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# Cigarette smoking as a risk factor associated with oral leukoplakia

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**BACKGROUND:** *It is well known that oral leukoplakia is the most common precancerous lesion of the oral mucosa. Although tobacco and alcohol are known to be major risk factors for oral leukoplakia worldwide, there are no data on risk factors for oral leukoplakia in our country. The aim of our study was to analyze the association between oral leukoplakia and smoking habit, with attention to the duration and quantity of smoking.*

**METHODS:** *The study population consisted of 352 patients aged 40-70 years. Prior to the clinical examination, each subject answered a standardized questionnaire regarding tobacco-smoking habits. Oral leukoplakia was diagnosed and grouped according to internationally accepted criteria. Chi-square test was used for statistical analysis.*

**RESULTS:** *Of the entire sample, 279 were smokers and 73 non-smokers. Oral leukoplaka was found in 53 subjects and among them 50 were smokers and 3 were non-smokers. All smokers had only used cigarettes. The relative risk of developing oral leukoplakia increased with duration of cigarette smoking habit. The majority of smokers with leukoplakia (74.0%) smoked more than 20 cigarettes per day compared to 34.5% of those without leukoplakia. The highest prevalence of leukoplakia (33.3%) was found in subjects who used cigarettes and alcohol.*

**CONCLUSION:** *In view of these results, cigarette smoking is significantly related to the etiology of oral leukoplakia.*

**KEY WORDS:** *Smoking; Leukoplakia, Oral; Risk Factors; Precancerous Conditions; Tobacco*

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## INTRODUCTION

Oral leukoplakia is a precancerous or potentially malignant lesion, which means that in this morphologically altered tissue, cancer is more likely to occur than its apparently normal counterpart (1). In general, it is more or less accepted as an overall statement that approximately 5 percent of all leukoplakias will transform into cancer in an average period of 5 years (2).

Tobacco smoking is an important risk factor for precancerous lesions of the mouth. Smokers have a significantly higher prevalence of leukoplakia compared with non-smokers (3-5), and the frequency of the habit has a positive dose-response relationship (6,7). It has also been demonstrated that there is a dose-response relationship for tobacco use and the risk of malignant transformation of oral leukoplakia (7,8).

However, women without smoking habits have significantly higher risk of malignant transformation of oral leukoplakia than women who smoke (2). It has been shown that most carcinomas develop from leukoplakias on the lateral borders of the tongue or in the floor of mouth (9). In a recent study, Schepman et al. (10) reports that leukoplakias in the floor of mouth are significantly more often present in smokers than in non-smokers. On the contrary, leukoplakias on the borders of the tongue are significantly more common among non-smokers than smokers.

Alcohol is an important risk factor, having a multiplicative synergistic carcinogenic effect with tobacco (11,12).

It has been found that heavy smokers (more than 20 cigarettes per day) who do not consume alcohol have a two- to four-fold increased risk of developing oral cancer than a tobacco and alcohol abstainers. A person who heavily smokes and drinks (over 21

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units per week) has a six to fifteen times greater risk (13,14).
The aim of our study was to analyze the association between oral leukoplakia and smoking habit, with attention to the duration and quantity of smoking.

## PATIENTS AND METHODS

The study population consisted of 352 patients aged 40-70 years. The nature and the purpose of the study were briefly outlined to each subject and then they signed an informed consent form.
Prior to the clinical examination, each subject answered a standardized questionnaire regarding tobacco-smoking habits. Alcohol drinking habits were also recorded. After completing the questionnaire, each subject was given an examination form with a number corresponding to the random number on the questionnaire to ensure anonymity. This study was blind and the examiner was not told of the tobacco history of each examinee.
The subjects were divided into two groups according to their smoking habits. Persons who had never smoked were considered to be non-smokers. The smokers were defined as regular smokers for any period of time, but at least 1 year before the study. Former smokers were not included in the study. All subjects exclusively smoked manufactured (commercial) cigarettes. The amount smoked was calculated after summing and averaging the number of cigarettes per day in different periods of the lifetime of all subjects. Smokers were divided into three groups according to the number of cigarettes used per day: 10 or fewer cigarettes, 20 or fewer cigarettes, and more then 20 cigarettes.
According to the duration of tobacco smoking habit, smokers were divided into 5 groups. One examiner performed oral examination. All patients were examined sitting in a dental chair, with artificial light and using mouth mirrors. Lesions were recorded on the WHO standard recording form for oral mucosal diseases (1). The clinical diagnosis of oral leukoplakia was based on the criteria as provided by the WHO and modified by Axell (15).
The questionnaire and examination data were tabulated and the results analyzed with chi-square test at the 0.05 level significance.

## RESULTS

A total of 352 subjects were examined. Out of these, 279 were smokers and 73 were non-smokers. Oral leukoplaka was found in 53 subjects and among them 50 were smokers and 3 were non-smokers.
The prevalence of leukoplakia by duration of cigarette smoking habit is shown in Table 1. The prevalence of leukoplakia increased as the years of duration increased. The highest relative risk was found for the duration of 10 years and more. Duration of use was an important contributory factor and was also evident when comparing the differences in the mean duration of use between smokers with and without leukoplakia. The mean duration of use was longer (10.3 years) in smokers with leukoplakia than in those without (5.6 years).

