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Original/*Cáncer*

Red meat, micronutrients and oral squamous cell carcinoma of Argentine adult patients

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Abstract

Introduction: **the identification of risk group of oral cancer allows reducing the typical morbidity and mortality rates of this pathology.**

Objetive: **it was analyzed the role of red meat, macronutrients and micronutrients on Oral Squamous Cell carcinoma (OSCC) in a case–control study carried out in Cordoba, Argentina.**

Methods: **case-control study 3:1, both genders, aged 24-80 years. Dietary information was collected using a quali-quantitative food frequency questionnaire. The logistic regression was applied for assessing the association among case/control status and daily red meat/macronutrient/micronutrients/energy intake.**

Results: **micronutrients and minerals in the diet that showed high significant median values of common consumption in cases relative to controls were iron, phosphorus, vitamins B1, B5, B6, E and K and selenium. The association measurement estimated by logistic regression was showed that a significant association between red meat, fat, daily energy, phosphorous, vitamin B5, vitamin E, and selenium intake and OSCC presence.**

Conclusions: **a high intake of fats, phosphorus, vitamin B5, vitamin E, and selenium intake and red meat appears to be related to the presence OSCC in Cordoba, Argentina. In relation to red meat consumption and risk of OSCC, the future research should center of attention on reducing the complexity of diet and disease relationships and reducing variability in intake data by standardizing of criteria in order to implement simple strategies in public health for recognizing risk groups of OSCC.**

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Key words: *Oral squamous cell carcinoma. Daily diet. Argentina.*

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CARNE ROJA, MICRONUTRIENTES Y CARCINOMA ORAL DE CÉLULAS ESCAMOSAS EN PACIENTES ADULTOS ARGENTINOS

Resumen

Introducción: **la detección de grupos de riesgo de cáncer oral permite reducir las tasas de morbilidad y mortalidad típicas de esta patología.**

Objetivo: **se analizó el rol de carnes rojas, macronutrientes y micronutrientes en pacientes con carcinoma oral de células escamosas (COCE) en un estudio de casos y controles llevado a cabo en Córdoba, Argentina.**

Métodos: **estudio de casos y controles 3:1, ambos sexos, con edades comprendidas entre 24-80 años. La información sobre la dieta fue recogida mediante un cuestionario de frecuencia de alimentos cuali-cuantitativo. La regresión logística se aplicó para evaluar la asociación entre el estado caso/control y la ingesta diaria de carne roja/ macronutrientes/micronutrientes/energía.**

Resultados: **los micronutrientes y minerales de la dieta que mostraron valores medios significativos de consumo común en los casos relativos a los controles eran hierro, fósforo, vitaminas B1, B5, B6, E y K y selenio. La medición de la asociación estimada por regresión logística mostró una asociación significativa entre carne roja, grasas, energía diaria, fósforo, vitamina B5, vitamina E, ingesta de selenio y presencia de COCE.**

Conclusión: **un alto consumo de grasas, fósforo, vitamina B5, vitamina E, selenio y carne roja parece estar relacionado con la presencia de COCE en Córdoba, Argentina. En relación con el consumo de carne roja y el riesgo de COCE, la investigación futura debería centrar su atención en la reducción de la complejidad de las relaciones de la dieta y la enfermedad, así como en reducir la variabilidad de los datos de ingesta mediante la estandarización de los criterios de admisión a fin de aplicar estrategias sencillas en salud pública para el reconocimiento de grupos de riesgo de COCE.**

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Palabras clave: *Carcinoma oral de células escamosas. Dieta diaria. Argentina.*

Abbreviations

OSCC: oral squamous cell carcinoma.
DNA: deoxyribonucleic acid.
WHO: World Health Organization.
DTE: Daily Total Energy intake.
OR: Odds Ratio.
CI95%: confidence intervals of 95%.

