Cancer Letters ■■ (2015) ■■–■■

Contents lists available at ScienceDirect

Cancer Letters

journal homepage: www.elsevier.com/locate/canlet

Mini-review

Radon exposure and oropharyngeal cancer risk

Tania Salgado-Espinosa [a], Juan Miguel Barros-Dios [a,b,c], Alberto Ruano-Ravina [a,b,*]

[a] Department of Preventive Medicine and Public Health, University of Santiago de Compostela, Spain
[b] CIBER de Epidemiología y Salud Pública, CIBERESP, Spain
[c] Service of Preventive Medicine, University Hospital Complex of Santiago de Compostela, Spain

ARTICLE INFO

Article history:
Received 17 June 2015
Received in revised form 18 August 2015
Accepted 19 August 2015

Keywords:
Oropharyngeal neoplasms
Systematic review
Radon

ABSTRACT

Oropharyngeal cancer is a multifactorial disease. Alcohol and tobacco are the main risk factors. Radon is a human carcinogen linked to lung cancer risk, but its influence in other cancers is not well known. We aim to assess the effect of radon exposure on the risk of oral and pharyngeal cancer through a systematic review of the scientific literature. This review performs a qualitative analysis of the available studies. 13 cohort studies were included, most of them mortality studies, which analysed the relationship between occupational or residential radon exposure with oropharyngeal cancer mortality or incidence. Most of the included studies found no association between radon exposure and oral and pharyngeal cancer. This lack of effect was observed in miners studies and in general population studies. Further research is necessary to quantify if this association really exists and its magnitude, specially performing studies in general population, preferably living in areas with high radon levels.

Introduction

Oropharyngeal cancer is the eleventh most common cancer in the world [1]. Oral cancer incidence is globally growing, especially in developing countries. This is due to the increasing prevalence of some risk factors and population ageing. In Europe, incidence and mortality rates for both sexes are 11 per 100.000 and 4.7 per 100.000 for males and females, respectively [2]. In Spain, the estimated incidence and mortality rates are 8.8 per 100.000 and 2.4 per 100.000 for oral cavity cancer, and 3.3 per 100.000 and 1.6 per 100.000 for pharyngeal cancer for men and women, respectively [3].

Oral and pharyngeal cancers are multifactorial diseases. Tobacco and alcohol are the most important risk factors. Between 43 and 60% of oral cavity, pharynx or nasopharynx cancers may be due to tobacco consumption with or without alcohol consumption [4]. These two factors acting together produce a synergistic multiplicative effect that significantly increases the risk [5]. Other forms of tobacco consumption such as betel quid are also important factors that contribute to the risk especially in Asiatic regions [6].

There are also specific risk factors depending on the oral cavity region: excessive solar exposition is the most important factor for lip cancer, and Human Papillomavirus is a risk factor for pharyngeal cancer principally, and its incidence is growing [7]. Moreover, unhealthy diets without fruit and vegetable consumption, or a low sociocultural level with no access to medical assistance or no oral hygiene education, preclude a higher oropharyngeal cancer risk [8].

Radon is a noble radioactive gas. It emanates from rocks and soils and tends to concentrate in closed spaces such as houses or indoor workplaces. When radon gas is inhaled, densely ionising alpha particles emitted by deposited short-lived decay products of radon can interact with biological tissues leading to DNA damage. Cumulative exposure to decay products of radon in low concentration is related to a higher oncogenic risk. Radon was classified as a human lung carcinogen in 1988 by the IARC and nowadays there is strong evidence about its relationship with lung cancer in the general population [9]. Residential radon was recently included as an exposure to avoid in the last version of the European Code Against Cancer [10].

Although there is strong evidence of the relationship between residential radon and lung cancer, the possible association with other neoplasms is under discussion. Published studies have found an association between residential radon and leukaemia, central nervous system [11], skin cancer [12] and oesophageal cancer [13]. We could not find any study assessing exclusively the possible relationship between oral and pharyngeal cancer and radon, but it is possible to extract data from larger studies where many cancer types have been analysed. Knowing that radon can damage by inhalation, and the carcinogenicity of α particles, it might be biologically plausible that radon exposure could pose a risk for oral and pharyngeal cancers.

We aim to analyse the possible association between radon exposure and cancers of the oral cavity and pharynx through a systematic review of the scientific literature.

* Corresponding author. Tel.: +34 881 812267; fax: +34 881 872282.
E-mail address: alberto.ruano@usc.es (A. Ruano-Ravina).

http://dx.doi.org/10.1016/j.canlet.2015.08.025
0304-3835/

Please cite this article in press as: Tania Salgado-Espinosa, Juan Miguel Barros-Dios, Alberto Ruano-Ravina, Radon exposure and oropharyngeal cancer risk, Cancer Letters (2015), doi: 10.1016/j.canlet.2015.08.025

Table 1
Quality scale used to score the included studies.

Item assessed	Characteristic	Weight
Total sample size	200–500	0
	501–1000	1
	>1000	2
Number of never smoking cases	<150	0
	151–400	1
	>400	2
Covariable adjustment (number)	2 (age and sex)	0
	>2	2
Study design	Hospital-based case–control study	0
	Population-based case–control study	1
	Cohort study	2
	Pooling study	3
Radon measurements	Not specified or charcoal	0
	Alpha-track or other	1
Total		10

Materials and Methods

We made a systematic review of the scientific literature using MEDLINE and EMBASE databases in order to find all the articles analysing the possible relationship between radon exposure and oral or pharyngeal cancer. We used a combination of free text words and MeSH terms in order to find all the available publications. We decided to perform an exhaustive search instead of a pertinent search in order to find all the available papers on the topic at the cost of obtaining many useless works that were disregarded. All results were merged and duplicates were excluded. Articles obtained from both databases were highly overlapped.

