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Effects of Smoking Form of Tobacco on Periodontal Health: A Review

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ABSTRACT: Cigarette smoking is a risk factor for several diseases, and recent evidence strongly suggests an adverse effect on periodontal health. Nevertheless, the nature of the relationship between smoking and periodontal disease is not clear. Smoking causes defects in neutrophil function, impairs inflammatory and immune responses to periodontal pathogens, and exerts both systemic and local effects. Smoking is associated with an increased rate of periodontal disease in terms of alveolar bone loss and attachment loss, as well as pocket formation. Nicotine, the major component of cigarette smoke, may weaken host defenses to the bacterial invasion induced by plaque.

Keywords: periodontal disease; smoking; periodontitis; gingivitis; nicotine

INTRODUCTION

Cigarette smoking represents a major preventable cause of human disease.[1] Tobacco smoke contains over 3800 chemicals, including carbon monoxide, hydrogen cyanide, and reactive oxidizing radicals, and sixty of these chemicals are known or suspected to be carcinogens.[2] Smokers have significantly elevated risks of all-cause mortality and developing a variety of pathological conditions.[1] A direct causal relationship between smoking exposure and the prevalence and the severity of periodontal disease has been firmly established (American Academy of Periodontology 1996, Grossi et al. 1994).[3,4] According to the National Health and Nutrition Examination Survey III, smokers were four times as likely to have periodontitis as persons who had never smoked after adjusting for age, gender, race/ethnicity, education, and income/poverty ratio. The use of tobacco products, in general, and smoking products, in particular, is the major preventable risk factor for the initiation and progression of periodontal diseases. [5-7] A meta-analysis of data from six such studies involving 2361 individuals indicated that current smokers were nearly three times more likely to have severe periodontitis than nonsmokers. The detrimental impact of long-term smoking on the periodontal and dentate status of older adults has been clearly demonstrated.[8] The most marked difference between smokers and nonsmokers in probing depths or attachment loss occurs in the maxillary lingual area and mandibular anterior teeth, suggesting a local effect of smoking.[9] It has also been firmly established that smoking cessation is associated with decreased mortality, lower risk of developing a variety of diseases, and increased life expectancy.[1]

Clinical Parameters Of Periodontium Affected By Smoking Gingival Diseases

Gingivitis

Several cross-sectional investigations have indicated that smokers may present with lower levels of gingival inflammation to a specific level of plaque than nonsmokers. This was evidenced using both the gingival index and the dichotomous evaluation of bleeding on probing.[1]Nair et al. followed 27 individuals for 4–6 weeks during a verified successful period of quitting smoking and found bleeding doubled (from 16% to 32%) during this period.[10]

Acute Necrotizing Ulcerative Gingivitis:

Pindborg (1947) was one of the first investigators to study the relationship between smoking and periodontal disease. He determined that tar in the smoke exerted a direct irritating effect on the gingiva giving rise to gingivitis and that nicotine could cause contraction of the capillaries, thus interfering with the nutrition of the gingiva which consequently became less resistant to infection.[11]

Periodontitis:

Smokers have a higher proportion of sites with deeper probing depths and clinical attachment loss compared with nonsmokers.[4,12,13] The observed effects have been confirmed in different studies and in different populations after correcting for a variety of potential confounders.[14]

Cigarette Smoking as a Risk Factor for Periodontitis :

Although the direct cause for periodontitis is oral bacterial infection, its progression and severity depend on a number of genetic and environmental factors.[14] Several epidemiological studies in different population demonstrate a relationship between smoking and periodontal disease.[15,16] Cigarette smoking is arguably the strongest behavioral risk factor for the incidence and progression of periodontitis.[17] It is also important to note that although nonsmokers universally respond better to periodontal treatment than do smokers, there is nevertheless substantial evidence of clinical improvement in smokers after treatment, indicating that smoking as a risk factor will compromise rather than prevent tissue healing.[18] Some of the mechanisms by which smoking affects periodontitis are elucidated in Table 1.[19]

