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The usage of the maximum inactive concentration as an analogue of the biological impact index for preventive health monitoring of chemical industry workers

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ABSTRACT. ***Introduction.*** In modern conditions of industrial production and enterprises, the problem of ensuring sanitary and hygienic requirements at the workplaces of employees who meet the established requirements of the legislation of the Russian Federation remains urgent. Problems associated with the possibility of contact with chemicals also remain relevant and have not lost their significance. When studying approaches to assessing the impact of industrial toxicants on the body of employees, the current and generally accepted method in the Russian Federation is the calculation method of “stay dose load”, which serves to substantiate the connection between the violation of the health status of workers and the accumulation of xenobiotics in the body. In order to prevent the accumulation of toxicants and organize measures to prevent occupational diseases, periodic medical and preventive examinations of employees are used, which are prescribed based on the results of a special assessment of working conditions, for workplaces with a recorded fact of exceeding the maximum permissible concentration in the air of the working area of harmful substances, typical for production. Today, in large enterprises where there is a chemical factor, the activities of industrial sanitary laboratories are aimed at registering the presence of chemicals in the air of the work area. Depending on the hazard class of the substance and the specifics of the technological process, the frequency of sampling and analysis is established. However, in order to implement measures aimed at preventing occupational diseases of workers, it is necessary to review approaches to the implementation of preventive monitoring. ***The purpose*** of the work is to prevent the negative effects of toxic substances on the body of workers and to take measures to organize a biomonitoring system at enterprises with potentially dangerous harmful substances. ***Materials and methods.*** A systematic analysis of modern literary sources and regulatory documentation in the field of occupational hygiene has been carried out. By the method of comparative analysis, domestic and foreign principles and practice of using approaches to assess the negative impact on the body of toxicant workers are compared. ***Conclusions.*** In order to organize preventive monitoring of the body condition of workers in contact with chemicals, it is necessary to supplement existing procedures for monitoring the working environment, such as special assessment of working conditions and production control, with a biomonitoring system to obtain a complete understanding of the impact of toxicants on the human body and subsequently assess the health risk.

Keywords: workplaces, maximum permissible concentration of air in the working area, maximum inactive concentration, chemical factor, biological exposure indices, selenium, occupational diseases

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Применение максимально недействующей концентрации как аналога индекса биологического воздействия для превентивного мониторинга здоровья работников химической отрасли

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РЕЗЮМЕ. ***Введение.*** В современных условиях деятельности промышленных производств и предприятий остается актуальной проблема обеспечения санитарно-гигиенических требований на рабочих местах сотрудников, отвечающих установленным нормам законодательства Российской Федерации. Проблемы, связанные с вероятностью контакта с химическими веществами, также остаются актуальными и не потеряли свей значимости. При изучении подходов по оценке влияния на организм работников промышленных токсикантов общепринятым в Российской Федерации является расчетный метод «стажевой дозовой нагрузки», который служит для обоснования связи нарушения состояния здоровья работников с накоплением в организме ксенобиотиков. В целях профилактики накоплений токсикантов и организации мер по предупреждению профессиональных заболеваний применяются периодические медико-профилактические обследования работников, которые назначаются на основе результатов проведенной специальной оценки условий труда, для рабочих мест с зафиксированным фактом превышения предельно допустимой концентрации в воздухе рабочей зоны вредных веществ, характерных для производства. В настоящее время на крупных предприятиях, где присутствует химический фактор, деятельность санитарных лабораторий направлена на фиксацию присутствия в воздухе рабочей зоны химических веществ. В зависимости от класса опасности вещества и особенностей технологического процесса по согласованию с местными органами Роспотребнадзора устанавливается периодичность отбора проб и их анализ. Однако для того, чтобы осуществлять мероприятия, направленные на предупреждение профессиональных заболеваний работников, необходимо пересмотреть подходы к осуществлению превентивного мониторинга. ***Целью*** работы является превентивное выявление негативного влияния на организм работников токсических веществ и принятие мер по организации системы биомониторинга на предприятиях, имеющих потенциально опасные вредные вещества. ***Материалы и методы.*** Проведен систематический анализ современных литературных источников, нормативной документации в области гигиены труда. Методом сравнительного анализа сопоставлены отечественные и зарубежные принципы и практика применения подходов по оценке негативного влияния токсикантов на организм работников. ***Выводы.*** Для организации превентивного контроля состояния организма работников, контактирующих с химическими веществами, необходимо дополнить существующие процедуры контроля состояния производственной среды, такие как специальная оценка условий труда и производственный контроль, системой биомониторинга для получения полного представления о воздействии токсикантов на организм человека и последующей оценки риска его здоровью.

