

Impact of occupational activity on development risk of malignant mesothelioma

Кәсіби қызметтің ісік мезотелиоманың дамуына әсері

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24 жылдың ішінде (1981–2004) Свердлов облысының 66 муниципальді бөлімшесі ішінен 32-сінде 125 мезотелиоммен морфологиялық верификацияланған жағдай тіркелді. Науқастық 1 жылдың ішінде 0,2-ден 27,1-ге дейін өсті. Облыс бойынша мезотелиома ауруына шалдыққан адамдар саны әлемдік деңгейге, яғни жылына миллион халыққа 1–2 жағдайға, жетті. Асбест экспозициясымен анықталған байланыс 12,0 % жағдайда анықталған. Барлық жағдайларда ауруға шалдыққандар XX ғасырдың 50–60-жылдарында сипат алған асбесттің жоғарғы деңгейдегі экспозициясының әсеріне ұшыраған. Авторлардың ойынша, асбест және хризотил-асбест аурудың дамуында жетекші этиологиялық фактор бола алмайды. Бұл ауру-сырқаттың полиэтиологиялық сипаты бар.

В статье рассмотрена картина заболеваемости мезотелиомой в Свердловской области за длительный период. За 24 года (1981–2004) в 32 из 66 муниципальных образований Свердловской области выявлено 125 случаев морфологически верифицированных мезотелиом. Заболеваемость варьировала от 0,2 до 27,1 случая на 1 миллион населения в год. В среднем по области заболеваемость мезотелиомой находится на уровне мировой фоновой — 1–2 случая на миллион населения в год. Достоверная связь с экспозицией асбеста выявлена в 12,0 % случаев. Во всех случаях больные подвергались воздействию повышенных уровней асбестовой экспозиции, характерных для 50–60-х годов XX в. По мнению авторов, асбест и в частности хризотил-асбест, не является ведущим, а тем более облигатным этиологическим фактором развития заболевания. Заболевание имеет полиэтиологический характер.

Introduction

Mesothelioma is a rare neoplasm of serosal surfaces (such as pleura, peritoneum, pericardium and others) [1]. The most common form of these neoplasms is malignant pleural mesothelioma, peritoneal and pericardium mesotheliomas occur tenfold rarer, and mesotheliomas of other localizations are the most uncommon. The median latency of the disease is 32 years but it may range from 5 to 70 years.

Overseas annually hundreds of articles on mesothelioma are published, especially in context of occasional mesotheliogenic potency of asbestos.* To our knowledge the first article on this issue was published in 1933. In 40–50s of the XXth century single papers on this issue were published. In 1960 the results of J.Wagner's study on association between mesotheliomas and exposure to crocidolite asbestos, were published, and later this study was recognized as classical [1]. From 70s of the XXth in western countries the most common etiological factor of mesothelioma was an inhalation of asbestos dust, primarily of amphibole asbestos (especially tremolite asbestos), that play a major role in causing the disease [2].

Not denying the role of amphibole asbestos in causing mesothelioma, a number of authors are skeptical about mesotheliogenic potency of chrysotile asbestos [3, 4]. Recent reports more often indicate that mesotheliomas may occur after exposure to other chemical (man-made mineral fibres, 9.10-dimethyl-1.2-benzaanthracene, nickel, beryllium, mineral, lead, polyurethane, ethylene oxide), physical (radioactivity), biological (Friend's virus (MC 29) and SV40) and many other carcinogenic agents [2–4].

Background incidence of mesothelioma is 1–2 cases per 1 million per year. In different countries incidence of mesothelioma varies widely from 0.15 to 29.01 cases per 1 million per year [1]. Mesothelioma incidence rates have been increasing throughout the industrialized countries in Western Europe, USA, Australia traditionally oriented to predominant use of amphiboles. The incidence in these countries varies from 4.33 in South Africa to 29.01 cases per 1 million per year in Belgium, at the average 8.06 cases as in USA. Mesothelioma

* Asbestos is generic commercial name for a naturally occurring group of six different mineral fibers that differ in mineralogical structure, physicochemical properties and biological aggressivity and are uniform only on fibre structure. As these groups differ from each other on important features, which play the main role for its use, the types of asbestos are classified into two groups: serpentine and amphiboles. Serpentine includes magnesium silicate – chrysotile asbestos (white asbestos). The second group includes iron silicates, are known as amphiboles (actinolite, amosite (brown asbestos), anthophyllite, crocidolite (blue asbestos) and tremolite) [4].

lioma incidence rates in countries traditionally using chrysotile varies from 0.15 (Ecuador) to 4.81 per 1 million per year in Latvia, at the average 1.51 — for instance, in Estonia.

