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Study the level of thymus stromal lymphopoietin in the blood of persons exposed to asbestos

Abstract. *Asbestos dust is classified as a carcinogen by the International Agency for Research on Cancer. Asbestos particles, binding cations, leach the cell environment. The initiation of the release of dust particles activates the NF-kB signaling cascade, which in turn includes the synthesis of pro-inflammatory cytokines, such as thymus stromal lymphopoietin (TSLP). The increased level of these cytokines is directly related to malignant processes in the body.*

The aim of the study is to study the level of TSLP in the blood serum of people exposed to asbestos.

The material for the study was cytokines isolated from the blood serum of 40 exposed to asbestos and 50 healthy people. Peripheral blood samples were collected from workers of the Zhitikara asbestos mining company of the city of Kostanay. The content of the main TSLP levels in blood serum was determined by ELISA the Human TSLP ELISA Kit (Biorbyt Ltd, UK, No. orb138077). The optical density of the reaction products was determined using a spectrophotometer with a wavelength of 450 nm.

The concentration of TSLP in the blood serum were increased 3 times in persons exposed to asbestos compared to the control group ($p = 0.000011$).

The concentration of the level of TSLP can serve as a diagnostic biomarker of a number of diseases that are induced by asbestos.

Keywords: *cytokines, thymus stromal lymphopoietin, asbestos exposure, asbestos.*

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Introduction

Asbestos is a mineral fiber that is part of rocks and is widely used by industry [1]. All identified forms of asbestos have been classified by the International Agency for Research on Cancer as carcinogens for humans. [2]. Kazakhstan is one of the five largest asbestos producers in the world and produces about 230 thousand tons of chrysotile asbestos per year, of which 95% is exported [3].

Thymus stromal lymphopoietin (TSLP) is an immune cytokine originating from epithelial cells that regulates the inflammatory response mediated by Th2 cells. TSLP promotes the initiation and maintenance of an immune response, is a marker of defects in the differentiation of the epidermal barrier and is strongly involved in the pathogenesis of asbestos [4].

When breathed, large fiber particles generally land in the upper respiratory system, where they can be easily expelled from the body with the aid of villi. Asbestos causes lung cancer, laryngeal cancer, pleural mesothelioma, stomach cancer, esophageal cancer, colon cancer, and rectum cancer because they infiltrate the lower respiratory system and irritate the lungs [5]. The risk of disease depends on the duration and intensity of contact, as well as on the type, length and thickness of the inhaled fibers. Recent findings suggest a genetic tendency linking asbestos exposure to idiopathic pulmonary fibrosis, another fibrotic lung disease [6]. A number of observations indicate that immune

responses regulate the manifestations of the disease in asbestos. The T-cell cytokine γ-interferon reduces fibroblast proliferation and fibrosis. The radiologically assessed degree of asbestos in persons exposed to asbestos is inversely proportional to the reaction of T cells [7].

The aim of the research is to study the level of thymus stromal lymphopoietin in the blood serum of people exposed to asbestos.

Materials and methods of research

Cytokines were isolated from the blood serum of healthy and asbestos-exposed individuals. Peripheral blood samples were collected from workers of the Zhitikara asbestos mining company of Kostanay. The study included 40 participants exposed to asbestos dust (aged 24 to 63 years). The control group includes 50 healthy individuals (aged 39 to 69 years). Sampling was carried out by the National Research and Production Center of Transfusiology of the city of Astana. Informed consent to the use of biological materials in the study was obtained from all participants of the study. A medical institution staff collected the material, which was accompanied by a detailed questionnaire. The following were the selection criteria for the control group: absence of acute neurological, autoimmune, allergic or chronic diseases (Table 1).

Measurements of the concentration of thymic stromal lymphopoietin (TSLP) were determined using the Human TSLP ELISA Kit (Biorbyt Ltd, UK, no. orb138077) definitions according to the manufacturer's instructions. The optical density of the reaction products was determined using a spectrophotometer with a wavelength of 450 nm.

Statistical analyses were carried out using the MedCalc and Post Hoc Tukey HSD program. Correlation analysis was carried out using Spearman's criterion. Statistical reliability was established at $p<0.05$. Correlation analysis was carried out using the Pearson criterion. Statistical reliability was established at $p <0.05$.

Table 1

Parameters of the studied and control groups

Parameters	Study group	Control group
Gender	male -30 female -10	male -29 female-21
Average age (years)	male -44 female-48	male -45 female -52
Work experience (years)	10 years or less -20 More than 10 years - 20	- -
Smoking status	Smoking -21 Non- smoking -17 Ex- smoking -2	Smoking -10 Non- smoking -38 Ex- smoking -2
p <0.05 compared to the control group		

Results

Levels of TSLP in the serum of people exposed to asbestos showed a significant difference from the control ($p = 0.000011$). TSLP was 3 times higher in the study group compared to the control group (F ratio = 21,89429) (Fig. 1). In the control group, the level of thymus stromal lymphopoietin was 194 pg/ml, while in the asbestos-exposed group it was 610 pg/ml.

