ГРОМАДСЬКЕ ЗДОРОВ'Я

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Modern aspects of the problem of influence of heavy metals in the environment on women's reproductive health

Introduction. The current situation in Ukraine is characterized by the deterioration of the environment, which requires comprehensive and effective actions from the public health system, aimed, among other things, at the early detection of negative environmental factors and the prevention of their influence. Chemical factor from the standpoint of hygienic significance occupies a priority place in the spectrum of harmful factors of the conditions of human existence, and heavy metals are the most dangerous environmental pollutants, which have a wide range of negative consequences from violations of the trace element composition to toxic effects and effects on the generative function of a person. External exposure to cadmium, as one of the widespread toxicants, is especially dangerous for pregnant women.

The aim of the study. Determination of the influence of cadmium contained in environmental objects on the level of internal pollution of the body of pregnant women and the frequency of manifestation of preeclampsia among women of the Dnipropetrovsk region.

Materials and methods. The research program included an assessment of the cadmium content in life-saving environmental facilities and biological substrates of 89 healthy pregnant women by the atomic absorption method, as well as a retrospective analysis of data of the primary statistical documentation on the complication of pregnancy.

Results. It was established that cadmium is constantly present in environmental objects in concentrations that are within the limits of normative values, but exceed the background levels and the results of research conducted in the territories of the ecological-geochemical optimum. Regardless of the relative sanitary and hygienic well-being of environmental objects in terms of cadmium content, an increase in its concentrations in biosubstrates is noted – the level of the metal in the blood and urine of women in industrial areas is significantly higher compared to the control ($p<0,01$), the content of cadmium in the urine of 36-50% of women in the studied areas of Dnipro exceeds the standard level. At the same time, the frequency of preeclampsia in practically healthy pregnant women has a direct correlation with the level of internal contamination of the body with cadmium.

Conclusion. The results indicate an increase in the level of internal pollution of the body of the inhabitants of the industrial region due to technogenic influence, especially among sensitive sections of the population – pregnant women, which causes a violation of the adaptation systems of a woman's body during pregnancy, which is accompanied by the further development of various complications, in particular, preeclampsia.

Key words: pollution, impact, adult population, pregnant women, heavy metals, cadmium, biosubstrates, blood, urine, genitourinary system, preeclampsia, industrial region.

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Сучасні аспекти проблеми впливу важких металів довкілля на репродуктивне здоров'я жінок

Вступ. Сучасна ситуація в Україні характеризується погіршенням стану довкілля, що потребує від системи громадського здоров'я комплексних та ефективних дій, спрямованих, у тому числі, на раннє виявлення негативних факторів довкілля та профілактику їх впливу. Хімічний фактор з позиції гігієнічної значущості посідає пріоритетне місце у спектрі шкідливих чинників умов існування

людини, а важкі метали найнебезпечніші забруднювачі навколишнього середовища, які мають широкий спектр негативних наслідків від порушень мікроелементного складу до токсичного ефекту і впливу на генеративну функцію людини. Зовнішні експозиції кадмію, як одного з розповсюджених токсикантів, особливо небезпечні для вагітних жінок.

Мета дослідження. *В*изначення особливостей впливу кадмію, що міститься в об'єктах довкілля, на рівень внутрішнього забруднення організму вагітних та частоту прояву прееклампсії у жінок Дніпропетровської області.

Матеріали та методи. Програма досліджень включала оцінку вмісту кадмію в життєзабезпечуючих середовищах довкілля та біологічних субстратах 89 здорових вагітних жінок атомно-абсорбційним методом, а також ретроспективний аналіз даних первинної статистичної документації про ускладнення вагітності.

Результати. Встановлено, що кадмій постійно присутній в об'єктах довкілля в концентраціях, що знаходяться в межах нормативних значень, однак перевищують фонові рівні та результати досліджень, проведені на територіях еколого-геохімічного оптимуму. Не зважаючи на відносне санітарно-гігієнічне благополуччя об'єктів довкілля за вмістом кадмію, відзначається підвищення його концентрацій у біосубстратах – рівень металу в крові та сечі жінок промислових районів достовірно вищий порівняно з контролем ($p<0,01$), вміст кадмію у сечі 36-50% жінок досліджуваних районів м. Дніпро перевищує нормативний рівень. При цьому частота прояву прееклампсії у практично здорових вагітних жінок має пряму кореляційну залежність від рівня внутрішнього забруднення організму кадмієм.

