Tobacco Use and Oral Disease

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Abstract: Tobacco use is a risk factor for oral cancer, oral mucosal lesions, periodontal disease and impaired healing after periodontal treatment, gingival recession, and coronal and root caries. Available evidence suggests that the risks of oral diseases increase with greater use of tobacco and that quitting smoking can result in decreased risk. The magnitude of the effect of tobacco on the occurrence of oral diseases is high, with users having many times the risk of non-users. There is a clear benefit to quitting tobacco use. The risks of oral cancer and periodontal disease decline as time from cessation increases, and some oral mucosal lesions may resolve with cessation of smokeless tobacco use. Smoking accounts for half of periodontal disease and three-fourths of oral cancers in the United States. Because tobacco accounts for such a high proportion of these diseases, comprehensive tobacco control policies are required to make progress in reducing the burden of tobacco-related oral diseases. Effective treatments to prevent tobacco use and increase cessation are available and need greater implementation. Dental practices may provide a uniquely effective setting for tobacco prevention and cessation.

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Key words: mouth neoplasms, periodontitis, gingival recession, mucosal lesions, coronal caries, root caries, cigarette smoking, cigars, pipes, snuff, chewing tobacco

Tobacco use is one of the most important risk factors for oral diseases including oral cancer, oral mucosal lesions, periodontal disease, and cleft lip and palate. In addition, chewing tobacco users appear to have more dental caries than non-users. All of the major forms of tobacco used in the United States—cigarettes, cigars, pipe tobacco, and smokeless tobaccos (chewing tobacco and snuff)—have oral health consequences. This review discusses the evidence for the effect of tobacco on each of the most prevalent oral diseases (except cleft lip and palate, which is discussed in the following article).

Consequences of Tobacco Use

Oral Cancer

Cigarettes, cigars, pipes, and smokeless tobaccos (chewing tobacco and snuff) cause oral cancer.[1,2] The evidence is based on the magnitude of the risks observed, the higher risks associated with greater amounts of tobacco used or longer duration of use, the reduction in risk with tobacco cessation, the consistency of the findings for oral cancer across numerous cultures and countries (see also the article by Dr. Newell Johnson in this issue), and strong biological plausibility.

Based on population-based case-control studies, cigarette smokers have risks of oral cancer two to five times that of nonsmokers.[3,4] The risks increase with the numbers of cigarettes smoked and years smoked (see Table 1).[3-8] Although epidemiologic studies consistently report that oral cancer risks decline with the number of years of abstinence from cigarettes, it can take many years for risks to reach those of nonsmokers (Table 1).[3,5,7,8] Cigarette smokers with oral cancers face additional health consequences, as cigarette smoking is a risk factor for further primary cancers.[9] The strong association of cigarette smoking with oral cancer in many cultures is confirmed in studies published in the past fifteen years in countries as diverse as Brazil, France, China, and India.[10-13] Alcohol use is also a major risk factor for oral cancer. Heavy smokers who drink alcohol heavily have many times the risk of oral cancer as that expected from the independent effects of smoking and alcohol intake.[3]

With cigar smoking increasingly popular, cigar sales have increased 50 percent since 1993.[14] Cigar smokers are seven to ten times more likely to develop oral cancer than nonsmokers.[14] Risks increase with both the depth of inhalation and the number of cigars smoked per day.[14] Former cigar smokers have a lower risk of oral cancer than current smokers,[15] but even after ten years of abstinence, ci-

