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FEATURES FUNCTIONING OF THE DETOXIFICATION SYSTEM AT THE THREAT TERMINATION OF PREGNANCY AS A CONSEQUENCE OF ACCUMULATION OF ^{137}CS

A. A. Zhyvetska-Denysova[1], I. I. Vorobiova[1], L. A. Lozova[1], V. B. Tkachenko[1], O. A. Voloshyn[2], S. M. Tolkach[1], O. V. Shamaieva, S. K. Stryzhak[1]

State Institution «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» [1], Shupyk National Healthcare University of Ukraine[2] (Kyiv, Ukraine)

Summary

To date, there is no consensus on the pathogenesis of miscarriage. In modern life, human health is significantly influenced by environmental factors. In this regard, 37 years after the accident at the Chornobyl nuclear power plant, the question of remote cytogenetic and hereditary effects in the offspring of parents affected by radiation remains relevant. Ecosystems contaminated with radioactive substances are a source of exposure for humans. Internal irradiation is the cause of reproductive losses. Radiation stress affects the course of redox processes in the body. Biochemical indicators are markers of the influence of environmental factors on a person. The study is dedicated to determining the state of peroxide hemostasis in the case of miscarriage.

Aim: *to determine the peculiarities of the functioning of the detoxification system in case of miscarriage due to the accumulation of 137Cs.*

Material and methods. *The first (research) group included women with reproductive losses in anamnesis and signs of termination of the current pregnancy; the second (control) group included women with an uncomplicated history and course of pregnancy. Additionally, the first group was divided into subgroups according to pregnancy outcomes: A – 38 women who gave birth at 37-40 weeks, despite the complicated course of the current pregnancy, B – 13 women who gave birth at 28-36 weeks + 6 days, C – 9 women who birth at 22-27 weeks + 6 days. The state of peroxide hemostasis in women was studied using biochemical studies. Accumulation of ^{137}Cs with different activity was detected in the placentas of the examined women of both groups using β-spectrometry. Morphological examination of placentas was performed according to the protocol. The severity of placental damage was studied by Olympus BX51 and Axioskop 40 microscopes. Analyzing the results revealed a relationship between biochemical indicators, the activity of ^{137}Cs, and pregnancy scenarios.*

Statistical data analysis was performed using Microsoft Excel (2016) and Fisher angular transformation. The difference between comparative values was considered significant at $p < 0.05$ (probability index greater than 95 %).

Permission to conduct research was obtained from the Medical Ethics Committee of the SI «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» (protocol No 3 of 07.06.2017).

Scientific research work is to «Develop the latest and improve existing technologies for diagnosis, prevention, and treatment of premature termination of pregnancy in women with miscarriage taking into account the passport of the placenta» (2018-2020). Code VN.20.00.02.18, state registration number 0118U000039, KPKV 6561040.

Results. *It has been confirmed that the state of the environment plays a decisive role in the pathogenesis of miscarriage. It has been proven that placental dysfunction caused by abnormal oxidative stress due to the action of incorporated ^{137}Cs leads to pregnancy termination. As a result of the depletion of the antioxidant reserve, the compensatory capabilities of the placenta decrease. It was established that activity in the placenta up to 1.0 Bq/kg of ^{137}Cs does not affect the course of gestation. The compensatory capacity of the placenta remains preserved even with the accumulation of 1.1 to 4.4 Bq/kg of ^{137}Cs. At the same time, it is possible to prolong the pregnancy until the term of timely delivery. Internal irradiation with an activity of 4.5-10.4 Bq/kg of ^{137}Cs causes damage to the stroma of the maternal surface of the placenta and premature birth at 28-36 weeks + 6 days. At the same time, newborns are viable due to the preservation of compensatory reactions in the placenta. Accumulation of more than 10.4 Bq/kg of ^{137}Cs causes antenatal death of the fetus and early premature birth due to damage to maternal and fetal structures of the placenta. An increase in the content of malondialdehyde and a decrease in the activity of superoxide dismutase in the blood indicate the severity of radiation damage.*