Висновки. Отримані нами результати свідчать про зростання рівня внутрішнього забруднення організму мешканців промислового регіону, обумовлених техногенним впливом, особливо у чутливих верств населення – вагітних, що викликає порушення систем адаптації організму жінки під час вагітності та супроводжується подальшим розвитком різних ускладнень, зокрема прееклампсії.

Ключові слова: забруднення, вплив, доросле населення, вагітні, важкі метали, кадмій, біосубстрати, кров, сеча, сечостатева система, прееклампсія, промисловий регіон.

Introduction. The health of the population of Ukraine is a multifaceted concept that includes the following medical indicators: population, age and gender composition, indicators of birth rate, incidence and prevalence of diseases, disability, and mortality. Recently, the medico-demographic situation in Ukraine causes concern and reflects the unsatisfactory state of health of the population of Ukraine [1]. The main reasons for the deterioration of the health of the population of Ukraine are social, ecological and economic factors. In particular, anthropogenic transformation of natural ecosystems in some regions of Ukraine, in particular in the Dnipropetrovsk region, is accompanied by man-made load both on the environment and on the population. At the same time, the morbidity and mortality rates of the region's population are higher than the national level [2, 3].

Among the chemically harmful pollutants, heavy metals absolutely rightfully occupy the leading place. They form a significant group of toxicants and determine the active anthropogenic pressure on environmental objects, and therefore on the human body, causes a significant increase in the morbidity of the population, the appearance of a new, environmentally determined pathology. Therefore, the problem of studying peculiarities of the impact of heavy metals on a human being, cadmium compounds in particular is relevant [4].

Cadmium is a toxic heavy metal that enters the environment through various natural and anthropogenic processes, which is especially relevant due to the rapid development of industry and modern technologies. It is a potential threat to most organisms, including humans. Cadmium by its nature does not decompose, therefore, after entering the environment, it remains in circulation. With advancing industrialization, the amount of this polluting toxic metal is increasing at an alarming rate. Humans are exposed to cadmium through ingestion (drinking or eating) or inhalation (breathing) [5, 6, 7]. It is a poison of polytropic action, which determines the diversity of pathogenetic mechanisms of its influence. Low levels exposure to cadmium may lead to damage to the kidneys, liver, skeletal system, and cardiovascular system, as well as to deterioration of sight and hearing. Along with strong teratogenic and mutagenic effects related to cadmium, it also shows adverse effects at low doses on both human male and female reproduction and affects pregnancy or its outcome [8], including the manifestation of toxic nephropathy. In addition, according to the IARC classification [9], cadmium belongs to category 1 carcinogens (substances that are carcinogenic to humans). Along with pronounced toxic properties of cadmium, a negative manifestation of its influence on the body is the ability to imitate the function and behaviour of essential trace elements. For example, like zinc, cadmium binds to albumin in plasma. As a result, the homeostasis of calcium, zinc and iron is disturbed [10].

With the increased content of cadmium in the human environment, its concentration in the biological mediums increases. The peculiarity of the harmful effects of cadmium is its rapid absorption by the body and slow release, which leads to the accumulation of this metal in the tissues [4, 5]. In this regard, the problem of the long-term effects of cadmium on the sensitive population, in terms of possibly hidden, time-varying changes in the body, which have negative consequences in manifestation of reproductive complications during pregnancy is of particular interest. In connection with the above, the aim of the study was to determine the influence of cadmium contained in environmental objects on the level of internal pollution of the body of pregnant women and the frequency of manifestation of nephropathy among women of the Dnipropetrovsk region.

Methodology and methods of research. Research was conducted in two industrial districts of Dnipro – Industrial and Novokodatsky, and the control city – Novomoskovsk, which was chosen as the control area, which most closely meets the requirements of contrast: it contains a small number of industrial objects, the volume of solid emissions into the air is 10 times lower than in the city of Dnipro. Ecological and hygienic studies of the quality of life-sustaining objects of the environment – atmospheric air, drinking water and food products was carried out in the residential areas of the observation areas. Hygienic assessment of the obtained concentrations was carried out in accordance with the existing hygienic regulations and literature data. The next step was the biomonitoring of

metals, which considers the method of determining the degree of danger of environmental factors and is necessary for hygienic studies. The content of lead and cadmium in environmental objects and the human body was determined by the atomic absorption method. Epidemiological studies were carried out by means of a retrospective analysis of the data of the primary statistical documentation as for the complication of pregnancy of the residents of the monitoring areas.

