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BIOCHEMICAL SIGNS OF CHILDREN'S MICROSATURNISM

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For industrialized areas, the problem of the anthropogenic pollution of the environment is not only relevant, but it also exacerbates at a qualitatively new level due to a significant deterioration of almost all the indicators of the population health, especially children's health. Among the wide variety of the factors that affect the people, the leading place belongs to the chemical one, in the spectrum of which the special place is occupied by the heavy metals and such a global and potentially dangerous toxicant as lead is on the first place.

The purpose of research was to assess the lowdose effect of lead on the microelement state and prenosological indicators of the health of preschool children living under conditions of constant exposure to it.

Material and methods. The obtained data testify to the constant presence of lead in environmental objects city Dnepr in concentrations for the most part do not exceed permissible ones, however, in 1.5-1.6 times higher than in unpolluted areas. Hygienic monitoring of the content of lead, copper and zinc in the air, water and food products of two industrial regions of the city of Dnipro and a "conditionally clean" region of a non-industrial city were carried out. The degree of influence of lead load was estimated with using a dose-dependent approach using biomonitoring and specific biochemical parameters. To assess the prenosological state of health of the child population, 46 and 57 children from preschool institutions in the observation areas aged 5 to 6 years old and 20 children from the control area were simultaneously examined according to a similar scheme.

Results and discussion. The average content of lead in the blood of 70-100% of children from the industrial areas is 1.6-5 times higher than the standard and 9.5-30 times higher than the control one. In the urine of 33-66% of the surveyed children from the industrial areas and 12% of children from the control one the lead concentration is 6.4-12.8 times higher than the standard. Hair of preschoolers contains lead in concentrations that correspond to the permissible level, but 2-3.5 times higher than that of children in the control area, found in 73-78% of those surveyed. The concentration of lead in the teeth of children from industrial regions is 4.6 times higher than the normative level recommended by the World Health Organization, and in nails it is 3.2 times higher than the background values. The content of copper in all biosubstrates of children is determined at the physiological level, and zinc is lower by 49-80%. The increased content of lead in biosubstrates is accompanied by an increase of the activity of δ -ALA in the urine of children from the industrial areas by 1.2 and 1.9 times compared with the recommended norm, it was observed in 51-89% of the examined.

Conclusion. The revealed biochemical disorders in the organism of children indicate the beginning of the development of microsaturnism, which, on the background of violations of the microelement status, is the ground for the search for effective measures of reducing the "lead pressure" on the health of the child population.

Keywords: environment, lead, children's health, biosubstrates.

Research relation to the programs, plans, and department themes. The work is a fragment of the research "Hygienic diagnostics of the formation of ecologically dependent microelements in the population of the industrial region and their prevention". The state registration number is 0114U005582.

Introduction. The constant increase of technology-related impact on the human health is an inherent part of industrialized areas [1, 2], on the other hand, the lack of vital elements in the environment contributes to the deterioration of public health. Widespread chemical environmental toxicants include lead, which is included by the WHO in the list of priority pollutants, the so-called "black dozen" [3, 4]. Taking into account

the fact that lead is able to accumulate and remain in the body for a long time, it is especially dangerous for children [5]. Nowadays it is also important to identify regional features of the microelement status of children, who are living in the conditions of constant pollution by heavy metals (HM), including the lead and to establish the degree of its impact on the body to develop the recommendations for the prevention measures of environment-related conditions in children. It is important to note that the prolonged intake of this toxicant in the body mostly occurs in concentrations that do not exceed the relevant hygienic standards. However, high cumulative properties, active involvement in the metabolic processes and enough long period of elimination cause a permanent increase of its content in the body. That's why, one of the promising areas in this context is the study of biological media of the human body, which, due to the increased sensitivity and selectivity of chemical analysis can be reliable and informative bioindicators that more accurately reflect changes in the human health.

