

Smoking and Periodontal Diseases

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Context: The aim of this review was to examine evidences for the association between smoking and periodontal disease, to discuss possible biological mechanisms whereby smoking may adversely affect the periodontium, and to consider the effect of smoking on periodontal treatment.

Evidence Acquisition: A web-based search in PubMed and Google Scholar was performed to identify publications regarding the effects of smoking on various aspects of the periodontal disease process and to find an explanation for the possible association between smoking and the progression of periodontitis. We evaluated the articles published in English language between 1990 and 2013 with the search terms "periodontal health and smoking", "periodontal treatment and smoking", and "tobacco smokers and oral hygiene".

Results: Of the total yield of 145 identified publications, 72 were selected for this literature review. The results of the selected papers reflect the effect of smoking on oral hygiene, gingival inflammation and vasculature, gingival crevicular fluid, subgingival microflora in periodontitis, fibroblast function, genetic polymorphism, initiation and progression of periodontal disease and its effect on passive smokers, and host response to periodontal treatment.

Conclusions: Smoking is a significant risk factor for impaired periodontal health and treatment.

Keywords: Periodontitis; Tobacco; Smoking; Gingival

1. Context

Tobacco smoking is a risk factor of several serious diseases such as lung cancers, myocardial infarctions, cardiovascular disease, chronic ischaemic heart diseases, and strokes. Smoking affects the prevalence, extent, and severity of periodontal diseases. Many studies have shown that the possibility of detecting periodontitis is higher in smokers than in nonsmokers. With a high prevalence of smokers in many countries, the association between cigarette smoking and periodontal diseases is a significant public health problem. The aim of this review was to examine evidence for the association between smoking and periodontal disease, to discuss possible biological mechanisms whereby smoking may adversely affect the periodontium, and to consider the effect of smoking on periodontal treatment.

2. Evidence Acquisition

2.1. Search Strategy

The search of the articles in electronic databases was conducted using the following search term combinations: "periodontal health and smoking", "periodontal treatment and smoking", and "tobacco smokers and oral hygiene". A total of 72 publications were obtained through focusing on articles related to the effect of smoking on periodontal health and treatment outcomes.

2.2. Inclusion Criteria

Publications were included for evaluation if they were published in English language between 1990 and 2013 and were listed in electronic databases Medline/PubMed. Publications were included for the review if the widespread effects of smoking on periodontal health or responds to periodontal treatment (surgical, nonsurgical, or regenerative) were reported.

2.3. Selection of Studies and Data Extraction

Using the abovementioned search terms, titles and abstracts of the publications identified by electronic databases were initially screened by two independent reviewers. Publications were included for full text evaluation if the study design and content of the abstracts met the inclusion criteria and matched the focused question. Full text assessment and data extraction were performed by the reviewers without any disagreements.

2.4. Excluded Studies

Publications were excluded if they did not meet the inclusion criteria (i.e. if they were considered case reports, animal or in vitro experiments, educational statements, or expert opinions). In addition, some publications with similar titles about the effects of another narcotic material such as alcohol, opium, heroin, or marijuana on periodontal tissue were excluded.

3. Results

Of the total yield of 145 publications identified with electronic search, 72 were selected for this literature review. The results of the selected papers reflected the effect of smoking on oral hygiene, gingival inflammation and vasculature, gingival crevicular fluid (GCF), subgingival microflora in periodontitis, fibroblast function, genetic polymorphism, initiation and progression of periodontal disease and its effect on passive smokers, and host response to periodontal treatment.