Introduction

Head and Neck Carcinoma, of which the majority are squamous cell carcinomas of the head and neck, is the sixth most prevalent cancer in mankind and presents high morbidity and low rates of survival[1]. Oral Cancer includes tongue, buccal mucosa, lip, soft and hard palate, gums and mouth base cancer[2]. Several human squamous cell carcinomas have been associated to certain risk factors including, but not limited to, smoking, drinking hot beverages, red meat, poor oral health, and low intake of fruits and vegetables. Among the epigenetic factors associated with cancer, environmental, socioeconomic and lifestyle characteristics have been described as risk factors for some cancers. Food is regarded as an important environmental factor linked to the occurrence of this disease[3-5]. Within dietary habits, it is known that diets low in fruits and vegetables, fish, vitamin C and other non-oxidants foods and high in red meat, is associated with an increased risk of developing oral cancer. Recent studies support evidence that dietary components may affect the process of carcinogenesis through epigenetic mechanisms. Epigenetic modifications are heritable changes in gene expression that do not require changes in the DNA (deoxyribonucleic acid) sequence[6].

However, most of these studies have addressed the association of individual foods or nutrients, and limited attention has been paid to the analysis of their joint effect by considering defined dietary profiles[7]. In complex pathologies such as oral cancer, the interaction of different environmental factors along with the expression of several genes makes it highly difficult to identify the additive or interactive effects of genes, the environment, and socio-cultural context that feature the disease; and as a result, the diagnoses are not accurate. The challenge of the multifactorial phenotypes is to achieve a valid strategy for identifying risk individuals at the population. These strategies may be addressed to screening population or generating causal predictive models for early detection, interpreting the root causes that create the condition[8].

Since prevention and early diagnosis have the greatest potential for public health and are most effective long-term for cancer control, action must be taken in training of health professionals, mainly dentists and doctors; and identifying biomarkers and methods of population monitoring and tracking for early detection of precancerous lesions in the process of malignization, or early signs of malignancy in incipient tumorigenic lesions, or prevention of recurrence in patients after surgery for a malignant lesion[9]. Nowadays a large number of studies reports a role of diet in cancer prevention and treatment; however it is necessary to define the bioactive dietary components allowing a protective or risk effect in the population.

Objective: it was analyzed the role of selected red meat, macronutrients and micronutrients on Oral Squamous Cell carcinoma in a case–control study carried out in Cordoba Argentina.

Methods

Case-control study 3:1, both genders, carried out between 2011 and 2013. The filiations and type of nutritional dietary intake data were collected in medical-odonto-stomatological clinical records. Clinical data were registered in a specific clinical form with socio-cultural, psychosocial, genetic, environmental, anthropometric, medical and dental sections. Examinations of the oral cavity were performed by dentists previously calibrated, through visual inspection and palpation of oral mucosa, teeth and removable / fixed denture, tongue, lip, cheek, and risk habits were also registered. The risk lifestyle habits were assessed according following criteria: *Smoker*: current consumption of at least one cigarette / day over a 1-year minimal period; *Alcohol*: current consumption of 2 drinks / week over a 1-year minimal period. It was considered three categories of risk habits: a) No smoke or/and alcohol (without risk habits); b) Smoke or Alcohol drinking, c) Smoke and Alcohol consumption. The occupational exposure to carcinogens (considering if you worked in risk industries such as textile, rubber, coal, dyes, leather, herbicides, automotive, plastics and chemicals) was named "workplace with risk".

This study was approved by the Research and Ethics Committee of the Ministry of Health of the province of Córdoba (No. 1378) and all subjects signed informed consent forms. Patients who were under therapeutic medication such as corticosteroids or chemotherapy drugs that modify or alter the clinical behavior of malignant oral lesions were excluded. Patients diagnosed with other cancers, systemic diseases, chronic alcoholism and drug addiction were also excluded.

Selection of cases

All the cases were ≤ 80 years old at diagnosis (age range 23-83 years, mean 58.96 years) and were drawn from the Clinical Office of the Stomatology Clinic "A", (Faculty of Dentistry, National University of Córdoba, Argentina). A total of 27 newly diagnosed with hematoxiline/eosine routine technique and classified by International Classification of Diseases (ICD-10) codes C00 to C14 were considered eligible for the study.

Selection of controls

In the same time period and at the same place, 86 patients ≤ 80 years old (age range 21-86 years, mean 59.06 years) with non-neoplastic diseases not related to smoking, drinking and without recent changes in their diet were considered eligible for this study. The controls were matched to the cases for gender and age (± 5-year).

Dietary assessment

A food intake frequency questionnaire (quali-quantitative) validated by Navarro et al., 2001[10], was administered to cases and controls at the clinical office by trained nutritionists at the stomatological clinical office after clinical examination and anatomopathological diagnosis.