Conclusions. *Internal exposure to ^{137}Cs disrupts the architecture and functional capacity of the placenta. Extreme effects depend on the activity of ^{137}Cs, the compensatory capabilities of the placenta, and the pregnant woman's body. Activation of lipid peroxidation acts as a biochemical amplifier of radiation exposure. An increase in the blood of malondialdehyde, diene conjugates, and free SH groups is associated with the severity of radiation damage. An early marker of primary placental dysfunction, premature birth, and antenatal fetal loss is an increase in MDA content in the blood by 12.0 % and a decrease in SOD by 6.5 % relative to permissible values. An early marker of exhaustion of the compensatory reserve is an increase in the content of MDA in the blood by 23.3 % and a decrease in SOD by more than 18.2 % relative to the permissible values. Decompensation of adaptation mechanisms in the system «mother-placenta-fetus» leads to antenatal losses.*

Key words: *Pregnancy Failure; Placenta; 137Cs; Lipid Peroxidation; Glutathione; Antioxidant Protection System.*

Introduction

Reproduction of the population of Ukraine in the conditions of an unfavorable demographic situation is a task of national importance. Modern achievements in obstetric science ensure that a woman realizes the function of motherhood, starting from the stage of fertilization until the birth of a healthy child. An obstacle is the problem of pregnancy failure, associated with stillbirth, early neonatal morbidity, and mortality. The frequency of miscarriage in Ukraine and the world reaches 25 % [1-3]. According to various authors, up to 50-70 % of reproductive losses occur in the first, 18-20 % – in the second, and 7-30 % – in the third trimesters of pregnancy [1-4]. The risk of pregnancy loss after first miscarriage is 13-17 %, second to 24 %, third to 30 %, and fourth to 40 % [4]. The factors of pregnancy failure are various [1-9]. In almost 80 % of women, termination of pregnancy occurs due to a violation of adaptation in the «mother-placenta-fetus» system under the influence of immune and endocrine deregulation [1-3, 6, 7]. Sexually transmitted infections are the cause of reproductive losses in 67 % of women. The introduction of molecular diagnostics revealed a hereditary predisposition to miscarriage [1,3]. Usually, 90 % of women have a combination of several factors. Despite a wide range of known factors, it is not always possible to establish the reason for termination of pregnancy in 41.2 % of women [1,2,5]. There is no doubt about the connection between miscarriage and environmental and social factors of modern life [2,6-9].

In recent years, more attention has been paid to the influence of the environment, lifestyle, and concomitant diseases on fetal development and pregnancy outcomes. WHO experts identified the derivatives of human health, among which the environmental factor was assigned the second in terms of influence. Medicine is powerless against diseases associated with environmental pollution. The consequences for human health depend on the scale of environmental pollution.

The ecology of Ukraine deteriorated due to the accident at the Chornobyl NPP (ChNPP), which has no analogs in the number of radionuclides entering the environment, the area of damage, and the consequences [11,12]. Contaminated ecosystems are a source of human exposure. Over time, the ecology of Ukraine has improved due to the decay, fixation, and redistribution of isotopes in the environment, as well as the creation of safe living conditions. However, the issue of remote cytogenetic and hereditary effects in the offspring of parents affected by radiation remains relevant.

The most dangerous for humans 37 years after the accident is ^{137}Cs due to contamination of soil, water, plant, and animal products, which enters the body through the biological chain of plants – digestive tract of animals – foods [13-15]. Agriculture and the food industry are highly developed in Ukraine. Thanks to established logistics connections, the consumer receives food from different regions of the country. Therefore, living in a territory free of radionuclides does not guarantee the appropriate purity of food products. The effects of ^{137}Cs entering the human body through food are associated with absorption into the blood and accumulation in organs and systems with increased radiosensitivity, for example, in stem cells capable of division. Fetoplacental and immune systems are donors of stem cells.

Internal radiation is one cause of reproductive losses [8,9]. Internal radiation suppresses cell division and tissue differentiation in the pre-implantation and implantation period, as well as during placentation, increasing the risk of death of the embryo and fetus. The possibility of penetration of radionuclides through the placenta has been proven experimentally. In the second half of gestation, radiation exposure can cause a teratogenic effect. By the way, low-power long-term internal irradiation causes more pronounced changes in cell membranes than powerful one-time external irradiation [15,16].

Accumulation of ^{137}Cs in the placenta represents radiation stress. The general pattern of any stress is an adaptive reaction associated with the tension of the sympathoadrenal and hypothalamic-pituitary-adrenal systems. Radiation disrupts redox in the body and leads to excess production of free radicals that damage vital structures [16,17]. An excess of free radicals affects reproduction. Internal irradiation ^{137}Cs disrupts the placental architecture, synthesis of hormones, and uteroplacental and placental-fetal microcirculation [8,9]. Pregnancy scenarios depend on the activity and speed removal of ^{137}Cs from the body, preservation of compensatory capabilities of the placenta, and proper functioning of the antioxidant system. Biochemical indicators are markers of environmental influence on pregnancy. Therefore, our attention is focused on the biochemical aspects of miscarriage caused by the accumulation of ^{137}Cs.