3.1. Cigarette Smoking and Oral Hygiene (Dental Plaque)

There are higher levels of oral debris in smokers than in nonsmokers and this may be due to personality traits leading to decreased oral hygiene habits, increased rates of plaque formation, or a combination of the above (1). Wilson explained that dental deposits of smoking make dental surface uneven; hence, dental plaque annexes easier (2). Increase in anaerobic plaque bacteria is due to the reduction of oxidation-reduction potential (Eh) by cigarette smoking (1). In three-day-old plaque, the proportion of gram-positive bacteria was statistically higher in smokers in comparison with nonsmokers (2). There are some controversial findings. Bergstrom et al. found no difference in mean plaque index scores amongst 285 musicians (31% smokers and 69% nonsmokers). In addition, they found no quantitative difference in the growth rates of plaque between smokers and nonsmokers (3).

3.2. Calculus Formation

Many authors suggested that tobacco smoking was associated with increased accumulation of supragingival and subgingival dental calculi. Although smokers had more calculi than nonsmokers, the effect of smoking was independent of the number of present calculi. There have been consistent reports of more calculi in smokers than in nonsmokers (4). The pH of pipe smoke is higher than cigarette smoke and the pipe smokers tend to circulate the smoke around the mouth while cigarette smokers inhale it; therefore, some authors claimed that supragingival calculi were significantly more in pipe smokers than in cigarette smokers (5). Moreover, the smoking cycle is much longer in pipe smokers than in cigarette smokers, causing pipe smokers to salivate more. There is a strong and independent effect of tobacco smoking on subgingival calculus deposition. The subgingival calculus load increase with increasing smoking exposure, suggesting a dose dependent association (6). There is a strong association between tobacco smoking and supragingival calculus. The occurrence and severity of supragingival calculi were similar between those who had stopped smoking in the distant past and those who had never smoked; it shows that the effect of smoking is reversible (7).

3.3. Smoking and Gingival Inflammation

Preber et al. noticed that gingival bleeding, average number of bleeding sites after periodontal probing, which are the first signs of gingival inflammation, and periodontal disease were less frequently expressed in smokers with longer history of smoking. Although, it was noticed that passionate smokers had significantly greater plaque index, was reduced in smokers (27%), than in non-smokers (40%) (8). Anil explained that nicotine causes vasoconstriction in peripheral blood vessels and reduces the objective clinical signs of gingival inflammation and therefore, masks the clinical marker of bleeding on probing often used by dentists to monitor periodontal health (9). Induced vasoconstriction impairs gingival blood vessels and reduces the amount of oxygen and blood elements that supply gingival with nutritive elements (8-10). The effect of smoking on experimental gingivitis was evaluated in a group of dental students. This study revealed that the number of gingival bleeding sites, the amount of gingival exudates, and the number of gingival sites with distinct redness were significantly lower in smokers than in nonsmokers with comparable levels of plaque indexes (3). Bergstrom et al. found that the intensity of vascular reaction after 28 days of plaque-induced gingivitis in smokers was only 50% of that observed in nonsmokers (11). Clinical signs of gingivitis in smokers are less frequent than nonsmokers, and this is independent of plaque (10). According to Palmer et al. measurement, smoking does not compromise blood flow in the periodontal tissues (12). Moreover, tobacco smoking can reduce permeability of peripheral blood vessels (10). Bergstrom et al. compared smokers and nonsmokers in an oral hygiene intervention program. In their study, the plaque index decreased in both groups, but gingival bleeding was significantly lower in smokers than in nonsmokers. They concluded that the clinical expression of gingivitis, i.e. chronic inflammation, in response to plaque is suppressed in smokers (3).

3.4. Effect on the Gingival Vasculature

Smokers have less vascular density, reduced lumen area, and increased epithelial thickness in comparison with nonsmokers; however, these changes are not statistically significant (10). In one study researchers found a high proportion of small to large vessels in smokers than in nonsmokers; however, there was no difference between them regarding the vasculature density (13).

