Epidemiologic Study of Squamous Cell Carcinoma of the Mouth and Oropharynx

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SUMMARY

Objective: To establish the relationship among demographic variables, clinical-pathological factors, habits, stage and prognostic of squamous cell carcinoma of the mouth and oropharynx.

Method: Retrospective observational study of 552 patients. The variables studied were: gender, ethnics, age, smoking and alcohol consumption, staging and follow-up.

Results: A prevalence of males over females in a 5:1 ratio; a prevalence of Caucasians over the other ethnics in a 3:1 ratio. Regarding risk factors, association of smoking and alcohol consumption was stable, mainly in patients in advanced stage (III and IV), showing connection between the carcinogens and these stages. Regarding location, a clear prevalence of the inferior portion of the oral cavity was found, but only in the tongue the diagnosis could be early done. It was also highlighted that early diagnosis was not found in the oral cancer. The survival rate was 25.5%. At the end of the study an increase in cases of initial stages (I and II), and a decrease in advanced cases (III and IV) in the period between 2000 and 2004 was verified.

Conclusion: There was a higher incidence of oral and oropharyngeal cancer in men, the carcinogens were present in all stages of the disease, the recurrence and the follow-up interruption were the usual determinants of death and the advanced stages III and IV were prevalent.

Key words: squamous cell carcinoma, mouth, oropharynx, epidemiology.

INTRODUCTION

Malignant neoplasias of oral cavity is a serious issue for public health in Brazil and worldwide. According to the valuations of Instituto Nacional do Câncer do Ministério da Saúde (National Institute of Cancer – Health Ministry) done in 2004, oral cancer is the seventh most frequent malignant neoplasia in Brasil (1). There are many factors contributing for such increase. Aging originated from social-economic development prevents early deaths and allows the establishment of diagnosing programs for the disease, with improvement of population statistical controls. Therefore, urbanization and technological development expose people to diseases caused by food additives, pesticides, pollution, smoking and alcohol. These two last ones are responsible for the risk of an oral cancer in up to 140 times (1).

Cancer in Brazil is a rather worrying issue. The increase of occurrence of the disease and consequent death are at the top of the rank of the world. Besides, diagnosis, which can be easily done by finding neoplasm, is usually done when in advanced stages (III and IV), what can define the bad results of surviving this disease, independent on the therapy. There is also a lack of information in how to prevent oral and oropharynx cancer from both population and professionals, what determines delay of diagnosing and therapy (1).

Knowing the epidemiological behaviour of squamous cell carcinoma of the mouth and oropharynx allows a proper planning of preventive resources, diagnosing and therapy for it. The target of this study is to establish relation between demographical factors, clinical-pathological period, staging and follow-up of the disease.

METHOD

This study presents retrospective epidemiological information on 552 patients diagnosed with squamous cell carcinoma of the mouth and oropharynx, treated at Department of Head and Neck Surgery and ENT at Hospital Heliópolis, Hosphel, São Paulo, from 2000 to 2004. It was approved under the number 541 by the Ethics Committee in Research of the Hospital Heliópolis on June 12th, 2007. Records of patients consisted of the following data: name, process code, gender, age, ethnics, alcohol use, smoking habits, place of lesion, TNM classification (which categorizes primary tumor – T, lymphonodal metastasization – N, and distant tumor – M) and follow-up.

According to variables of the study: age was standardized in full year of age; gender (male and female); ethnics (Caucasian, black, brown and yellow Asian skin) and habits (alcohol and smoking). Regarding alcohol and smoke consumption, there were "yes/no" questions. Regarding the amount of consumption, it was scaled: (+) more than 10 cigars with filter/day or two cigars with no filter/day; (++) more than 20 cigars with filter/day or four cigars with no filter/day; (+++) more than 30 cigars with filter/day or six cigars with no filter/day and (++++) more than 40 cigars with filter/day or more than six cigars with no filter/day. Regarding alcohol, (+) consume a dose/day for distilled drinks or half carafe/day for fermented ones; (++) consume two doses/day for distilled drinks or one carafe/day for fermented ones; (+++) consume three doses/day for distilled drinks or 1 ½ carafe/day for fermented ones and, (++++) consume four doses/day or more for distilled drinks or two carafes/day for fermented ones. Regarding place, it was observed oral cavity and oropharynx. Staging followed TNM (2) classification. In relation to follow-up, patients were classified as alive without being affect by the disease, alive affected by it, dead from a different reason and dead from the disease.