TABLE 1: HOW SMOKING ALTERS THE ETIOLOGY AND PATHOGENESIS OF PERIODONTAL DISEASE

PROPOSED MECHANISMS FOR THE NEGATIVE PERIODONTAL EFFECTS OF SMOKING[19]
Increased prevalence of periopathogens
Difficulty in eliminating pathogens by mechanical therapy
Vascular alterations
Altered fibroblast attachment and function
Negative local effects on cytokine and growth factor production
Altered neutrophil function
Decreased IgG production
Decreased lymphocyte proliferatio

Effects Of Nicotine on The Periodontal Tissues :

While nicotine is the primary psychoactive component, and addiction to it is the main reason for people subjecting themselves to frequent and high doses over many years, one must appreciate that tobacco smoke contains thousands of different compounds. Many of these are directly noxious/poisonous to living organisms and cells, and nicotine may be unfairly blamed for most of these properties. Moreover, it is also very important to appreciate that most of the harmful effects of tobacco products will result from systemic exposure through absorption in the lungs rather than topical absorption in the oral cavity[21]. A regular heavy smoker exposes himself/herself to these compounds many times per day for several minutes at a time. Although increasing evidence is being presented for the harmful effects of passive smoking, the periodontal literature is generally confined to active smoking. Many smokers develop the habit in their teenage years and continue it throughout their life. No other drug is administered so frequently or over such a time period as smoking. This is to emphasize the fact that the detrimental effects on the periodontium are derived from long term chronic exposure and bear little relationship with the effects that can be measured on a single exposure. Cotinine, a metabolite of nicotine, can be measured in the serum/plasma and saliva, and is a better measure of tobacco smoke exposure as it has a longer half-life than nicotine (18 h compared with 1 - 2 h). Smokers would be expected to have serum cotinine levels of over 14 ng/ml, and this could be as high as 1000 ng/ml. Resting plasma nicotine levels are much lower (5 - 50 ng/ml), and are maintained by the individual to satisfy their craving for nicotine. Because nicotine is so rapidly absorbed from the lung and transport to the brain is rapid, very high peak levels can be measured in the brain. It is important to understand these variations in relation to levels tested in in-vitro experiments . Some early studies suggested that smokers experienced less gingival bleeding than non-smokers .[22,23] This observation was confirmed in a comparative study of 10 heavy smokers (at least 20 cigarettes per day) and 10 non-smokers who had similar levels of periodontitis .[38] These authors cited the potential vasoconstrictive effect of nicotine previously reported by Clarke .[20] The reduced bleeding on probing was further demonstrated in a study by Bergstrom & Bostrom .[24] Gingival bleeding was lower in 130 smokers (median [interquartile range, IQR] bleeding score 19.0 [13.0]) than 113 non-smokers (median [IQR] bleeding score 32.0 [20.3]), with similar levels of periodontitis ($p < 0.001$). Tobacco smoke contains carbon monoxide, which is detectable in the breath of smokers and can be used to assess compliance in quit-smoking programmes .[10] Oxygen saturation of haemoglobin is affected and attempts have been made to measure this in the gingival tissue of smokers and non-smokers. Hanioka and coworkers [40] showed variable results. In healthy gingiva, smokers did appear to have lower oxygen saturation, determined using tissue reflectance spectrophotometry, whereas in the presence of inflammation, the converse was shown. The same group of workers [25] also examined the oxygen tension in the pockets of 34 non-smokers and 27 heavy smokers with mild to moderate periodontitis. They showed that the pocket oxygen tension was significantly lower in smokers (mean 21.9 mm Hg) compared with non-smokers (mean 33.4 mm Hg [$p < 0.0001$]). This could have an impact on the pocket microflora. The vasculature has also been examined in histological and immunocytochemical studies. In a very limited study of one histological section from three smokers and four non-smokers, Mirbod and coworkers [26] found that there were a high proportion of small vessels compared with large vessels in smokers compared with non-smokers, but no difference in the vascular density. The region chosen for study was the connective tissue beneath the external gingival epithelium, which was therefore remote from the pocket wall/sulcus and the inflammatory lesion. Sonmez and colleagues [27] did not show differences in the density or number of Factor VIII labelled vessels in gingival tissues obtained at the time of periodontal surgery from 38 smokers and 36 nonsmokers. The orientation and location of the specimens were not described. A more comprehensive

