



EFFECT OF TOBACCO ON ORAL MUCOSA – A REVIEW

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ABSTRACT

Tobacco use in any form has the potential to profoundly alter the systemic and oral health of the individual. So it has been recognized to be a significant risk factor for periodontitis affecting the prevalence, extent and severity of disease. It has usually been necessary to rely on the vast body of medical literature that describes the noxious effects of smoking, and to apply this knowledge to the pathogenesis of periodontitis. Therefore, many of these mechanisms may be implied or speculative. The purpose of this review will attempt to build on previous studies in the periodontal literature and make attempts to primarily consider evidence that directly pertains to the periodontal tissues.

KEYWORDS: *Nicotine, cigarette smoking, smokeless.*

INTRODUCTION

Periodontal disease is considered as an opportunistic infection and the host responses to the oral micro flora challenges become an important factor in the progression of the disease. The wide ranging impact on the host, cigarette smoking, smokeless tobacco & its interrelationship has been topic of interest for the last 10-15 yrs.^[1-8]

Tobacco is a plant grown for its leaves, which can be prepared in varied manners with the objective of altering their flavor, smell and pharmacological properties. It is considered an addictive substance because it contains the chemical nicotine.^[9] Nicotine is an alkaloid found in the nightshade family of plants (solanaceae) at constitutes approximately 0.6–3.0% of dry weight of tobacco with biosynthesis taking place in the roots and accumulation occurring in the leaves.^[10-13] Unlike cigarettes, chewing tobacco contains 28 carcinogens, including tobacco-specific nitrosamines, other cancer-causing substances include formaldehyde, acetaldehyde, crotonaldehyde, hydrazine, arsenic, nickel, cadmium, benzopyrene and polonium.^[13]

Classification

Smokeless tobacco exists in two major forms: Snuff & Chewing tobacco.

Snuff can be moist or dry. Moist snuff is usually taken orally. This product is sold in small round cans, in which the snuff is loosely packed, or in small, tea-bag-like sachets. Dry snuff, which is less commonly used, is usually inhaled through the nose.

Chewing tobacco is coarser than snuff and exists in three forms: Loose leaf (sold in a soft package or pouch), Plug (sold in small block) and twist (dried tobacco leaves that are twisted into strands).^[14]

The products of smokeless tobacco available in India are:^[15]

Pan: This is home made from a variety of ingredients including betel leaf, tobacco (optional), chopped betel (areca) nut, a variety of perfumes and other additives assembled into a quid, which is then sealed with lime paste and placed in the back of the jaw or inner gum. The tobacco content varies depending on the maker and the user's preferences. Paan seems to be less popular than the readymade packets of paan masala/gutkha.

Pan Masala/Gutkha: Commercially manufactured, chewable product containing tobacco, betel nut, catechu, lime, colouring and flavoring agents. Also known as Guthka, it is usually placed in the buccal vestibule and referred to as a "chaw" or "quid" of chewing tobacco.

The quid may be retained in the mouth for hours, and the user expectorates the saliva that mixes with the tobacco extract. Gutkha is often sold in brightly coloured packages (resembling sweets); some are chocolate flavoured and others sold as mouth fresheners.

Zarda (Khaini): Chewing tobacco mixed with a variety of coloring's, spice essences and perfumes. The tobacco is usually shredded or boiled and may contain betel nuts. Often chemical sweeteners are added.

Supari: Ayurvedic term for betel (areca) nut. Its use is culturally bound; used in religious and cultural festivals. Thin slices of the nut may be eaten on their own or mixed with a variety of substances including slaked lime and spices. Most significantly they may be mixed with tobacco products or wrapped in a betel leaf.

Cigarette smokers: Cigarette is defined as a cylindrical roll of shredded or ground tobacco that is wrapped in paper and a cigarette filter has the purpose of reducing the amount of smoke, tar and fine particles inhaled during the combustion of a cigarette. Filters also reduce the harshness of the smoke and keep tobacco flakes out of the smoker's mouth.^[16]

Smokers are subjects who have been smoking at least 15 cigarettes/per day for one year. They can be classified as Heavy smokers who smoke 31 cigarettes/per day. Light smokers are who smoke 9 or less cigarettes/per day.^[6] Previous smokers are one who has quit smoking a year or more before diagnosis.

Bidis: A thin, often flavored indian cigarette made of tobacco wrapped in a tendu leaf or temburni leaf they are common throughout India and south-east Asia and are especially appealing to young smokers.