Ключевые слова: рабочие места, предельно допустимая концентрация воздуха рабочей зоны, максимально недействующая концентрация, химический фактор, индекс биологического воздействия, селен, профзаболевания

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

INTRODUCTION

Publicly available online data provides indirect insight into the development of new technologies aimed at meeting Russia's economic needs in various fields, such as instrument engineering, the IT industry, and other related sectors.

The intensification of production technology development is also driven by the national needs for import substitution of raw materials, supplies, components, assemblies, machine parts, and equipment required for the aforementioned branches of the economy. Equipment and production technologies imported into Russia do not always comply with safety standards, including the equipment's potential to emit harmful substances into the environment.

Numerous workers are exposed to various pollutants at their workplaces, such as chemicals in the form of vapors, aerosols, and dust, which under certain conditions can adversely affect their health. In assessing the impact of toxicants entering the workplace air, it is customary to consider only the inhalation pathways of xenobiotic exposure. However, some of these substances can pose a greater health risk through dermal absorption. Therefore, an approach focused on comprehensive health screening and the implementation of biological monitoring for workers is warranted.

Inadequate control of occupational exposure to pollutants can lead to health deterioration. Some diseases caused by workplace hazardous substances (occupational diseases) may only manifest after a considerable latency period following initial exposure. Consequently, even the most effective treatment of an occupational disease will not prevent similar cases among other workers unless the sources of harmful exposure are eliminated. Hence, the risk of recurrence will remain persistently high. This underscores the critical importance of proactive strategies to protect the health of personnel handling hazardous substances, as well as others who may be indirectly affected by these work activities.

AIM

The aim of this study is to develop a framework for a preventive health biomonitoring system for chemical industry workers, utilizing the Maximum Inactive Concentration (MIC) as an analogue to the Biological Exposure Indices (BEI).

MATERIALS AND METHODS

Currently, two principal approaches are employed to control the levels of hazardous substances in workplace air: 1) the Special Assessment of Working Conditions (SAWC) procedure[1], and 2) the implementation of Production Control[2].

The existing SAWC procedure, as currently practiced, is designed to document the factors of the work environment and labor process at specific workplaces based essentially on the data provided by the employer commissioning the assessment. It is an open secret that violations of this procedure occur, leading to the recording of all environmental factor levels at or below established regulatory limits. Consequently, unscrupulous employers reduce costs by avoiding supplementary payments and compensations for hazardous working conditions, justifying this by claiming to protect workers' health through the provision of personal protective equipment. The inevitable result of such practices is an increase in occupational disease rates in the Russian Federation.

To monitor the content of harmful substances in workplace air, accredited measurement methods listed in the register of the accreditation body (the State Information Fund for Ensuring Measurement Uniformity, SIF UMI)[3] are used. This can create a discrepancy, as the assessment of a chemical compound's concentration in the air may be impossible if no certified measurement method for it exists or has been developed.

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[1] Federal Law No. 426-FZ of December 28, 2013 "On the Special Assessment of Working Conditions". Available at: https://www.consultant.ru/document/cons_doc_LAW_156555/ (accessed: June 8, 2024).

[2] Federal Law No. 52-FZ of March 30, 1999 "On the Sanitary and Epidemiological Welfare of the Population". Available at: https://www.consultant.ru/document/cons_doc_LAW_22481/ (accessed: June 8, 2024).

[3] The official website of the "State Information Fund for Ensuring Measurement Uniformity — SIF UMI". Available at: https://oei.by/mvi/index (accessed: June 8, 2024)..