This questionnaire includes two sections: a) bio-socio-cultural characteristics, anthropometric measurements and lifestyle; b) daily food intake, which allows to evaluate dietary exposure in the past (5 years before time of the interview). Additionally, a photographic food atlas, also validated Navarro et al., 2001[11], and Nutrio software were used 1.2[12] for assessment the nutritional composition analysis (average daily consumption in grams of each food, vitamines A (g), E (mg), C (mg) y B6 (mg), phosphorous (mg), selenium (μg) y zinc (mg) and total energy intake.

Macronutrients were categorized as follows: carbohydrate: low (<45), normal (45-65), high (>65) percent of Daily Total Energy intake; proteins: low (<10), normal (10-35), high (>35) percent of Daily Total Energy intake; total fats: low (<20), normal (20-35), high (>35) percent of Daily Total Energy intake (g).

Statistical analysis

Statistical description of data was expressed by average ± standard error and median value in quantitative variables or relative/absolute frequencies in qualitative variables.

Data analysis was as follows:

- The Fisher Test was performed to evaluate associations among qualitative variables.
- Mann Whitney U test for proving Ho: median of consumption are equals between cases and controls are performed because normal distribution of data was not proved
- T Student test for comparison average of % energy between cases and controls was used.
- It was estimated the Spearman coefficient between red meat and specific compounds of this food.
- It was estimated of measures of association (odds ratio –OR- and their confidence intervals of 95% -CI95%-) between the presence of disease and intake of red meat or compounds of red meat were built simple and multiple logistic models respectively. The intake of different compounds of diet intake were incorporated as continuous variables.

For all tests, it set $p<0.05$ for statistical significance. The software used was STATA 13.

Results

General charactheristics

Patients with Oral Squamous Cell Carcinoma (OSCC) presented lesions in tongue (11; 42.0 %), palate (2; 6.3%), lip (3; 9.6%), buccal mucosa (4; 16.2%), gum (4; 16.2%) and floor of the mouth (3; 9.6%). It is noteworthy that patients with OSCC presented at the clinical and/or cytology examination a significantly higher percentage of chronic trauma (16; 58%; p-value=0.0001), candidiasis (14; 51%; p-value=0.0001), plus a greater percentage of patients with OSCC work in an environment of risk (8; 31%; p-value=0.0429). Meanwhile, the "risk lifestyle habits" variable showed a significant association between consumption of alcohol and tobacco with the case/control condition (Table I).

Daily Dietary Intake

Regarding the Daily Total Energy intake (DTE) showed that the cases consumed a average of 3355.01 kcal/day significantly higher than control DTE. In addition the proteins and lipids consumed in the diet had a significantly higher average consumption in cases. The average red meat consumption showed a slight non-significant increase in cases (207.67 g/day) than in controls (153.71 g/day) (Table II). In relation to the macronutrient categories (% of DET), it was observed a 59% (16) low intake of carbohydrate; 96.3% (26) normal intake of protein, and 70.4% (19) high intake of total fats intake in cases.

In cases, micronutrients showed a high significant average values of consumption were iron, phosphorus, vitamins B1, B5, B6, E and K and selenium (Table III).

Generally, the association of red meat consumption and macro-micronutrients and energy intake showed a high or medium association (Table IV). In other hand the multiple or bivariate association measurement estimated by logistic regression was showed that a significant association between red meat, fat, DET, phosphorous, vitamin B5, vitamin E, and selenium intake and OSCC presence (Table V).

Table I
Anthropometric and lifestyle characteristics studied

Anthropometric and lifestyle characteristics	*Controls (n=86; F=41 / M=45)*			*Cases (n=27; F=12; M=15)*			*p-values*
BMI *							
Female	25.73	(0.66)	24.56	24.67	(1.12)	25.30	0.9746a
Male	27.59	(0.51)	27.02	26.68	(1.13)	26.90	0.5625a
Age (years)*							
(F)	62.71	(2.00)	62.00	61.92	(4.77)	67.00	0.9322a
(M)	55.73	(2.29)	56.00	56.29	(3.93)	53.00	0.7846a
Risk lifestyle habits**							
No smoke or/and alcohol		45 52.3%			13 48%		
Smoke habit (current consumption of at least one cigarette/day over a 1-year minimal period) **or** Alcohol drinking (current consumption of 2 drinks/ week over a 1-year minimal period)		27 31.4%			4 15%		**0.0358b**
Smoke and Alcohol drinking		14 16.3%			10 37%		
Workplace**							
With risk		8 13.0%			11 31.0%		**0.0429b**

Value reported: *Average (Standard Error) Median; **Absolute and Relative% Frequencies (RF calculated over total of controls or cases). [a]MannWhitney U p-values; [b]Irwin-Fisher p-values. p<0.05 indicates a statistical significance.

