Oral Diseases (2004) 10, 346–348

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Oral Medicine

The prevalence of oral leukoplakia in 138 patients with oral squamous cell carcinoma

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OBJECTIVES: To determine the relationship between oral leukoplakia (OL) and oral squamous cell carcinoma (OSCC), and to evaluate possible differences between those carcinomas with and without associated leukoplakia.
MATERIAL AND METHODS: A total of 138 patients were studied at the Stomatology Service of the University General Hospital, Valencia, Spain. These patients were divided into two groups: group 1, patients with oral cancer and leukoplakia, and group 2, patients with OSCC but with no associated premalignant lesions. The relationship between this precancerous lesion and the OSCC was evaluated, as well as the possible clinical and histological differences between the tumours of the two groups.
RESULTS: Leukoplakia was detected in 27 (19.56%) patients with OSCC. No differences were found between the two groups regarding age and tumour location. However, statistically significant differences were observed with respect to the form, tumour stage and the presence of adenopathies in the cancers with and without leukoplakia; in that the tumours associated with leukoplakia were diagnosed as being at a more initial stage.
CONCLUSIONS: Those patients with OL associated with oral cancer presented with tumours at a less advanced stage than those where no associated leukoplakia existed.
Oral Diseases (2004) **10**, 346–348

Keywords: oral leukoplakia; squamous cell carcinoma

Introduction

The fact that some oral leukoplakias (OLs) undergo malignant transformation during their clinical evolution (Pindborg *et al*, 1968; Silverman *et al*, 1984; Schepman *et al*, 1998) and that white lesions are found on the borders of some oral squamous cell carcinomas (OSCC) (Hogewind *et al*, 1989; Schepman *et al*, 1999), lends support to the concept that OL is a potentially malignant lesion.

A certain debate exists with respect to the prevalence of OL in patients diagnosed with OSCC. The published percentages of which vary from approximately 15 to 60% (Table 1). In the same regard, the frequency of malignant transformation of OL fluctuated between 0 and 20% in observations made over a period of 30 years (Silverman *et al*, 1984).

The objectives of this study were to determine the association between OL and OSCC and to evaluate the possible differences between OSCCs with and without an associated leukoplakia.

Material and methods

In the present study, 138 patients were examined and histologically diagnosed with OSCC at the Stomatology Service of the University General Hospital of Valencia (Spain). All patients were observed in the period between October 1997 and July 1999.

In the first instance, the simultaneous presence of OL and OSCC was examined, basing our pathological diagnosis on the criteria established by Axell *et al* (1996). In this respect, we considered two groups of patients: group 1, corresponding to those cases with OSCC and with an associated leukoplakia and group 2, formed by patients with OSCC, but with no leukoplakia.

Details of patients were obtained with respect to their age, sex, tobacco and alcohol consumption, and the symptoms and moment of evolution of the tumoral lesions. Moreover, a clinical description of the lesions was made with respect to location, size and clinical form and stage of the tumour (International Union Against Cancer, 1992). The grade of histological differentiation was obtained by either diagnostic or operative biopsy.

Comparative statistics were calculated by means of the chi-square and Student's *t*-test. Statistical significance was considered for a *P*-value of <0.05.

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Received 13 June 2003; revised 23 November 2003 and 30 January 2004; accepted 19 March 2004

Table 1 Studies with simultaneous occurrence of oral squamous cell carcinoma (OSCC) and oral leukoplakia

Authors	*Country*	*Number of patients with OSCC*	*Percentage with oral leukoplakia*
Weisberger (1957)	USA	275	60.0
Chierici *et al* (1968)	USA	874	15.0
Bouquot *et al* (1988)	USA	61	36.1
Hogewind *et al* (1989)	Holland	212	48.0
Pinholt *et al* (1997)	Denmark	100	33.0
Scheifele and Reichart (1998)	Germany	101	15.8
Schepman *et al* (1999)	Holland	100	47.0
Present study (2003)	Spain	138	19.6

Results

The presence of OL was observed in 27 (19.57%) of the patients with OSCC (group 1), the 111 (80.03%) remaining patients with OSCC did not present any associated premalignant lesions (group 2).

The characteristics of both groups are shown in Table 2. No statistically significant differences were observed in either group with regard to age, sex and tobacco consumption. The mean age in group 1 was 57.93, while 60.63 in group 2. However, a higher alcohol consumption within group 2 than in group 1 patients was observed, and furthermore the number of symptoms was also higher in group 2 patients, resulting in statistically significant differences between the two groups ($P = 0.004$).