Statistical processing and mathematical analysis of the research results was carried out by calculating relative and average values, their reliability criteria [11]. Statistical processing was carried out using Microsoft Excel and STATISTICA 6.1 statistical software package (license number AGAR909E415822FA). The difference was considered significant at $p<0,05$.

Results and discussion. The results of the studies show that cadmium is constantly defined in in life-supporting objects of the environment of industrial areas within the limits of maximum permissible concentrations, but exceed the background levels. In the control city xenobiotic is determined in the air and drinking water samples periodically, with statistically-valid lower content than in the districts of Dnipro.

The level of cadmium in the blood of women ranges from 0,01 to 0,17 μg/ml 1). This value in women of group I averages 0,062±0,004 mg/ml, which is significantly ($p<0,01$) lower than in pregnant women of group II – 0,092±0,006 mg/ml. The content of cadmium in the blood of the control group is 0,028±0,002 μg/ml, which is significantly lower ($p<0,01$) than in Dnipro women. By the average and maximum values, cadmium in the blood of the inhabitants of the observation areas does not exceed the normative content – 0,3μg/ml. But in 96,7% of pregnant women in the Novokodatsky district, the concentration of cadmium in the blood is higher than 0,02 μg/ml, which is considered to be the limit of presence of metal for this toxicant. In the Industrial district in 18% of the examined subject's presence of cadmium in the blood has been identified.

Regarding the content of cadmium in another biosubstrate of pregnant women – urine, a more pronounced variation of individual levels of xenobiotic concentrations in the study areas was revealed – from 0,006 to 0,253 μg/ml. Its average concentrations for women of Industrial District is 0,079 ± 0.01 μg/ml, which is practically at the level of the normative value – 0,08 μg/ml. But for women of Novokodatskiy District, the average value of cadmium in urine is higher by 10% than the standard and makes up 0,089 ± 0,006 μg/ml. Despite the fact that the average concentration of this metal in the urine of women in group I is by 11% lower than in the group II, no statistically-valid evidence of this difference was obtained ($p> 0,05$). The concentration of cadmium in the urine of women of control city is on average 0,034 ± 0,004 μg/ml, which does not exceed the normative one and reliably ($p<0,01$) lower than in women of Dnipro. In addition, up to 50% of women of industrial districts, the level of cadmium in urine is higher than the standard. In the control group, only 7,7% of pregnant women have an increased value of this indicator.

As is known, cadmium is characterized by a pronounced nephrotoxic effect, in the pathogenesis of which a significant role is played by the generation of ROS, an increase in the level of TNF-α, the regulation of Nrf2 and, ultimately, abnormal gene expression, deregulation of cell proliferation and resistance to apoptosis [4]. The increased excretion of the xenobiotic in the body of pregnant women, probably, reflects the stress of the body's adaptive processes, which is to a certain extent caused by its increased toxic effect during this vulnerable period for women.

The largest amounts of cadmium are registered in the body of the inhabitants of the Novokodatsky district. Thus, its average content in the blood exceeds the data of the industrial region by 1,5 times, and in urine – by 0,01 μg/ml. Compared to the city of Novomoskovsk, the average value of cadmium in the blood is 3,3 times lower and in urine it is 2,6 times. Correlation analysis revealed a statistically significant ($p<0,05$) positive relationship between the concentration of cadmium in the blood and its content in the urine in the three groups.

Most often, preeclampsia of pregnant women were registered with residents of the Novokodatsky district – 9,72±0,76% and had a significant association with cadmium content in drinking water and biosubstrates of pregnant women ($r=0,54-0,76$; $p<0,05$). Considering reliably increased cadmium content in the organism of women of the II group in comparison to the data of other areas surveyed, it is possible to assume an unfavorable man-made influence on the system of adaptation of women's body during pregnancy with the further development of nephropathy.

