

Revisiones**Larynx cancer and occupational exposure to asbestos****Cáncer de laringe y exposición laboral al amianto****Borin Mario, A.^{1,3}; Ventura García, M.^ª Ángeles^{1,3}; Coca Simón, María del Pilar^{2,3}**

1. Hospital General Universitario Gregorio Marañón, Madrid. Spain.

2. Hospital La Princesa, Madrid. Spain.

3. Teaching Unit of Occupational Health of Comunidad de Madrid. Madrid. Spain.

Recibido: 23-04-15

Aceptado: 25-05-15

Correspondencia

Mario Borin

marioborin@gmail.com

This work has been carried out as part of the Scientific Program of the National School of Occupational Medicine of the Carlos III Health Institute under an agreement with the Teaching Unit of Occupational Medicine of the Community of Madrid, Spain.

Abstract

Summary: The occupational exposure to asbestos fibers it's a known health risk. Laryngeal cancer due to inhalation of asbestos dust is included in Annex II of RD 1299/2006. Epidemiological studies up to date, have obtained conflicting results regarding the association.

Objectives: Identifying the latest scientific evidences of an association between laryngeal cancer and occupational exposure to asbestos, to know the risk of having laryngeal cancer according to the frequency of exposure to asbestos, to know other vulnerabilities factors, and to identify the type of laryngeal cancer more frequent to said occupational exposure.

Methods: A systematic review of articles of scientific evidence collected from different databases (Medline, OSH, Scopus, IBECs, ILO) conducting a literature search for MeSH descriptors (laryngeal neoplasms, occupational exposure, work exposure, asbestos) of articles published between 1999 and 2014, in humans, only original items, with a sample size larger of 30, in spanish, english, french, italian and portuguese. Duplicate studies, non original studies and prevalence studies with no control group were excluded. Following this systematic reading was performed by evaluating the evidence level of the studies with the SIGN criteria.

Results: 107 articles were collected through the literature search, after applying inclusion/exclusion criteria a total of 6 items were selected (4 case-control studies, 1 cohort study and 1 meta-analysis). Of these, 2 case-control studies and the cohort study achieved a statistically significant association between occupational exposure to asbestos and laryngeal cancer. The meta-analysis suggests association, although without obtaining statistical significance, while the remaining case-control studies reported a non statistically significant association between laryngeal cancer and occupational exposure to asbestos.

Discussion/Conclusion: Based on the results, it is evidenced an existence of discrepancy regarding the association between laryngeal cancer and occupational exposure. A statistically significant increased risk of presenting laryngeal cancer with an increased frequency of exposure to was exposed. Regarding vulnerability factors in one of the largest studies, a higher risk of laryngeal cancer for workers exposed to asbestos was proposed if were to be exposed to silica dust and cotton dust also. Regarding the type of laryngeal cancer, a study achieved a statistically significant association, for the epiglottic localization.

It would be advisable to conduct further studies of an observational design, with a larger duration and a larger sample size in order to increase the statistical significance and to minimize the possibility of research biases.

Med Segur Trab (Internet) 2015; 61 (239) 284-294

Keywords: *Laryngeal neoplasms, occupational exposure, occupational disease, asbestos.*

Resumen

Resumen: Es conocido el riesgo para la salud que supone la exposición laboral a las fibras del amianto. El cáncer de laringe debido a la inhalación de polvo de amianto está incluido en el anexo II del RD 1299/2006. Hasta la fecha los estudios epidemiológicos realizados han obtenido resultados controvertidos con respecto a dicha asociación.

Objetivos: Identificar las últimas evidencias científicas de la asociación entre la exposición laboral al amianto y el cáncer de laringe, conocer el riesgo de presentar cáncer de laringe acorde a la frecuencia de exposición al amianto e identificar el tipo de cáncer de laringe más frecuente en relación a dicha exposición laboral.

