Original Article

Meta-analysis of case-referent studies of specific environmental or occupational pollutants on lung cancer

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Abstract

BACKGROUND: Meta-analysis is a statistical tool for combining and integrating the results of independent studies of a given scientific issue. The present investigation was initiated to investigate case-referent studies of lung cancer risk from specific environmental and occupational pollutants, using detailed individual exposure data. **MATERIALS AND METHODS:** To examine the risk of lung cancer associated with environmental and occupational pollutants, a meta-analysis of published case-control studies was undertaken using a random effects model. For this study, the papers were selected for review from electronic search of PubMed, Medline and Google Scholar during 1990-2006. The principal outcome measure was the odds ratio for the risk of lung cancer. Twelve study reports detailing the relationship between the lung cancer and the type of exposure were identified. **RESULTS:** The odds ratio of asbestos, cooking fuel, cooking fumes, motor and diesel exhaust related to lung cancer were 1.67, 1.99, 2.52 and 1.42 (P<0.001), respectively. The odds ratio of metal fumes related to lung cancer was 1.28 (0.001<P<0.01). The combined odds ratio for the environmental and occupational exposure related to lung cancer was 1.67 (P<0.001). **CONCLUSIONS:** The meta-analysis of the present study shows the magnitude association between asbestos, cooking fumes, cooking fuels, motor and diesel exhaust, with lung cancer risk. Lung cancer risk may be reduced by controlling exposure levels.

Key words: Environmental, lung cancer, meta-analysis, pollution

Introduction

Epidemiologic studies from many countries have shown elevated risks of lung cancer in urban or industrially polluted areas, even when adjustment for smoking has been attempted.[1,2] Although, in several epidemiological studies exposure to diesel motor emissions (DME) show an elevated lung cancer risk, it is still controversial whether DME is a human carcinogen.[3] A number of occupations or occupational exposures are established or suspected risk factors for lung cancer. The International Agency for Research on Cancer has identified some occupational exposure factors as being carcinogenic to the human lung like metal fumes and asbestos.[4] While there is little controversy over the carcinogenic effect of asbestos, there is considerable uncertainty about the magnitude of the lung cancer risk.[5-7]

Also, cooking practices and exposure to cooking fumes and cooking fuel increase the risk of lung cancer.[8]

Until studies are pooled, meta-analysis offers the best opportunity for characterizing existing information. As far as, the methods of meta-analysis of different kind of studies are different, in this article, we present a meta-analysis of completed case-referent studies of environmental and occupational pollutants related to lung cancer. The present study is focused on lung cancer risk in relation to five environmental and occupational exposure factors; asbestos, cooking fuel, cooking fumes, metal fumes, motor and diesel exhaust. Given the results from the previous studies, one of the

unsolved problems is the magnitude of the exposures effect. So, the present study was launched to answer the following question:
How much is the magnitude of asbestos, cooking fuel, cooking fumes, metal fumes, motor and diesel exhaust related to lung cancer risk?

Materials and Methods

For this study, the papers were selected for review from an electronic search of PubMed, Medline and Google Scholar during 1990-2006. In the first step, the articles were retrieved using "lung cancer" and "case-control" from MeSH heading and keywords. Then at least one of the following MeSH headings and keywords such as "asbestos", "diesel exhaust", "metal fumes", "motor exhaust", "cooking fumes", "cooking fuel" and "pollution" were searched. The references to articles were crosschecked by the authors. The cited references in obtained studies were also reviewed to include all relevant articles. We did not attempt to locate unpublished studies.

We selected studies if they met the following eligibility criteria: they were case-control studies published as a paper in English and they focused on environmental and occupational pollutants. The outcome of all published studies was regarding the odds ratio of lung cancer. The disease was lung cancer and did not refer to any stage or classification of cancer. We classified the exposures as follows: diesel exhaust, motor exhaust, residents of industrial area and diesel motor emissions as "diesel and motor exhaust"; asbestos as "asbestos"; metals, iron and steel foundries and metal smelter as "metal fumes"; cooking fumes and lack of a separate kitchen as "cooking fumes"; cooking fuels, biomass fuel and mixed fuel as "cooking fuels". Also, based on what was in the original papers, we considered the exposures as environmental vs. occupational.

Over the period of sixteen years, 130 articles were found of which twelve articles were relevant to the defined criteria.[3,8-18]

Two researchers performed data collection and extraction independently. Differences in data extraction were resolved by discussion. Consistency and analysis were performed with a random effects model. Analysis involved the calculation of a common estimate of odds ratio between lung cancer and environmental and occupational pollutants with 95% confidence interval and a Chi-squared test of heterogeneity between the studies. The meta-analysis was performed using NCSS and PASS 2000 Released December 2005. The software requires the input of the number of cases and controls into a two-by-two table to calculate the combined odds ratio (OR) and 95% confidence interval (CI). Additional subgroup analyses were carried out to examine the effects of the type of exposure as well as environmental and occupational pollutants.