Table 1. Recent U.S. case-control studies of tobacco and oral cancer

Author, (# cases, controls)	# cigarettes per day	Odds ratios by gender		Duration	Odds ratios by gender		Years since quitting cigarettes	Odds ratios by gender	
Blot, 1988[1] (1114, 1268)		*M*	*F*	*Years smoked cigarettes*	*M*	*F*		*M*	*F*
	Nonsmokers	1.0	1.0	Nonsmokers	1.0	1.0	Nonsmokers	1.0	1.0
	1-19	1.2	1.8	1-19	0.8	1.0	Never quit	3.4	4.7
	20-39	2.1	3.6	20-39	1.9	2.9	1-9	1.1	1.8
	40+	2.8	6.2	40+	3.6	5.0	10-19	1.1	0.8
							20+	0.7	0.4
Spitz, 1988[2] (185, 185)				*Packyears (# cigarettes per day X years smoked)*					
				Nonsmokers	1.0	1.0	Nonsmokers	1.0	1.0
				1-24	1.8	1.5	< 5	6.1	9.8
				25-49	4.0	9.0	5-14	2.2	4.5
				50+	7.5	12.0	15+	1.0	.5
Marshall, 1992[2] (290, 290)				*Packyears (# cigarettes per day X years smoked)*	*Both genders*				
				0	1.0				
				1-20	1.3				
				21-30	2.7				
				31-40	2.9				
				41-50	7.0				
				51-70	7.7				
				71+	5.7				
Mashberg, 1993[3] (359, 2280)		*Both sexes*		*Years smoked cigarettes*	*Both genders*			*Both genders*	
	Minimal smoking	1.0		Nonsmokers and 1-15	1.0		Minimal smoking	1.0	
	6-15	4.0	16-30	0.7	3-10	1.3			
	16-25	4.4	31-45	1.5	11+	0.5			
	26-35	5.6	46+	1.9					
	36+	4.0							
Schwartz, 1998[5] (284, 477)								*Both genders*	
							Never quit	1.0	
							Current: > 20	5.5	
							Current: 1-19	2.2	
							Past: > 20	2.5	
							Past: 1-19	0.9	
Hayes, 1999[4] (342, 521)		*M*	*F*					*M*	*F*
	Non-smoker	1.0	1.0				Never quit	1.0	1.0
	1-9	0.9	2.2				Recent use	7.5	14.1
	10-19	2.8	4.3				2-9	4.1	8.7
	20-39	6.0	6.4				10-19	2.0	2.1
	40+	4.9	28.2[6]				20+	1.2	0.8

1 Adjusted for age, alcohol consumption, age, race, study location, and respondent status
2 No adjustments made
3 Adjusted for age, race, and alcohol drinking
4 Adjusted for age and alcohol use
5 Adjusted for age, sex, and average number of alcoholic beverages per week
6 Based on 6 cases and 2 controls

gar smokers still have three times the risk for oral cancer of non-users.[16]

In contrast to the rising prevalence of cigar smoking, the prevalence of pipe smoking has been declining.[17] In large cohort studies, pipe smokers had a 2.0 to 3.5-fold increased risk of developing oral cancer compared to persons who did not smoke.[18] In one case-control study of oral cancer in Brazil, the odds ratios associated with pipe smoking were as high as eleven to twenty-eight, depending on the anatomic site involved.[12] As has been observed for cigarettes and for cigars, quitting pipe smoking leads to a reduction in risk compared to continuing, but pipe smokers who have quit for ten or more years still have a risk three times greater than that of nonsmokers.[16]

Smokeless tobacco, in the forms of chewing tobacco and snuff, is also linked to oral cancer. Currently, the primary users of these products are white adolescent and young adult males, Native Americans, and Alaskan Natives.[17] Based on analyses that excluded smokers, smokeless tobacco users experienced risks of oral and pharyngeal cancer that were about four to six times higher than non-users.[3,19] In the one study that examined dose-response relationships, it was found that risks of oral cancer increased with years of use to about fifty-fold for snuff users after fifty or more years of use.[19] Another study compared the proportion of smokeless tobacco users from a sample survey of Americans with the proportion of users from a nationally representative case-control study of persons who died of oral cancer. Although this study did not find a link between smokeless tobacco and oral cancer,[20] the study design had significant limitations. Studies have not been conducted to examine the effect of quitting smokeless tobacco use on the risk of oral cancer.