Incidence of mesothelioma in Russia is unknown [5]. In Russia a national register of mesothelioma doesn't exist, and because of its' rarity mesotheliomas haven't been emphasized in official oncological statistics. Only in 1994 in St. Petersburg population cancer register mesotheliomas were classified as individual group of malignant neoplasms.

During the XXth century in Russia only 4 epidemiological studies of mesothelioma were conducted: local studies in Asbest [6] and Yekaterinburg [7], and two regional studies in the Republic of Karelia [8] and a pilot study in Sverdlovsk region [9]. The studies show that only in 12.0–29.4 % of cases an occupational exposure to asbestos may cause of mesothelioma [7–9].

So, currently we haven't got reliable data on epidemiology of the mesothelioma in Russia and role of occupational factors, particularly asbestos, for developing this neoplasm. For clarification of range of statements on this issue we conducted comprehensive epidemiological analysis of mesothelioma in Sverdlovsk region, one of the most industrial administrative territories in Russian Federation.

The population of Sverdlovsk region is more than 4.5 million people, about 4.6 thousands of enterprises are situated here where about 2.1 million people are employed and more than 550 thousands from them work in harmful and dangerous conditions, and more than 100 thousands of people are exposed to substances, products, industrial processes and factors with proved carcinogenic potency and likely cancerogenic for the man [10].

In this region the largest deposit of chrysotile asbestos in the world named Bazhenovskoye, which is characterized by absolute absence of contamination with tremolite asbestos, is situated. The deposit is a part of eastern gabbro peridotite pack in Middle Ural, which also includes Alapayevskoye, Ostaninskoye and Rezhevskoye deposits of chrysotile asbestos. In the region there are 4 leading enterprises on asbestos production and field technological institute. In Sverdlovsk region more than 15000 of workers occupationally contact with chrysotile. Moreover situated in the region Sysert district is high in anthophyllite asbestos (Sysert region), there are 29 industrially significant deposits of anthophyllite and deposits of other amphiboles, development of which has been ceased.

Materials and Methods

As primary data we used official records of Sverdlovsk regional oncologic dispensary on new-onset diseases with clinicoradiologic diagnosis of mesothelioma for the period from 1981 to 2004. In all cases included into the study the diagnoses were confirmed using standard pathomorphological studies, and re-examination of histologic specimens was carried out. The data on population size in different areas and in Sverdlovsk region as a whole were obtained in regional statistical department.

Collected data were processed using recommended descriptive and cross epidemiological research methods. Incidence of mesothelioma was calculated per 1 million per year and was standardized by direct method, both for the region as a whole and for every municipal unit where they were revealed.

For all patients included into analysis it were studied occupational history personally or through relatives, and paraoccupational and environmental exposures to asbestos using special questionnaire developed by the group of international experts, for identifying potential asbestos exposure. Findings were specified in personnel department of enterprises where the patients with mesothelioma worked.

For all patients with occupational exposure to asbestos the value of total dust load on full weight of dust, received for the whole period of work activity was calculated.

Results

For 24 years (from 1981 to 2004) 226 diseases with primary clinicoradiologic diagnosis mesothelioma were registered in Sverdlovsk region. In 125 (55.3 %) cases the primary diagnosis was confirmed after morphological re-examination, and 101 (44.7 %) cases were excluded from the study because the primary diagnosis mesothelioma was proved incorrect. In addition 24 cases of lung cancer with pleural lesion, 19 cases of metastases of other cancers, 12 cases of pleuritis of nonneoplastic etiology and one case of complicated pancreatitis were revealed. In 14 cases intravital and postmortal morphological verifications were not carried out, in 28 cases primary materials were lost and 3 patients were inhabitant of other regions.

From 125 verified mesotheliomas 116 (92.8 %) cases were pleural mesotheliomas, 7 (5.6 %) were peritoneal mesotheliomas and 2 (1.6 %) were pericardial mesotheliomas. In 112 (89.6 %) patients malignant neoplasms were revealed (including extrapleural) and in 13 (10.4 %) patients benign types of «mesothelioma»

were revealed. By term «benign mesothelioma» we nominally mean localized mainly fibrous neoplasmes of pleura. Among malignant mesotheliomas on histologic type tumors of epithelioid type (72.9 %) prevailed, less often there were mesotheliomas of sarcomatous (13.6 %) and biphasic (10.2 %) types.