Métodos: Se realizó una revisión sistemática de artículos de evidencia científica recolectados de distintas bases de datos (Medline, OSH, Scopus, IBECs, ILO) realizando una búsqueda bibliográfica por descriptores MeSH (cáncer de laringe, exposición laboral, exposición ocupacional, asbesto) de artículos publicados entre 1999 y 2014, en humanos, artículos originales exclusivamente, con un tamaño muestral mayor de 30, en castellano, inglés, francés, italiano y portugués. Se excluyeron estudios duplicados, estudios no originales y estudios de prevalencia sin grupo control. Posterior a esto se realizó una lectura sistemática evaluando el nivel de evidencia de los estudios con los criterios SIGN.

Resultados: Se recolectaron 107 artículos a través de la búsqueda bibliográfica, tras aplicar criterios de inclusión/exclusión se seleccionaron un total de 6 artículos (4 estudios caso-control, 1 estudio de cohortes y 1 meta-análisis). De estos, 2 estudios de caso-control y el estudio de cohortes obtuvieron una asociación estadísticamente significativa entre la exposición laboral al amianto y el cáncer de laringe. El meta-análisis sugiere asociación, aunque sin obtener significación estadística, mientras que los 2 restantes estudios de caso-control reportaron una asociación no estadísticamente significativa entre el cáncer de laringe y la exposición laboral al amianto.

Discusión/Conclusión: En base a los resultados, se evidencia la existencia de discrepancia en cuanto a la asociación, entre la exposición laboral al amianto y el cáncer de laringe. Se evidenció un aumento del riesgo de presentar cáncer de laringe, estadísticamente significativo con el aumento de la frecuencia de exposición al amianto. Respecto al tipo de cáncer de laringe, un estudio consiguió una asociación estadísticamente significativa, para el localizado a nivel epiglótico.

Sería recomendable seguir realizando estudios de diseño observacional, de mayor duración y tamaño muestral para así aumentar la significación estadística y minimizar la posibilidad de sesgos.

Med Segur Trab (Internet) 2015; 61 (239) 284-294

Palabras clave: *Cáncer de laringe, exposición ocupacional, enfermedad profesional, amianto.*

INTRODUCTION

Laryngeal cancer has an annual incidence of 4.5 in Spain and ranks 10th in frequency of tumors¹. Its incidence worldwide is highly variable but there are countries, such as Central and Eastern Europe as well as Mediterranean countries where the incidence has increased².

The most common histological type is squamous. You can submit three locations: supraglottic, glottic (vocal cords) and subglottic (relatively rare). Neoplasms of supraglottic localization as well as those of the oropharynx, are usually presented with local metastatic nodules, while the glottic level manifest with dysphonia and so are diagnosed relatively early, so they usually have a better prognosis than the other localizations³.

Laryngeal cancer is associated with non-occupational factors such as consumption of tobacco and alcohol, with known synergistic effect and dose-response relationship. Other factors associated with laryngeal cancer are race, diet and oral hygiene, with a strong socioeconomic gradient. Although association with exposure to asbestos is controversial³.

In Spain for years, many companies have used asbestos in their production processes, especially in construction related activities. Although the marketing and use of asbestos are prohibited since 2002⁴.

The word asbestos is Greek and means inextinguishable. Asbestos is a rock that belongs to the family of silicates and which is subdivided into six minerals, three of which are used by the industry: chrysotile (white asbestos), crocidolite (blue asbestos) and amosite (brown asbestos). On microscopic examination there is a huge amount of agglomerated fibrils. Are so thin (5 microns long and 3 meters wide) that may be 50,000 to 1 mm in diameter. It is precisely this filamentous structure that confers remarkable qualities asbestos their absorption and insulation. It is fireproof, resistant to high temperatures (its melting point is 1500 degrees Celsius), is unchanged by bacteria, resistant to electricity, not spent, is stronger than steel and it's cheap.

His large-scale exploitation began in the late XIX century. Most used asbestos in the production of cement products, for producing tiles, panels and pressure pipes; as fire protection in walls and beams of buildings and to increase the fire resistance of cellulose and textile industry. Is known health risk posed by occupational exposure to asbestos fibers and that the latency period can be long.

The main health effects resulting from this exposure are asbestosis (pulmonary fibrosis), lung cancer and mesothelioma (pleural or peritoneal), association with other malignancies (gastrointestinal or laryngeal carcinomas) having also found. There is also an unconfirmed suspicion that asbestos can cause other cancers (kidney, ovarian, breast)⁵.