Another significant factor compromising the objectivity of workplace assessment regarding chemical hazards is the sampling frequency and the specific time interval chosen for evaluation. According to SAWC guidelines, measurements must be conducted during the most intensive work shift, at peak equipment productivity and during the most demanding associated technological operations. In practice, this requirement is often disregarded during SAWC procedures, which calls into question the reliability of the obtained results.

RESULTS

Therefore, it can be concluded that the outcomes of a Special Assessment of Working Conditions (SAWC) may not accurately reflect the true state of the air quality in the workplace. Consequently, workers exposed to hazardous substances may be referred for mandatory periodic medical examinations. However, the preventive value of these examinations is compromised because the employer officially reports the absence of a chemical hazard.

A solution could be the implementation of a targeted biomonitoring program within the framework of enhanced occupational health examinations, using approaches analogous to Biological Exposure Indices (BEI). BEI represent guideline values for interpreting biomonitoring results. They serve as an additional tool for assessing the adverse effects of toxicants on workers and are instrumental in confirming exposure to a specific chemical agent[1].

A substantial array of methods for detecting xenobiotics in the human body exists and is employed in evidence-based medical practice in Russia. To establish regular monitoring of industrial toxicants and their metabolites in biological samples from workers, it is imperative to create a dedicated subsidiary structure within current specialized medical institutions for occupational disease research. This structure should have a sector-specific focus on existing enterprises and be based on biomonitoring. Concurrently, it is necessary to develop an algorithm for implementing approaches that enable the early identification of health deviations in workers exposed to industrial toxicants.

The potential application of an analogue to BEI for organizing preventive health surveillance of workers with a confirmed chemical hazard at their workplaces is of significant interest.

One feasible approach to implementing xenobiotic detection can be illustrated using exposure to selenium compounds as an example.

Selenium finds wide application across numerous industrial sectors, both in the form of various salts and as a metallic powder. It is used in semiconductor technology, the production of high-quality alloys, pharmaceuticals, and the paint, varnish, and glass industries. The primary industrial uses of selenium are summarized in Figure 1.

Current estimates indicate a slight upward trend in global selenium consumption, including for the production of vitamin supplements and other goods [1].

The leading global selenium producers are Japan (accounting for 30–50% of world output), Canada (16–20%), Belgium (10–14%), and Germany (7%). Russia's share in global selenium production does not exceed 7% [2, 3].

At present, selenium production in the Russian Federation is carried out by three metallurgical companies: Norilsk Nickel (Nornickel), the Ural Mining and Metallurgical Company (UMMC), and the Kyshtym Copper Smelting Plant [4, 5].

Selenium production technologies remained virtually unchanged until the end of the 20th century. The dominant method was the roasting-selenide process, introduced in the 1970s at the Norilsk and Almalyk Mining and Metallurgical Combines and at the Ural Electrolytic Copper Plant (UralElectroMed). Copper

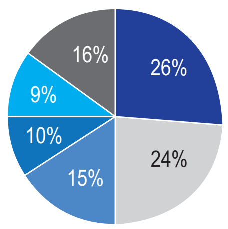

Fig. 1. **Differentiation of industrial spheres of selenium application**

Рис. 1. Распределение областей промышленности по применению селена

[1] International Labour Organization. Encyclopedia. Available at: https://www.iloencyclopaedia.org/ru/part-iv-66769/biological-monitoring-65407 (accessed: June 16, 2024)..

slimes generated during the electrolytic refining of copper anodes were the primary industrial source of selenium.

Modern hydrometallurgical copper processing technologies implemented at metallurgical plants, primarily the SX-EW (Solvent Extraction — Electrowinning) process, developed in the 1980s by companies such as Phelps Dodge Corp. and Placer Dome, prevent the formation of anode slimes. These slimes were the traditional source of selenium [4, 6]. Current best practices focus on recovering selenium from various industrial process solutions and electrolytes.