Statistics was observed through tables linked to distribution of nominal variables (gender, ethnics, risk factors, place of lesion, follow-up and year of diagnosing) or numbers (age, time of smoking and drinking habits in absolute-relative frequencies and measures of central and dispersion tendency, according to year of diagnosis and period (gathering in initial period (I and II and advanced III and IV). It was used a Qui-square test for the statistical inference (hypothesis test) of the non-parametric nominal variables distributed in association tables. For the continuous numerical variables, comparison was made with parametric tests according to the possibilities of event of independent variable - Student´s-t non-paired test for the period distribution (bivariate analysis) and analysis of one-step variation (one way ANOVA) for the distribution of diagnosis year (multivariate analysis). In the association tables the statistical significance was described with an asterisk followed by the presentation of the value of the associated probability to the event (p). The cases with no statistical significance were signed with 'NS'. In all cases of analysis, it was chosen a alpha error below 5% ($p<0.005$) for the rejection of voided hypothesis.

RESULTS

According to Table 1, in relation to gender, male prevailed (456 cases) over female (95 cases), establishing a 5:1 ratio. In the quinquennium, the male incidence remains with no expressive alteration, varying from 79.2% to 89.2%. Regarding females, in the same period, there was a quite expressive percentage varying from 10.8% to 20.8%. However, there was no significant statistical

variations, though it was noticed a light tendency for the increase on female cases comparing to the beginning of the researched period.

Regarding ethnics, there was predominance on Caucasians, with 75.3% in relation to Black ones with 14.7%, Brown ones with 9.3% and Yellow ones with 0.7%, adding up 551 cases, presenting a 3:1 ratio. Such variations remained the stable during the period of the analysis.

Regarding risk factors, association between smoking and drinking habits is very expressive on mouth and oropharynx cancer (values can vary from 77.1% to 83.9% per year), adding up 443 patients (80.3%) of all patients studied in this association. Once, the isolated use of alcohol and tobacco (1.4% and 10.3%) was not so expressive, as well as not making use of those limited to 8%, which was not statistically significant.

Regarding the place of lesion, there was a neat predominance on the floor of the mouth, adding up 317 patients (57.5%), followed by oropharynx adding up 140 patients (25.3%), then palate and lips adding up 11 cases and (6.5%) for both. The initial diagnosis place was not significant.

Regarding the follow-up, there were 220 patients who died from cancer (40%), follow-up missing occurred for

Table 1. Distribution of variables according to year of inclusion of the patients.

Variables	Year of inclusion					Total
	2000	2001	2002	2003	2004	
Gender^{NS} (n = 551)						
Male	56 (84.8)	83 (89.2)	76 (79.2)	103 (81.7)	138 (81.2)	456
Female	10 (15.2)	10 (10.8)	20 (20.8)	23 (18.3)	32 (18.8)	95
Ethnics^{NS} (n = 550)						
Caucasian	52 (78.8)	65 (70.7)	75 (77.3)	90 (72.0)	132 (77.6)	414
Black	7 (10.6)	16 (17.4)	15 (15.5)	17 (13.6)	26 (15.3)	81
Yelllow	1 (1.5)	0 (0.00)	1 (1.0)	1 (0.8)	1 (0.6)	4
Brown	6 (9.1)	11 (12.0)	6 (6.2)	17 (13.6)	11 (6.5)	51
Risk factors^{NS} (n = 552)						
Smoking	4 (6.1)	10 (10.2)	12 (12.4)	11 98.7	20 (11.8)	57
Alcohol	0 (0.00)	0 (0.00)	0 (0.00)	3 (2.4)	5 (2.9)	8
Both	55 (83.3)	78 (83.9)	76 (78.4)	103 (81.7)	131 (77.1)	443
None	7 (10.6)	5 (5.4)	9 (9.3)	9 (7.1)	14 (8.2)	44
Place of lesion^{NS} (n = 552)						
Tonsil bed	7 (10.6)	12 (12.9)	8 (8.2)	10 (7.9)	17 (10.0)	54
Retromolar Area	2 (3.0)	1 (1.1)	4 (4.1)	8 (6.3)	15 (8.8)	30
Floor of the mouth	15 (22.7)	25 (26.9)	21 (21.6)	30 (23.8)	42 (24.7)	133
Tongue	19 (28.8)	21 (22.6)	21 (21.6)	19 (15.1)	33 (19.47)	113
Gum	5 (7.6)	9 (9.7)	6 (6.2)	9 (7.1)	12 (7.1)	41
Lips	4 (6.1)	2 (2.2)	4 (4.1)	14 (11.1)	11 (6.5)	35
Jugal Area	1 (1.5)	0 (0.00)	4 (4.1)	6 (4.8)	3 (1.8)	14
Palate	3 (4.5)	8 (8.6)	13 (13.4)	11 (8.7)	11 (6.5)	46
Oropharynx	10 (15.2)	15 (16.1)	16 (16.5)	19 (15.1)	26 (15.3)	86
Period* (n = 525)						
Period I	5 (7.6)	2 (2.4)	1 (1.1)	7 (5.8)	23 (14.0)	38
Period II	7 (10.6)	17 (20.0)	16 (17.8)	32 (26.7)	41 (25.0)	113
Period III	9 (13.6)	20 (23.5)	28 (31.1)	23 (19.2)	36 (22.0)	116
Period IV	45 (68.2)	46 (54.1)	45 (50.0)	58 (48.3)	64 (39.0)	258
Follow-up** (n = 550)						
Death from cancer	34 (51.5)	35 (37.6)	42 (43.3)	57 (45.6)	52 (30.8)	220
Death from other reasons	0 (0.00)	2 (2.2)	0 (0.00)	3 (2.4)	0 (0.00)	5
Follow-up missing	23 (34.8)	33 (35.5)	30 (30.9)	42 (33.6)	57 (33.7)	185
Alive with disease	0 (0.00)	10 (10.8)	14 (14.4)	6 (4.8)	20 (11.8)	50
Alive without disease	9 (13.6)	13 (14.0)	11 (11.3)	17 (13.6)	40 (23.7)	90