A systematic review that identified and assessed 35 prospective and 17 retrospective studies found no increased risk of laryngeal cancer in asbestos exposed, while a multicenter case-control study found a marginally significant excess risk for cancer of the larynx and hypopharynx, after adjusting for non-occupational factors such as social class, diet and consume alcohol and tobacco. Subsequent studies have found an association between exposure to asbestos and laryngeal cancer⁶⁻⁸.

Laryngeal cancer due to inhalation of asbestos dust has been included in Annex II of Royal Decree 1299/2006: supplementary list of occupational diseases is suspected and whose inclusion in the schedule of occupational diseases could be considered in the future³.

Despite its ban in 2001, the incidence of related diseases asbestos exposure has become a serious public health problem worldwide. Also due to its large latency period (between 20 and 50 years), it is anticipated that the pathology secondary to occupational exposure to asbestos in the late 70 will reach its peak incidence around 2010-2015.

OBJECTIVES

This systematic review aims to identify the latest scientific evidence of an association between occupational exposure to asbestos and laryngeal cancer.

The following specific objectives were formulated:

- Know the risk of laryngeal cancer, according to the frequency of occupational exposure to asbestos.
- Know vulnerability factors for laryngeal cancer in workers exposed to asbestos.
- Know the location of most frequent laryngeal cancer in relation to occupational exposure to asbestos.

MATERIALS AND METHODS

A search of scientific articles was performed, of articles published between 1999-2014 (last accessed date 30/11/2014), including one meta-analysis published in 1999 and 2012.

The consulted databases were MEDLINE, OSH, SCOPUS, IBECs and ILO, using descriptors and search equations below in [Table 1](#).

Table 1. Databases and search equations

Database	Descriptors, search equation
MEDLINE	1. Free search, limited by date and species (human only) Búsqueda libre, limitada por fecha y sólo en humanos: asbestos exposure laryngeal cancer Filters: Publication date from 1999/01/01 to 2014/12/31; Humans.
	2. Descriptors Search: ((«Laryngeal Neoplasms»[MeSH Terms]) AND Asbestos[MeSH Terms]) AND (((«Occupational Diseases»[MeSH Terms]) OR «Occupational Medicine»[MeSH Terms]) OR «Workplace»[MeSH Terms]) OR «Occupational Exposure»[MeSH Terms]).
	3. Descriptors Search limited by species (humans only): ((«Laryngeal Neoplasms»[MeSH Terms]) AND Asbestos[MeSH Terms]) AND (((«Occupational Diseases»[MeSH Terms]) OR «Occupational Medicine»[MeSH Terms]) OR «Workplace»[MeSH Terms]) OR «Occupational Exposure»[MeSH Terms]) Filters: Humans.
	4. Search limited by descriptors, species and publication date. ((«Laryngeal Neoplasms»[MeSH Terms]) AND Asbestos[MeSH Terms]) AND (((«Occupational Diseases»[MeSH Terms]) OR «Occupational Medicine»[MeSH Terms]) OR «Workplace»[MeSH Terms]) OR «Occupational Exposure»[MeSH Terms]) Filters: Publication date from 1999/01/01 to 2014/12/31; Humans.
IBECs (Virtual Library of Health Science).	Free search: CANCER AND LARINGE\$ AND ASBESTO\$.
International Labour Organization (ILO)	Free search: ASBESTOS EXPOSURE LARYNGEAL CANCER.
OSH UPDATE + FIRE	Búsqueda a través de raíz y descriptores: Search by root and descriptors: «LARYNGEAL CANCER» OR «LARYNGEAL DISEASES» OR «LARYNX CANCER» OR «LARYNX CARCINOMA» OR «LARYNX CARCINOMAS» OR «LARYNX TUMORS» AND ASBESTOSS.

