tobacco smokers and decreases after quitting[16]. Polymorphonuclear Neutrophils (PMNs) isolated from the smoker's peripheral blood or saliva showed functional changes in chemotaxis, phagocytosis, and oxidative burst[17,18]. The increased release of potentially tissue-destructive products by smokers' neutrophils in the peripheral circulation could be one possible mechanism for this increased neutrophil-mediated damage. Besides, nicotine has proven to slow down apoptosis and thereby cause the prolongation of the life of neutrophils in tissues[19].

Proteases Derived from Neutrophils

Tobacco smoking causes a large rise in neutrophil elastase and Matrix Metalloproteinases (MMPs) in humans. It lowers levels of important endogenous MMP inhibitors, such as tissue inhibitors of MMP-1 while enhancing collagen-degrading enzyme activity[18].

Neutrophil Respiratory Burst

According to studies, cigarette smoke constituents hinder neutrophils' respiratory bursts, reducing their ability to kill plaque bacteria[18].

Neutrophil Migration and Chemotaxis

The kinetics of f-Actin may be affected by tobacco smoke, causing neutrophil motility and migration to be hampered. Migration of neutrophils decreases the expression of selectins while increasing the expression of adhesion integrins, resulting in chemotaxis and phagocytosis[18].

3.2 Effect on T Lymphocytes

In smokers, the total number of lymphocytes is elevated in bronchoalveolar lavage fluid whereas the cluster of differentiation4 (CD)4 cell subpopulation is decreased resulting in a lower CD4/CD8 ratio while in peripheral blood, it remains unchanged[20].

3.3 Effect on B lymphocytes and Immunoglobulins (Ig)

Tobacco smoke has been shown to have an impact on both cell-mediated and antibody-mediated immunity which is interconnected. Suppression of antibody-forming cell responses by nicotine in rats appears to be caused by a disruption in antigen-mediated T-cell signaling[20]. These results are backed up by studies that show smokers and periodontitis patients have lower serum IgG levels. IgE levels are significantly higher in smokers, although this is not related to increased skin reactivity. When smokers are compared to non-smokers, salivary immunoglobulin A levels are found to be substantially lower[21].

3.4 Effect on Natural Killer (NK) Cells

Smoking has a reversible effect on NK cells which function like cytotoxic T cells and cytolytic activity may improve even after a month of quitting[20].

3.5 Impact on Cytokines, Growth Factors and Other Enzymes

Gingival Crevicular Fluid (GCF) of smokers has increased expression of prostaglandin-E2, matrix

metalloproteinase-8 (MMP-8), neutrophil elastase, and tumour necrosis factor-α[21]. Furthermore, nicotine and bacterial lipopolysaccharide together exhibited a synergistic effect, increasing the development of inflammatory cytokines[22]. Byron *et al.*, found that mononuclear cells isolated from the peripheral blood of smokers produced considerably more interleukin-4 (IL-4) than non-smokers[23].

Tappia *et al.* found that when smokers are exposed to bacterial lipopolysaccharides, they produce considerably more TNF and interleukin-6, as well as the acute phase protein α2-macroglobulin. The chemical mediators involved in bone remodeling are also affected by cytokine variations[24].

The pro-inflammatory cytokines such as tumour necrosis factor, interleukin -1, and interleukin-6 stimulate the expression of inhibitor protein Osteoprotegerin (OPG) and Receptor Activator of Nuclear Factor-Ligand (RANKL) are required for bone remodeling and resorption. Smoking causes a decrease in OPG concentration as well as a change in the ratio of RANKL/OPG; smokers express a higher RANKL/OPG ratio[25].

3.6 Effect on Fibroblast Function

Gingival Fibroblasts

Smokers' gingival fibroblasts appear to be less vulnerable to the cytotoxic impact of an excessive amount of nicotine possibly due to tolerance building. Intermediate filaments, actin, and microtubules are disturbed resulting in a reduction in cell viability[20]. Chang *et al.* discovered that nicotine causes changes in the expression of Cox-2 mRNA of gingival fibroblasts[26].

PDL Fibroblasts

Strong smokers had slightly less cell attachment to the root surface in comparison to non-smokers[20].