Due to the hierarchy of antioxidant mechanisms, pro- and antioxidant balance is maintained in the body under normal. It is known that any pathological process occurs against the background of activation of pro-oxidant reactions. Lipid peroxidation (LPO) is considered the most weighty oxidative process. LPO is a mechanism for realizing the toxicity of xenobiotics. Intermediate and final products of LPO have cytotoxic and mutagenic effects. An excess of LPO products disrupts the energy supply of cells, the synthesis of proteins and nucleic acids, and enzymatic reactions. Numerous studies confirm the importance of radiation-induced oxidative stress for the pathology [16, 17]. Activation of LPO caused by internal irradiation leads to the mobilization of antioxidant protection.

Antioxidant mechanisms are universal [18,19]. There are four lines of antioxidant protection in the human body, which sequentially neutralize the products of POL. Glutathione participates in three of them. In the first stage, lipophilic xenobiotics are transformed into hydrophilic under the influence of cytochrome P450 (CYP)-dependent microsomal monooxygenases associated with phospholipids of the endoplasmic. In the first stage, active participation of catalase, superoxide dismutase (SOD), and ceruloplasmin ensures the transition of toxic substances into oxygen and water. During the second stage, hydrophilic metabolites enter into conjugation with glutathione, forming non-toxic products easily excreted. Conjugation reactions occurring on the endoplasmic membrane protect the cell from the outside. Conjugation reactions in the cytosol can reduce toxic effects inside the cell. Enzymes of the second phase of detoxification: arylamine acetyltransferase, sulfotransferase, glucuronosyltransferase, and glutathione-S-transferase, due to weak specificity, neutralize a large group of xenobiotics.

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In the third stage, conjugated derivatives are removed from the body through the lungs, kidneys, and intestines. The fourth line of defense is responsible for the reparative regeneration of damaged molecules due to the restoration of disulfide bonds of proteins and antioxidants [18, 19].

Thus, the conjugation of xenobiotics with glutathione is at the heart of the detoxification. Among antioxidants, glutathione (γ-L-глутаміл-L-цистеїніл-гліцин) has a high reducing potential and cellular concentration. The L-isomer of glutathione is biologically active. The intracellular pool of glutathione includes reduced (GSH) and oxidized (GSSG) forms, mixed disulfides, and thioesters. Functioning of biological membranes, transmission of nerve impulses, cell proliferation, synthesis of prostaglandins, metabolism of proteins, carbohydrates, nucleic acids, and apoptosis are provided by γ-glutamyl and sulfhydryl groups of glutathione. However, the primary function of glutathione is to detoxify xenobiotics. The detoxifying effect of glutathione is associated with the sulfhydryl (SH) group. GSH protects cytochrome P450 from the harmful effects of reactive oxygen species and peroxide compounds with the help of glutathione peroxidase [18,19]. The depletion of endogenous glutathione reserves slows down detoxification processes.

Conjugation and reduction reactions are catalyzed by glutathione-S-transferase (GST) in the cytosol, microsomes, and mitochondria. The highest activity of GST is registered in the liver, kidneys, and intestines [18,19]. In reactions with glutathione, GST neutralizes electrophilic xenobiotics without damaging cells.

The purpose is to determine the features of the functioning of the detoxification system in case of miscarriage due to the accumulation of ^{137}Cs.

Material and methods

According to the study plan, pregnant women were divided into groups. The first (research) group included 60 women with reproductive losses in anamnesis and signs of termination of the current pregnancy. The second (control) group consisted of 30 women with an uncomplicated anamnesis and course of pregnancy. Additionally, the first group was divided into subgroups according to pregnancy outcomes: A – 38 women who gave birth at 37-40 weeks, despite the complicated course of the current pregnancy, B – 13 women who gave birth at 28-36 weeks + 6 days, C – 9 women who birth at 22-27 weeks + 6 days. The average age of the examined in both groups was 33.4 ± 5.2 years. Most women were from Kyiv and the region (69.4 %); from the western, eastern, and central of Ukraine – 8.2 %, 5.5 %, and 16.9 % of pregnant women, respectively.