The majority of the OSCCs were found on the tongue and floor of the mouth with no differences existing between the groups. Whereas statistically significant differences were observed between both groups with regard to other clinical parameters such as tumour – clinical characteristics ($P = 0.002$), clinical stage of the tumour ($P < 0.001$) and the presence of adenopathies upon palpation ($P = 0.002$). Approximately 95% of group 1 patients were diagnosed with initial stages I and II, as opposed to 47% of the patients in group 2. In addition, group 1 patients (those with associated OL) presented more incipient erythroplakic and leukoplastic clinical forms, and fewer adenopathies upon extraoral examination.

Histopathologically, no differences were observed in the grade of differentiation between the carcinomas with or without an associated leukoplakia. However, in the anatomopathological studies of the extirpated adenopathies, differences were observed in both groups with regard to tumoral infiltration. Group 2 patients (those patients who presented oral cancer alone) had a greater number of extirpated tumour-positive adenopathies than patients in group 1 (those with leukoplakia and OSCC).

Table 2 Clinical differences between the two groups[a]

	Group 1, N *(%)*	*Group 2,* N *(%)*	P-*value*
Gender			
Men	14 (51.9)	85 (76.6)	0.010
Women	13 (48.1)	26 (23.4)	
Tobacco			
Smokers	14 (51.9)	79 (71.2)	0.055
Non-smokers	13 (48.1)	32 (28.8)	
Alcohol			
Drinkers	9 (33.3)	73 (65.8)	0.002
Non-drinkers	18 (66.7)	38 (34.2)	
Symptoms			
None	11 (40.7)	15 (13.5)	0.004
Discomfort	10 (37.0)	48 (43.2)	
Pain	6 (22.2)	48 (43.2)	
Location			
Lip	2 (7.4)	7 (6.3)	0.835
Tongue	13 (48.1)	47 (42.3)	0.585
Floor of the mouth	6 (22.2)	35 (31.5)	0.342
Palate	2 (7.4)	9 (8.1)	0.904
Buccal mucosa	3 (11.1)	25 (22.5)	0.185
Gingiva	4 (14.8)	18 (16.2)	0.858
Clinical forms			
Erythroplakic	3 (11.1)	6 (5.4)	0.002
Leukoplastic	6 (22.2)	3 (2.7)	
Exophytic	3 (11.1)	11 (11.7)	
Ulcerated	14 (51.9)	67 (60.4)	
Mixed	1 (3.7)	22 (19.8)	
Regional lymph node metastasis	1 (3.7)	37 (33.3)	0.002
Tumoral stage			
I	17 (63.0)	28 (25.2)	< 0.001
II	9 (33.3)	25 (22.5)	
III	1 (3.7)	14 (12.6)	
IV		44 (39.6)	

[a]Group 1, patients with leukoplakia and oral squamous cell carcinoma (OSCC) and group 2, patients with OSCC without associated leukoplakia.

Discussion

In the present study, we observed the simultaneous presence of OL in 20% of the patients with OSCC, in accordance with the other published studies in the medical literature (Chierici *et al*, 1968). However, the published percentages vary between 15 and 60% (Table 1). These findings, and the fact that some leukoplakias undergo malignant degeneration (Silverman *et al*, 1984; Schepman *et al*, 1998), lend support to the concept of OL as a potentially malignant lesion. For this reason oral leukoplakia requires strict follow-up.

Age is an influencing factor in the incidence of oral cancer, but does not seem to be relevant in this study, since the average age of the patients with leukoplastic lesions associated to OSCC was 57.9 years at the time of diagnosis of the malignant disease. Moreover, this age was similar to the average age of the group of patients that presented oral cancer alone (60.6 years old). Neither did Silverman *et al* (1984) observe that age was a specific factor in the malignant transformation of OL.

In this study, no sex predilection was observed among those patients who presented simultaneous leukoplastic lesions along with the oral neoplasia, which agrees with the studies of Bouquot *et al* (1988) and Schepman *et al* (1999). However, in the clinical follow-up studies of OL, it was observed that women presented a greater risk for malignant progression of their leukoplastic lesions (Banoczy, 1977; Silverman *et al*, 1984).

Tobacco has classically been considered as an important risk factor in the development of oral cancer. However, Einhorn and Wersall (1967) determined an eight times higher risk that these lesions would undergo malignant transformation in non-smoker patients. It does not seem very clear why the absence of this habit is associated with a greater risk of malignant transformation. It is speculated that in the suppression of tobacco other factors of greater importance in the initiation or promotion of carcinogenesis could exist. We found a higher prevalence of smokers in the second group ($P = 0.055$).