4. The Effects of Tobacco Smoking on Oral Physiology

4.1 Tobacco and Gingival inflammation

The clinical indications of inflammation in smokers are less apparent compared to non-smokers. Though there are few observable variances in the vascularity of healthy gingiva among smokers and non-smokers, microcirculation of the former appears to be disturbed when compared to the latter[24]. Reduced number of crevicular Polymorphonuclear Neutrophils (PMNs) and crevicular phagocytosis may diminish lysosomal enzyme release resulting in less inflammation in superficial layers of periodontal tissue. Persistent hypoxia of periodontium induced by smoking exacerbates periodontal disease[26].

Cotinine is a by-product of nicotine metabolism, reported to have peripheral constrictive action on capillaries of gingiva causing variations in the diameter of blood vessels penetrating gingival tissue and reducing clinical signs like oedema, bleeding, and redness[27,28].

Trikilis *et al.,* reported that smokers may have a lower subgingival temperature because their periodontal cells are less active[29].

Greyish discoloration and gingival hyperkeratosis are seen in heavy smokers and epithelial alterations were identified as hyperplastic, keratotic, and hyperkeratotic[24].

Vukadin Bajagic *et al.,* published a study that found that the epithelial base and stratum corneum thickness is less *in* non-smokers compared to smokers. Inflammatory clinical symptoms in the gingival tissue can be reduced with increased epithelial thickness. Reduction in the number of crevicular Polymorphonuclear Neutrophils (PMNs) and crevicular phagocytosis may limit lysosomal enzyme release resulting in less inflammation in the surface layers of the periodontium[30].

Holde *et al.,* reported that tobacco smoking significantly reduces the site-specific association between plaque and bleeding on probing (BOP) in a dose-dependent manner[31].

Although smoking causes peripheral vasoconstriction, it is preceded by vasodilation in some individuals. Its use has also been linked to a reduction in peripheral blood vessel permeability[25]. Smoking for a prolonged period can cause a reduction in gingival bleeding masking the clinical sign of bleeding on probing[32].

Greater epithelial thickness, lesser vascularity, and decreased area of lumen were found in tobacco smokers than observed in non-smokers, according to histomorphometric research[33].

Bergstrom together with his co-workers conducted a study on twin pairs from the older cohort of the Swedish twin registry and discovered that twins with a high lifetime smoking exposure had more alveolar bone loss and missing teeth than their counterparts who smoked for a short time. Gingival bleeding was also found to be less common in the high-exposure population, suggesting

that its significance as a symptom and sign of periodontitis could be diminished as a result of smoking[34].

4.2 Tobacco and Plaque and Calculus Formation

In studies examining the association between smoking and oral hygiene, researchers found mixed results. Smokers were found to have worst oral hygiene and noticeably more plaque deposits than non-smokers. Plaque deposits tended to increase as cigarette intake increased[35]. However few studies revealed that there were no changes in mean PI index scores between smokers and nonsmokers[36,37].

The calcium content in fresh saliva is higher in smokers and serves as the primary source of calcium phosphates[38].

4.3 Tobacco and Gingival Crevicular Fluid (GCF) Secretion

In a study conducted by Luhtra *et al.,* the average GCF volume was reported to be lesser in smokers when related to gender- and age-matched non-smokers of equivalent health status. When compared to baseline levels, GCF volumes were shown to be lower soon after smoking and after 10 minutes increased transiently[39]. Morozumi *et al.,* also found similar findings indicating a lower overall GCF volume. A decrease in gingival blood flow is associated with lower GCF volumes in tobacco smokers[40].

4.4 Tobacco and Periodontal Health

Adler *et al.,* reported a significant correlation between the prevalence of palatal pockets ≥6 mm for subjects who smoked > 20 cigarettes per day in contrast to non-smokers[41].

In a cross-sectional study done by Velidandla *et al.,* reported that tobacco smokers have more number of sites with pocket depth ≥5 mm, with less number of sites with shallow probing depth and deep pockets between 4-7 mm particularly on the lingual aspect of these teeth, and was more prevalent in the anterior region[42].

5. Impact of Tobacco Smoking on outcomes of Periodontal Therapy

The changes in the immune and inflammatory response[43] or the pathogenic floral persistence in smokers after treatment[44] affect smokers' response to periodontal treatment.

