Risk Factors for Developing Laryngeal Cancer in Adult Population at the Hospital Español in Mexico City

Luz María Durán de Alba and Francisco Miguel Roa Castro
Servicio de Otorrinolaringología, Hospital Ángeles Lomas, México DF, Mexico

Introduction: Laryngeal cancer is the most frequent head and neck cancer. Considerable geographic differences exist in its incidence by gender. In Spain, there is male predominance (>90 %). Numerous authors have documented exposure to tobacco and/or alcohol as the main risk factors for laryngeal cancer. Gastroesophageal reflux, genetics, occupational factors, and also human papilloma virus are also cited.
Patients and method: The present study involved 43 patients diagnosed with laryngeal cancer and 130 healthy control subjects. The goal was to establish the frequency affecting both sexes and to identify the risk factors of those born in Spain but living in Mexico. Odds ratios (OR) for each risk factor were analyzed using univariate analysis.
Results: A considerable predominance of laryngeal cancer was found in males (90.6 %). Tobacco (OR=6.56) and alcohol consumption (OR=3.04) are significant risk factors with a multiplier effect. Gastroesophageal reflux does not show any significant OR. Occupational exposure had a significant OR=37.28.
Conclusions: The main advantage of this type of studies is the ability to design strategies to modify the risk factors. Male predominance and risk factors were no different from other findings reported in Spain, except for the considerable risk relating to occupational exposure.

Key words: Cancer. Laryngeal cancer. Risk factors.

Factores de riesgo de desarrollo de cáncer de laringe en la población adulta del Hospital Español de México
Introducción: De los diversos tipos de cáncer de cabeza y cuello, el cáncer de laringe es el más frecuente. El patrón geográfico de su incidencia difiere en uno y otro sexo. En España, predomina en varones (> 90 %). Numerosos autores documentan que los principales factores de riesgo de cáncer de laringe son la exposición al tabaco y/o el alcohol. También se señala al reflujo gastroesofágico, factores genéticos, factores ocupacionales y el virus del papiloma humano.
Pacientes y método: Se realiza un estudio en 43 pacientes con cáncer de laringe y 130 controles sanos, teniendo como objetivo conocer la frecuencia de afección en cada sexo e identificar los factores de riesgo en pacientes con cáncer de laringe nacidos en España y residentes en México. Se analiza la razón de momios (OR) de manera univariable para cada uno.
Resultados: Se encuentra un predominio importante de cáncer de laringe en varones (90,6 %). El tabaquismo (OR = 6,56) y el alcoholismo (OR = 3,04) son importantes factores de riesgo, con un efecto multiplicativo. La enfermedad por reflujo gastroesofágico no demostró tener una OR significativa. Se evidencia un riesgo significativo (OR = 37,28) por exposición ocupacional.
Conclusiones: La ventaja evidente de este tipo de estudios consiste en que permite diseñar estrategias para incidir en los factores de riesgo. El predominio de afección en varones y los factores de riesgo no difieren de lo publicado de pacientes en España, con excepción del importante riesgo de la exposición ocupacional.

Palabras clave: Cáncer. Laringe. Factores de riesgo.

INTRODUCTION

Laryngeal cancer is considerably less common than other types of cancer, such as breast, prostate, and colon cancer; however, there are important psychological and socioeconomic implications involved when the main organ of speech production is affected, as it impacts an individual's ability to communicate.[1]

Correspondence: Dr. L. Durán de Alba.
Servicio de Otorrinolaringología. Hospital Ángeles Lomas.
Vialidad de la Barranca No. 22. Col. Valle de las Palmas, CP 52763.
Huixquilucan. México.

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Of the different types of head and neck cancer, laryngeal cancer is the most common. In the United States there is a recorded annual incidence of some 10 000 cases.[2] The geographical distribution of the incidence of laryngeal cancer differs across genders; for instance, in the European Union, highest estimated incidence rates in males correspond to the Southern countries, whereas the highest incidence rates in females are reported in Ireland, Denmark, Belgium, and the United Kingdom. In Spain, the incidence of laryngeal cancer in males is very high (second only to France) and it is very common in the Basque Country, Zaragoza, and Murcia. Five-year mortality for this type of cancer is estimated to be 30%.[3,4]

Numerous studies provide evidence that the leading causal factors of laryngeal cancer are exposure to tobacco and/or alcohol. In this regard, different authors indicate a dose-dependent relation between smoking and laryngeal cancer. Likewise, alcohol use has been documented to have a multiplier effect on the risk a smoker has of developing laryngeal cancer.[5-7]

Willet[8] (2000) and Bossetti et al[9] (2002), among other authors, indicate that increased consumption of certain fruits and vegetables (mainly citric fruits) provides a protective effect against epithelial carcinoma of the head and neck, particularly the consumption of antioxidants such as vitamin C, folates, lycopenes, and flavonoids. Likewise, low consumption of canned meats and butter is also recommended.

