A multifactorial analysis of radon exposure and lung cancer in the Middle Urals, Russia

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BACKGROUND: *We conducted a case-control study of residential radon and lung cancer in the town of Pervouralsk, the Middle Urals, Russia.*

METHODS: *We administered questionnaires to collect personified data on 200 cases of lung cancer and 237 controls. A complex of 26 known risk factors of lung cancer characterized each study participant. Concentrations of radon and thoron in residences of all cases and controls were measured using solid track detectors and MarkovñTerentyev aspiration method. Radiological risk was assessed using BEIR VI model. We also applied a multifactor analysis based on mathematical methods of pattern recognition to establish the contribution of residential radon/thoron in the development of lung cancer.*

RESULTS: *Results of our multifactor epidemiologic study showed that the contribution of natural radionuclides in the development of lung cancer in the population dwelling in multistory blocks of flats in cities of the Middle Urals, Russia ranged from 0.5-1%.*

CONCLUSION: *Comparison of the two methods allowed us to conclude that this contribution assessed in the multifactor analysis was more precise and correct.*

KEY WORDS: *Lung Neoplasms; Radon; Air Pollutants, Radioactive; Russia*

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INTRODUCTION

In 1987 the International Agency for Research of Cancer (IARC) evaluated radon and its decay products as human carcinogens (1). Large epidemiologic studies conducted in Western Europe in the '90s showed that this radioactive gas accounted for 50 to 90% of a radiological dose (2). Very high residential concentrations of radon were measured in Sweden and Finland (3-5). They were 5,000 times higher than its airborne concentrations. In Great Britain and the U.S.A. some concentrations of residential radon were 500 times higher than airborne ones (6).
Natural background radiation is rather high in the Middle Urals, Russia. There are over 1,000 local clusters of natural radioactive uranium, thorium and uranium/thorium mineralization and about 350 reservoirs with high contents of natural radionuclides approaching maximum allowable concentrations of the World Health Organization.
Results of radiation studies conducted by the Institute of Industrial Ecology of the Ural Branch of the Russian Academy of Sciences in the Middle Urals confirmed increased residential levels of radon. In some Ural towns radon concentrations were >100 Bq/m^3 in 30% of investigated residences and in 11% of residences the level of radon exceeded the criterion of safe residence. The results of this study also showed that the major part of the territory of the Middle Urals, including the biggest cities of Yekaterinburg, Nizhni Tagil, Pervouralsk, Kamensk-Uralsky and some others, were located within areas with high radon exposure (7). Based on data of the Ural Geological Committee, the dose of γ-radiation in Yekaterinburg, the capital of the Middle Urals, ranges from 8-10 μr/hr, Nizhni Tagil - 6-9 μr/hr, Pervouralsk - 5-7 μr/hr (8). A high contribution of thoron in the dose of radiation formed by natural radionuclides is a distinctive feature of the Middle Urals. High levels of radionuclides of thorium decay series in ore and building materials account for thoron accumulation in residences. On the whole, the dose of natural and industrial background radi-

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ation in the Urals comprises 70% of the total dose from all sources of ionizing radiation.

High natural background radiation in the Middle Urals accounts for the increased radiation dose of the population. So far, its medical and biological consequences have not been studied completely. In this connection, it was important to conduct special clinical and epidemiologic studies to establish adverse health effects of exposure to natural radionuclides, if any.

MATERIALS AND METHODS

Study design

The study was conducted in the town of Pervouralsk typical of the Middle Urals chosen for the following reasons:

The dose of γ-radiation in Pervouralsk ranges from 5 to 7 μr/hr;

The size of population is sufficiently large for a good epidemiologic study; on January 1, 1998 it was 164,500 people; the migration is insignificant;

The incidence of malignant newgrowths in the town is high. In 1998 the incidence rate was 350 per 100,000 people, 17% higher than the average regional rate. A large number of cancer cases allowed us to form representative study groups;

The proximity of Pervouralsk to the Regional Center of Yekaterinburg provided additional favorable conditions for high-grade diagnostics of malignancies and their morphological verification.