Table 1

Average concentrations of cadmium in the blood and urine of pregnant women – residents of Dnipro and Novomoskovsk (M ± m)

Observation groups		Cadmium, μg/ml	
		blood	urine
I	Industrial District Dnipro (n = 33)	0,062±0,004	0,079±0,01
II	Novokodatskiy District Dnipro (n = 30)	0,092±0,006	0,089±0,006
III	Novomoskovsk (n=26)	0,028±0,002	0,034±0,004
Reliability		p I-II>0,05 p II-III<0,01 p I-III<0,01	p I-II>0,05 p II-III<0,01 p I-III<0,01
Physiological limits of norm	standard	0,02	-
	metal carrier	0,02-0,3	-
	intoxication	> 0,3	0,08

Conclusions. It has been established that cadmium is constantly determined in the atmospheric air, drinking water and food products of the observation areas, which forms a complex effect on the state of the inhabitants. Concentrations of the xenobiotic in the experimental and control areas have a significant difference both in the environment and in the body, this indicates the effect of external exposure of the toxicant on the content of cadmium in the body of women. Examination of residents of industrial areas established a significant content of cadmium in the organism of pregnant women, and despite the fact that the average concentration of the toxic metal in the blood of pregnant women was within the normal range, its level in the urine exceeds the permissible values in almost every second woman living in the most polluted district of the Dnipro. The internal content of the studied xenobiotic has a correlation with the frequency of preeclampsia in pregnant women. Taking into account the fact that cadmium is a natural antagonist of zinc, an extremely important trace element for a pregnant woman, the above results indicate the likelihood of an increase in the toxic effect of the abiogenic metal on the course of pregnancy in practically healthy women.

Prospects for further research. The results of the study allowed to scientifically substantiate the need for further research to develop and implement effective measures to prevent the negative impact of heavy metals on the reproductive health of women living in industrialized regions to reduce technogenic load on critical populations, increase the adaptive reserves of the body of pregnant women.

REFERENCES

1. Chorna VV., Khliestova SS., Humeniuk NI., Makhniuk VM., Sydorchuk T.M. Pokaznyky zakhvoriuvanosti i poshyrenosti ta suchasni pohliady na profilaktyku khvorob. *Visnyk Vinnytskoho natsionalnoho medychnoho universytetu*, 2020;24(1):158-164.
2. Yuntunen HM., Onul NM. Osoblyvosti zakhvoriuvanosti dorosloho naselennia Dnipropetrovskoi oblasti na urolohichni khvoroby. *Dovkillia ta zdorovia*. 2023;4:11-15.
3. Kryvych IP., Chumak YuIu., Husieva HM. Suchasnyi stan zdorovia naselennia Ukrainy. *Dovkillia ta zdorovia*. 2021;3:4-12.
4. Balali-Mood M., Naseri K., Tahergorabi Z., Khazdair MR., Sadeghi M. Toxic mechanisms of five heavy metals: mercury, lead, chromium, cadmium, and arsenic. Front Pharmacol. 2021;12:643972.
5. Saini S., Dhania G. Cadmium as an environmental pollutant: ecotoxicological effects, health hazards and bioremediation approaches for its detoxification from contaminated sites. 2020. 10.1007/978-981-13-3426-9_15.
6. Satarug S. Cadmium sources and toxicity. Toxics. 2019;7:25. doi: 10.3390/toxics7020025.
7. David Johane Machate. Anthropogenic hyperactivity for natural resources increases heavy metals concentrations in the environment: Toxicity of healthy food and cancer risks estimated. Journal of Trace Elements and Minerals. 2023;4:100057. https://doi.org/10.1016/j.jtemin.2023.100057.
8. Kumar S., Sharma A. Cadmium toxicity: effects on human reproduction and fertility. Rev. Environ. Health. 2019;34:327–338. doi: 10.1515/reveh-2019-0016.
9. IARC. Available from: https://ec.europa.eu/health/scientific_committees/ opinions_layman/en/electromagnetic-fields/glossary/ghi/iarc-classification.htm
10. Schaefer HR., Dennis S., and Fitzpatrick S. Cadmium: mitigation strategies to reduce dietary exposure. J. Food Sci., 2020;85(2):260–267. doi:10.1111/1750-3841.14997
11. Hruzieva TS., Lekhan VM., Ohniev VA. et al. Biostatystyka: pidruchnyk dlia studentiv; under the editorship T Hruzieva TS., Vinnytsia: New Book, 2020:384