histological comparison of smokers and non-smokers was presented by Rezavandi and coworkers [28] who labelled the vessels by immunocytochemical staining to the von Willebrand factor, ICAM-1 and E-Selectin. They reported that a significantly larger number of vessels were observed in inflamed tissues of nonsmokers than smokers ($p < 0.05$). Baab & Öberg [29] were the first researchers to question the vasoconstrictive action of nicotine (from cigarette smoking) on gingival tissues. In a Laser Doppler Flow (LDF) study of 12 young regular smokers, they showed that gingival blood flow rose by about 25% during smoking, was maintained for 5 min. and then gradually declined to baseline values. This was associated with an increase in heart rate and systolic and diastolic blood pressure. They confirmed that the blood flow to the skin of the forearm did decrease slightly, demonstrating the differences in response between peripheral skin responses and those in the head and neck. It was interesting to note that 3 of their subjects felt light headed after smoking, suggesting that the inhalation dose was greater than they normally experienced. Animal studies have shown that local nicotine delivery negatively impacts bone healing [30], which may be related to inhibited expression of various growth factors [31] and delayed revascularization [32]. These findings might help explain the diminished treatment response to surgical periodontal procedures, especially that involving tissue regeneration. This means that tobacco smoking may exert a masking effect on gingival symptoms of inflammation, which might give smoking patients a false sense of assurance of gingival health [33]. Smoking upregulates the expression of pro-inflammatory cytokines, such as interleukin-1, this contributes to increased tissue damage and alveolar bone resorption [34]. Interleukin-1 genotypepositive smokers are more susceptible to severe adult periodontitis [34].

Effect of Smoking on the Microbiology of Periodontitis

Studies have failed to demonstrate a difference in the rate of plaque accumulation of smokers compared with nonsmokers, suggesting that if an alteration in the microbial challenge in smokers exists, it is due to a qualitative rather than quantitative alteration in the plaque. Several studies report a similar microbial profile of dental plaque in smokers compared with nonsmokers with regard to the ability to detect suspected periodontal pathogens in the subgingival plaque biofilm.[35-37] However, in smokers, such suspected periodontal pathogens are recovered in shallower areas without clinical periodontal breakdown.[38] More recent studies that utilize molecular techniques capable of characterizing previously unknown bacteria or those that are difficult to culture have provided evidence of distinct microbial profiles and patterns of biofilm colonization in smokers and nonsmokers.[39,40] Winkelhoff and Tijhof [41] compared the subgingival microflora of treated and untreated smokers and nonsmokers. They found the most pronounced microbiological characteristics of smokers appeared to be the presence of Bacteroidesforsythus, Peptostreptococcus micros, Fusobacterium nucleatum, and Campylobacter rectus in the absence of Actinobacillus actinomycetemcomitans and Porphyromonas gingivalis. In addition, these pathogenic bacteria were more prevalent in the maxilla than the mandible.[42]

Impact of Smoking on the Physiology:

The clinical signs of inflammation are less pronounced in smokers when compared with nonsmokers. Although no significant differences in the vascular density of healthy gingiva have been observed between smokers and nonsmokers, the response of the microcirculation to plaque accumulation appears to be altered in smokers when compared with nonsmokers.[43] Fewer crevicular polymorphonuclear neutrophils (PMNs) and less crevicular phagocytosis could conceivably decrease the release of lysosomal enzymes and thus decrease the level of inflammation in the superficial layers of the periodontal tissues. Smoking-induced chronic hypoxia of periodontal tissues causes greater severity of periodontal disease seen in smokers.[44] Trikilis et al. found that subgingival temperatures are lower in smokers than nonsmokers. The decreased subgingival temperature in smokers might reflect the reduced activity of periodontal cell.[45] Tobacco and some of its components such as nicotine have been found to have adverse effects on cells of the periodontium, including gingival fibroblasts and cells of the immune system. An in vitro study done by Tanur et al. showed that the nature of cell attachment to root surfaces is altered by nicotine.[46] Cigarette smoke condensate may interfere in myofibroblastic differentiation. Results of the study by Silva et al. showed that cigarette smoke, but not nicotine, may significantly alter cell viability, cell migration, and myofibroblastic differentiation in gingival mesenchymal cells.[47] Nicotine also caused a dose-dependent inhibition of fibronectin and Type I collagen production. The inhibition of collagen production by nicotine was accompanied by ~700 and 400% increase in collagenase activity at nicotine concentrations of 0.075% and 0.05%, respectively. Nicotine may stimulate transcription of the collagenase gene, either directly or through inducing the production of cytokines by the fibroblasts themselves.