Table II
Dietary energy, macronutrients and red meat consumption in controls and cases

		Average (DS) Median of daily intake		*p-values[a]*	*% energy*		*p-values[b]*
		Controls	*Cases*		*Controls*	*Cases*	
Macronutrients (g/day)	Carbohydrates	303.28(131.87) 280.95	344.47 (113.43) 334.40	0.0797	43.56	41.07	0.1087
	Proteins	107.41 (43.15) 96.30	127.89 (45.80) 118.10	**0.0253**	15.36	15.24	**0.0111**
	Fats	113.58 (69.70) 94.90	158.94 (89.97) 141.40	**0.0062**	36.70	42.64	**0.0065**
Fibers (g/day)	Total	15.22 (6.54) 14.47	17.61 (6.03) 16.62	0.0625			
DTE	kcal/day	2784.66(1250.37)2462.74	3355.01(1008.48)3515.90	**0.0058**			
Red Meat	(g/day)	190.82(144.46) 153.71	252.68 (182.34) 207.67	0.0628			

[a] Mann Whitney U test for proving Ho: median are equals between cases and controls. [b] T Student test for proving Ho: average %energy are equal between cases and controls. Bold letters indicated statistical significance at p<0.05 level.

Discussion

Cancer is a complex pathology, and its incidence and survival index are closely related to social, cultural and socio-economic determinants of health. Low-income countries are usually the most exposed to environmental risk factors such as infectious agents, tobacco and alcohol consumption, unhealthy diet; adding to this, at times, poor access to health care systems and health education. Cancer is largely preventable, many different types of cancers can be prevented by early detection in their development stage, thus reducing its morbidity and mortality rates[9,13].

The number of patients in this study (three years) was small; in our previous work carried out between 2000 and 2007 in a population of 406 subjects, 16%

Table III
Micronutrients in controls and cases

Micronutrients	*Controls*			*Cases*			*p-values**
	Average	*DS*	*Median*	*Average*	*DS*	*Median*	
Iron (mg/day)	18.88	8.50	17.58	22.44	8.23	21.04	**0.0288**
Calcium (mg/day)	776.68	364.13	693.15	915.25	469.48	935.68	0.1779
Phosphorus (mg/day)	1431.03	571.52	1323.85	1761.34	552.79	1636.40	**0.0030**
Vit A (μg/day)	1376.92	1031.76	1039.29	1657.39	939.27	1735.57	0.1093
Vit B1 (mg/day)	1.14	0.44	1.12	1.35	0.40	1.33	**0.0246**
Vit B2 (mg/day)	2.13	0.98	1.89	2.31	0.93	2.04	0.2867
Vit B5 (mg/day)	20.29	9.24	18.18	25.53	9.74	22.70	**0.0045**
Vit B6 (mg/day)	1.28	0.60	1.25	1.58	0.60	1.35	**0.0198**
Vit C (mg/day)	189.14	132.69	156.11	197.42	178.66	124.43	0.8206
Vit E (mg/day)	6.28	4.23	4.85	10.51	8.05	8.43	**0.0030**
Se (μg/day)	106.69	51.78	95.87	142.88	47.33	145.20	**0.0015**
Zinc (mg/day)	11787.87	7039.30	8849.61	12850.75	5663.66	11616.66	0.1358
Vit K (mg/day)	782.84	378.90	670.42	942.03	355.40	869.40	**0.0225**

*Mann Whitney U test for proving Ho: median are equals between cases and controls Bold letters indicated statistical significance at p<0.05 level.

Table IV
Spearman Coeficient between red meat and macronutrients in case or control groups

Association Variables		*Total subjects (n=110)*	
		Spearman Coefficient	*p-value*
Red meat	Carbohydrate	0.42	**0.0001**
	Protein	0.75	**0.0001**
	Fat	0.83	**0.0001**
	Vitamin B1	0.55	**0.0001**
	Vitamin B5	0.68	**0.0001**
	Vitamin B6	0.59	**0.0001**
	Vitamin K	0.65	**0.0001**
	Iron	0.75	**0.0001**
	Se	0.46	**0.0001**
	Phosphorous	0.64	**0.0001**
	DET	0.76	**0.0001**

Bold letters indicated statistical significance at p<0.05 level, and association

(65 patients) presented oral cancer; this result showed that the clinical office attended 6 to 10 patients per year with oral squamous cell carcinoma[14].