Accumulation of ^{137}Cs with different activity was detected in the placentas of women of both groups using β-spectrometry. Placentas of the control incorporated no more than 1.0 Bq/kg of ^{137}Cs. The activity of ^{137}Cs in the placentas of women of the first group was related to pregnancy outcomes. According to measurement, about 1.1-4.4 Bq/kg of ^{137}Cs accumulated in placentas of subgroup A. The activity of ^{137}Cs in subgroup B was 4.5-10.4 Bq/kg and in subgroup C – 10.5-38.0 Bq/kg. A morphological examination of the placentas was performed according to the protocol [20]. The degree of placental damage was studied using Olympus BX51 and Axioskop 40 microscopes. The state of peroxide hemostasis was determined using a dynamic biochemical study of the blood of pregnant women.

Statistical data analysis was performed using Microsoft Excel (2016) and Fisher angular transformation. The difference between comparative values was considered significant at $p < 0.05$ (probability index greater than 95 %).

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Results and discussions

The most common cause of reproductive losses is placental dysfunction [7,21], which in pregnant women of the first group was formed under the influence of internal irradiation ^{137}Cs [8,9]. Of course, the decisive factor was the absorbed dose of radiation.

According to the data of β-spectrometry, the accumulation of ^{137}Cs with a specific mass of up to *1.0 Bq/kg* was found in the placentas of the control group without damage to its architectonics.

In the placentas of the first group, violations of the histological structure were determined as a result of irradiation with incorporated ^{137}Cs.

The placentas of subgroup A contained *1.1-4.4 Bq/kg* of ^{137}Cs. Foci of ischemic infarction were found on the maternal surface of 30 % of placentas. The decidual membrane in 50 % of the samples had «afunctional zones» formed due to the convergence of intermediate and terminal villi with stroma fibrosis. An accumulation of fibrin was detected in the intervillous space. The villi were walled-up fibrin. A decrease in area and perfusion of villi increases the risk of chorionic infarction and, accordingly, pregnancy failure.

Subgroup B included placentas from premature births at 28-36^{+6} weeks by viable children. Intraplacental accumulation of *4.5-10.4 Bq/kg* ^{137}Cs caused damage to the maternal stroma. Areas of ischemia were found on the maternal surface. The decidua are represented by «afunctional zones» and signs of exfoliation. Dystrophic changes inhibit oxygen transport from the intervillous space to the umbilical cord. Insufficient placental oxygenation, synthesis of inflammatory mediators, and activation of phagocytosis lead to fetal distress, cervical remodeling, amnion rupture, and premature birth.

Subgroup C included placentas from early premature labor by a dead fetus. Accumulation of *10,5-38,0 Bq/kg* ^{137}Cs causes damage to maternal and fetal structures in the placentas of subgroup C. Chronic radiation stress due to the accumulation of 10,5-38,0 Bq/kg ^{137}Cs contributes to the development of systemic endothelial dysfunction, activation pro-inflammatory response, and pro-coagulation potential. Depletion of the compensatory ability of subgroup C placentas occurs due to acute inflammation of the decidua, immaturity of intermediate and terminal villi,

and a global decrease in vascular perfusion. Hence, internal exposure ^{137}Cs above 10.4 Bq/kg is fatal to the fetus.

The mechanism for realizing the toxicity of xenobiotics, in particular radionuclides, is lipid peroxidation (LPO) [17-19,22]. Any powerful impact on the body initiates LPO, the intermediate and final products of which are cytotoxic and mutagenic. An increased content of malondialdehyde (MDA), diene conjugates (DK), lipid hydroperoxides, and anion-radical oxygen was found in the blood of women of the first group (Table 1).

Table 1

Indicators of LPO in the blood of examined women in the dynamics of pregnancy, M±m

Groups	n	Trimester of pregnancy	Diene conjugates, um. od/ml	Lipid hydroperoxides, μmol / ml	Malonic dialdehyde, μmol / ml	O, OH, H_2O_2
First (research) group	70	1st	62.8 ± 4.1[1]	2.1 ± 0.06[1]	149.6 ± 3.8[1]	63.8 ± 3.6[1]
		2nd	36.8 ± 3,2[1]	2.1 ± 0.07[1]	144.4 ± 2.6[1]	54.3 ± 4.3[1]
		3rd	46.8 ± 2.1[1]	3.3 ± 1.1[1]	152.2 ± 3.1[1]	58.6 ± 2.5[1]
Second (control) group	30	1st	27.9 ± 1.2	1.7 ± 0.04	128.4 ± 3.7	35.3 ± 2.8
		2nd	29.5 ± 1.2	1.8 ± 0.06	136.4 ± 2.9	36.4 ± 1.7
		3rd	31.1 ± 2.9	2.0 ± 0.14	142.6 ± 3.6	38.7 ± 1.9

Note: [1]the probability of difference with control, p < 0.01.