Results

Characteristic of case-referent studies of environmental and occupational pollutants on lung cancer from published studies based on what was in the original articles are shown in Table 1. As can be seen in the Table, the highest value for OR is related to cooking fumes for women in China (5.90; 95% CI (2.1-16.0)). Table 2 shows the results of meta-analysis for environmental and occupational pollutants related to lung cancer. As the Table shows, the odds ratio of asbestos, cooking fuel, cooking fumes, motor and diesel exhaust related to lung cancer were respectively 1.67, 1.99, 2.52, 1.42 and 1.39 ($P<0.001$). As well as, the odds ratio for metals fumes related to lung cancer was 1.28 ($0.0001<P<0.01$).

The Chi-square test for homogeneous studies showed that the null hypothesis was rejected. On the other hand, some studies had different effects. So, for analysis of data a random effects model was used.

Figure 1 shows the forest plot of odds ratio for different types of environmental and occupational pollutants. As the Figure shows the highest value of odds ratio for environmental and occupational pollutants is related to cooking fumes, whereas the lowest value is related to metal fumes.

Figure 2 shows the forest plot of odds ratio for environmental and occupational pollutants. The odds ratio for environmental pollutants was 1.99 (95% CI; 1.59-2.48) and for occupational pollutants was 1.49 (95% CI; 1.33-1.64), but there was not any statistical difference for risk of the occupational pollutants compare to the environmental pollutants related to lung cancer ($P>0.05$). Overall, the odds ratio for environmental and occupational pollutants related to lung cancer in this meta-analysis was 1.67 (95% CI; (1.47-1.87)).

Discussion

The main purpose of this study was to obtain a better understanding and magnitude of the relation between environmental and occupational pollutants with human lung cancer, according to meta-analysis.

Table 1: Characteristic of case-referent studies of environmental and occupational pollutants on lung cancer from published studies

Study	Kind of exposure	Exposure group	Sex	Country	Odds ratio (95% CI for OR)	Smoking status
Gustavsson P, 2000	Diesel exhaust	Occupational	Men	Sweden	1.35 (1.10-1.64)	Adjusted for smoking
Gustavsson P, 2000	Motor exhaust	Occupational	Men	Sweden	1.36 (1.12-1.65)	Adjusted for smoking
Gustavsson P, 2000	Asbestos	Occupational	Men	Sweden	1.83 (1.42-2.36)	Adjusted for smoking
Gustavsson P, 2000	Metals	Occupational	Men	Sweden	1.20 (0.96-1.50)	Adjusted for smoking
Nyberg F, 2000	Diesel exhaust	Environmental	Men	Sweden	1.41 (0.97-2.05)	Adjusted for smoking
Nyberg F, 2000	Asbestos	Occupational	Men	Sweden	1.47 (1.10-1.97)	Adjusted for smoking
Jockel KH, 1998	Asbestos	Occupational	Men and women	Germany	1.62 (1.28-2.05)	Adjusted for smoking
Jedrychowski W, 1990	Iron and steel foundries	Occupational	Men	Poland	1.48 (1.08-2.01)	Adjusted for smoking
Barbone F, 1995	Residents of industrial area	Environmental	Men	Italy	1.40 (1.00-2.10)	Adjusted for smoking
Liu Q, 1993	lack of a separate kitchen	Environmental	Women	China	5.90 (2.10-16-00)	Adjusted for smoking
Liu Q, 1993	lack of a separate kitchen	Environmental	Men	China	2.40 (1.40-4.20)	Adjusted for smoking
Sobue T, 1990	Cooking fuels	Environmental	Women	Japan	1.77 (1.08-2.91)	Non-smokers
Zhong L, 1999	lack of a separate kitchen	Environmental	Women	China	2.09 (1.58-3.57)	Non-smokers
Besso A, 2003	Metal smelter	Environmental	Men	Sweden	1.51 (0.90-2.54)	Adjusted for smoking
Kleinerman R, 2000	Cooking fumes	Environmental	Women	China	1.56 (1.00-2.50)	Non-smokers
Bruske_hohlfeld I, 1999	Diesel motor emissions	Occupational	Men	Germany	1.43 (1.23-1.67)	Adjusted for smoking
Behera D, 2005	Biomass fuel	Environmental	Women	India	5.33 (1.70-16.70)	Non-smokers
Behera D, 2005	Mixed fuel	Environmental	Women	India	3.04 (1.10-8.38)	Non-smokers

Meta-analysis is a statistical tool that combines or integrates the results of several studies to provide increased power for the combined studies.[19] About the methods of meta-analysis of different kind of studies being different, in the present paper, only case-referent studies were considered.

Epidemiological studies show that occupational exposure to asbestos, are associated with an increased risk of developing lung cancer.[9,10,20,21] However, the potential confounding effect from asbestos exposure may not have been fully controlled in many studies.[22] As expected, our study confirmed the well-known association between environmental exposure to asbestos (greater than 0.03 fibers/ml, over 30 years exposure) and lung cancer.