It was observed in this study, a high prevalence of cancers located in the tongue in relation to other anatomical sites in the oral cavity. The tongue was reported as the most frequently affected site, for example, in Japan, Taiwan, Thailand, Yemen, India and Iran[15]. The site of occurrence depends on the predominant risk factors in the particular geographical region; It is known that oral cancers that develop in the anterior two thirds of the tongue are usually prevalent in developing countries, while pharyngeal cancers are more common in developed countries and East Central Europe[16].

Smoking and drinking habits are the most recognized risk factors for the development of oral cancer in developing countries of the Caribbean and South America. The tobacco smoking habit is one of the

Table V
Logistic regression for OSCC presence and red meat / macronutrients / dietary energy /micronutrients.

Logistic Model	*Food, macro and micronutrients*	*Odds Ratio*	*Std. Err.*	*P>0.05*	*[95% Conf.Interval]*	
Multiple	Iron	0.979360	0.070918	0.773	0.849776	1.128705
	Phosphorous	1.003941	0.001467	**0.007**	1.001069	1.006821
	Vitamin B1	0.563975	0.656171	0.623	0.057664	5.515856
	Vitamin B5	1.210738	0.117397	**0.049**	1.001186	1.464151
	Vitamin B6	0.189221	0.173698	0.070	0.031304	1.143781
	Vitamin E	1.177298	0.083595	**0.022**	1.024345	1.353091
	Se	1.017942	0.008447	**0.032**	1.001519	1.034634
	Vitamin K	0.997317	0.002065	0.194	0.993278	1.001373
	Carbohydrate	1.014693	0.007747	0.056	0.999621	1.029992
	Protein	0.964195	0.018915	0.063	0.927826	1.001990
	Fat	1.045927	0.019763	**0.017**	1.007901	1.085388
	DET	0.996023	0.001735	**0.022**	0.992627	0.999429
Simple	Red Meat	1.003306	0.001360	**0.015**	1.000644	1.005975

Bold letters indicated statistical significance at p<0.05 level

most important factors for the development of these cancers in the world, it's estimated that worldwide, its responsible for approximately 41% of head and neck cancers in men, and 15% in women. In countries such as India, tobacco consumption is combined with the chewing of betel and drinks high alcohol content[17]. A high percentage of patients with OSCC showed chronic trauma (58%). Emerging risk oral cancer factors have been proposed, such as chronic irritation from dental factors. Studies undertaken by us suggest that the chronic mechanic trauma is, together with other factors, an important risk factor in patients with oral cancer diagnosis[14].

In relation to other risk lifestyle habits for OSCC, the bibliography is still controversial and scarce. Food is one of the factors related to the ocurrence of cancer; for example, it is known that in dietary habits, a diet poor in fruits and vegetables is associated with an increased risk for oral cancer. Our results showed that the energy consumed, as well as protein and fat intake, showed a significant average increase in cases. Epidemiological evidence shows that there is a relationship between overweight and obesity and carcinogenesis[18], having the endocrine system and metabolism as the main target. Disturbances in the above mentioned systems modify the bioavailability of growth factors, steroid hormones and inflammatory markers. For example, elevated serum concentrations of insulin lead to hyperinsulinemia, an event causing a reduction in the adhesion proteins of the growth factor similar to insulin, which promotes the synthesis and biological activity of such event. This factor regulates cell growth depending on the available energy as well as the nutrients from diet and body reserves. While it is not easy to estimate the effect of energy consumption in relation to cancer risk, mechanisms have been identified linking physical activity with an inhibitory effect of the carcinogenic process such as reducing fat reserves, changes in activity related to the levels of sex hormones, altering the immune system function, reducing the generation of free radicals, and others[19].