3.5. Effect of Smoking on Gingival Crevicular Fluid

In a study by Holmes, compared crevicular fluid flow in smokers (in the areas physically exposed to smoke, and in areas not physically exposed to smoke), and non-smokers with clinically healthy gingiva. Smokers had significantly less GCF flow than nonsmokers (14). Kinane and Radvar investigated the responses of smokers and nonsmokers to instrumentation with and without subgingival anti-

microbials. After therapy, GCF volume decreased less in smokers than in nonsmokers, regardless of treatment modality; however, the actual mean GCF volumes still remained lower in smokers than in nonsmokers (15). Moreover, smoking tends to reduce the flow of the gingival fluid exudates. In a study by Bergstrom et al., the degree of gingival redness, bleeding from gingival margin, and the gingival fluid exudate increased in smokers and nonsmokers during four weeks of experiment (3). There are an higher levels of TNF- α and decreased levels of IL-1 α , IL-1 β , enzyme elastase, cytokines, and possibly polymorphonuclear leukocytes (PMNs) in GCF of smokers in comparison with nonsmokers, which justifies the lower levels of gingival inflammation observed clinically and histologically in smokers (16). The reasons for the reduction of elastase concentration in GCF are not clear. Elastase is not detected in normal serum and is produced locally by the PMNs cells; therefore, vasoconstriction is not the reason for the reduction of elastase concentration in smokers (17). It may be due to less functional or reduced PMNs in the gingival crevices of smokers as a result of reduced vascularity of the region (17, 18). In addition, all smokers had detectable salivary and GCF cotinine. Mean GCF cotinine was as four times high as mean salivary cotinine levels. Individuals who smoked ≥ 20 pack-years of cigarette had significantly higher saliva and GCF cotinine levels in comparison to those smoked < 20 pack-years ($P \leq 0.05$) (18).

3.6. Smoking and Subgingival Microflora in Periodontitis

Many authors investigated the association between cigarette smoking and the prevalence of periodontal pathogens using PCR techniques (19). Microbiological studies showed that in comparison with nonsmokers, smokers had a higher prevalence of bacterial species related to periodontal disease including *Porphyromonas gingivalis*, *Bacteroides forsythus*, *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia*, and *Fusobacterium nucleatum* (20). In another study using molecular analyses techniques for six putative periodontal pathogens, current smokers displayed an increased risk for harboring *Treponema denticola* (OR = 4.61) (21). On the other hand, some authors reported no differences between smokers and nonsmokers with respect to the detection of periodontal pathogens (19). In a study that included equal numbers of smokers and nonsmokers with generalized aggressive periodontitis, no significant differences in the incidence of any of the pathogenic species was reported (22). Gomes et al. evaluated 25 smokers and 25 never-smokers aged 33 to 59 years old. Real-time PCR quantified *P. gingivalis*, *Micromonas micros*, *Dialister pneumosintes*, *A. actinomycetemcomitans*, and total bacteria in subgingival samples. Similar amounts of total bacteria and *P. gingivalis* were observed in both groups. Significantly higher numbers of *D. pneumosintes* and *M. micros* were present in smokers and associated with moderate and deep pockets. When heavy

smokers were considered, higher counts of total bacteria, *M. micros*, and *D. pneumosintes* were observed (19). Haffajee et al. stated that after scaling and root planning (SRP), significant clinical improvements were seen in subjects who had never smoked or who were past-smokers, but not in current smokers. The rate of *P. gingivalis*, *B. forsythus*, and *T. denticola* among current, past, and never smokers were similar before therapy while these rates decreased after SRP in all subjects except in current smokers (23).