The age of patients (67 men and 58 women) varied from 12 to 70 years, at an average 55.9 ± 1.0 years, 55.9 % of patients were productive age. Age and sexual differences at the diagnosis in cases of malignant and benign types of neoplasmes of different localizations and lesion area were not statistically significant.

Unless one case of pleural mesothelioma revealed during autopsy the lifetime of patients from the diagnosis of malignant mesothelioma ranged from 10 days to 1.10 years, at an average 7.1 ± 0.8 months which is equivalent of results mentioned by Russian and foreign publications [1].

The interactive study of incidence of mesothelioma showed that despite of some increased incidence in 1985–1990 in the region the tendency to stabilization and even decrease is observed (Table 1).

Table 1

Total rates of incidence of mesothelioma on Sverdlovsk region

Rates	Period of observation, years					Total
	1981–1985	1986–1990	1991–1995	1996–2000	2001–2004	
Absolute	20	39	25	21	20	125
Incidence per 1 million per year	0.88	1.67	1.04	0.97	1.11	1.11
The portion of patients with mesothelioma in total regional cancer morbidity, %	0.036	0.063	0.039	0.032	0.036	0.041
The portion of patients with pleural mesothelioma in total regional respiratory cancer morbidity, %	0.19	0.31	0.21	0.19	0.25	0.23

Mesotheliomas were revealed in 32 from 55 municipal units of Sverdlovsk region. The bulk of neoplasmes was diagnosed in municipal unit Yekaterinburg — 50 cases (40.0 %), Asbest — 12 cases (9.6 %), Serov and Pervouralsk — 7 cases (5.6 %) and Kamensk-Uralsky — 6 cases (4.8 %) (Figure).

The incidence varied from 0.2 (Nizhny Tagil) to 27.1 cases per 1 million per year (Novoasbest), at an average 1.1 cases per 1 million per year for the period of study. In 16 (50 %) municipal units and in the region as a whole an average incidence of mesothelioma is agreed with global background level, i.e. 1–2 cases per 1 million per year.

In areas with enterprises on mining and manufacture of asbestos the incidence varied from 4.3 (Asbest — mining of chrysotile) to 27.1 cases per 1 million per year (Novoasbest — mining of crocidolite), and in Sysert antophyllit province the incidence was 7.1 cases per 1 million per year. In towns Sukhoy Log and Beloyarsky, where enterprises «Sukholozhskasbo cement» and «Beloyarskaya factory on asbestos board production» (which use chrysotile asbestos) are situated, mesotheliomas were not revealed.

Occupational exposure to asbestos was revealed only in 15 (12.0 %) patients (Table 2). During labour activity 11 (8.8 %) patients occupationally contacted with chrysotile asbestos and 4 (3.2 %) patients — with amphiboles, including 3 patients contacting with crocidolite and one patient contacting with tremolite. 7 from 15 patients worked at «Uralasbest», JSC (chrysotile), three patients — at mining and concentration complex Anatolyevsky (crocidolite) and three patients — at different motor transport enterprises in Yekaterinburg (chrysotile). One patient worked at talc plant Shabrovsky (tremolite) and one patients worked at «UralATI», JSC (chrysotile).

The age of patients with occupational exposure to asbestos varied from 37 to 75 years, at an average 55.7 ± 2.6 years and was equal to corresponding figures for all patients with mesothelioma (55.9 ± 1.0 years). The age of patients at the first contact with asbestos varied from 18 to 27 years, at an average 21.5 ± 1.1 years; and work experience varied from 3 months to 45 years, at an average 21.3 ± 3.2 years. Mesotheliomas developed during 13–68 years after beginning of exposure, at an average — after 33.9 ± 3.8 years. It is important to note that occupational activity of patients with occupational exposure to asbestos in all cases was in conditions of high levels of exposure, which were common to 50–60s years of the XXth century [11].

The labor activity of patients not associated with asbestos was presented by wide range of occupations, including 46 workers (36.8 %), 17 technologists (13.6 %), 13 clerks (10.4 %), 9 medicine workers (7.2 %) and 7 scientific workers (5.6 %). In 15 patients (12.0 %) the area of working activity wasn't revealed but at they didn't work at enterprises on mining, processing and manufacture of asbestos on Sverdlovsk region. In one case (0.8 %) the patient with malignant mesothelioma was 12-years-old boy.