The purpose of the research was to evaluate the low-dose effects of lead on micronutrient status and pre-nosological health indicators of preschool children's health, who are living in the conditions of its constant exposure.

Material and methods of research. Hygienic monitoring and comparative characterization of the lead, copper and zinc content in the various life-supporting objects of the environment: atmospheric air, water and food of two industrial districts of Dnipro and "conditionally clean" area of non-industrial city, which was selected as a control, during 15 years. To assess the pre-nosological state of health of the child population, 46 children from one of the children's preschool institutions (CPI) of Dnipro of the first industrial district and 57 children of CPI of the second one, aged from 5 to 6 years were examined at the same time. To compare determinant of health of the children from industrialized areas, an assessment of 20 children of the control area was conducted according to the similar scheme. The choice of children population was done due to the significant intensity of metabolic processes due to its intensive growth and development in combination with infantility of regulatory systems, which caused the significant sensitivity to the chemical environmental factors. The above-listed, in combination with a probable deficiency of essential elements in the child's body at this important age, conduct the reduction its resistance and ability to adapt to the environment.

All experiments were conducted in accordance with the Council of Europe Convention "On the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine Application of Biological and Medicine Achievements (ETS No. 164)" dated 04.04.1997, and the Helsinki Declaration of the World Medical Association (2008). Parents of each study patient signed an informed consent to participate in the study and all measures to ensure anonymity of patients were taken.

Considering that the most informative markers of the influence of chemical elements in ecological and hygienic researches and early clinical diagnosis of microelementosis are those tissues and organs that are able to deposit and accumulate these elements, the content of lead, copper and zinc were found out in children's indicator bioenvironments: venous blood, hair, baby teeth, nails. The choice of selected bioenvironments was, firstly, due to the fact that microelement composition of blood and urine were the first to respond to increasing levels of chemical elements [6], secondly, due to the fact that nails, baby teeth and hair were informative material for a long-term HM income through the special mechanism of microelement actions: they rigidly fixed the composition and ratio of substances that got into them during their growth [7].

The studies were performed by atomic absorption spectrophotometry on an atomic absorption spectrophotometer (AAS-1N) in the propane-butane-air mixture and inductively coupled plasma spectrometry according to the existing methods [8, 9]. To study the effect of the lead on the body of children, a biochemical marker of its constant exposure - the content of delta-aminolevulinic acid in urine (δ-ALA) was studied. The concentration of δ -ALA in urine increases in proportion to the increase of lead in the blood, due to its ability to block SH - groups of enzymes of porphyrin metabolism, and therefore this enzyme is classified as an early and specific indicator of microsaturnism. Determination of δ-ALA activity in urine was performed by biochemical method [10]. The analysis of the results was performed in comparison with existing physiological norms [8].

Statistical processing of research results included the calculation of the primary statistical indicators; identification of differences between groups on statistical grounds; establishing the relationship between variables using the licensed software packages for statistical analysis Statistica v.6.1 (StatsoftInc., USA, license number AJAR909E415822FA), Microsoft Excel. Pearson and Spearman correlation coefficients were used to determine the relationships between the studied traits. Correlations were considered statistically significant at p <0.05 [11].

Research results. During the hygienic monitoring of lead, copper and zinc it was found that in the air of the monitored residential areas of the industrial city metals were detected in the concentrations that did not exceed the maximum allowable concentrations on average, except for copper, where the concentration exceeded by 4.3 times. At the same time, the results of research of the lead content in the air of the monitored areas in comparison with the control one indicated its statistically significant excess of both maximum and average monthly concentrations (p <0.001).

Comparing our results with the average data of other industrial cities, it was determined that the content of copper and zinc in the atmosphere of the observation areas exceeds 1.5-2 times the corresponding data in unpolluted areas [12].

In the tap water of the observation areas, lead, copper and zinc were registered in concentrations that were not higher than the corresponding TLV on average annual values. In some periods, the lead content in the water of industrial areas was observed at the level of the TLV. At the same time, the concentrations of these metals exceeded the literature data for drinking water from the surface water intakes in technologically uncontaminated areas in 16; 1.5; and 3 times, respectively [13].