**Table 1.** Relative risk of leukoplakia by duration (years) of tobacco smoking habit

| Duration (years) | Subjects with leukoplakia | Subjects (n) | Prevalence of leukoplakia (%) | Relative risk of leukoplakia |
|---|---|---|---|---|
| 1. none | 3 | 73 | 4.1 | - |
| 2. ≤ 2 yr. | 4 | 75 | 5.3 | 1.0 |
| 3. ≤ 4 yr. | 6 | 62 | 9.7 | 2.0 |
| 4. ≤ 6 yr. | 10 | 60 | 16.7 | 3.4 |
| 5. ≤ 8 yr. | 13 | 50 | 26.0 | 5.2 |
| 6. ≥ 10 yr. | 17 | 32 | 53.2 | 10.6 |

2.- 3. p>0.05; 2.- 4. p<0.05; 2.- 5. p<0.001; 2. - 6. p<0.001; 4. – 5. p<0.05; 4. – 6. p<0.001; 1. - 2.3.4.5.6. p<0.001

The presence of leukoplakia increased with the number of smoked cigarettes per day. The majority of smokers with leukoplakia (74.0%) smoked more than 20 cigarettes per day compared to 34.5% of those without leukoplakia. This difference was also highly significant ($p<0.001$)(Table 2).

**Table 2.** Number and frequency (%) of subjects according to the number of cigarettes per day

| | With leukoplakia n (%) | Without leukoplakia n (%) | Significance |
|---|---|---|---|
| ≤ 10 cig/day | 3 (6.0) | 131 (57.2) | p< 0.001 |
| ≤ 20 cig/day | 10 (20.0) | 19 (8.2) | p< 0.05 |
| > 20 cig/day | 37 (74.0) | 79 (34.5) | p< 0.001 |

The prevalence of leukoplakia in subjects with smoking and alcohol habits is shown in Table 3. The highest prevalence of leukoplakia (33.3%) was found in subjects who used cigarettes and consumed alcohol. The difference between non-smokers and users of smoking tobacco only and smoking tobacco users who also consumed alcohol was statistically significant.

**Table 3.** Prevalence of leukoplakia by tobacco and/or alcohol habit

| Tobacco or alcohol habit | Number of subjects with leukoplakia | Number of subjects without leukoplakia | Prevalence of leukoplakia (%) |
|---|---|---|---|
| 1. None | 3 | 73 | 4.1 |
| 2. Smoking only | 32 | 175 | 18.2 |
| 3. Smoking and alcohol | 18 | 54 | 33.3 |
| 4. Alcohol only | 0 | 12 | 0.0 |

1.- 2. p<0.001; 1.- 3. p<0.001; 2.- 3. p<0.05

## DISCUSSION

The present study documented the prevalence of leukoplakia among tobacco smoking users as compared with non-smokers and identified factors that may affect such prevalence.
Patients over 40 year of age were included in this study, since this is the age group in which oral leukoplakia occurred more frequently. This is in accordance with previous studies (3,15-20).

Moreover, an increase in the incidence or prevalence of leukoplakia with any population group should raise concern about the possible malignant transformation of oral leukoplakia and subsequent rise in the incidence of oral cancer with that group (2,4,9). In this study, in the entire study population cigarette smoking was the only smoking habit. The higher percentage of smokers (94.3%) than non-smokers (5.7%), points to the accepted role of smoking tobacco use in the development of oral leukoplakia. This result supports previous findings (3,16,17,19).

The results of this study showed that the longer the duration of smoking habits the higher the prevalence of oral leukoplakia. The peak time for the development of leukoplakia was after 4 years of cigarette smoking use. Also, smokers with leukoplakia had a statistically longer mean duration of use (10.3 years) than did smokers without leukoplakia (5.6 years). It is also important to note that the peak time for development of leukoplakia was nearly the mean duration of smoking habits of those without leukoplakia. Moreover, the duration of smoking habits associated with a significant increased risk of developing oral leukoplakia. In fact, those who smoked more than 10 years had nearly 11 times greater risk of developing leukoplakia than non-smokers.

In this study, the number of cigarettes used per day significantly related to the presence of oral leukoplakia, which is in agreement with previous study (6). There is clear evidence to suggest that cessation of tobacco use may result in the regression or disappearance of oral leukoplakia and increased risk falls to a level close to that of a person who has never smoked (7,8,21). This information could be helpful in motivating patients to stop smoking.

Statistically significant association between the prevalence of leukoplakia and the use of alcohol and cigarettes was found in this study. Previous studies (11,13,22) have suggested a synergistic effect of joint exposure to alcohol and tobacco - i.e. the combined effect of both these agents is greater than simply adding the effects of each together. The aim of this study was not to analyze the type of alcoholic beverage with the prevalence of leukoplakia. However, it seems that the total amount of alcohol (14) and the duration of alcohol consumption (23) are more important factors than the type or constitution of alcoholic beverage consumed.

## CONCLUSION

The present study showed that there is not only a relationship between cigarette smoking habit and oral leukoplakia, but several factors appear to be associated with its presence. The duration of smoking habits, the number of cigarettes smoked per day, and alcohol and cigarette use all were significantly associated with the presence of oral leukoplakia.

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