Two groups were considered to research the long-term and short-term impacts of asbestos, based on the work experience of people in the study group.

Comparing the groups by the categories presented in Table 1, the following trends can be noticed: the results for the working for more than 10 years and the working for less than 10 years are similar (606 pg/ml and 613 pg/ml). Nevertheless, the concentration of TSLP in the control group is 194 pg/ml. Serum TSLP concentrations in individuals with less than 10 years of experience and with more than 10 years of experience differ significantly from the control group (p = 0.000067) (Fig. 2).

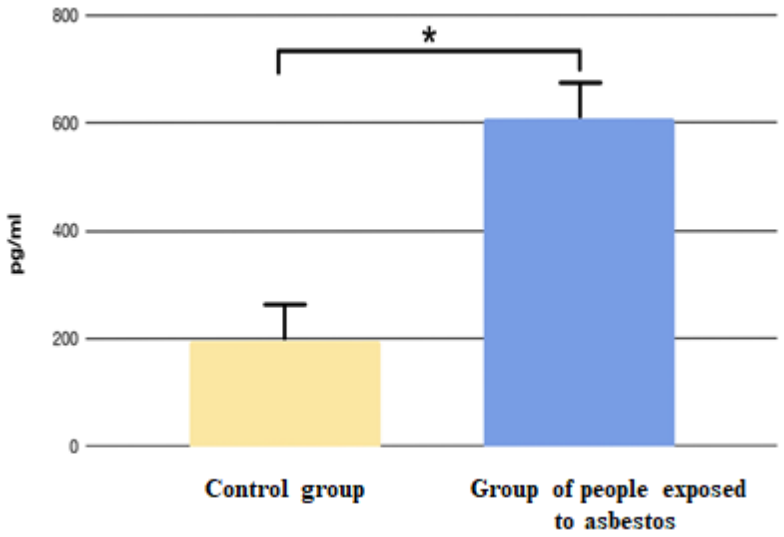

Figure 1. Levels of TSLP in blood serum of persons exposed to asbestos and control groups (F-ratio = 21.89429, *p = 0.000011)

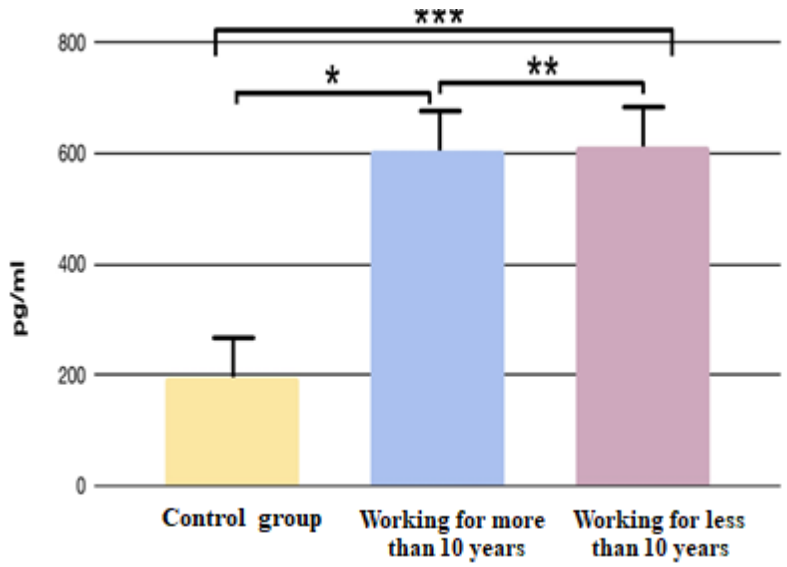

Figure 2. TSLP concentrations in the control group and according to work experience (F-ratio = 10.81762, p= 0.000067, *p = 0.00612, **p= 0.99904, ***p = 0.0054)

The concentration of TSLP in the blood serum of smokers and non-smokers had no significant differences with the control group.

As a result of the findings, we know that asbestos causes inflammatory reactions and excessive cytokine production, which further activates a cascade of reactions and prompts the activation of cells such as: dendritic cells, B cells, T cells, cells of innate immunity, which in turn provokes inflammatory diseases and in some cases oncology [8-11].

It has been proved that the level of TSLP has a direct relationship with various diseases, an increased amount of this cytokine indicates various inflammatory reactions [12; 13].