On the other hand, the human papilloma virus (HPV) has been proven to be an aetiological agent in various proliferative disorders of the head and neck. The HPV serotypes that have been isolated in laryngeal samples with cancer[10,11] are serotypes 16, 18, 31, and 33. In 75% of the biopsies from patients with laryngeal cancer of epithelial cells, Pou et al[12] found the herpes simplex virus, yet found no viral isolate in several benign diseases of the larynx, which indicates the possible participation of the herpes simplex virus as a co-carcinogen.

Chronic inflammation of the larynx cause by gastroesophageal reflux disease (GERD) is an important risk factor for laryngeal cancer, as published by Vaezu et al[13] in an important case-control study.

Some publications[14-18] point to passive exposure to cigarette smoke, occupational exposure to substances such as asbestos, diesel, the liquids used in the metal-mechanical industry, and products derived from the rubber industry as possible causal factors. Bravo et al[19] have reported cases due to exposure to silica, as well as cases in woodworkers, largely in the furniture-making industry.

Cancer of the head and neck has demonstrated genetic predisposition in first degree relatives.[20]

The objective of this work consists in identifying the risk factors associated with laryngeal cancer in the adult population attending hospital in view of the fact that there are no studies in this regard at this hospital. It is noted that this disease is preventable to a certain degree in some cases if the factors amenable to modification can be identified, thus making it possible to implement strategies aimed at decreasing its frequency.

PATIENTS AND METHOD

A retrospective case-control study was carried out in the ENT and Head & Neck Surgery Department at the Hospital Español, by means of medical chart review covering from January 1, 1990 to December 31, 2000. Cases were defined as 43 adult patients, 39 (90.6%) of whom were male and 4 (9.3%) females, with ages ranging from 56 to 96 years (mean, 65.8 [7.3]), born in Spain and having lived in Mexico for at least 20 years and with a pathology diagnosis of laryngeal cancer. Moreover, a group of controls was created consisting of 115 males (88.4%) and 15 females (11.6%) with a mean age of 62.6 (8.9) years (range, 57-88), also born in Spain, who were matched for their year of birth, time of residence in Mexico and gender by means of systematic sampling of the medical charts of individuals deemed healthy who went to the hospital for an annual medical check-up at the Department of Preventive Medicine at the same hospital.

The following risk factors for laryngeal cancer were recorded in each history: all forms of tobacco use, consumption of alcoholic beverages, and a diagnosis of GERD by means of oesophagogastric endoscopic examination, history of occupational exposure to carcinogenic substances, and family history of laryngeal cancer.

Dates were analyzed using descriptive statistics with conventional methods. Risk factors were compared between both groups using univariate descriptive statistics with odds ratio (OR) using the G-Statt v.2 statistical software.

RESULTS

Forty-two patients (98%) had a pathology diagnosis of epidermoid cancer and 1 (2%) had a diagnosis of lymphoepithelial carcinoma. Twenty-one patients (48%) were found with stage I disease; 6 (13%) displayed stage II disease; 5 (11%) had stage III disease; and 11 (24%) presented stage IV disease. The location of the carcinoma at the time of diagnosis included 6 patients (13.9%) with disease located in the supraglottis; 29 (67.4%) presented disease located in the glottis; 1 (2.3%) had the disease located in the subglottis; and 7 (16.4%) of the patients had transglottic disease.

Insofar as tobacco use is concerned, 35 patients (81.3%) reported smoking 40 cigarettes/day on average (OR=6.56; 95% confidence interval [CI], 2.82-15.26). In the control group, 56 individuals (40%) smoked a mean of 8 cigarettes/day. Thirty patients (69.7%) were regular consumers of alcohol (OR=3.04; 95% CI, 1.45-6.37) (Table 1). On stratification of 29 patients with concomitant alcohol and tobacco use, the risk of laryngeal cancer in these patients rose to OR=21.75 (95% CI, 2.76-171.08) (Table 2). The univariate results of 13 patients (30.2%) with a diagnosis of GERD presented an OR=0.40 (95% CI, 0.19-0.85).