In our study significant association between the red meat consumption and OSCC presence was established. In according with this result a case-control study of 4000 subjects showed a significant increase of developing oral cancer in the group of consumers of red meat. Other research suggested that high consumption of processed meat was significantly associated with an increased risk of oral cavity and oropharynx cancer, but these authors are not reported significantly association among total meat, red meat or white meat and the risk of oral cancer[20]. Moreover, a recent research reported a widespread consumption of red meat in Cordoba (Argentina) population [4,21].

Meanwhile, other epidemiological studies have shown that the consumption of fiber, fish, vitamin C and other non-oxidizing food, has a protective effect against the risk of developing oral cancer[22], in this study a significant consumption between cases and controls in fiber and vitamin C was not observed. The median consumption of micronutrients and minerals such as iron, phosphorus, vitamins B1, B5, B6, E and K and selenium, were higher in patients with OSCC.

It is known that *selenium* is an essential mineral and crucial for the cell to function properly. However these metalloids such as arsenic and selenium may in-

duce or prevent cancer. Both are responsible for carcinogenesis, cytotoxicity and genotoxicity in humans. Selenium produces adverse effects by modifying the thioredoxin reductase. Both arsenic and selenium react with glutathione and S-adenosylmethionine to form a Arsenic-Selenium complex, which can be secreted to the cell exterior. Authors such as Sun et al., 2014[23] suggest that low levels of selenium may reduce the toxicity of arsenic by means of exocytosis; aversely, high concentrations of selenium can increase the toxicity of arsenic due to the reaction with S–adenosylmethionine and glutathione, and modify the structure and function of the arsenite methyltransferase enzyme. Selenium is one micronutrient whose deficiency and toxic concentrations are very close each other. It was observed that meat, chicken, fish and eggs are protein-rich foods containing high levels of Se. Meat showed large variations in Se concentration. It has reported that Se levels in meat products ranged from 55.0 to 329 ng/g; these values were higher than in other food groups[24].

Another essential element for the human body is *iron*. Because of its ability to accept and donate electrons. Iron is an essential component of molecules that act as sensors, transporters and accumulators, and enzymes involved in energy production. This element is essential for the cell division process because the enzymes that synthesize deoxyribonucleotides are iron-dependent; and the deregulation of iron homeostasis has been associated to diseases such as cancer, inflammatory and neurodegenerative diseases. In relation to carcinogenesis only a few studies link the pathological process with iron[25]. It is known that red meat supplied heme iron, which is more bioavailable than non-heme iron. In the experimental studies in rats it was observed that heme iron contributes to carcinogenesis by generating free radicals and inducing oxidative stress[20, 26].

The above mentioned vitamins have been found increased in patients with OSCC. Some vitamins, such as vitamin E, has been associated with anticarcinogenic effects, for having compounds such as tocopherol, which has antioxidant and anti-inflammatory capacity[27]. However, this vitamin, and vitamins B1, B5, B6 and K have no proven effect in relation to oral cancer.

For example, epidemiological researches in colorectal carcinogenesis have shown influence role of vitamin B6 over synthesis and methylation DNA. Besides animal models have demonstrated that vitamin B6 suppress cell proliferation, reduce the number of tumors in the colon, inhibit angiogenesis, suppress nitric oxide, and reduce oxidative stress, all of which are associated with preventing carcinogenesis[28]. Some studies in cancer centers in the United States seek to identify an effective combination of antioxidant supplements that are preventative of recurrence and/or secondary neoplasia in patients with head and neck cancer; although these agents are not always malignant preventive[29]. It is well known that micronutrients are required for the protection of genome stability. It is thought that a fundamental early event in carcinogenesis is the keeping the DNA stability. This highlights the importance of dietary intake on cancer risk based on the effects of diet on epigenetic events rather than structural changes in the DNA[30].

Cancer prevention is one of the best strategies Public Health can rely on, because it is a low-cost method and highly effective over time. Recognizing risk population groups allows for early diagnosis and intervention at early stages of the disease, this being a time with high potential for healing. Epidemiologically, recognizing of food patterns is reaching new levels of interest in South American countries but is usually not implemented[21]. People's diet is part of a complex behavior and its influenced by the culture to which the population belongs. The complexity of the diet makes it difficult to assess the role of different dietary components in relation to oral carcinogenesis. In relation to red meat consumption and risk of OSCC, the future research should center of attention on reducing the complexity of diet and disease relationships and reducing variability in intake data by standardizing intake criteria in order to implement simple strategies in public health for recognizing risk groups of OSCC.

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Conflict of interest statement

None declared.

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