In the present study, statistically significant differences were found among patients with and without leukoplakia with regard to the alcohol factor, in that those patients with OSCC and OL consumed less alcohol than the other patients. Here, we should point out that the majority of those patients who consumed alcohol were also smokers. On the contrary, Schepman *et al* (1998) did not observe any correlation between the alcohol drinking habits of men and women with respect to the malignant transformation of their oral leukoplastic lesions.

Pain increases ones notion of malignant neoplasia, in a way that while pain is not normally associated with an oral leukoplastic lesion, and only 25% of patients may manifest slight discomfort, 50% of the patients with leukoplakia at the moment of oral neoplasia diagnosis perceive pain (Silverman *et al*, 1984).

In our study, we observed that 77% of the patients with leukoplakia and OSCC either did not present pain or simply felt slight discomfort, while 43.2% of the patients in the second group experienced moderate-to-severe pain, probably because there were more patients at advanced stages in this group.

Many studies reflect where malignant transformation of leukoplakia occurs. These are located on the lateral borders of the tongue or on the floor of the mouth, these locations being considered as high risk (Kramer *et al*, 1978; Schell and Schonberger, 1987). We did not find any locations especially associated with OL and OSCC, in accordance with Silverman *et al* (1984), Hogewind *et al* (1989) and Schepman *et al* (1999).

On the basis of our results, we conclude that those patients who present an OL associated with an OSCC present less advanced tumoural stages than those cancers without OL. It is logical to suppose that OL was the initial condition, and that the OSCC in its evolution and growth could cause any previous leukoplastic area to disappear.

References

Axell T, Pindborg JJ, Smith CJ, van der Waal I (1996). Oral white lesions with special reference to precancerous and tobacco-related lesions: conclusions of an international symposium held in Uppsala, Sweden, May 18–21 1994. International Collaborative Group on Oral White Lesions. *J Oral Pathol Med* **25:** 49–54.

Banoczy J (1977). Follow-up studies in oral leukoplakia. *J Maxillofac Surg* **5:** 69–75.

Bouquot JE, Weiland LH, Kurland LT (1988). Leukoplakia and carcinoma in situ synchronously associated with invasive oral/oropharyngeal carcinoma in Rochester, Minn., 1935–1984. *Oral Surg Oral Med Oral Pathol* **65:** 199–207.

Chierici G, Silverman S Jr, Forsythe B (1968). A tumor registry study of oral squamous carcinoma. *J Oral Med* **23:** 91–98.

Einhorn J, Wersall J (1967). Incidence of oral carcinoma in patients with leukoplakia of the oral mucosa. *Cancer* **20:** 2189–2193.

Hogewind WF, van der Waal I, van der Kwast WA, Snow GB (1989). The association of white lesions with oral squamous cell carcinoma. A retrospective study of 212 patients. *Int J Oral Maxillofac Surg* **18:** 163–164.

International Union Against Cancer (1992). *TNM atlas. Illustrated guide to the TNM/pTNM classification of malignant tumours*. Springer-Verlag: Berlin.

Kramer IR, El-Labban N, Lee KW (1978). The clinical features and risk of malignant transformation in sublingual keratosis. *Br Dent J* **144:** 171–180.

Pindborg JJ, Jolst O, Renstrup G, Roed-Petersen B (1968). Studies in oral leukoplakia: a preliminary report on the period prevalence of malignant transformation in leukoplakia based on a follow-up study of 248 patients. *J Am Dent Assoc* **76:** 767–771.

Pinholt EM, Rindum J, Pindborg JJ (1997). Oral cancer: a retrospective study of 100 Danish cases. *Br J Oral Maxillofac Surg* **35:** 77–80.

Scheifele C, Reichart PA (1998). Oral leukoplakia in manifest squamous epithelial carcinoma. A clinical prospective study of 101 patients. *Mund Kiefer Gesichtschir* **2:** 326–330.

Schell H, Schonberger A (1987). Site-specific incidence of benign and precancerous leukoplakias and cancers of the oral cavity. *Z Hautkr* **62:** 798–804.

Schepman KP, van der Meij EH, Smeele LE, van der Waal I (1998). Malignant transformation of oral leukoplakia: a follow-up study of a hospital-based population of 166 patients with oral leukoplakia from the Netherlands. *Oral Oncol* **34:** 270–275.

Schepman K, van der Meij E, Smeele L, van der Waal I (1999). Concomitant leukoplakia in patients with oral squamous cell carcinoma. *Oral Dis* **5:** 206–209.

Silverman S Jr, Gorsky M, Lozada F (1984). Oral leukoplakia and malignant transformation. A follow-up study of 257 patients. *Cancer* **53:** 563–568.

Weisberger D (1957). Precancerous lesions. *J Am Dent Assoc* **54:** 507–508.