Not a single patient reported having a family history of laryngeal cancer. Five patients (11.6%) had a history of occupational exposure, 3 were exposed to nickel, 1 to aluminium and asbestos, and 1 patient had on-the-job contact with substances used in the textile industry. An OR=37.28 (95% CI, 2.01-685.45) was revealed (Table 1).

DISCUSSION

Important life functions converge in the larynx, such as eating, breathing, and speech production. The co-ordinated functioning of the structures that comprise it is necessary for human existence.[21]

The diagnosis of laryngeal cancer is made relatively early during the course of the disease due to alterations in speech production and the airways. The feeling the patient has of constant secretion in the throat, later accompanied by changes in their voice quality (which becomes scratchy, low volume and with modifications in the rhythm, without evidence in the earliest stage of changes in pitch) leads the ENT specialist to suspect the diagnosis.[22]

Epithelial cell carcinoma is the most common type of cancer in the larynx (more than 90% of cases), which accounts for 26% of the different types of cancer affecting the head and neck.[23]

Most patients who develop this disease are male, and the maximum incidence occurs during the sixth decade of life. The ratio of males to females is believed to be 5:1; however, there has been an increasing incidence in women starting in the fifties, probably due to the increase in smoking and alcohol use.[23] In this study, this disease was found in 90.6% of males and 9.3% of females.

Many authors have reported that this type of malignancy is preventable to a certain degree. The results of the univariate analyses conducted in this study point out that the number one risk factor is occupational exposure, on the basis of the fact that 5 cases were reported in the patient group and no one presented this factor in the control group. The literature indicates that more than 95% of patients with laryngeal cancer have a history of smoking. In this work, we have detected a proportion of 81%, who reported smoking an average of 40 cigarettes/day. Falk et al[24] indicated a relative risk 4.4 times higher in individuals who smoke 10 cigarettes a day; this risk increased to 10.4 times higher for people smoking 20 cigarettes a day, which confirms a dose-dependent effect. The results of the univariate analysis performed in this study confirm the importance of smoking and alcohol use as risk factors for laryngeal cancer. Furthermore, the multiplying effect of tobacco and alcohol use is confirmed, with an important increase in OR. Goodsell (2006) and Nishimoto et al (2004) postulated that the influence of alcohol use in the risk of laryngeal cancer may be due to the alcohol dehydrogenase present in the mucosa or to the bacteria of the oropharynx that turns ethanol into acetaldehyde, a known carcinogen.[24-26] In our study, the OR increased considerably when the association of both factors was contemplated, as indicated in the literature.

Occupational exposure was an important risk factor, as 5 cases were recorded in the group of patients and none in the control group. It is worth highlighting that no adjustments were made for tobacco use and/or alcohol.

In the present study, oesophageal reflux did not emerge as a risk factor, although various authors have demonstrated its role in the development of different types of aerodigestive cancers, laryngeal cancer among them, with a relative risk 2.4 times higher.

Table 1. Risk Factors for the Development of Laryngeal Cancer[a]

Risk Factor	*Cases*	*Controls*	*Total*	*OR (95% CI)*
Tobacco use				
Yes	35	52	87	6.56 (2.82-15.26)
No	8	78	86	
Total	43	130	173	
Alcohol use				
Yes	30	56	86	3.04 (1.45-6.37)
No	13	74	87	
Total	43	130	173	
GERD				
Yes	13	67	80	0.40 (0.19-0.85)
No	30	63	93	
Total	43	130	173	
Occupational exposure				
Yes	5	0	5	37.28 (2.01-689.45)
No	38	130	158	
Total	43	130	173	

[a]CI indicates confidence interval; GERD, gastroesophageal reflux disease; OR, odds ratio.

Table 2. Smoking as a Risk Factor for Laryngeal Cancer in Patients Who Consume Alcohol[a]

Risk Factor	*Cases*	*Controls*	*Total*	*OR (95% CI)*
Tobacco use				
Yes	29	32	61	21.75 (2.76-171.08)
No	1	24	25	
Total	30	56	86	

[a]CI indicates confidence interval; OR, odds ratio.

It is important to highlight the fact that interesting research has been conducted investigating the role of HPV and the influence of different serotypes has been established in the genesis of this disease; however, in this study we have found only one patient in whom HPV was documented, probably due to the fact that viral isolation has only become available fairly recently.

No family history of laryngeal cancer was found in our patients; however, a genetic predisposition has been demonstrated in first degree relatives and it has been posited that the genetic foundations for this susceptibility is found in the DNA cell repair systems, in the efficacy of cell systems to metabolize carcinogens, and in the control systems of the cell cycle or in a combination of all of these.[22,27]

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