Other Non-cigarette forms of tobacco are Cigar which is defined as any roll of tobacco wrapped in leaf tobacco, or in any substance containing tobacco and which is typically smoked without a filter.^[17]

The prevalence of cigar consumption has been progressively decreasing worldwide; of 30% of the English population who were regular smokers in 2002, only 5% were cigar smokers. It should be borne in mind that cigar smoke is more alkaline than that of cigarettes, thereby facilitating its dissolution and absorption by the oral mucosa. This makes it possible to achieve the desired dose of nicotine without the need to inhale the smoke into the lungs. Despite the fact that cigar smokers do not inhale, cigars can cause nicotine dependence, because they make high levels of nicotine available so rapidly. The smoke contains a class of highly carcinogenic compounds (nitrosamines, hydrocarbons and aromatic amines) at levels significantly higher than those found in cigarette smoke. Since cigar smoke contains higher concentrations of toxins and cancerous

substances than does cigarette smoke, it also contributes to increasing the risk of lung cancer.^[18]

Pipe: The prevalence of regular pipe use among American men dropped from 14% in the 1960s to 2% in the 1990s, remaining rare among women (< 0.1%).

Nevertheless, most pipe or cigar smokers are former-cigarette smokers, who might retain some of the techniques of smoke inhalation, despite the irritation the smoke provokes in the airways. In addition, there is a causal relationship between pipe smoking and mortality due to lung, laryngeal, esophageal and oropharyngeal cancer.^[18]

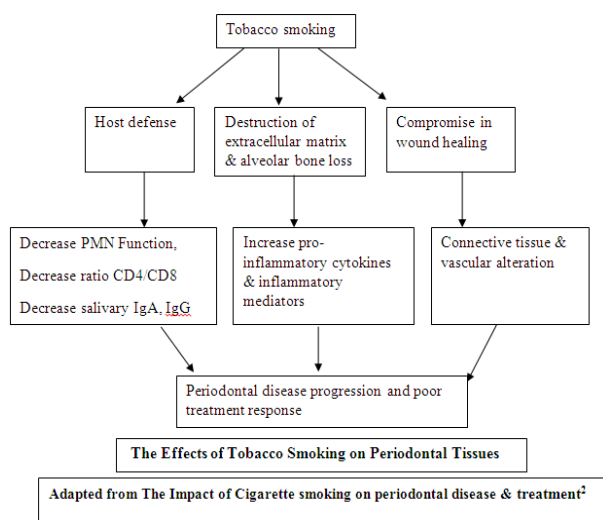
Narghiles are also known as water pipes, gozas, hookahs, shishas. It has been suggested that the narghile originated in India and has been widely used for over 400 years. However, in recent years, a true rebirth of its use has been observed, principally among young people, including those in western countries. Its nicotine content is estimated at 2-4%, compared with 1-3% for the tobacco used in cigarettes. Similarly, the proportion of carbon monoxide in narghile smoke is greater than that reported for cigarette smoke, and it is increased by the burning of the coal used in that modality. However, since the quantity of nicotine inhaled is an important regulator of the quantity of tobacco smoked, narghile smokers have to inhale larger quantities of smoke and is therefore exposed to larger quantities of cancerous substances and noxious gases. This fact puts narghile smokers and passive smokers of narghile smoke at risk for the same diseases caused by cigarette smoking, such as cancer, heart disease, respiratory disease.^[18]

The use of smokeless tobacco is probably less lethal than is the use of cigarettes. However, there is no doubt that all forms of tobacco use significantly increase the risk of developing diseases and of premature death among their users.

Pathophysiology

Smoking has major effects on the host response, but there are also a number of studies that show some microbiological differences between smokers and non-smokers. Smoking has a long-term chronic effect on many important aspects of the inflammatory and immune responses. Histological studies have shown alterations in the vasculature of the periodontal tissues in smokers. Smoking induces a significant systemic neutrophilia, but neutrophil transmigration across the periodontal microvasculature is impeded. Neutrophils have shown decreased chemotaxis, phagocytosis, and adherence in smokers. Integrin expression and protease inhibitor production is also affected. Protease release from neutrophils may be an important mechanism in tissue destruction. Tobacco smoke has been found to affect both cell-mediated immunity and humoral immunity. Antibody production is another protective host mechanism that is altered by smoking. Smoking

generally decreases serum IgG concentrations and decreases IgG₂ antibody production in patients with periodontitis.^[13] It has widespread systemic effects, many of which may provide mechanisms for the increased susceptibility to periodontitis and the poorer response to treatment.^[13] In vitro studies have shown detrimental effects of nicotine and some other tobacco compounds on fibroblast function, including fibroblast proliferation, adhesion to root surfaces and cytotoxicity.^[13]