In our study we used data collected by the Institute of Industrial Ecology of the Ural Branch of the Russian Academy of Sciences in a number of studies of environmental pollution and occupational hazards at industrial plants of Pervouralsk in the past.

According to existing epidemiologic data, lung cancer is actually the only one medico-biological effect of radon exposure (9-14). At the same time, many different factors contribute to the development of lung cancer. According to the opinion of experts of the World Health Organization, the contribution of environmental factors in cancer morbidity is about 80%. As for lung cancer, many specialists think that smoking plays the major role in forming predisposition to this disease. The contribution of smoking in lung cancer is 70-90%, whereas the contribution of natural radiation is considered as very moderate - about 3% (15). Thus, to adequately assess the influence of radon exposure on the development of lung cancer, it was necessary to adjust for many confounders of carcinogenic risk.

Because of all mentioned above, we supposed that standard epidemiologic methods were insufficient for the study of residential radon and lung cancer. These methods allow one to eliminate effects of two to three confounders, whereas we had to adjust for a lot of them. We were of opinion that incomplete control of confounders could distort the contribution of residential radon. A cohort study involving a multifactor data analysis was the most adequate way of solving our task. We did not have to adjust for confounders because the analysis of their whole aggregate was performed at the same time. We had already successfully tested such a study technique in a number of epidemiologic studies of cancer (16-19).

The experimental group consisted of 200 lung cancer cases that got the disease in 1995-1998. The diagnosis of lung cancer was thoroughly verified instrumentally in all cases and morphologically in 70% of them. The control group included 237 people without malignant newgrowths randomly chosen in Pervouralsk according to the following criteria:

a) The age and gender of the controls should reflect the age and gender structure of the adult population of the town.

b) The proportion of controls dwelling in different districts of the town should be close to that of the whole population;

c) Occupational structure of controls should reflect that of the whole population.

Thus, we tried our best to match the controls to the population structure of Pervouralsk.

We used a specially developed questionnaire to collect personified data on all study participants. The questionnaire contained 84 questions divided into 26 classes of known risk factors of lung cancer: age, gender, nationality, workplace and length of service, occupational exposure to carcinogens, family history, chronic lung diseases, smoking and alcohol abuse, the source of drinking water, household characteristics (floor number, a gas cooker, type of building material, plastic wall cover, synthetic carpeting), the level of environmental pollution in the residential area, equivalent equilibrium concentrations (EEC) of residential radon and thoron. The majority of these risk factors need no explanation, so let us comment on just a few of them. The degree of soil contamination with Cr VI, B(a)P, and the complex of 12 toxicants in the residential area were evaluated on the basis of data collected by the Institute of Industrial Ecology in 1996.

When there were no measurements of waterborne radon, the type of a drinking water source was considered a marker of radon exposure. Upon this, we made an assumption that the level of radon was lower in open reservoirs than in artesian wells.

One of the most important constituents of our study was to determine the concentrations of radon and thoron in residences of the study participants. At present, concentrations of radon and its decay products are mainly measured by aspiration and solid track detectorsí methods. We applied the latter method to measure residential radon, the period of exposure being 1.5 months. Thoron was measured by Markov-Terentyev one-time aspiration method. Measurements were made in bedrooms and sitting rooms where people spent most of their time. The study of exposure lasted from November 1997 to April 1998. In the Middle Urals this time period could be considered relatively homogeneous in climatic and temperature conditions.

According to the standards of radiation safety (SRS-96) (20), a complex effect of radon and thoron is represented by “Equivalent Equilibrium Concentration of Radon Isotopes (EEC)” (C) estimated as follows:

$$C = 0.5 \text{ EEC of radon} + 4.6 \text{ EEC of thoron}$$

We needed an effective mathematical method of the multifactor data analysis essential for our study. We thought it possible to perform a high-quality analysis only based on a complex approach. Judging by our large experience in conducting similar investigations, a multifactor analysis based on mathematical methods of pattern recognition seemed the most appropriate.