Malondialdehyde is a marker of LPO intensification [17] (Table 2). In the blood of women of subgroups B and C, starting from the early stages of pregnancy, increased content of MDA was observed compared to the indicators of subgroup A: in the 1st trimester by 12.7 %, in the 2nd and 3rd trimesters by 5.3 % and 6, 0 % (p < 0.05) respectively; compared to the control group: in the 1st trimester by 17.4 % and 23.3 %, in the 2nd and 3rd trimesters, respectively, by 10.7 % and 11.5 % (p < 0.05). In pregnant women of subgroup A, the content of MDA exceeded that of the control group only in the 1st trimester (+8.7 %) (p < 0.05). The difference between subgroups B and C during gestation is 5.3 %. The increased content of MDA in women of the first group from the 1st trimester of pregnancy indicates the early onset of placental dysfunction. Thus, a high content of MDA in the blood of pregnant women can be considered an early marker of placental dysfunction, premature birth, and antenatal fetal loss.

Table 2

Dynamics of MDA in the blood of examined pregnant under the influence of 137Cs, M ± m

Groups & subgroups		n	MDA, μmol/ml		
			before 12 weeks	13-24 weeks	25-36 weeks
First (research) group	A	30	139.6 ± 4.1[1]	137.6 ± 2.9	144.5 ± 3.2
	B	20	150.8 ± 2.6[1, 2]	144.0 ± 2.0[1, 2]	152.1 ± 2.9[1, 2]
	C[NB!]	20	158.4 ± 4.2[1, 2, 3]	151.6 ± 2.9[1, 2, 3]	160.0 ± 3.2[1, 2, 3]
Second (control) group		30	128.4 ± 3.7	136.4 ± 2.9	142.6 ± 3.6

Notes: [1]the probability of difference with control, p < 0.05;
[2]the probability of difference with subgroup A, p < 0.05;
[3]the probability of difference with subgroup B, p < 0.05;
[NB!] for subgroup C – 25-27+6 weeks.

The activity of superoxide dismutase (SOD), catalase, glutathione peroxidase, and reduced glutathione in the blood reflects the functioning of the antioxidant defense system [18, 19]. In the blood of pregnant of the first group, a deficiency of reduced glutathione, slowed activity of SOD, catalase, and glutathione peroxidase was detected, which indicates inhibition of detoxification mechanisms (Tables 3-5). Depletion of the glutathione reserve leads to an increase in the number of free radicals in the body. Activity SOD is a marker of oxidative stress. SOD is found in oxygen-consuming cells. Manifestation of oxidative stress in pregnant of the first group is a decrease in SOD activity after 25 weeks. In the blood of women of subgroups B and C, reduced content of SOD was found compared to subgroup A: in the 1st trimester by 6.5 % and 12.2 %, in the 2nd trimester by 5.9 % and 21.7 %, and in the 3rd trimester by 10, 7 % and 31.3 %, respectively (p < 0.05); compared to the control group: in the 1st trimester by 13.0 % and 18.2 %, in the 2nd trimester by 11.4 % and 26.3 %, in the 3rd trimester by 17.1 % and 36.2 %, respectively (p < 0.05). The difference between subgroups B and C is 6.0 % in the 1st trimester, 16.8 % in the 2nd trimester, and 23.0 % in the 3rd trimester (p < 0.05). Thus, inhibition of antioxidant protection due to the exposure of 137Cs leads to the depletion of compensatory reactions in the «mother-placenta-fetus» system. A pronounced lack of SOD in the blood during pregnancy should be considered a marker of placental dysfunction, premature birth, and antenatal fetal loss.

Defects in LPO and antioxidant protection against the background of a decrease of glutathione in the blood and the activity of glutathione peroxidase inevitably lead to the pathology of cell membranes with the development of organ and tissue hypoxia. An increase in the content of malondialdehyde in the blood and a decrease in the activity of superoxide dismutase are associated with the severity of radiation damage. Accumulation of reactive oxygen species with the subsequent formation of insoluble, denatured, and mutant proteins threatens the destruction of cells [18, 19, 22]. Overexpression of CO_2 triggers pregnancy termination mechanisms, such as arachidonic cascade and synthesis of prostaglandins.