5.1 Non-Surgical Therapy

Periodontitis can be treated effectively with non-surgical periodontal therapy which is a combination of professional mechanical plaque removal and oral hygiene instructions[44,45]. However, numerous studies revealed that smokers respond to nonsurgical therapy unfavorably[46–50].

Preber *et al.,* looked at improvements in smoker's pocket depth after non-surgical periodontal treatment and observed less drop in probing depth compared to non-smokers on entire surfaces of the dentition studied. The maxillary anterior region showed the greatest difference between classes[51].

In their studies, Rinvert *et al.,* and Jin *et al.,* discovered comparable results[49,50].

According to Heasman *et al.'s* analysis of clinical evidence, most of the studies revealed that in response to periodontal therapy, smokers achieved reduced clinical attachment gain[51].

In a cohort study, Dietrich *et al.,* assessed the connection between cigarette use, smoking cessation, and the incidence of tooth loss. The results revealed a significant relationship between smoking cessation and a reduction in the risk of tooth loss similar to that of never smokers after 10 to 20 years of quitting[52].

Data from the US National Health and Nutrition Examination Survey from 2009 to 2012 revealed that 13.1% of non-smokers, 19.3% of ex-smokers, and 34.5% of current smokers had periodontitis. Additionally, the likelihood of having periodontal disease decreases with time since the cessation of smoking[53].

According to Shim *et al.,* smokers have a less favourable response to periodontal treatment and healing mechanisms after scaling and root planning compared to non-smokers which may be attributed to the less clinical attachment level gain[54].

5.2 Surgical Treatment

Tobacco smokers had a poor response to surgical treatment than nonsmokers[55,56].

Scabbia *et al.,* found that, even though all of the periodontitis patients were given supportive periodontal therapy monthly for half-yearly, smokers displayed much fewer reduction of deep pockets and comparatively less

clinical attachment gain than non-smokers after open flap access surgery[55].

Kaldahl *et al.,* reported that smokers continued to show lower pocket reduction and clinical attachment benefit and heavy smokers reacted less favourably to periodontal therapy than light smokers in a 7-year longitudinal comparative analysis on the effects of different treatment modes such as supra gingival scaling, root planning, modified Widman flap, and respective osseous surgery. These variations were noticeable right after therapy was completed and remained for the next seven years of supportive periodontal therapy. Present smokers had more degradation at the furcation areas over the 7 years period than former smokers and non-smokers[56].

5.3 Periodontal Plastic Surgery

A systematic review by Chambrone *et al.,* showed that tobacco smoking negatively influences the reduction of gingival recession reduction and clinical attachment level gain following root coverage procedures. The meta-analysis reported a high statistically significant reduction in gingival recession ($P < .001$) and clinical attachment level gain ($P < .001$) for non-smokers in comparison to smokers who underwent treatment for gingival recession with subepithelial connective-tissue grafts. In addition, non-smokers showed a remarkably greater number of sites with complete root coverage in contrast to smokers ($P = .001$)[57].

Smoking was reported to have major impact on the self-curing capacity of periodontal tissues[58], presumably by interfering with the vascular[59–61], and immunological systems[62,63]. Additionally Nicotine was also shown to have impact on gingival fibroblast proliferation in vitro, boosts collagenase activity[64], and decreases the synthesis of fibronectin and type I collagen by fibroblasts[65]. Furthermore, hampered oxygen transport and metabolism due to carbon monoxide or enzyme poisoning by hydrogen cyanide, in turn, diminish the oxidative metabolism required for the cellular repair[66]. Further research is required to identify the mechanisms by which cigarette smoking adversely affects the long-term results following root coverage procedures even though these changes could contribute to the poorer healing reported for smokers.

5.4 Regenerative Therapy

Tobacco smoke deleteriously affects the regenerative treatment in furcation and interproximal defects, whether employing membranes or osseous graft alone, or osseous graft in combination with membranes. It also has a detrimental impact on the results of bone grafts and Guided Tissue Regeneration (GTR) used to treat infrabony defects[67]. When compared to that in non-smokers, less than half the attachment benefit was shown by smokers a year after GTR therapy for deep infrabony defects[68,69].

5.5 Implant Therapy

Moy and Bain initially compared the results of dental implants placed in tobacco smokers and non-smokers and discovered that smokers had a substantially higher number of failures than nonsmokers[70].

Several other studies have since confirmed smoking as a principal cause of dental implant failure[71,72].