The essence of the main task of pattern recognition called “teaching with a teacher” was as follows. We defined a set of characteristics (in this case, carcinogenic risk factors) used for the description of observations, i.e. cases and controls. Each observation was recorded as a numerical vector the coordinates of which were the values of chosen risk factors. The task was to construct mathematically a rule of decision allowing us to divide the combined multitude of chosen vectors into those of cases and controls. The criterion of quality of this rule was the percent recognition of cases and controls not included in the procedure of teaching (20% of all observations). We found confidence intervals using Bernulliís independent statistical tests. The percent of correctly classified observations ranging from 80% to 100% indicated a satisfactory recognition of cases and controls using the rule of decision, and proved a strong association between the complex of carcinogenic factors under study and the lung cancer.

The tasks solved in the course of mathematical processing of the questionnaire data were as follows:

- Assessment of sufficiency of the chosen complex of factors for the reliable description of differences between cases and controls;
- Quantitative assessment of each factorís relative significance, the value interpreted as the strength of effect on the development of lung cancer;
- Definition of the direction of each factor’s effect treated as an increase or decrease in the probability of developing the disease under exposure to this factor.

Sufficiency was evaluated by discriminant analysis. Estimating differences between mean values of factors in cases and controls assessed relative significance of each factor. We analyzed relative distribution of factors in cases and controls to establish the direction of effects of risk factors. All tasks were solved in the package of applied programs “KVAZAR” (21).

It was of great interest to compare the results of our study of residential radon and thoron and lung cancer with the results of mathematical models of risk assessment.

There are two major radiation risk assessment models ñ additive (the model of absolute risk) and multiplicative (the model of relative risk). Until recently, both models were considered equal. However, according to the recent publications of the International Committee for Radiological Protection - 60 (22,23) and 65 (5) the multiplicative model is more appropriate for lung cancer studies. We used BEIR VI model (24) in our study.

RESULTS AND DISCUSSION

We first analyzed whether the data obtained on 26 risk factors were sufficient for a reliable description of differences between cases and controls. The best results of recognition were 87.2% in controls and 89.7% in cases achieved in the analysis of a complex of 12 most significant risk factors, when analyzed samples were formed randomly. On the whole, we obtained very close results of the analysis of sub-complexes of 11-15 risk factors.

High results of pattern recognition gave us grounds to think that the chosen complex contained risk factors of lung cancer significant for the population under study. It should be also noted that those results were obtained using three different algorithms of recognition based on methods of “potential functions”, “committees of seniority” and “committees with the logic of the majority”, thus increasing the reliability of our study results.

Using a special algorithm (25) we calculated the confidence interval (CI) 81%-96%. We, therefore, concluded that the size of both case and control groups was sufficient for establishing a reliable association between residential radon and lung cancer.

After that, we analyzed relative significance of each factor and interpreted its value as the strength of its effects on lung cancer. The results are shown in Table 1.

Table 1 shows that the contribution of both residential radon and thoron in the development of lung cancer was found insignificant. The factor of the floor number did not rank high either (see rank 19). The rest of the results quite agree with the traditional list of risk factors of lung cancer. Such factors as smoking, gender, age, chronic lung diseases in the past, occupational exposure to carcinogens rank the highest.

Then we established the direction of each factor’s effect. The risk of lung cancer was found much higher in men. Again, this result corresponds to common knowledge that lung cancer is more prevalent among men as they are more inclined to smoke, and are exposed to occupational hazards more often, etc.

Table 1. Relative Significance of Risk Factors of Lung Cancer in Pervouralsk

Rank	Risk Factor	Relative Significance
1.	Duration of smoking	1.00
2.	Gender	0.88
3.	Intensity of smoking	0.71
4.	Chronic lung diseases in the past	0.70
5.	Age	0.50
6.	Alcohol abuse	0.26
7.	Duration of occupational exposure to carcinogens	0.26
8.	Place of work	0.24
9.	Type of building material	0.17
10.	Marital status	0.16
11.	Source of drinking water	0.14
12.	Linoleum flooring	0.13
13.	Benign newgrowths	0.12
14.	Duration of living in Pervouralsk	0.12
15.	Living area per person	0.09
16.	Benzo(a)pyrene contamination of soil in the residential area	0.04
17.	Nationality	0.04
18.	Soil pollution in the residential area	0.03
19.	Floor number	0.03
20.	Cr^{6+} contamination of soil in the residential area	0.02
21.	Occupational stress	0.01
22.	**EEC of radon**	**0.01**
23.	**EEC of thoron**	**0.01**
24.	**Total EEC of radon and thoron**	**0.007**
25.	Diabetes	0.004
26.	Gas cooker	0.001

The factors of duration and intensity of smoking ranking 1 and 3 fully agree with the statement that smoking causes lung cancer. The same refers to the factor of alcohol abuse ranking 6.