The results of the analysis of HM content in the regional food products show that lead is constantly detected, but in concentrations not exceeding the TLV, except for the group of dietary fats (2.5 times). There was a significant (p < 0.05) excess of the average annual concentrations of the lead in the local food products of industrial areas compared to the control one. The obtained results of the lead content in the food coincided with similar data of other authors for the industrial areas [14]. Moreover, the microelement composition of food did not correspond to the biological value. Thus, if the concentrations of copper were at the lower levels of biological values, the zinc content was up to 5 times lower than the biological norm [15]. In contrast to the results of the study of lead in products of the control area, the inverse pattern of copper content was found: content of fats was increased by 1.7 times and zinc content was by 1.2-2 times higher in meat and milk, respectively, compared with products of the industrial areas.

From the standpoint of the toxicokinetic patterns, biomonitoring of abiotic metals in different biosubstrates has different informativeness regarding the time of entry of these substances into the body. Thus, if the blood is an indicator of the recent arrival, the urine - of the long-termed one. This fact is mainly due to the renal route of excretion of HM from the body, for example, 75% of lead is excreted by this way [1]. In the analysis of the obtained results, the increased content of lead in the biosubstrates of the examined children of industrial areas has been found. These data confirmed the regular intake of the lead from the various environmental objects, which in different ways forms its complex effect on the child's body and could further lead to the manifestation of symptoms of saturnism. Thus, the reference content of lead in the blood

of the examined children, residents of the first industrial district, was by 1.6 times, the second was almost 5 times higher than the normative level (p<0.001). In the blood of children from the control area, lead was determined in an average amount that corresponded to the limits of physiological fluctuations and background values in children of uncontaminated areas. The average content of copper in the blood was at the physiological level in children of all areas of observation. However, the amount of zinc was below the normal level by 7-49% (p<0.001), which was especially dangerous against the background of increased lead content in the body, as it could conduce the formation of zinc deficiency in children [16].

Our previous studies [5, 12] showed that HM had different intensities of renal elimination from the body depending on the degree of their essentiality. These data were the evidence of the presence of differentiated elimination of biologically different values of HM in the body and was one of the manifestations of general biological laws of adaptation in conditions of industrial-related influences. Due to the above-listed, the results of lead content in the urine of examined children of both industrial and control areas were analyzed. The results showed that this metal was determined in concentrations higher than the normative [13, 17] by 6.4-11.2-12.8 times (p<0.001), respectively, which could be regarded as a metal carrier or the initial stage of intoxication of the body.

These data were typical for 33-66% of preschoolers in the industrial areas and 12% of the control one. The fact that the lead content in the urine of children from the relatively clean area also exceeded the norm may be the evidence of the long-term intake of small concentrations of this xenobiotic from the environment. In terms of copper and zinc, their average concentrations in children of different areas were at the level that exceeded the limits of physiological fluctuations, which confirmed the assumptions about the antagonistic interaction of these microelements with lead.

The hair of the monitored preschoolers of industrial districts contained lead in concentrations that were by 2-3.5 times higher than in children of the control district, but were at the limiting level of 8-9 μ g/g recommended by I. M. Trachtenberg and others [18, 19].

It should be emphasized that 73-78% of the surveyed children in industrial areas had a higher content of lead in their hair than the standard. The average content of zinc in the hair of children of the second industrial area was 80% of physiological value, in the hair of children of the first area the concentration of zinc was even lower and comprised 40%. The copper content was normal in the first area, and in the second was 48% of norm. Deficiency of micronutrients in chil-

dren was probably associated with their deficiency in children's nutrition, which was unbalanced, as well as with some metabolic disorders in the body due to biological antagonism of these vital elements with lead [16, 18].