Database	Descriptors, search equation
SCOPUS	1. Free search: (TITLE-ABS-KEY («LARYNGEAL NEOPLASMS»)) AND («ASBESTOS») AND («OCCUPATIONAL EXPOSURE»).
	2. Search limited by publication date 1999-2014: (TITLE-ABS-KEY («LARYNGEAL NEOPLASMS»)) AND («ASBESTOS») AND («OCCUPATIONAL EXPOSURE») AND (LIMIT-TO (PUBYEAR, 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR, 2012) OR LIMIT-TO (PUBYEAR, 2011) OR LIMIT-TO (PUBYEAR, 2010) OR LIMIT-TO (PUBYEAR, 2009) OR LIMIT-TO (PUBYEAR, 2008) OR LIMIT-TO (PUBYEAR, 2007) OR LIMIT-TO (PUBYEAR, 2006) OR LIMIT-TO (PUBYEAR, 2005) OR LIMIT-TO (PUBYEAR, 2004) OR LIMIT-TO (PUBYEAR, 2003) OR LIMIT-TO (PUBYEAR, 2002) OR LIMIT-TO (PUBYEAR, 2000) OR LIMIT-TO (PUBYEAR, 1999)).
	3. Search limited by publication date and only original articles in the medicine and environmental science area: (TITLE-ABS-KEY («Laryngeal Neoplasms») AND TITLE-ABS-KEY («Asbestos») OR TITLE-ABS-KEY («Occupational Exposure») OR TITLE-ABS-KEY («Occupational Medicine») OR TITLE-ABS-KEY («Occupational Diseases») OR TITLE-ABS-KEY («Workplace») OR TITLE-ABS-KEY («Occupational,Accident»)) AND SUBJAREA (mult OR medi OR nurs OR vete OR dent OR heal) AND PUBYEAR > 1998 AND PUBYEAR < 2015R nurs OR vete OR dent OR heal) AND PUBYEAR > 1998 AND PUBYEAR < 2015

Based on inclusion and exclusion criteria (Table 2 and 3) articles were selected for further systematic reading.

Table 2. Inclusion criteria

Variables	Inclusion Criteria
Topic.	Occupational exposure relationship between asbestos and laryngeal cancer.
Publication date.	Published between 1999-2014.
Sample size.	n>30 (in cross-sectional studies).
Population.	Humans, with occupational exposure.
Publication language.	Spanish, English, French, Italian, Portuguese.

Table 3. Exclusion criteria

Variables	Exclusión Criteria
Duplicates.	Among databases consulted and authors.
Non-original studies.	Reviews, editorials letters, expert opinions, etc.
Design type.	Prevalence studies without control group.

Once selected and evaluated, the abstracts of the articles were reviewed by each of the researchers independently, and controversies found were discussed in a joint team review, evaluating the inclusion or exclusion in the systematic review.

Subsequently the full text articles were obtained through the National Library of Health Sciences, of the Institute of Health Carlos III.

To facilitate reading and systematic analysis a data information capture table was designed. including aspects related with: article identification, method, results and conclusions (Table 4).

Table 4. Studied variables in the systematic reading of articles

Identificación	Método	Resultados y conclusiones
Titles.	Study design.	Limitations.
Author.	Sample size.	Results.
Publication year.	objectives.	Evidence level.
Population.	Explosure variable.	SIGN (Criteria) ⁹ .
	Effect variable.	
	Bias control.	

The evidence level of the collected articles were controlled via SIGN criteria⁹. The results were the following: Goodman¹³ 1+, Purdue⁷ 2++, Ramroth¹⁰ 2+, Marchand¹² 2+, Berrino⁶ 2+, Elci¹¹ 2+.