We established the following inclusion criteria: a) regarding the study population: we included miners and the general population, b) language: we included papers published in English and Spanish, c) study design: we included meta-analysis, systematic reviews, cohort studies (based on incidence or mortality), case–control studies and cross-sectional studies, d) sample size: we did not establish any limit, and, e) publication period: we included all the papers retrieved, independently on the publication date. We used a standardised table to extract information homogeneously from each paper and which served to build evidence tables.

We built a quality scale to rank the quality of the included studies. This quality scale was adapted from a previously published scale to assess published studies on residential radon and lung cancer risk in never smokers [14]. The scale appears in Table 1 and reflects different items with a range from 0 to 10 points, 10 points being the best study. The scale considered the study design, sample size, number of included cases, covariables considered and follow up time (for cohort studies) or study setting (for case–control studies). Two reviewers applied the scale to the included studies, and if discrepancies were present they were solved by consensus. The scale was easy to use and there were very few discrepancies between the reviewers of the included papers.

It was not possible to perform a meta-analysis because of the heterogeneity of the available studies, so we made a qualitative synthesis of the information.

Results

The search resulted in the inclusion of 13 articles, all of them written in English. Eleven were studies on miners, and the other two were performed on the general population. The studies were published between 1988 and 2014, and were carried out in Europe or North America except for one study in Japan. The characteristics of the included studies are shown in Table 2.

Included studies are mostly mortality studies, where the number of observed deaths from oral or pharyngeal cancer is compared with the number of expected deaths for a population with similar characteristics, or where the excess of relative risk is calculated for radon exposure for a given unit of time (Excess Relative Risk/Working Level Months).

Miner studies

Some studies that obtained observed vs expected deaths (O/E or SMR) did not have a significant number of observed cases. This is the case of the iron miners study in Sweden [16], where there are no events of oropharyngeal cancer in a cohort of 1294 miners followed between 1951 and 1990. In the French cohort of uranium miners [24] the result O/E is 0.82 with three observed cases. In the Colorado Plateau cohort [19] the obtained results are given separately for white miners, with 6 observed cases and a rate O/E = 0.86 in a sample of 3358 subjects. There were no cases for American Indian miners in a sample of 779 subjects. The fluorspar miners study in Terranova [15] observed an O/E = 2.74 for oropharyngeal cancer (6 cases), and O/E = 9.78 for salivary gland cancer (2 cases), in a sample of 2224 subjects. This last study is the only study where we can observe an increasing mortality in relation with radon exposure.

Table 2
Description of the included studies.

Author (year)	Location of the study	Studied population	Study design	Observed effect	Observations	Score
H.I. Morrison (1988) [15]	Terranova (Canada)	Fluorspar miners	Mortality in a cohort study	O/E = 2.74 oropharynx O/E = 9.78 salivary glands	Oropharynx: 6 cases observed Salivary glands: 2 cases observed	5
M. Timarche (1993) [24]	France	Uranium miners	Mortality in a cohort study	O/E = 0.82	3 cases observed	4
Sarah C. Darby (1995) [16]	Sweden	Iron miners	Mortality in a cohort study	O/E = 0	No events observed	4
Sarah C. Darby (1995) [16]	Meta-analysis	Miners	Mortality in 11 cohort studies	O/E = 0.52		6
Wemin Ye (1998) [17]	Japan	General population	Mortality in a cohort study	O/E = 0.64	2 cases observed	7
B. Vacquier (2008) [25]	France	Uranium miners	Mortality in a cohort study	O/E = 0.91		5
M. Kreuzer (2008) [18]	Germany	Uranium miners	Mortality in a cohort study	O/E = 0.80		5
M.K. Schubauer-Berigan et al. (2009) [19]	United States	Uranium miners	Mortality in a cohort study	O/E = 0.86 for white miners; O/E = 0 for American Indian miners	White miners: 6 cases American Indian miners: 0 cases	5
M. Kreuzer (2010) [26]	Germany	Uranium miners	Mortality in a cohort study	ERR/100WLM = 0.047 oral ERR/100WLM = 0.164 pharynx	p = 0.481 oral p = 0.114 pharynx	5
L. Walsh (2010) [20]	Germany	Uranium miners	Mortality in a cohort study	ERR/100WLM = 0.045 oral ERR/100WLM = 0.163 pharynx	95% CI –0.085; 0.175 oral 95% CI –0.042; 0.367 pharynx	6
M. Kulich (2011) [21]	Czech Republic	Uranium miners	Incidence in a cohort study	RR = 0.48	95% CI 0.21–1.12	6
Michelle C. Turner (2012) [22]	Unites States	General population	Mortality in a cohort study	HR = 0.80	95% CI 0.59–1.80	9
M. Kreuzer (2014) [23]	Germany	Uranium miners	Mortality in a cohort study	ERR/100WLM = 0.077 pharynx ERR/100WLM = 0.033 mouth and tongue	p = 0.20 p > 0.5	7

Please cite this article in press as: Tania Salgado-Espinosa, Juan Miguel Barros-Dios, Alberto Ruano-Ravina, Radon exposure and oropharyngeal cancer risk, Cancer Letters (2015), doi: 10.1016/j.canlet.2015.08.025