Factors Contributing To Negative Impact of Smoking on the Periodontium

Age, Sex and Smoking

Women between the ages of 20-39 yrs and men between 30-59 yrs who smoke cigarettes have about twice the chances of having periodontal disease as compared non-smokers.^[19] Thomson, Garito, Brown^[20] found the effects of smoking on periodontal status to be more pronounced in younger women. This was in spite of the fact females and younger subjects were generally periodontally healthier than their male and older counterparts. On contrary Calsina, Ramon, Echeverria found that the effect of smoking on periodontal tissues are more in men than in women.^[21]

Smoking and Anug

Pindborg (1947) was one of the first investigators to study the relationship between smoking and periodontal disease. He discovered a higher prevalence of acute necrotizing ulcerative gingivitis in smokers. Preexisting gingivitis, emotional/psychic stress and smoking forms a triad of interrelated predisposing factors in the etiology of the disease. Karadachi, Clarke^[10] noted smoking activates the release of epinephrine and promotes contraction of peripheral vessels reducing blood flow to the gingiva. Severe reduction of blood flow induced by sepsis, stress and smoking may cause loss of vitality to the most vulnerable regions of the gingival epithelium, leading to the onset of ANUG.

Interaction between Smoking and Systemic Health Status

The combination of smoking with other systemic factors further enhances the risk of periodontal destruction. In an Erie County Pennsylvania study the combination of diabetes and heavy smoking in an individual over the age of 45 years who harbored *Porphyromonas gingivalis* or *Tannerella forsythesis* resulted in an odds ratio of attachment loss 30 times that of a person lacking this risk factors.^[22]

Smoking also increases the risk of attachment or bone loss in AIDS and HIV serotype patients.^[23]

Maternal cigarette smoking could affect intrauterine growth (and possibly gestational duration) through several mechanisms.^[24] The most likely mediators are carbon monoxide and nicotine. Carbon monoxide can interfere with oxygen delivery to the fetus in two ways: by displacing oxygen from haemoglobin, and by shifting the oxyhaemoglobin dissociation equilibrium to the left, so that less oxygen is released to the fetal tissues for a given partial pressure of oxygen.^[25]

Nicotine is an appetite suppressant and is believed to result in rapid increase in maternal catecholamines and consequent uterine vasoconstriction.^[26] Tobacco smoke also contains cyanide compounds, and a third possible mechanism for a smoking effect involves cyanide-mediated interference with fetal oxidative metabolism.^[27]

The effect of smoking on birth weight appears to depend on the period in pregnancy when the mother smoked, and in particular, is more marked for smoking during the last trimester.^[28] Butler, Goldstein, Ross found that smoking after the fourth month of pregnancy was critical in reducing birth weight.^[29]

Smoking and oral flora

Powerful reducing agents such as the carbon monoxide contained in tobacco smoke produce a substantial immediate reduction in redox potential at mucosal surfaces. The powerful physico-chemical reducing activity of carbon monoxide is probably a direct mechanism for promoting the growth of anaerobes at superficial sites rather than simple anaerobiosis.^[30] Smoking could cause a lowering of the oxidation-reduction potential, and this could cause an increase in anaerobic plaque bacteria. Data from the Erie County Study demonstrated that current smokers were 3.1 times more likely to exhibit *Actinobacillus actinomycetemcomitans* infection and 2.3 times more likely to be infected with *Bacteroides forsythus* than former or never smoker.^[8] In another study, smokers were eleven times more likely to have a positive BANA reaction than nonsmokers. A positive BANA reaction indicates the presence of *Porphyromonas gingivalis*, *Treponema denticola*, or *Bacteroides forsythus* which hydrolyze the trypsin substrate.^[31] One explanation for these findings is that these pathogens may be more

difficult to eliminate in smokers. After scaling and root planing, fewer current smokers were negative for and *Porphyromonas gingivalis*, *Bacteroides forsythus* ($p < 0.008$), compared to never smokers and former smokers. Renvert, Dahlen, Wikstrom reported *Actinobacillus actinomycetemcomitans* was more difficult to eliminate in smokers.^[32] Another possible explanation is that smoking may alter the quality of the flora. A lower oxygen tension in the periodontal pocket of smokers may be favorable for the growth of anaerobic bacteria.^[33] On the other hand several studies have indicated that the types of bacteria in smokers and nonsmokers did not vary significantly.^[34-35]

Smoking and Gingival Bleeding

Bleeding from the gum margin is an important early symptom of gingivitis, and gingival bleeding on probing is now widely used in clinical examination as a means of identifying active lesions in periodontal disease. Some early studies suggested smokers expressed less gingival bleeding than nonsmokers.^[36,37] They were also able to show a dose-response effect, which was confirmed in a much larger study of 12,385 general population subjects from the National Health and Nutrition Examination Survey: Part III. This reduced response in smokers has also been elegantly shown in studies using the experimental gingivitis model.^[36]