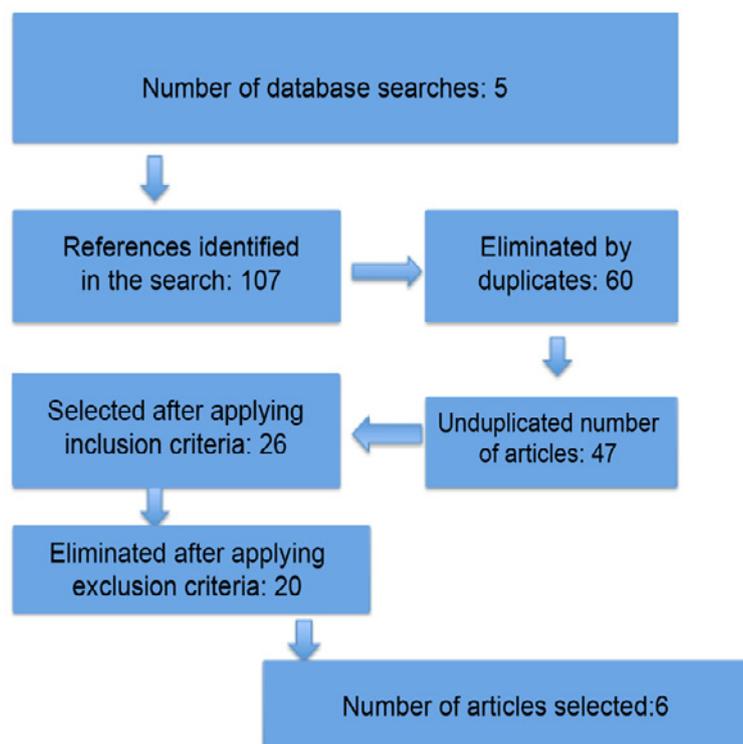
RESULTS

Table 5 shows the total number of items recovered in each of the databases searched. All this applying the various search equations and the number selected for systematic review according to the selection process exemplified in (Figure 1) items.

Table 5. Number of retrieved articles and selected

Databases	Recovered items	Selected items
MEDLINE.	13	6
IBECS.	3	-
OSH UPDATE.	35	-
SCOPUS.	52	-
ILO.	4	-
Total items.	107	6

Figure 1. Search results



A total of 107 references, 60 of which were removed for being recovered duplicate. He then proceeded to read summaries, after that 21 items were eliminated for failing to meet any criteria for inclusion, and 20 meet any of the exclusion criteria. Total items were selected for systematic reading 6.

The type of design of the studies included in this review were: 1 meta-analysis, one cohort study, 4 case-control studies.

The following general information about each item in descending chronological order says.

- RAMROTH H.¹⁰ 2011, conducted a case-control study collected between 1998 and 2000, with a total sample of 73 cases and 158 controls. The measure of association used was the Odds Ratio, divided into two groups: the first taking into account any asbestos exposure (OR 1.2, 95% CI 0.84 to 1.9) and the second only employee exposure to asbestos insulation works (OR 1.0, 95% CI 0.67 to 1.6). The study controls for confounders (snuff, alcohol, educational level and degree of exposure). The result of the study is not significant for the association.
- PURDUE, M.⁷ 2006, conducted a cohort study with a sample of 477 non-exposed and 66 exposed to asbestos in varying degrees of exposure (33 long, 29 moderately exposed and 4 highly exposed). His measure of association was the RR in unexposed 1.0, and always exposed 1.9 (95% CI 1.2-3.1), moderately exposed 2.3 (95% CI 1.4-3.8) and highly exposed 0.8 (95% CI 0.2-3.3) showing and a positive correlation between exposure to asbestos and labor-related laryngeal cancer.
- BERRINO, F.⁶ 2003, a study conducted from 1979 to 1982 cases and controls with a sample of 1010 cases of laryngeal / hypopharyngeal cancer and 2176 controls. Subsequently eliminating subjects older than 55 years later, leaving a sample of 315 cases and 819 controls. Confounding factors such as tobacco, alcohol consumption and diet were monitored. The measure of association used was the Odds Ratio.
Specific objectives and frequency of exposure to asbestos were raised. 151 workers exposed to possible exposure frequency, had a result of: OR 1.7 (95% CI 1.0-2.8); and 67 workers exposed to probable frequency of exposure had an OR of 2.7 (95% CI 1.4-5.2). Coming to the conclusion that the result is statistically significant for those with probable exposure frequency, compared to possible frequency of exposure with no significant result.
- ELCI, O.¹¹ 2002, conducted a case-control study of 150 cases and 250 controls by evaluating the relationship between exposure to asbestos and labor-related laryngeal cancer using to measure association Odds Ratio with a score of 1 (95% CI 0.8-1.3), expressing a non-significant result for the association.
- MARCHAND¹² 2000, conducted a study of the relationship of larynx and hypopharynx cancer with occupational exposure to asbestos case-control. Data were collected in France between 1989-1991, with a sample of 315 cases of laryngeal cancer and 305 controls.
As a measure of association used the Odds Ratio (OR 1.24, 95% CI 0.83 to 1.9). In turn he made a division of laryngeal cancer according to location (epilaringe, glottis and subglottis). Took account control potential confounders the tobacco, alcohol and age. A statistically significant relationship between the epiglottis cancer (OR 2.22, 95% CI 1.05 to 4.71) was found and occupational exposure to asbestos, while the results for which others were not statistically significant locations.
- GOODMAN¹³. 1999, performed a meta-analysis consisting of 69 cohort studies reported morbidity and mortality, to determine the magnitude of association between occupational exposure to asbestos and lung cancer as well as cancer research different locations. A meta-SMR for each type of cancer (lung, laryngeal, esophageal, stomach, colorectal, kidney, bladder, or urethra, prostate) reporting