Impact of Smoking on Immunology:

Periodontitis is associated with an alteration in the host-bacterial balance that may be initiated by changes in the bacterial composition of subgingival plaque, changes in the immune response, or a combination of both elements.[48] A number of studies have shown that cigarette smoking may affect the host response by altering the immune response in local tissue. Smoke exposure impairs f-actin kinetics, resulting in the damage of the neutrophil cytoskeleton (Ryder et al. 1998).[48]

Effect on Oral Polymorphonuclear Neutrophils:

Neutrophils, obtained from the peripheral blood or saliva of smokers, have been shown to demonstrate functional alterations in chemotaxis, phagocytosis, and oxidative burst.[49,50] One possible mechanism for this elevated neutrophil-mediated destruction may simply be the elevation of neutrophils in smokers seen in the peripheral blood which may lead to increased secretion of potentially tissue-destructive products. In addition, nicotine may prolong the lifespan of neutrophils in tissue by delaying the process of programmed cell death (apoptosis).[51]

Effect on Monocytes :

The effects of nicotine on monocytes were not restricted to inhibition of the production of oxygen radicals. It also interfered with secretion of the pro-inflammatory cytokine, interleukin 1β (IL-1β). In periodontitis, IL-1β activates fibroblasts and osteoclasts to destroy the periodontal ligament and the alveolar bone. Eventually, the immune response to prolonged infection by periodontal pathogens would overwhelm any short-term anti-inflammatory effect of nicotine.[52]

Effect on Circulating Polymorphonuclear Neutrophils :

Circulating PMNs from smokers have been shown to have normal phagocytosis but depressed chemotaxis when testing is performed rapidly after cigarette smoking. This effect is lost after overnight abstinence from smoking, suggesting the presence of a labile substance.[53]

Effect on Antibody and Lymphocyte Response:

Nicotine and the water-soluble fraction from whole cigarette smoke can suppress the in vitro secondary antibody response.[54] Salivary immunoglobulin A has been found to be significantly decreased in smokers when compared with nonsmokers.[55] Production of antibody essential for phagocytosis and killing of bacteria, specifically IgG2 levels to periodontal pathogens, has been reported to be reduced in smokers versus nonsmokers with periodontitis.[56]

Effect on Cytokines, Growth Factors, and Other Enzymes :

Elevated levels of tumor necrosis factor-α, prostaglandin-E2 , neutrophil elastase, and matrix metalloproteinase-8 have been demonstrated in the gingival crevicular fluid(GCF) of smokers.[57] Wendell et al. demonstrated that nicotine can directly stimulate human gingival fibroblast IL-6 and IL-8 production in vitro. In addition, combination of nicotine and lipopolysaccharide had a synergistic response, upregulating inflammatory cytokine production.[58] IL-4 production by peripheral blood mononuclear cells of smokers was significantly higher than that of nonsmokers (Byron et al. 1994).[59] Bergstrom et al. (2001) observed that for patients with periodontitis, the concentration as well as the total amount of GCF, α-2-macroglobulin and α-1-antitrypsin, was lower in smokers as compared to nonsmokers, which led to increased tissue damage due to increased activity of elastase and collagenase.[59]

How Smoking Effects the Response to Periodontal Therapy

Nonsurgical Therapy:

The majority of clinical research supports the observation that pocket depth reduction is more effective in nonsmokers than in smokers using nonsurgical periodontal therapy, including oral hygiene instruction, scaling, and root planing. In addition, gains in clinical attachment as a result of scaling and root planing are less pronounced in smokers than in nonsmokers.[60-66] Wan et al. found that at 12 months after nonsurgical therapy, smokers presented with a significantly higher percentage of residual pockets. In addition, smokers showed less probing pocket depth (PPD) reduction in sites with initial PPD ≥5 mm.[67] The inhibitory effect of smoking on treatment response is more pronounced at initially deeper sites.[68] Darby et al. found that nonsmokers with aggressive periodontitis had significantly greater probing depth reduction (2.4 mm) compared with patients with aggressive periodontitis who smoke (1.3 mm).[69] It can be concluded that smokers respond less well to nonsurgical therapy than nonsmokers. However, in the presence of excellent plaque control, these differences may be minimized.

Antimicrobial Therapy:

In a 9-month, placebo-controlled, randomized trial in which smokers and nonsmokers were treated by scaling and root planing with and without sub-antimicrobial doxycycline, Preshaw et al. concluded that adjunctive sub-antimicrobial dose doxycycline enhanced therapeutic outcomes in all groups with smokers taking doxycycline, showing approximately the same magnitude of clinical improvement as nonsmokers on placebo.[70] On the other hand, in studies where adjunctive systemic amoxicillin and metronidazole[71] or locally delivered minocycline microspheres[72] enhanced the results of mechanical therapy, there was a greater difference between the control and experimental treatments within smokers as compared to within nonsmokers. These and, in the case of tetracycline derivatives, anticollagenase activity. Unique regimens that sequence systemic antimicrobial therapy or combine local antimicrobial delivery with host modulatory therapy might offer clinicians and patients options that address microbial and host response alterations in smokers.[73]

Surgical Therapy :

The clinical benefit seen in nonsmokers following nonsurgical therapy has also been observed following surgical treatment (Ah et al. 1994).[74] The most impressive report of clinical attachment gain in nonsmokers (5.2 mm) compared with smokers (2.1 mm) was observed by Tonetti et al., who carried out guided tissue regeneration (GTR) of infrabony defects using Gore-Tex membranes and with a follow-up period of 1 year. They also concluded that higher plaque levels that are seen consistently in smokers compared with nonsmokers will also have influenced the clinical outcomes.[75] When expanded polytetrafluoroethylene

membranes were utilized in GTR procedures at recession sites, smokers had significantly less root coverage (57%) as compared to nonsmokers (78%).[76] The superior blood supply afforded by the subepithelial connective tissue graft might be more resistant to the effects of smoking as compared to the nonresorbable barrier membrane. However, root coverage following thick free gingival graft procedures is reportedly diminished by heavy cigarette smoking and there are conflicting reports on smoking's effect on the success of subepithelial connective tissue grafts.[76]

Implant Therapy:

The largest data set on the influence of smoking on implant success comes from the Dental Implant Clinical Research Group (DICRG) of the Department of Veterans Affairs, which is an 8-year, randomized, prospective clinical study that includes >2900 implants.[77] The 3-year data demonstrated that 8.9% of implants placed in smokers failed as compared to 6% in individuals who had never smoked or had quit smoking. The majority of implant failures in smokers occurred before prosthesis delivery; thereafter, the differences between smokers and nonsmokers tended to disappear.[78] A meta-analysis done by Bain reported that light smoking (average of 12 cigarettes/day) did not affect the success rate of either machined or dual acid-etched surface implants.[79]

CONCLUSION:

In view of the fact that smokers are two- to eight-fold more likely to have periodontitis than nonsmokers, smoking cessation should be an important treatment consideration for periodontal patients. This fact can be useful in patient education and may provide encouragement to patients contemplating cessation. Dental professionals are well positioned to provide smoking cessation advice to their patients because patients are likely to visit their periodontologists/dentists more often than their physician. Therefore, close collaboration of dentists/periodontologists and physicians is recommended in the treatment of smoking patients

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