Studies showed that the lead content in the nails of children in the industrial areas was 3.2 times higher than the normative values. The content of copper corresponds, and zinc was much lower than physiological values and data from literature sources (Cu - 11-53 μ g/g, Zn - 100 μ g/g) [17].

The content of lead in deciduous teeth, as a marker of long-term intake of this toxicant in children, in industrial areas exceeded the WHO recommended physiological norm by 4.6 times, in control children it was at its level [4]. The high content of lead was determined in the deciduous teeth of all examined children of the industrial areas.

The increase of the lead concentrations in the biosubstrates of the examined children was naturally accompanied by an increase of the activity of δ -aminolevulinic acid in the urine as a biochemical marker for this toxicant. Its level was higher than the recommended norm (1.6 mg/g creatinine) for children from the industrial areas by 1.2 and 1.9 times [20]. It should be emphasized that the increase in the concentration of δ -ALA was found in 51% of the surveyed children of the first industrial area and 89% of the second and indicated a tension of porphyrin metabolism in their body due to the exposure to lead. For children in the control area, this value was significantly lower. The level of δ -ALA in the urine of these children did not exceed the norm in all studies.

Discussion of the obtained results. Thus, in the conditions of industrial districts of the city there was a systematic and complex intake of such a priority regional pollutant as lead by the child's body. The fact of reducing the intake of micronutrients, especially copper and zinc, which are especially important for children's growth and development, is alarming. It should be emphasized that this circumstance, combined with the inherent biological antagonism of lead with these substances, generally potentiates its adverse effects on the health of children, which can cause the lead-associated changes [21]. Despite the relatively low external concentrations of HM in the objects of environment, such an abiotic metal as lead was determined in high concentrations in the body of children from the industrial areas, which can be explained by long-termed, constant and complex intake by body of the child with air, water, food, which forms a significant internal pollution [17, 22].

A comparative analysis of our biomonitoring data confirmed the assumption of a more significant technogenic associated load on the child's body in the industrial areas of the city.

Conclusion

- On the basis of long-term observations, we gave a hygienic assessment of the aspects of lead migration and certain metals in the system "source of pollution - environment - the child's body".
- 2. We determined a statistically significant (p<0.001) excess of lead content in the biosubstrates of children from the industrial areas compared with control area children: from 15.6 μ g/dl to 45.9 μ g/dl in the blood, from 0.16 μ g/ml to 0,32 mcg/ml in urine, from 5 mcg/g to 23.23 mcg/g in deciduous teeth, which was 5-7 times higher than the existing standards and was found in 50-100% of examined children, which proved the technogenic origin of the lead.
- 3. A certain deficiency of essential microelements, such as copper and zinc, increased the negative impact of lead on the body of one of the most sensitive parts of the population, children.
- 4. The obtained data on the relationship between the accumulation of macro- and micronutrients in children's biosubstrates and the ecological state of the environment in the place of residence of these children significantly expanded the possibilities of managing public health by correcting micronutrient imbalance.

Prospects for further research. The results of the conducted research allowed to scientifically substantiate the need for the further research on the development and implementation of effective measures to prevent the negative effects of lead on children of the industrial contaminated areas, in order to increase the adaptive reserves, accelerate rehabilitation and improve the health of children.

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УДК 614.7: 548.815/.819:616-074-053.2 БІОХІМІЧНІ ПОКАЗНИКИ ДИТЯЧОГО МІКРОСАТУРНІЗМУ Антонова О. В., Землякова Т. Д., Безуб О. В.

Резюме. *Метою роботи* було оцінити низькодозовий вплив свинцю на мікроелементний стан та донозологічні показники здоров'я дітей дошкільного віку, які мешкають в умовах постійного його впливу.

Проведено гігієнічний моніторинг вмісту свинцю, міді та цинку в атмосферному повітрі, воді та продуктах харчування двох промислових районів м. Дніпро та «умовно чистого» району непромислового міста. Для оцінки донозологічного стану здоров'я дитячого контингенту одночасно обстежено 46 та 57 дітей з дитячих дошкільних закладів районів спостереження віком від 5 до 6 років та 20 дітей контрольного району за аналогічною схемою.