3.7. Smoking and Fibroblast Function

As an attempt to determine the mechanisms involved in modulation of the periodontal tissues by smoking, the effect of cigarette compounds including nicotine and cotinine on the periodontal tissues were investigated through in vitro and in vivo studies (24). Cotinine at its highest concentration (10 $\mu\text{g/mL}$) inhibited attachment and growth of fibroblasts, but this was not statistically significant (25). In general, nicotine has been reported to adversely affect proliferation, attachment, and chemotaxis of periodontal ligament (PDL) cells and fibroblasts growth. Moreover, attachment to tissue culture plates was inhibited by its high concentrations (over 1 mg/mL); however, no effect was seen at concentrations comparable with plasma levels in smokers (26). Giannopoulou et al. showed that nicotine at high concentrations (100 to 25 $\mu\text{g/mL}$) was cytotoxic by inhibiting the vacuolation and proliferation of fibroblasts. They also confirmed that PDL cell proliferation and protein synthesis were inhibited in a dose-dependent manner. Cell attachment was significantly less on root surfaces obtained from heavy smokers in comparison with nonsmokers and healthy controls (27). In addition, regardless of its association with lipopolysaccharide (LPS) from periodontopathogenic bacteria, nicotine increases IL-6 and IL-8 production by human gingival fibroblasts (25). In another study, PDL cells were plated for one day and then were treated with various concentrations of cigarette smoke extract (CSE). It was concluded that CSE induces cell death at concentrations of $\geq 5\%$. PDL cells-induced collagen gel contraction was reduced at CSE concentrations of 1.5%. CSE selectively increased the expression of collagen V α 3, decreased collagen XI α 1, and increased the expression of matrix metalloproteinase 1 (MMP1), MMP3, and to a lesser extent MMP2 and MMP8. CSE also increased the expression of integrins α 1, α 2, and α 10 (collagen receptors) as well as integrin α 9 (a tenascin receptor) (28).

3.8. Genetic Polymorphism and Smoking

Exposing peripheral blood mononuclear cells to tobacco smoke for five minutes increased expression of 20 genes associated with periodontal pathogenesis (29). The levels of TNF- α and IL-8 in the GCF of smokers were higher (30). On the other hand, proinflammatory and anti-inflammatory cytokines were lower in association with smoking and its compounds. It showed that ciga-

rette smoke has potent inhibitors of both gene expression and protein production of IL-1 β , IL-8, IL-2, and TNF- α (31). Moreover, there was a significant genetic component in association with aggressive periodontitis (32); the disease status in young adults might contribute to it by interaction of cigarette smoking and various genetic polymorphisms (33).

3.9. Passive Smoking and Periodontal Status

Recent studies have suggested that passive smoking may be associated with periodontal diseases (34, 35). Many authors showed higher cotinine levels and greater attachment loss in passive smokers in comparison with unexposed group (36). Nishida et al. conducted a two-year longitudinal study and observed increased salivary levels of albumin, aspartate aminotransferase, and lactoferrin in passive smokers. The authors suggested that passive smoking might affect inflammatory response and may be associated with a greater risk for periodontitis progression (37). In addition, some authors showed statistically significant gingival pigmentation in passive smokers (38). In a cross-sectional study in the United States, the association between environmental tobacco smoke (ETS), and periodontal disease was investigated; it showed that among participants who had never used tobacco, those who were exposed to ETS were more likely to have periodontal disease in comparison to those who were not exposed to it (39). In another study, a dose-dependent association was seen between exposure to secondhand smoke and severe periodontitis (40). Although additional studies are necessary, it seems that passive smoking affects periodontal health negatively (37, 40).

3.10. Smoking and Host Response

Smokers have been shown to have reduced titers of salivary IgA and serum IgG, specifically IgG2 levels, against *A. actinomycetemcomitans*, *P. intermedia*, and *F. nucleatum* in patients with generalized early-onset periodontitis (34, 35, 41). The ability of tobacco products to decrease the proliferating capacity of T and B lymphocytes might contribute to this diminished production of protective antibodies (42). Few investigators have demonstrated suppressed phagocytosis by salivary PMNs, and have reported higher blood counts and reduced chemotaxis of PMNs in smokers in comparison with nonsmokers (43). In contrast, a few studies have found no significant difference in the chemotaxis ability of PMNs between smokers and nonsmokers (44). Nicotine increases intercellular adhesion molecule-1 (ICAM-1) and endothelial leukocyte adhesion molecule-1 (ELAM-1) in human umbilical vein cells (endothelial cells); moreover, it seems that nicotine increases soluble ICAM-1 in the serum of smokers. These changes in adhesion molecule may affect leukocytes binding to endothelial cells lining the capillaries and postcapillary venules and thus, may impede the recruitment of important host defense cells to the inflammation and micro-