Subtitle: NS = non significant difference ($p > 0.05$); * = significant difference; * $p < 0.001$; ** $p = 0.002$

Table 2. distribution of averages ± Standard deviation of continous variables of time and age, according to the advance of stage to diagnosis.

Variables	Stage to Diagnosis		Total
	Initial (I and II)	Advanced (III and IV)	
Age (years)[NS]			
Average ± standard deviation	57 ± 13	56 ± 12	56 ± 12
Smoking time (years)[NS]			
Average ± standard deviation	39 ± 13	39 ± 13	39 ± 13
Drinking time (years)[NS]			
Average ± standard deviation	34 ± 13	34 ± 12	34 ± 13

Subtitle: NS = non-significant difference (p > 0.05).

185 (33.6%). In the end, 405 patients died (73.3%), 90 of them are still alive (16.3%) and 50 ones (9%) are alive but with the disease. It can be considered that 140 patients (25.5%) belong to the alive-patient group, and 90 out of them are asymptomatic, what can confirm that 25.5% of patients survived to the therapy procedures.

Regarding smoking and alcohol habits, the average time of usage was 56 ± 13 years for former and 34 ± 13 for latter, with no either year-change or behavior observations during the average time of usage regarding carcinogens consumption.

When the same variables for initial (I and II) and advanced (III and IV) periods are considered, the facts repeat themselves, and no variations on age, tobacco and drinking which might alter their values at the beginning and end of the disease occur (Table 2).

In relation to variables distribution, regarding staging, initial (I and II) and advanced (III and IV), one of the distribution allows comparison between a light tendency to increase initial cases at the end of the 5-year period in relation to the beginning and a light decrease of advanced cases in the same period (table 3).

Regarding gender, there was a more balanced distribution on early diagnosis succeeding instability on advanced cases. In the initial periods the gender relation (male / female) was 3:1 ratio and in advanced periods was 5:1.

Regarding ethnics in initial periods, distribution shows a predominance of Caucasians in relation to the others, what is repeated in the advanced stages of the disease.

Regarding risk factors, alcohol and smoking association is expressive in the advanced periods (III and IV) in relation to the initial ones (I and II). This can explain that the association of carcinogens is obvious in advanced stages of the disease, and an expressive statistical significance.

Regarding place of lesion, the predominance of diagnosis in advanced stages is clear except for lip tumor, where diagnosis is done earlier, (75% for stages I and II and 25% for II and IV). This distribution is statistically significant (p=0.001).

Discussion

Among all epidemiological aspects of mouth and oropharynx cancer, there is predominance on males in a 5:1 ratio, according to literature (3-9). Therefore, the increase of it on females with higher consumption of carcinogens has been observed in the last decades (10-12).

Regarding ethnics, there is predominance of Caucasians over the other in a 3:1 ratio. This proportion has been the same in other groups in Brazil (5,10). Black and yellow skin patients are less affected by oral cancer in this study for different reason. Whereas black skin patients suffer from racism and do not have access to preventive programs, the yellow ones, for genetic reasons, are less affected by mouth and orpharyns cancer (5,6,9,10).