for laryngeal cancer, 157 with latency (95% CI 95-245) and 133 was calculated without latency (95% CI 114-155), an association between asbestos and laryngeal cancer is suggested, without accompanying statistical significance for dose-response effect. The study did not include confounding factors (such as consumption of snuff I alcohol) by limited information on the habit in different studies. Likewise, no clear association between asbestos and other cancers was observed, pushing the lung.

The following table (Table 6), collected globally various studies were collected for the systematic review examines the relationship between laryngeal cancer and occupational exposure to asbestos.

Table 6. Studies examining the relationship between laryngeal cancer and occupational exposure to asbestos

Author	Year	Design	Sample	Extent of association	IC = 95%	Level of evidence
H. Ramroth	2011	Case-Control	73 cases 158 controls	JSQ OR = 1.2 SCL OR = 1.0	0.84 - 1.9 0.67 - 1.6	2
Purdue M.P.	2006	Cohorts	33 exposed (always) 477 no-exposed	RR = 1.9	1.2 - 3.1	2
Berrino	2003	Case-Control	315 cases 819 controls	OR = 1.7 OR = 2.7	1.0 - 2.8 1.4 - 5.2	2
Elci , O.C.	2002	Case-Control	150 cases 250 controls	OR = 1	0.83 - 1.3	2
Marchand	2000	Case-Control	315 cases 305 controls	OR = 1.24 OR = 2.22	0.83 - 1.9 1.05 - 4.71	2
Goodman	1999	MTA	69 estudios de cohorts	Meta-SMR 157 with latency 133 without latency	95 - 245 114 - 155	1

Both Table 7, 8 and 9 grouped the studies according to analyze the frequency of exposure to asbestos and the risk of laryngeal cancer; analyzing the vulnerability factors for cancer of the larynx; and analyzing the most common location of laryngeal cancer in relation to occupational exposure to asbestos.

Table 7. Studies examining the frequency of exposure to asbestos and the risk of laryngeal cancer

Author	Design	Sample	Frequency of exposure	Extent of association	IC = 95%
H. Ramroth	Case-Control	73 cases 158 controls	0 horas 0-940 h 940-5280 h > 5280 h	OR = 0.95 OR = 1.9 OR = 0.89	0.51 - 1.8 1.1 - 3.4 0.49 - 1.6
Purdue, M.P.	Cohorts	209 N.E. 16 Exp. 2 Exp. 18 Exp.	Never Moderate High Consistently	RR = 1.0 RR = 2.3 RR = 0.8 RR = 1.9	1.4 - 3.6 0.2 - 3.3 1.2 - 3.1
Berrino	Case-Control	151 exp 67 exp	Posible Probablyniveo	OR = 1.7 OR = 2.7	1.0 - 2.8 1.4 - 5.2
Marchand	Case-Control	315 cases 305 controls	Cumulative level: Low Intermediate High	OR = 1.10 OR = 1.20 OR = 1.47	0.66 - 1.82 0.73 - 1.99 0.87 - 2.46

Table 8. Study that analyzes the various factors of vulnerability for developing laryngeal cancer in workers exposed to asbestos