Many carcinogens are found in mainstream tobacco smoke,[21,22] the smoke drawn into a smoker's mouth from the butt or mouthpiece of a cigar, cigarette, or pipe.[23] Tobacco-specific N-nitrosamines, aromatic amines, and polycyclic aromatic hydrocarbons present in mainstream tobacco smoke are considered major carcinogens contributing to the oral cancer risk from smoked tobacco products.[24] For smokeless tobacco, the nitrosamines formed during fermenting and curing occur at relatively high levels and are thought to be most important.[25] It is also becoming increasingly evident that certain inherited genotypes may predispose to tobacco-related oral disease. These represent genes involved in tobacco metabolism such as those coding for N-acetyl transferases, glutathione transferases, and P450 pathway enzymes.[26]

Other Oral Mucosal Lesions

Oral mucosal lesions are common in smokeless tobacco users and may develop even with relatively limited use. A survey of 17,027 U.S. adolescents conducted in 1986-87 determined that mucosal lesions were found in 27 percent of snuff and chewing tobacco users, in contrast to 0.4 percent among those who had never used smokeless tobacco.[27] These lesions were described as ranging from slight superficial wrinkling of the mucosa to thickened, furrowed white or gray mucosa. The prevalence of lesions increases with increasing duration of use; among snuff users, for example, the prevalence increased from 1.9 percent for users of less than one month to 38 percent among those who were users for more than two years. The corresponding percentages for chewing tobacco were 3.1 percent and 21 percent, respectively.

Major and minor league baseball players (N=1109) were the focus of a study of the oral effects of smokeless tobacco.[28] The authors defined leukoplakia as any white, opaque, or leathery appearing plaque not clinically characteristic of another type of white lesion. In this study the prevalence of leukoplakia was 1.4 percent among non-users of snuff versus 84 percent among those who used four or more cans of snuff per week.[28] There is some suggestion that these lesions can resolve with cessation. One study reported finding that 97.5 percent of the smokeless tobacco-related lesions in young male U.S. Air Force trainees resolved in six weeks after forced smokeless tobacco cessation.[29] However, the persistence of lesions in older males who have used smokeless tobacco for many years is unknown. Leukoplakia is considered a premalignant condition, with transformation rates varying from 3.6 percent to 17.5 percent in studies of Europeans and Americans.[30]

Cigarette smoking is also associated with oral leukoplakia (discussed in the article by Drs. Bánóczy, Gintner, and Dombi in this issue) and with oral mucosal conditions such as nicotinic stomatitis and hairy black tongue.[31]

Periodontal Disease

Cigarette smoking is a significant risk factor for periodontal disease and impaired healing after periodontal surgery (see also the article by Dr. Georgia Johnson). In studies with a cross-sectional design, an association between cigarette smoking and periodontal disease, measured by attachment loss, is consistently found. Population-based studies, which sample populations with a known probability, tend to have a higher level of generalizability than other studies. Two population-based epidemiologic studies have found that periodontitis is more common in smokers than nonsmokers.[32,33] The number of cigarettes smoked per day is an important determinant of risk, doubling the risk for those in the lowest use category and increasing it sixfold in the subgroup smoking more than thirty cigarettes per day.[33] Former smokers have lower rates of periodontitis than continuing smokers.[33]

Longitudinal studies suggest that periodontal disease may progress faster in smokers than in nonsmokers. North Carolina adults aged sixty-five or older were the subjects of a population-based cohort study of periodontitis in which, over the five-year follow-up, smokers experienced significantly greater attachment than nonsmokers.[34] Measuring the incidence of periodontal attachment loss, as was done in this study, has advantages over cross-sectional studies of periodontal disease etiology because the temporal relationships among the study variables are known.

Response to periodontal therapy is poorer in smokers than in nonsmokers. In one study, seventy-four patients were followed for up to seven years. The smokers had less periodontal depth reduction and less clinical attachment level gain after treatment than either prior smokers or nonsmokers.[35] Findings from other studies are also consistent with an adverse effect of smoking on healing after various forms of periodontal therapy.[36-40] One of these studies found that former smokers were similar to nonsmokers in their response to therapy,[37] suggesting that quitting smoking may promote healing.

Cigar and pipe smoking also are associated with periodontal disease, based on the Veterans Affairs Longitudinal Study.[41] Periodontal disease was measured by alveolar bone loss on radiographs of mesial and distal sites. Some individuals were followed for as many as twenty-three years. The percentage of persons with moderate to severe progression of periodontal disease was 8 percent in nonsmokers, compared to 13 percent in pipe smokers and 16 percent in both cigar smokers and cigarette smokers.