Effect on gingival blood flow and gingival vasculature

The data on possible changes of gingival blood flow from the results of human and animal experiments are contradictory.^[38] In smokers, gingival blood flow was significantly increased by cigarette smoking.^[39] However, intravenous administration of nicotine reduces the marginal temperature of gingival sites suggesting a decrease in gingival blood flow which leads to the hypothesis this phenomenon is caused by vasoconstriction induced by nicotine and stress.^[13] Later studies^[40] using laser Doppler flow compared the response to smoking a single cigarette in a group of light/occasional smokers and heavier habitual smokers. The changes in gingival blood were not statistically significant, but they did show quite dramatic differences in the response in the skin of the forehead. The light smokers responded with a significant increase in blood flow, but heavy smokers showed no response, indicating a high level of tolerance.^[40]

Mirbod, Ahing, Pruthi^[41] shows a higher percentage of smaller blood vessels and a lower percentage of larger vessels, but similar vascular density in smokers than non-smokers. However, the result of this study was only based on histological sections obtained from three smokers and four nonsmokers. Rezavandi, Palmer, Odell, Scott, Wilson^[42] relied on immunocytochemical staining showed significantly large numbers of vessels in inflamed tissues of non-smokers than smokers and proportion of the total numbers of vessels expressing ICAM-1 in non-inflamed tissues was greater in non-smoker. The results suggested that the inflammatory

response with periodontitis may not be accompanied by equivalent increase in vascularity. Data available to date seem to suggest that smoking exerts a chronic effect by impairing the vasculature of the periodontal tissues rather than a simple vasoconstrictive effect. The suppressed vasculature has contributed to less gingival redness, less bleeding on probing and may also lead to an impaired healing response by affecting the revascularization.^[13]

Alveolar Bone Loss

A dose-response effect on alveolar bone has been seen, accelerating the bone loss with higher amount and longer duration of tobacco consumption.^[43] The bone mineral content among smokers was found to be 10–30 % lower compared to non-smokers in a longitudinal cohort study, and it was speculated that constituents of tobacco smoke may alter the metabolism of vitamin D or influence hormonal states.^[44] In a group of 235 patients of whom 72 were smokers, radiographic analysis of bone height expressed as percentage of root length, revealed lower bone level for smokers, suggesting that smoking as risk factor for periodontal health.^[45] Smokers with generalized early onset periodontitis had more affected teeth and attachment loss than generalized early onset periodontitis patients who did not smoke.^[46] Haffajee, Socransky studied 289 patients with periodontitis and concluded that smokers had more attachment loss, deeper periodontal pockets, more missing teeth, fewer sites with gingival bleeding on probing and similar dental plaque level and gingival inflammation than those who never smoked.^[47] The observed pattern of attachment loss indicated more maxillary lingual loss suggesting possibility of local effect.

Smoking also has negative effects on bone metabolism. By the time women reach menopause, those who smoke one pack of cigarettes a day throughout their adult lives will have an average deficit in bone density of 5-8 %.^[11] Recent reports suggest that the combination of smoking and low systemic bone density negatively affects alveolar bone height^[48] and density in postmenopausal females.^[49] Estrogen metabolism is altered in female smokers and the estrogen deficiency is associated with elevations of IL-1, IL-6 and Tumor Necrosis Factor alpha, which affect both alveolar and systemic bone status.^[11]

Oxygen tension in the gingival tissues

Oxygen saturation of hemoglobin is affected by cigarette smoking, and attempts have been made to measure this in the gingival tissues. In healthy gingiva, smokers appear to have lower oxygen saturation determined by using tissue reflectance spectrophotometry, but in the presence of inflammation converse was shown.^[13] The same group of investigators also examined oxygen tension in periodontal pockets and demonstrated oxygen tension was significantly lower in smokers.

Smoking and Fibroblast Gingival fibroblast

Peacock, Sutherland, Schuster, Brennan (1993) were the only researchers to show a positive effect of nicotine on the proliferation and attachment of gingival fibroblast.^[50]

Significant inhibition of proliferation of gingival fibroblasts at very high concentrations of nicotine was demonstrated by Tipton, Dabbous (1995) who also showed reduction in the production of type 1 collagen and fibronectin and an increase in the collagenase activity in culture media.^[51]

Periodontal ligament fibroblasts

PDL fibroblast growth and attachment to tissue culture plates was inhibited by nicotine at high concentrations and no effects were seen at concentrations comparable with plasma levels in smokers.^[52] Nicotine at high concentrations was also shown to be cytotoxic by Giannopoulou, Geinoz, Cimasoni who confirmed the cell attachment was significantly less on root surfaces obtained from heavy smokers compared with non-smokers and healthy controls.^[53]

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 periodontologist s/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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