Author	Design	Sample	Vulnerability factors	Med. association	IC = 95%
Elci, O.C.	Case-Control	126c 227c	Silica powder	OR = 1,5	1,2 - 1,9
		109c 173c	Wood flour	OR = 1,1	0,8 - 1,4
		54c 74c	Cotton dust	OR = 1,3	0,9 - 1,9
		31c 37c	Grain dust	OR = 1,3	0,8 - 2,1

Table 9. Studies that analyze the most frequent location of laryngeal in relation to occupational exposure to asbestos

Author	Design	Sample	Location anatomical	Med. association	IC = 95%
Elci, O.C.	Case-Control	71 cases 250 controls	Supraglottic	OR = 1,0	0,8 - 1,4
		28 cases 250 controls	Glottic	OR = 0,8	0,5 - 1,2
		150 cases 250 Controls	All	OR = 1,0	0,8 - 1,3
Marchand	Case-Control	315 cases	Epilaringe†	OR = 2,22	1,05 - 4,71
		305 controls	Supraglottis Glottis-subglottis	OR = 1,27 OR = 1,44	0,58 - 2,78 0,73 - 2,83

† The epilaringe includes the free edge of the epiglottis, the back surface of suprahoide portion, the union of the three folds (the aryepiglottic fold, the arytenoid fold and interarytenoid fissures).

DISCUSSION AND CONCLUSIONS

The results of the systematic review of 6 studies reviewed (1 meta-analysis, one study cohort and 4 case-control)^{6, 7, 10-13} suggests a discrepancy regarding the association between exposure character work to asbestos and laryngeal cancer. It is noted that two recently published studies (study cohort and case-control study)^{6, 7} a significant positive association was demonstrated. As for the meta-analysis¹³ there is a suggestion of association, not being significantly positive. And in contrast observed a statistically significant relationship in the remaining three studies (case-control)¹⁰⁻¹².

But if we go deeper in those studies in which the crude OR gave no significant values in their results found that Elci¹¹ study finds a significant OR in the combined asbestos-silica exposure: OR = 1.5 (1.2 to 1.9). In the study of H. Ramroth¹⁰ to stratify by frequency of exposure is significant OR: OR = 1.9 (1.1 to 3.4). And finally in the study of Marchand¹², when stratified by location found an association to study the localization of the tumor epi-larynx: OR = 2.2 (1.05 to 4.71).

In this review we have tried a number of specific objectives. With respect to the frequency of exposure to asbestos and the risk of laryngeal cancer, a sample rate possible occupational exposure to asbestos and one with probable was taken. Giving a statistically significant for probable exposure and a nonsignificant result for possible exposure result. All data subjects and other non-occupational controlled variables such as tobacco, alcohol and diet⁶. Another study⁷ that assesses the frequency of exposure, showed an increased risk of laryngeal cancer for exposed constantly and moderately to asbestos. Showing results demonstrate a statistically significant association. However highly exposed, achieved a statistically significant result. We believe that this result could be seen influenced by the small sample size. The following study⁹ also takes into account the frequency of exposure to asbestos. To distinguish between a low or high exposure, classified into four groups according to the hours of work set (0 h, 0-940 h, 940-5280 h over 5280 h). Statistical data obtained after this classification suggest an increased risk.

However, after adjust to tobacco and alcohol use data obtained significantly decreased, found no statistically significant relationship. The latest study of case-control¹², shows that the risk of cancer increases with increasing cumulative exposure level. However, the results finally found a non-significant association.

Regarding vulnerability factors for cancer of the larynx in workers exposed to asbestos, we analyzed a study¹¹ where exposure to occupational dusts different character and the risk of laryngeal cancer was compared. Found statistically significant results for laryngeal cancer risk from exposure to silica dust (often moderate and high exposure) being the results adjusted for age and alcohol consumption. While other exposures to wood dust, grain and cotton was not statistically significant relationship was evident.

Regarding the most frequent anatomical location laryngeal cancer was found in a study of case-control, a statistically significant relationship between occupational exposure to asbestos and laryngeal cancer, localized at the epilaringe level¹².

The other study¹¹ which analyzed the risk according to anatomic location, shows no statistically significant results for different locations (supraglottic and glottic) susceptible of laryngeal cancer from exposure to asbestos. The difficulty in the study to estimate and identify asbestos exposure could prevent the result of finding a meaningful relationship.