bial challenge site (34). It has been shown that alveolar macrophages from smokers exhibit reduced expression of class II MHC. This may eventually lead to a reduction in the humoral immune response to invading organisms (35). Interestingly, seroconversion following hepatitis B vaccine occurs much more slowly in smokers than in nonsmokers; moreover, the frequency of subjects showing an immune response is lower in smokers (45). Shivanai et al. quantified neutrophils in the gingival connective tissue of smokers and nonsmokers with chronic periodontitis, and concluded that neutrophil apoptosis was significantly more in nonsmokers. Except clinical attachment loss, which was more in smokers, plaque and bleeding index were equal in both groups (46).

3.11. Smoking and Periodontal Disease

Bergstrom et al. declared that probing depth (PD), alveolar bone loss, and tooth mobility were significantly increased in smokers (3). Many authors stated that cigarette smokers had significantly fewer teeth than nonsmokers (47). The effect of smoking in tooth loss is due to periodontal disease not to caries (47). Gomes et al. showed that visible plaque index, gingival bleeding index, and bleeding on probing were similar in smokers and nonsmokers; however, regardless of tooth surface, periodontal PD in buccal/lingual sites and clinical attachment loss were more in smokers than in nonsmokers (19). Severe periodontal disease with increased bone loss, greater periodontal attachment loss, gingival recession, and periodontal pocket formation are more frequent in smokers (47). Many authors declared that effect of cigarette consumption and periodontal attachment loss were dose dependent (48). Destructive effects of smoking on periodontal tissues may be mainly from systemic side effects and almost independent of the site within the mouth although some additional local effects may be present in areas such as anterior palatal sites (49). Comparing clinical parameters of periodontal disease between smokers and nonsmokers showed that clinical symptoms were more severe and manifested by higher number of deep pockets and gingival recessions, more excessive loss of epithelial insertion, and accelerated alveolar bone loss; however, gingival bleeding was reduced in these patients (47, 50). An additional analysis of gingival tissue adjacent to periodontitis sites showed that MMP-2 levels were higher in the exposed than in unexposed animals. This finding suggests that MMP-2 might be one of the molecules responsible for the increased tissue degradation in the periodontal tissues of smokers (51).

3.12. Periodontal Treatment in Smokers

It has been demonstrated that smoking has an adverse effect on all forms of periodontal therapy and that up to 90% of the refractory periodontitis patients are smokers (52). Numerous studies have shown that smoking compromises PD and/or attachment gain out-