Smokeless tobacco users appear to have more gingival recession at facial sites than non-users, according to data from the baseball players study,[8,42] This finding corresponds to the location in the mouth where the smokeless tobacco lesions occurred and to where the tobacco was placed. Recession increased within a one-year period in smokeless tobacco users by 0.36 mm, while no change was observed for non-users.[42]

Periodontal disease results from a complex interplay of environmental (e.g., tobacco, bacteria) and host-related factors (e.g., genetic factors, immunological status, age, diabetes).[43] The ways in which smoking may contribute to periodontal disease risk and impaired healing are reviewed in the article by Dr. Georgia Johnson.

Caries

The high proportion of sugar in chewing tobacco[44, 45] has been a cause for concern. Data from the multipurpose health survey, the Third National Health and Nutrition Examination Survey, conducted from 1988 to 1994 was used to examine the relationship between chewing tobacco and other forms of tobacco use and decayed or filled coronal or root surface caries. Chewing tobacco users had slightly higher mean numbers of decayed and filled coronal surfaces than persons using other forms of tobacco. In addition, the mean number of decayed and filled root surfaces for those who used chewing tobacco was four times higher than for those who did not use tobacco.[46] Mean numbers of decayed and filled root surfaces rose with increasing numbers of chewing tobacco packages used per week and duration of use in years. The mechanism suggested was that high levels of fermentable sugars in chewing tobacco stimulate the growth of cariogenic bacteria.

Aphthous Ulcers

Aphthous ulcers appear to occur less frequently in smokers than in nonsmokers.[47,48] Smoking cessation results in worsening of aphthous ulcers, and resumption of smoking improves the condition.[49] One explanation is that smokers develop mucosal hyperkeratinization, which better protects the mucosal surface from ulceration.[49]

Discussion

Tobacco in its many forms is a risk factor for oral cancer, oral mucosal lesions, periodontal disease, gingival recession, and coronal and root caries. Available evidence suggests that the risks of oral diseases increase with greater use of tobacco and that ceasing to use tobacco can result in decreased risks. The magnitude of the effect of tobacco on the occurrence of oral diseases is generally very high, with users having many times the risks of non-users. Tobacco use leads to additional consequences for persons with periodontal disease and oral cancer. Tobacco adversely affects healing after periodontal treatment, while among persons with oral cancer, continued use of tobacco increases the risk of a second primary cancers. There is a clear benefit to quitting tobacco use because the risks of oral cancer and periodontal disease decline with increasing time after smoking cessation and some oral mucosal lesions may resolve with cessation of smokeless tobacco use. The risk of oral cancer appears to decline to the level of nonsmokers in most studies, but it may take two decades or more for this to occur.

Several biological mechanisms appear to be responsible for the increased risks of oral and dental diseases among tobacco users (see the article by Dr. Georgia Johnson for further discussion). Although tobacco contributes to the pathogenesis of oral diseases through many pathways, some may have a greater impact on the disease burden than others. Among the many carcinogens in tobacco smoke, the polycyclic aromatic hydrocarbons, aromatic amines, and nitrosamines are very significant. As smokeless tobacco products are not burned, the tobacco-specific nitrosamines may be the main etiologic factor in smokeless tobacco-related oral cancers. The effect of tobacco on the immune system plays a major role in the development of periodontal disease and in impaired healing after treatment for the disease. The risk for caries may be elevated in users as a consequence of the high amounts of sugar in chewing tobacco. There is an increasing recognition that genetic factors play a role in the development of tobacco-related oral diseases. Genetic factors affecting susceptibility to oral cancers include genotypes affecting metabolism of tobacco carcinogens[50] and DNA repair.[26] Specific genotypes for interleukin-1 are associated with adult periodontal disease.[51,52]

It has been estimated that smoking accounts for half of all periodontal disease[33] and 91 percent of oral cancers among males and 59 percent of oral cancers among females.[53] Because tobacco accounts for such a high proportion of periodontal disease and oral cancer, controlling tobacco use will be important if we are to make progress in reducing the burden of tobacco-related oral diseases. Effective treatments to prevent tobacco use and increase successful quitting[54] are available and need to be more widely adopted. Dental practices may provide a uniquely effective setting for prevention and cessation of smoking and smokeless tobacco use.[55,56]

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