Середній вміст свинцю в крові 70-100% дітей промислових районів в 1,6-5 разів вище нормативного і у 9,5-30 разів - контрольного. У сечі 33-66% обстежених дітей промислових районів і 12% дітей контрольного концентрації свинцю вище нормативу у 6,4-12,8 разів. Волосся дошкільнят містять свинець в концентраціях, які відповідають допустимому рівню, але в 2-3,5 рази вищі, ніж у дітей контрольного району, що виявлено у 73-78% обстежених. Концентрація свинцю в зубах дітей промислових районів за середніми значеннями у 4,6 рази вища за нормативного рівня, рекомендованого Всесвітньою організацією охорони здоров'я, а в нігтях - у 3,2 рази перевищує фонові значення. Вміст міді в усіх біосубстратах дітей визначений на рівні фізіологічного, а цинку – нижчий на 49-80%. Підвищений вміст свинцю в біо-субстратах супроводжується збільшенням активності δ-АЛК в сечі у дітей промислових районів в 1,2 і 1,9 рази у порівнянні з рекомендованою нормою, що спостерігалося у 51-89% обстежених.

Виявлені біохімічні порушення в організмі дітей свідчать про початок розвитку мікросатурнізму, що на фоні порушень мікроелементного статусу, є обґрунтуванням пошуку ефективних засобів зниження «свинцевого пресингу» на здоров'я дитячого населення.

Ключові слова: довкілля, свинець, здоров'я дітей, біосубстрати.

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БИОХИМИЧЕСКИЕ ПОКАЗАТЕЛИ ДЕТСКОГО МИКРОСАТУРНИЗМА Антонова Е. В., Землякова Т. Д., Безуб О. В.

Резюме. *Целью работы* было оценить низкодозовое влияние свинца на микроэлементное состояние и донозологические показатели здоровья детей дошкольного возраста, проживающих в условиях постоянного его воздействия.

Проведен гигиенический мониторинг содержания свинца, меди и цинка в атмосферном воздухе, воде и продуктах питания двух промышленных районов г. Днепр и «условно чистого» района непромышленного города. Для оценки донозологического состояния здоровья детского контингента одновременно обследовано 46 и 57 детей из детских дошкольных учреждений районов наблюдения в возрасте от 5 до 6 лет и 20 детей контрольного района по аналогичной схеме.

Среднее содержание свинца в крови 70-100% детей промышленных районов в 1,6-5 раз выше нормативного и в 9,5-30 раз – контрольного. В моче 33-66% обследованных детей промышленных районов и 12% детей контрольного концентрации свинца выше норматива в 6,4-12,8 раз. Волосы дошкольников содержат свинец в концентрациях, которые соответствуют допустимому уровню, но в 2-3,5 раза выше, чем у детей контрольного района обнаружено в 73-78% обследованных. Концентрация свинца в зубах детей промышленных районов по средним значениям в 4,6 раза выше нормативного уровня, рекомендованного Всемирной организацией охраны здоровья, а в ногтях – в 3,2 раза превышает фоновые значения. Содержание меди во всех биосубстратах детей определен на уровне физиологического, а цинка – ниже на 49-80%. Повышенное содержание свинца в биосубстратах сопровождается увеличением активности δ-АЛК в моче у детей промышленных районов в 1,2 и 1,9 раза по сравнению с рекомендуемой нормой, наблюдалось в 51-89% обследованных.

Выявленные биохимические нарушения в организме детей свидетельствуют о начале развития микросатурнизма, что на фоне нарушений микроэлементного статуса, является обоснованием поиска эффективных средств снижения «свинцового прессинга» на здоровье детского населения.

Ключевые слова: окружающая среда, свинец, здоровье детей, биосубстраты.

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