After four years, Bain established a smoking cessation protocol and discovered in his research that individuals who continued to smoke had a statistically significant failure rate compared to those who accepted the protocol. As all of the failures happened before the prosthetic was installed, it was unlikely that they were induced by prosthetic overload or other external factors[73].

During smoking, nicotine gets absorbed into the vascular bed of oral mucosa, it produces notable local vasoconstrictive impact according to Shuler and Armitage, and Turner[74,75]. As a result, a dental implant can be potentially vulnerable.

Lindquist *et al.,* reported that heavy smokers had substantially more marginal bone loss around implants than those who smoked infrequently[76].

5.6 Effect of Smoking on Wound Healing

Nitrogen oxide (NO), hydrocyanic acid, carbon monoxide (CO), and nicotine in tobacco smoke have been identified to have an impact on wound healing[77].

Grossi *et al.,* examined how cigarette smoking affects the non-surgical treatment clinically and microbiologically and concluded that in relation to non-smokers and former smokers, a reduced drop in subgingival Porphyromonas *gingivalis* and Tannerella *forsythia was* observed in smokers, implying that smoking impairs periodontal healing[78].

Wound healing involves 3 three stages: inflammatory, proliferative, and tissue remodeling. Hypoxia has been shown to surge the chances of surgical site infection possibly due to decreased neutrophil bactericidal activity[79]. Smoking causes elevated plasma levels of adrenaline and noradrenaline which induces peripheral vasoconstriction and diminished polymorphonuclear neutrophil activity[80].

5.7 Influence of Quitting Smoking on the Outcome of Periodontal Treatment

Bergstrom and colleagues conducted prospective research with a schedule for reinvestigation in 1992 and 2002 as the primary study base. The increase in the frequency of diseased sites was noticed in continuous smokers in comparison to that in former and non-smokers over the last ten years. When compared with non-smokers whose periodontal health stayed unaffected over a 10-year period, the data suggest that persistent smoking affects periodontal health as indicated by the increase in periodontally compromised sites and a loss of alveolar bone height. The health of periodontium of former smokers remained unaffected identical to that observed in non-smokers, showing that quitting smoking is favourable to the health of the periodontium[81].

Nair *et al.* reported that in addition to progress in the oral hygiene of individuals and a rise in gingival blood flow after quitting smoking, a hike in the incidence of bleeding, from 16 percent to 32 percent sites were noticed, on probing with a steady force probe[60].

A literature review by Johnson *et al.,* reported that there was a change towards a less pathogenic microflora and elements of immune-inflammatory responses have improved. The degree of bone and attachment loss decreases to clinical values between that in smokers and nonsmokers[81]. With increasing years since discontinuing smoking, the chances for periodontitis and tooth loss decrease[83,84], and improvement in the healing phase is observed[85,86]. 'Past smokers' implant success rates are comparable to 'never smokers'[87] and the therapeutic effect of non-surgical mechanical therapy in relation to clinical and microbiological characteristics was equivalent to that of non-smokers[88,89], indicating that cessation had a major role in modifying the subgingival biofilm[90], and a positive effect was found after periodontal surgeries[91]. A greater response and chances of success after implant and regenerative treatments were also observed after the cessation of tobacco smoking.

C- Reactive Protein (CRP) and neutrophil count were raised following smoking cessation of ten and twenty years correspondingly whereas tissue plasminogen activator antigen (t-PA), a sign of damage of endothelium, remained elevated for 5 years until returning to normal after 20 years[92]. A previous systematic review by Fiorini T *et al* and Preshaw PM *et al*., proposed a possibility of reversal of periodontitis ten years from quitting smoking considering an improved response to periodontal therapy was noticed after a year[93,94].

According to Yarnell, the restoration of systemic and local acute effects of smoking has been linked to the initial rapid drop in the level of proinflammatory molecules following smoking cessation[95].

6. Conclusion

Tobacco prevention has long been a public health issue around the world. The contribution of toxic substances in tobacco smoke to the development of periodontal diseases was ascertained. Numerous studies report the adverse effects of tobacco smoking on wound healing after periodontal treatment. Also, quitting smoking has a favourable impact on wound healing along with the maintenance of periodontal health. Dentists can assist patients in quitting smoking as well as maintaining good periodontal health during the maintenance phase of periodontal therapy.

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