Table 2

Occupational activity of patients with mesothelioma

Occupational activity	Number	
	Absolute	%
Associated with asbestos: automechanic, borer in mine, driver, screener, laboratory assistant, machinist of mineral processing equipment, carman, maintenance fitter, electrician	15	12.0
Not associated with asbestos but with different harmful occupational factors: gas welding operator, doser, tool maker, bricklayer, assembler, checker inspector, woodcutter, painter, metallurgist, mechanic, glazer, field engineer, brancher, vegetable grower, felt boot manufacturer, foreman, operator, maintenance fitter, maintenance fitter, joiner, builder, turner, tractor operator, filter operator in production of alumina, moulder, mine worker, electrician	46	36.8
Not associated with asbestos and without harmful occupational factors: accountant, military man, physician, geologist, parlormaid, dispatcher of aircraft-traffic control station, canteen manager, engineer, cameraman, constructor, laboratory assistant, nurse, musical worker, butcher, research assistant, cook, salesman, telephonist, charwoman of shop floor, medical assistant, seamstress, economist.	48	38.4
Pupil	1	0.8
The data on occupational activity are absent but patients didn't work at enterprises on mining and manufacture of asbestos	15	12.0
Total	125	100.0

Table 3

Some data of occupational history in patients with malignant mesothelioma with exposure to asbestos, $M \pm m$ (variations)

Feature, years	Contact with asbestos		Statistically significant differences. $p <$
	Chrysotile	Amphiboles	
Mean age at the diagnosis	63.0 \pm 2.5 (55–75)	48.3 \pm 2.7 (41–53)	0.05
Mean age at the first contact with asbestos	22.3 \pm 0.6 (18–21)	19.3 \pm 0.3 (19–20)	0.05
Mean work experience with asbestos	25.8 \pm 2.5 (10.5–45)	10.2 \pm 3.0 (5–18)	0.05
Period from the first contact with asbestos to development of the disease	36.6 \pm 5.2 (13–57)	26.7 \pm 4.2 (22–35)	–
Dust burden for a whole period of occupational contact. grams	609.0 \pm 61.2 (292.7–1062.6)	205.4 \pm 78.1 (72.6–369.4)	0.05

As the table 3 suggests in the group of patients with the exposure to amphibole asbestos mesotheliomas statistically significantly ($p < 0.05$) developed in earlier age, with less work experience and virtually in 3 times lower dust load, than in the group of patients with exposure to chrysotile asbestos. Malignant neoplasms also were diagnosed after shorter time from the first contact with asbestos, but in that case the differences were not statistically significant.

Conclusions

1. The first Russian integrated epidemiological study of mesothelioma in Sverdlovsk region showed that an average incidence of mesothelioma is agreed with global background level, i.e. 1–2 cases per 1 million per year.

2. Asbestos, particularly, chrysotile is not a leading, and moreover obligate causative factor for development of the disease. The disease has got pluricausal nature.

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Recent international medical research on asbestos concerning the use of chrysotile

Хризотилдың қолдануына қатысты асбест туралы ең жаңа халықаралық медициналық зерттеулер

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Мақалада ең жаңа медициналық зерттеулердің нәтижелеріне шолу жасалған. Бұл зерттеулерді 1998–2009 жылдар аралығында әр түрлі мемлекеттердің ғалымдары өткізген, мысалы, Австрия, Ұлыбритания, Греция, Израиль, Литва, Польша, Украина, ЮАР және тағы басқалары. Автордың ойынша, ең жаңа медициналық ғылыми мәлімет және практикалық тәжірибе нәтижесінде, өндірісте қауіпсіздік ережелерді сақтау айтулы кәсіптік асбесттен болған ауруларды азайтуға кепіл бола алады.

В статье сделан обзор результатов новейших международных медицинских исследований, касающихся возможности безопасного использования в контролируемых условиях хризотил-асбеста, его биологической активности в сравнении с амфиболами. Исследования проведены в 1998–2009 гг. учеными разных стран: Австрии, Великобритании, Греции, Израиля, Литвы, Польши, Украины, ЮАР и др. Новейшие медицинские научные данные и практический опыт, по мнению автора, подтверждают, что соблюдение правил безопасности на производстве гарантирует минимизацию случаев профессиональных асбестообусловленных заболеваний.

Asbestos is a common name of six natural fibrous minerals used in industrial products. There are two groups of these minerals: serpentine (chrysotile) and amphibole (crocidolite, amosite, anthophyllite, tremolite, and actinolite).

Particularly in the past decade the issue of health effects of these groups of minerals has become the topic of numerous discussions when it became the focus of numerous very different interests: medical, environmental, commercial, political, etc. Further in this article the question will be only about chrysotile since the use of amphiboles is banned by ILO Convention No.162 on Safety in the Use of Asbestos [1].