According to the study that level of TSLP was increased in the smooth muscles of the respiratory tract in patients with COPD [14], this suggests a link between cigarette smoke and TSLP. The generation of TSLP produced by cigarette smoke extract involves oxidative stress and TNF-aR activation. Thus, these limited data help to link TSLP with changes in the lungs caused by cigarette smoke [15]. Anzalone et. al, showed an increase in the number of cells expressing TSLP mRNA in the bronchi of patients with stable COPD and control smokers with normal lung function, indicating an additional role of TSLP in the immune pathogenesis of COPD [16].

All of these stimuli are likely to induce NF-kB-dependent TSLP expression in human lung epithelial cells. The production of TSLP can be stimulated by some pathogenic pathogens or repetitive environmental exposure, resulting to Th2-mediated human disease.

Conclusion

Asbestos dust enters the organism and damages tissues while also causing cytokine-induced inflammation and activating TSLP expression. This indicates that TSLP can be utilized as diagnostic biomarkers and that it has a wide range of applications in medicine.

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Асбест әсеріне ұшыраған адамдардың қанындағы тимустық стромальды лимфопоэтин деңгейін зерттеу

Аңдатпа. Асбест шаңы "Қатерлі ісікті зерттеу жөніндегі халықаралық агенттікте" канцероген ретінде қарастырылады. Катиондарды байланыстыратын асбест бөлшектері жасуша ортасын сілтілендіреді. Шаң бөлшектерін шығаруды бастау NF-kB сигнал каскадын іске қосады, ол өз кезегінде тимус стромальды лимфопоэтин (TSLP) сияқты қабынуға қарсы цитокиндердің синтезін қамтиды. Бұл цитокиндердің жоғарылауы организмдегі қатерлі процестермен тікелей байланысты.

Зерттеудің мақсаты-асбестке ұшыраған адамдардың қан сарысуындағы TSLP деңгейін зерттеу.

Зерттеу материалы ретінде асбест әсеріне ұшыраған 40 адамның және 50 сау адамның қан сарысуынан бөлінген цитокиндер зерттелді. Перифериялық қан үлгілері Қостанай қаласының Жітіқара асбест тау-кен байыту комбинатының қызметкерлерінен жиналды. Қан сарысуындағы TSLP негізгі деңгейінің құрамы Human TSLP ELISA Kit (Biorbyt Ltd, Ұлыбритания, № orb138077) жиыны пайдалана отырып, иммуноферменттік талдау әдісімен анықталды. Реакция өнімдерінің оптикалық тығыздығы толқын ұзындығы 450 нм болатын спектрофотометр көмегімен орнатылды.

Қан сарысуындағы TSLP концентрациясының құрамы бақылау тобымен салыстырғанда асбест әсеріне ұшыраған адамдарда 3 есе жоғары болды ($p = 0.000011$).

Тимус стромальды лимфопоэтин концентрация деңгейі асбест тудыратын бірқатар аурулардың диагностикалық биомаркері бола алады.

Түйін сөздер: цитокиндер, тимустық стромальды лимфопоэтин, асбест әсері, асбестоз

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Изучение уровня тимусного стромального лимфопоэтина в крови лиц, подверженных воздействию асбеста

Аннотация. Асбестовая пыль классифицирована как канцероген «Международным агентством по изучению рака». Частицы асбеста, связывая катионы, выщелачивают среду клетки. Инициация высвобождения частичек пыли активирует NF-kB сигнальный каскад, который в свою очередь включает синтез провоспалительных цитокинов, таких как тимусный стромальный лимфопоэтин (TSLP). Повышенный уровень данных цитокинов непосредственно связан со злокачественными процессами в организме.

Целью исследования является изучение уровня TSLP в сыворотке крови людей, подвергшихся воздействию асбеста.

Материалом для исследования являлись цитокины, выделенные из сыворотки крови 40-ка людей, подвергшихся воздействию асбеста, и 50 здоровых людей. Образцы периферической крови были собраны у работников Житикаринского асбестового горно-обогатительного комбината города Костанай. Содержание основного уровня TSLP в сыворотке крови определяли методом иммуноферментного анализа с использованием наборов Human TSLP ELISA Kit (Biorbyt Ltd, Великобритания, № orb138077). Оптическая плотность продуктов реакции устанавливалась с помощью спектрофотометра с длиной волны 450 нм.

Содержание концентрации TSLP в сыворотке крови было в 3 раза выше у лиц, подвергшихся воздействию асбеста, по сравнению с контрольной группой ($p = 0.000011$).

Концентрация уровня тимусного стромального лимфопоэтина может служить как диагностический биомаркер некоторого ряда заболеваний, которые индуцируются асбестом.

Ключевые слова: цитокины, тимусный стромальный лимфопоэтин, воздействия асбеста, асбестоз.

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