Table 2: Odds ratio and confidence interval of meta-analysis for environmental and occupational pollutants related to lung cancer

Type of exposure	OR	95% CI for OR		*P*-value
		Lower	Upper	
Asbestos	1.67	1.48	1.87	*P*<0.001
Cooking fuel	1.99	1.36	2.93	*P*<0.001
Cooking fumes	2.52	1.69	3.75	*P*<0.001
Metals fumes	1.28	1.08	1.52	0.001<*P*<0.01
Motor and diesel exhaust	1.42	1.26	1.59	*P*<0.001
Average	1.67	1.48	1.88	*P*<0.001

OR - Odds ratio, CI - Confidence interval

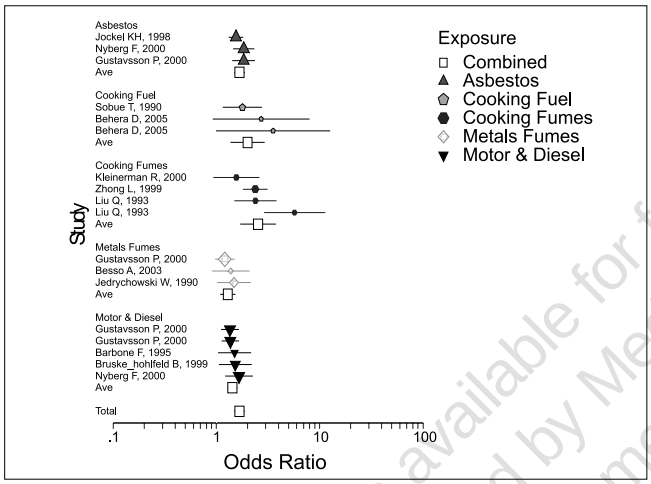

Figure 1: Forest plot of odds ratio for different studies

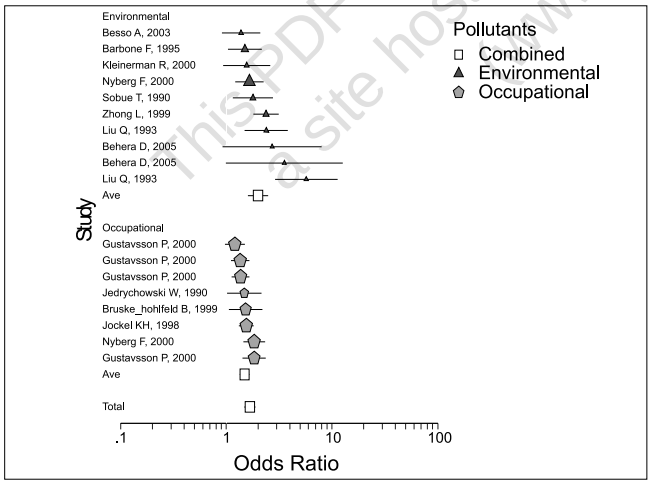

Figure 2: Forest plot of odds ratio for environmental and occupational pollutants

Also, significantly increased risks were observed in the metal industry, particularly in smelter and foundry workers.[23] International agency for research on cancer reported that welding of stainless steel is possibly associated with an increased risk of lung cancer.[24] The present meta-analysis showed that exposure to metal fumes (greater than 0.1 mg/m^3) is related to lung cancer.

Cooking practices, exposure to cooking fumes and a family history of cancer were found to increase the risk of lung cancer.[8] A trend in the association between lung cancer risk and factors pertaining to house and kitchen ventilation was observed and a decreasing risk of lung cancer was observed for several variables indicating better ventilation.[14] Also, different studies showed that some cooking fuels are related to lung cancer.[8,18] Our findings add further evidence to an association between cooking fume (more than 30 years exposure) and cooking fuel with lung cancer. Also it was found in this meta-analysis that it is a risk factor for lung cancer.

Air pollution data have indicated that lung cancer incidence is increased by 30-50% in areas with high ambient air pollution levels, compared with areas with lower levels.[25,26] Occupational exposure to diesel exhaust is widespread and the question of its carcinogenicity has been the focus of a large number of epidemiologic studies over the past years. Although, findings are contradictory, many evaluations seem to agree that occupational exposure to high levels of diesel exhaust for a prolonged period of time as well as non-occupational environments may be associated with an increased risk of lung cancer.[9,27-29] Furthermore, the results of the present meta-analysis showed exposure to motor exhaust (>1.1 mg of carbon monoxide/m^3) and diesel exhaust (>40 μg of nitrogen dioxide/m^3) increased the risk of lung cancer.

A single etiologic agent, cigarette smoking, is by far the leading cause of lung cancer, accounting for approximately 90% of lung cancer cases in the United States and other countries where cigarette smoking is common.[30,31] Since tobacco smoking is an established cause of lung cancer, in this meta-analysis we included only those studies in which the subjects were non-smokers or adjusted for smoking.

Conclusion

In this meta-analysis after excluding the effect of smoking on lung cancer, the relation between asbestos, cooking fuel, cooking fumes, metal fumes, motor and diesel exhaust with lung cancer was considered. So based on the combined OR, we observed that the relation between the specified risk factors and lung

cancer is still significant and the combined OR shows the magnitude of the relation.

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