We got quite expected results when analyzing occupational exposure to carcinogens. Risk of lung cancer increased with the years of hazardous exposure. As for the place of work, the risk of lung cancer was the highest among the workers of the plant of chromium salts' production, slightly lower - among those working at the plant of refractory materials and tube-rolling mills. Naturally, the risk was found the lowest among service and professional workers. It was not surprising that chronic lung diseases in the past and age ranked rather high - 4 and 5 respectively. Contamination of soil in the residential area with benzo(a)pyrene and Cr VI did not rank very high (16 and 20, respectively). It is obvious, however, that dwelling in areas with extremely high levels of carcinogens in soil is a risk factor of lung cancer.

The main objective of the study was to assess natural radionuclides as potential risk factors of lung cancer in Pervouralsk. We noted above that the contribution of radon and thoron in the development of lung cancer was found very moderate. We also found no distinct association between the trend in effects of these factors and lung cancer (Figure 1). Thus, those data prevented us from considering the exposure to natural radionuclides one of the most important risk factor of lung cancer in Pervouralsk.

We considered such factors as the floor number, type of building material and the source of drinking water indirectly associated with radon exposure. However, their correlation coefficients with EEC of radon and thoron were 0.033, 0.131, and 0.007, respectively, indicating that they could not be treated as markers of radiological exposure of population.

We were confident in the reliability of our study results as we found the expected effects of many well-known non-radiation carcinogenic risk factors, i.e. smoking, occupational exposure to carcinogens, age, benign newgrowths, etc., on the development of lung cancer. This conformity of our results with scientifically proved carcinogenic effects of those factors made us confident of the assessment of exposure to natural radionuclides.

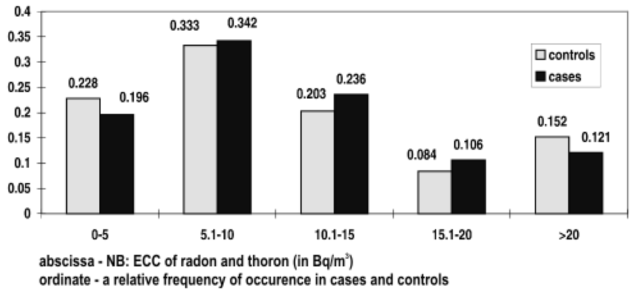

Figure 1. Relative distribution of total equivalent equilibrium concentration of residential radon and thoron in cases and controls

We assessed the contribution of residential radon and thoron in lung cancer using methods of pattern recognition and radiological risk assessment model BEIR VI. This allowed us to assess the reproducibility of results and the effectiveness of the two analytical methods. The results were significantly different. According to BEIR VI model the contribution of radon/thoron in lung cancer ranged from 7.2% to 33%. Specialists in cancer epidemiology understand that this contribution was overestimated. A comparison of the two analytical methods allowed us to conclude that the results of the epidemiologic analysis were more precise than those of the model that could be used only for obtaining preliminary estimates. The contribution of residential radon/thoron in the development of lung cancer assessed in the multifactor analysis is more precise and correct.

CONCLUSION

Results of multifactor epidemiologic studies show a small contribution of radionuclides in the development of lung cancer in the population of big cities of the Middle Urals, Russia.

It is necessary to conduct supplementary epidemiologic studies of residential radon and lung cancer in small towns and villages in the Middle Urals where the majority of population lives in one-story houses and indoor concentrations of radon and thoron in them can be higher than in multistory buildings of Pervouralsk.

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