During selenium extraction and refining, workplace air may become contaminated with various chemical compounds, including heavy metals and acid vapors. Workers directly involved in selenium production are at risk of exposure to these hazardous substances, which are released into the air from industrial equipment.

Consequently, a critical component of industrial hygiene is the systematic monitoring of airborne hazardous substances, coupled with health surveillance for employees exposed to such chemicals during their work[1, 2].

The time-weighted average Maximum Allowable Concentration (MAC) for selenium aerosol in workplace air is 2 mg/m³, classifying it as a hazard category 3 substance. For selenium dioxide aerosol, the maximum one-time exposure MAC is 0.3 mg/m³, while its time-weighted average MAC is 0.1 mg/m³, placing it in hazard category 1[3].

A method for detecting selenium hexafluoride (SeF_6) in workplace air, along with the rationale for setting its MAC (in vapor form) at 0.2 mg/m³ and assigning it to hazard category 1, was examined in a study by O.V. Gorbunova et al. [7].

Toxicological research on the effects of selenium hexafluoride in white outbred rats also led to the development of a bioindication method for selenium in biological matrices, specifically in the blood and urine of the test animals. This method was designed to establish an exposure test and for subsequent use in occupational hygiene control (biomonitoring) for workers handling the hazardous compound SeF_6 [7].

According to research data [8], selenium is excreted from the body via the kidneys. This finding supports the hypothesis that inhaled selenium hexafluoride, after undergoing metabolic transformations, is also partially eliminated in urine as various selenium compounds.

It is also established that selenium is present in the blood, including within the selenoenzyme glutathione peroxidase (GPx). GPx is detectable in virtually all human and animal tissues and biological fluids. Its enzymatic activity is significantly higher in blood plasma than in erythrocytes [9].

These considerations, together with the fact that blood and urine are the most accessible and convenient biological matrices for analysis, provided the rationale for selecting them as media for determining bodily selenium levels [10].

Dose- and time-response relationships for SeF-exposure — specifically, time-effect and concentration-effect curves — were established. Analysis of these relationships enabled an assessment of the compound's *general toxic effect* using a parameter S (following the methodology described in the source study [11]), which quantifies the deviation in the physiological state of exposed animals from that of controls. From this analysis, the *Maximum Inactive Concentration* (MIC) for chronic selenium hexafluoride exposure was determined to be 0.12 mg/m³. This MIC value can serve as a basis for designing biological monitoring programs for workers in hazardous occupations, as demonstrated for this specific xenobiotic in the doctoral thesis of O.V. Gorbunova [10].

In practice, however, such bioindication methods for harmful substances are employed merely as ancillary tools in evidence-based medical assessments and are not used to establish causality in occupational

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[1] Federal Law No. 426-FZ of December 28, 2013 "On the Special Assessment of Working Conditions". Available at: https://www.consultant.ru/document/cons_doc_LAW_156555/ (accessed: June 8, 2024).

[2] Federal Law No. 52-FZ of March 30, 1999 "On the Sanitary and Epidemiological Welfare of the Population". Available at: https://www.consultant.ru/document/cons_doc_LAW_22481/ (accessed: June 8, 2024).).

[3] Decree of the Chief State Sanitary Physician of the Russian Federation No. 2 of January 28, 2021 "On the Approval of Sanitary Rules and Norms SanPiN 1.2.3685-21 'Hygienic Standards and Requirements for Ensuring the Safety and (or) Harmlessness of Environmental Factors for Humans'". Available at: https://docs.cntd.ru/document/573500115 (accessed: June 16, 2024).

disease or poisoning cases. Consequently, bioindication methods are not widely adopted for health screening of workers exposed to chemical hazards. This limited uptake can be attributed primarily to the need for a complex infrastructure involving specialized medical institutions tailored to specific industrial sectors. Furthermore, numerous logistical and regulatory barriers hinder the implementation of such monitoring systems.

An urgent need to revise current occupational health monitoring frameworks was identified. The key challenges for implementing biomonitoring in Russia include:

- the necessity to establish and accredit a large number of specialized sector-specific analytical laboratories for personnel health screening;
- the development and validation of modern biomonitoring methodologies;
- the study of toxicokinetics of hazardous substances upon entry into the human body;
- the rationale for selecting specific biological matrices for analysis.