Regarding risk factors, the association between tobacco and alcohol is predominant, which is confirmed in three quarters of patients (3,13-16). The isolated chemical dependence is less frequent when alcohol or tobacco is isolated used. Thus, the use of those is normally associated and rarely in a isolated way (3,15).

There is predominance in clinical periods III and IV, though in initial periods I and II, diagnosis figure is low. Although programs of early detection of mouth and oropharynx cancer are a worry for doctors, the delay in diagnosing is common (11,17-21).

Table 3. Distribution of variables according to the advance of stage to diagnosis.

Variables	Diagnosis period				Total		p
	Initial (I and II)		Advanced (III and IV)				
	n	%	n	%	n	%	
Diagnosis Year (n = 525)							
2000	12	18.2	54	81.8	66	100	0.001
2001	19	22.4	66	77.6	85	100	
2002	17	18.9	73	81.1	90	100	
2003	39	32.5	81	67.5	120	100	
2004	64	39.0	100	61.0	164	100	
Gender (n = 524)							
Male	117	26.9	318	73.1	435	100	0.039
Female	34	38.2	55	61.8	80	100	
Ethnics (n = 523)							
Caucasian	122	30.8	274	69.2	396	100	0.304
Black	15	19.5	62	80.5	77	100	
Yellow	1	25.0	3	75.0	4	100	
Brown	13	28.3	33	71.7	46	100	
Risk factors (n = 525)							
Smoking	20	37.7	33	62.3	53	100	0.007
Drinking	5	62.5	3	37.5	8	100	
Both	110	25.8	317	74.2	425	100	
None	16	43.2	21	56.8	37	100	
Place of lesion (n= 525)							
Tonsil bed	12	23.1	40	76.9	52	100	0.001
Área retromolar	4	14.3	24	85.7	28	100	
Floor of the mouth	36	27.7	94	72.3	130	100	
Tongue	34	31.5	74	68.5	108	100	
Gum	8	20.5	31	79.5	39	100	
Lip	21	75.0	7	25.0	28	100	
Jugal Region	2	20.0	8	80.0	10	100	
Palate	12	26.7	33	73.3	45	100	
Oropharynx	22	25.9	63	74.1	85	100	
Follow- up (n = 523)							
Death from cancer	35	16.3	180	83.7	215	100	0.001
Death from other reasons	2	40.0	3	60.0	5	100	
Follow-up missing	42	24.0	133	76.0	175	100	
Alive with disease	22	46.8	25	53.2	47	100	
Alive without disease	49	60.5	32	39.5	81	100	

The number of patients who do not extend follow-up is large, once they search for specialized centers and, after the treatment, move residence or return to the previous one. 33% of missing patients in the first year of follow-up were considered dead from cancer and analyzed in group with a diagnosis of recurrence and death, according to literature (6,10,12,22,23).

Regarding age, in the fifth decade is more likely to occur. For consumption time of tobacco and alcohol, the average age is over 30. This happens in different types countries even with different habits from Brazil, such as India, where patients consume betel and tobacco (3,5,13,15).

As to the relation between cancer staging and habits for both stages I - II and III – IV, consumption rates of those are constant, which confirms that such relation are not direct connected (advance of disease versus carcinogens quantity) (3,7,13,15,18).

At last, if variables of study are correlated according to the advance of the neoplasm, one can establish constant frequencies during the five years of analysis, which affirms

that the incidence of mouth and oropharynx cancer is steady during analysis period (p=0.003) according to literature (6,9,19,20,24). Such period of distribution uniformity was also certified in the analysis of demographic variables (gender and ethnics) (3,5,6,8,18).

However, when analyzing risk factors (alcohol and tobacco), place of lesion and follow-up, one might affirm that the consumption of carcinogens, placing in the floor of the mouth and follow-up are expressive causes (p=0.001) of reserved prognosis of these malignant neoplasm, where local recurrences determine reserved prognosis of the disease (4,12,13,17,19,20,23-25).

Conclusion

One can conclude that: 1) squamous cell carcinoma of the mouth and oropharynx occurs mainly in males over females in a 5:1 ratio; 2) alcohol and tobacco are habits associated to squamous cell carcinoma of the mouth and oropharynx; 3) death from squamous cell carcinoma of the mouth and oropharynx is associated to disease recurrence and follow-up missing; 4) predominant finding of the advanced periods III and IV limited squamous cell carcinoma of the mouth and oropharynx prognosis.

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