Finally, as limitations of this review, we found:

- Lack of publications in the last four years.
- Few designs directed to the specific study of the relationship between laryngeal cancer and asbestos exposure.
- Not all studies controlled for confounding factors (age, alcohol, snuff, chronic exposure to non-occupational asbestos).
- Difficulty study of the subject by the latency period of cancer.
- Some studies with small sample size.

We conclude that further research on the association between laryngeal cancer and occupational exposure to asbestos are still needed additional observational, long lasting and with a larger sample size, so studies would get increased statistical significance and minimize the possibility of biases (age, alcohol, tobacco, chronic exposure to asbestos, etc). We also believe it is necessary to increase research that pose as an initial hypothesis the relationship between laryngeal cancer and occupational exposure to asbestos. Since most of the studies dealing with the association of lung cancer due to occupational exposure to asbestos.

BIBLIOGRAPHIC REFERENCES

1. G. López-Abente, M. Pollán, N. Aragonés, B. Pérez Gómez, V. Hernández Barrera, V. Lope, B. Suárez. Situación del cáncer en España: incidencia. Área de Epidemiología Ambiental y Cáncer. Centro Nacional de Epidemiología. Instituto de Salud Carlos III. 2004. Tabla 4.
2. Paget-Bailly S, Cyr D, Luce D. Occupational exposures and cancer of the larynx-systematic review and meta-analysis. *J Occup Environ Med* 2012 Jan;54(1):71-84.
3. Villanueva-Ballester, García-Gómez, Martínez-Vidal, Elvira-Espinosa, García-López, López-Menduiña, Coto-Fernández, Anes-del-Amo. Protocolo de vigilancia específica: Amianto (3era edición). Ministerio de sanidad, servicios sociales e igualdad. Sanidad 2013. NIPO en línea: 680-13-022-9.
4. López-Abente, García-Gómez, Menéndez-Navarro. Pleural cancer mortality in Spain: time-trends and updating of predictions up to 2020. *BMC Cancer* 2013;13:528.
5. García-Gómez, Artieda-Pellejero, Esteban-Buena. La vigilancia de la salud de los trabajadores expuestos al amianto: ejemplo de colaboración entre el sistema de prevención de riesgos laborales y el sistema nacional de salud. *Rev Esp Salud Pública* 2006 Ene-Feb N.1;80: 27-39.
6. Berrino F, Richiardi L, Boffetta P. Occupation and larynx and hypopharynx cancer: a job-exposure matrix approach in an international case-control study in France, Italy, Spain and Switzerland. *Cancer Causes Control*. 2003 Apr;14(3):213-23.

7. Purdue MP, Järholm B, Bergdahl IA, Hayes RB, Baris D. Occupational exposures and head and neck cancers among Swedish construction workers. *Scand J Work Environ Health* 2006;270-275.
8. Brown T, Darnton A, Fortunato L, Rushton L. Occupational cancer in Britain. *Br J Cancer* 2012;107: S56-S70.
9. Harbour R, Miller J, for the Scottish Intercollegiate Guidelines Network Grading Review Group. A new system for grading recommendations in evidence based guidelines. *BMJ* 2001; 323: 334-6.
10. Ramroth H, Ahrens W, Dietz A, Becher H. Occupational asbestos exposure as a risk factor for laryngeal carcinoma in a population-based case-control study from Germany. *Am J Ind Med* 2011;54(7):510-514.
11. Elci OC, Akpınar-Elci M, Blair A, Dosemeci M. Occupational dust exposure and the risk of laryngeal cancer in Turkey. *Scand J Work Environ Health* 2002;278-284.
12. Marchand J, Luce D, Leclerc A, Goldberg P, Orłowski E, Bugel I, et al. Laryngeal and hypopharyngeal cancer and occupational exposure to asbestos and man-made vitreous fibers: Results of a case-control study. *Am J Ind Med* 2000;37(6):581-589.
13. Goodman M, Morgan R, Ray R. Cancer in asbestos-exposed occupational cohorts: a meta-analysis. *Cancer Causes and Control* 10: 453±465, 1999.