Corresponding required measures at the enterprise level consist of:

- the timely identification of worker exposure to industrial toxicants and the implementation of protective measures;
- ensuring comprehensive coverage of at-risk worker groups for examination;
- the application of methods for ongoing control that enable the tracking of indicators related to the deposition of harmful substances in the body during work activities.

At the same time, global experience with Biological Exposure Indices (BEI) indicates their substantial benefits. This approach, focused on the early detection of health disorders among workers handling hazardous substances, delivers these benefits by reducing the incidence of occupational diseases related to chemical exposure [12]. However, studies demonstrate that occupational exposure limits enforced in the Russian Federation are more restrictive [3]. The numerical values of established Maximum Allowable Concentrations (MACs) for workplace air and Approximate Safe Exposure Levels (ASELs) differ significantly from corresponding BEI [8].

Nevertheless, BEI represent biomarkers that reflect the human body's response to chemicals absorbed via any route (e.g., inhalation, dermal, or oral). In some instances, BEI correspond to Threshold Limit Values (TLVs), defined as a “safe” level presumed not to induce adverse health effects. In others, they may represent the upper 95th percentile of biological response levels observed in a general population sample. Furthermore, certain BEI are non-numerical and provide only a qualitative indication of exposure. These indices are valuable for confirming that exposure to a specific chemical agent has occurred [13].

The data suggest that the Maximum Inactive Concentration (MIC), derived from continuous toxicological studies, could be considered an analogue to BEI [11]. An approach based on determining the MIC for different xenobiotics forms the basis for a risk-oriented concept in occupational risk assessment aimed at preventing toxicity-related occupational illnesses [14–16].

DISCUSSION

This study has evaluated the applicability of methodologies for assessing the adverse health effects of occupational chemical hazards. The conventional occupational hygiene assessment model in the Russian Federation relies on the Special Assessment of Working Conditions (SAWC) and routine production control. However, this model has been found inadequate for establishing an effective system for preventive health monitoring and the prophylaxis of occupational disease.

Consequently, instituting preventive health surveillance for workers in settings with chemical hazards requires the adoption of strategies centered on the early detection of substances to which exposure occurs during work activities.

This analysis has focused on two principal indicators for assessing chemical-related health impacts: the Biological Exposure Indices (BEI), standard in European and American practice, and the Maximum Inactive Concentration (MIC), utilized in the Russian context to validate exposure tests. The utilization of MIC holds potential for enabling the early identification of health impairments in workers and for mitigating the occupational risk associated with chemical factors.

A comparative analysis of the methodologies underpinning BEI and MIC application reveals that Biological Exposure Indices are not readily adaptable to the current occupational hygiene control framework in Russia. In contrast, the Maximum Inactive Concentration (MIC) presents a viable marker for the preventive diagnosis of health impairments in workers exposed to chemicals during the initial phases of exposure.

Therefore, within the current framework of the Russian Federation, a feasible preventive strategy can be implemented. This strategy involves assessing the adverse health effects on workers by applying analogues of the Biological Exposure Indices (BEI), such as the Maximum Inactive Concentration (MIC).

Currently, evaluating the adverse health effects of chemicals on workers relies on data from the Special Assessment of Working Conditions (SAWC), routine production control, occupational risk assessments, and periodic occupational health examinations.

This situation underscores the critical importance of ensuring safe and harmless working conditions for personnel at newly established or modernized workplaces. Furthermore, the current landscape of industrial advancement necessitates a revision of the methodologies used to assess workplace environmental factors that affect employee health.

CONCLUSIONS

Consequently, within the existing framework of legally mandated procedures, there is a clear need to implement preventive health monitoring for workers at industrial facilities where chemical hazards are present. This analysis highlights the significant promise of further research focused on developing systematic preventive monitoring and health assessment strategies for workers exposed to diverse industrial toxicants [17–21].

ADDITIONAL INFORMATION

Authors' contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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