comes following nonsurgical or surgical therapies (53, 54). Following nonsurgical therapy, including SRP and professional tooth cleaning, healing in terms of gingival bleeding reduction and pocket depth reduction was less favorable in smokers than in nonsmokers (55). A study by Grossi et al. showed that current smokers had less healing and reduction in subgingival *Tannerella forsythensis* and *P. gingivalis* after treatment in comparison to former smokers and nonsmokers, which suggests impaired periodontal healing in smokers (53). Machtei et al. considered the changes in attachment level and alveolar bone levels approximately one year after the hygiene phase of therapy. Nonsmokers had relatively stable bone height whereas smokers exhibited an annualized bone loss rate of 1.17 mm (56). These findings are in agreement with recent long-term results suggesting that tobacco smoking interferes with the healing process following nonsurgical periodontal therapy (57). Moreover, there are similar findings in response to surgical therapy. Ah et al. reported less PD reduction and attachment gain in smokers who were treated by periodontal surgery, which corroborated that smokers were poor candidates for successful periodontal care (58). A statistically significant difference was observed in the reduction of PD between smokers and nonsmokers at 12-month postsurgical follow-up after Widman flap surgery on 4 to 6 mm pockets (59). Preber and Bergstrom found that despite differences in levels of plaque accumulation, smokers had a statistically significantly PD reduction 12 months following surgery (59). Tonetti et al. performed a retrospective study that examined the effect of cigarette smoking on the healing response following guided tissue regeneration (GTR) in deep infrabony defects. This study indicated that smoking was a significant factor in determining the clinical outcome (60). A risk-assessment analysis indicated that smokers had a significantly greater likelihood of having a reduced probing attachment level gain following GTR than nonsmokers. Other investigators have found smoking to be detrimental to healing when using regenerative procedures with allografts (61). Studies in which recession sites were treated using connective tissue with a partial thickness pedicle graft, a coronally positioned flap alone or with a bioabsorbable membrane, found no difference in root coverage between smokers and nonsmokers (62). On the other hand, when guided tissue regeneration procedures were used, smokers had significantly less root coverage (57%) in comparison to nonsmokers (78%) (63). Long-term studies have indicated the association of smoking with recurrence of periodontitis during periodontal maintenance; the effect appeared to be dose dependent, with heavy smokers (> 10 cigarettes/day) presenting with higher levels of disease progression (1). Haas et al. studied the association between smoking and peri-implantitis. They stated that bleeding indices, mean peri-implant pocket depths, and mesial and distal peri-implant mucosal inflamma-

tion were higher in smokers, particularly in the maxilla. They concluded that risk of developing peri-implantitis particularly in the maxilla is higher in smokers (64). Recent studies have suggested that the adjunct use of local and systemic antimicrobial therapy may improve the clinical outcome of SRP and guided tissue regeneration in smokers (65). On the other hand, subgingival pathogens are more difficult to eliminate in smokers following SRP; microbiologic examination of these patients revealed that the adjunct use of locally delivered 10% doxycycline after SRP in smokers with chronic periodontitis may favor the elimination of *T. forsythensis* and *P. gingivalis* in a greater proportion of sites and may lead to better clinical outcomes than conventional mechanical therapy (66). Scabbia et al. concluded that there was little adjunctive effect of systemic metronidazole on nonsurgical therapy in smokers (54). On the other hand, a few studies have reported that adjunctive systemic amoxicillin and metronidazole or locally delivered minocycline microspheres could enhance the results of mechanical therapy (57).

4. Conclusions

Tobacco smoking has widespread systemic effects, many of which may provide mechanisms for the increased susceptibility to periodontitis and the poor response to treatment. Its effects are related to smoking duration as well as the number of consumed cigarettes. The smoking status of the family members may also be relevant to both behavioral influences and the potential consequence of passive smoking. It changes the human microflora and human immune response that leads to destruction of the supporting tissues of the tooth. As an environmental factor, smoking interfere with the host and the bacterial challenge associated with periodontal disease. The mechanisms by which tobacco use favors periodontal destruction still need complementary investigation. It seems that a downregulation of anti-inflammatory factors associated with an upregulation of proinflammatory cytokines is involved. While this review has primarily examined the effects attributed to nicotine and its metabolites, it should be stated that other byproducts of cigarette smoke might also have an effect on the progression of periodontitis. Moreover, treatments in patients with periodontal disease must be focused on understanding the association between genetic and environmental factors. We can identify our patients' risks and achieve better results only through individual approach. To pursue strategies of prevention, early detection of disease, and prompt intervention, the dental profession should continue to target and educate patients regarding the effects of smoking on periodontal health. In this way, dentistry will also make a significant contribution to the general health and well-being of our youth and future generation. It is hoped that the presented evidence of the harmful effects of smoking in this review might inspire dentists to encourage their patients to cease smoking.

Authors' Contributions

Study concept and design: Parviz Torkzaban; acquisition of data, analysis and interpretation of data, and drafting of the manuscript: Zahra Khalili; critical revision of the manuscript for important intellectual content: Zahra Khalili and Narges Ziaei.

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