Table 3

The activity of glutathione-S-transferase in examined pregnant, M±m

Groups & subgroups		n	GST activity, HDNB/mg protein/min
First (research) group	A	30	2.0 ± 0.1[1]
	B	20	1.8 ± 0.2[1]
	C	20	1.8 ± 0.2[1]
Second (control) group		30	3.9 ± 0.2

Note: [1]the probability of difference with control, p < 0.05;

Table 4

Dynamics of SOD in the blood of examined pregnant under the influence of ^{137}Cs, M±m

Groups & subgroups		n	SOD, um. od. act/ml/min		
			before 12 weeks	13-24 weeks	25-28-36 weeks
First (research) group	A	30	51.0 ± 2.6	57.6 ± 2.7	57.9 ± 2.3
	B	20	47.7 ± 2.8	54.2 ± 2.9	51.7 ± 2.4
	C[NB!]	20	44.8 ± 2.7[1]	45.1 ± 2.8[1, 2]	39.8 ± 2.2[1, 2]
Second (control) group		30	54.8 ± 3.6	61.2 ± 1.4	62.4 ± 2.6

Notes: [1]the probability of difference with control ma A підгрупи, p < 0.05;
[2]the probability of difference with subgroup B, p < 0.05;
[NB!] for subgroup C – 25-27[+6] weeks.

Table 5

Indicators of antioxidant protection in the blood of surveyed women in the dynamics of pregnancy, M ± m

Groups	n	Trimester of pregnancy	Catalase, μmol H_2O_2 ml	Superoxide dismutase (SOD), um. od. act /ml/min	Antioxidant activity (AOA), um. od. act /ml/min	Glutathione peroxidase, μmol / ml	Reduced glutathione, μmol / ml
First (research) group	70	1st	25.7 ± 1.5[1]	47.8 ± 2.7	1.4 ± 0.03[1]	2.2 ± 0.04[1]	2.8 ± 0.02[1]
		2nd	38.6 ± 2.4	52.3 ± 2.8[1]	1.3 ± 0.05[1]	3.2 ± 0.06[1]	3.3 ± 0.06[1]
		3rd	32.5 ± 2.1[1]	49.8 ± 2.3[1]	1.3 ± 0.03[1]	2.3 ± 0.04[1]	3.0 ± 0.04[1]
Second (control) group	30	1st	38.5 ± 2.2	54.8 ± 3.6	1.8 ± 0.03	2.6 ± 0.02	3.6 ± 0.03
		2nd	40.6 ± 1.8	61.2 ± 1.4	1.7 ± 0.02	2.5 ± 0.04	3.6 ± 0.02
		3rd	44.8 ± 1.9	62.4 ± 2.6	1.6 ± 0.03	2.6 ± 0.02	3.7 ± 0.03

Note: [1]the probability of difference with control, p < 0.01.

Thus, the incorporated ^{137}Cs disrupt the placental architectonics, which affects the course of pregnancy. Extreme effects depend on the amount of incorporated radioisotope and compensatory capabilities of the placenta. The functional ability of the placentas of subgroup A (1.1-4.4 Bq/kg ^{137}Cs) is preserved despite the circulatory disorders and dystrophic changes. Pathogenetic therapy allows pregnancy to be prolonged up to 37-40 weeks. Structural changes in the placenta due to the action of 4.5-10.4 Bq/kg of ^{137}Cs related to damage to the maternal stroma. Children of women of subgroup B were born viable at 28-36^{+6} weeks due to preservation of the compensatory capabilities of the placenta. The result of internal irradiation of 10.5-38.0 Bq/kg ^{137}Cs (subgroup C) was damage both to maternal and fetal structures of the placenta. Depletion of the compensatory capacity in the placentas of the subgroup C leads to the antenatal death of the fetus.

Conclusions

Internal exposure to ^{137}Cs disrupts the architecture and functional capacity of the placenta. Extreme effects depend on the activity of ^{137}Cs, the compensatory capabilities of the placenta, and the pregnant woman's body. Activation of lipid peroxidation acts as a biochemical amplifier of radiation exposure. An increase in the blood of malondialdehyde, diene conjugates, and free SH groups is associated with the severity of radiation damage. An early marker of primary placental dysfunction, premature birth, and antenatal fetal loss is an increase in MDA content in the blood by 12.0 % and a decrease in SOD by 6.5 % relative to permissible values. An early marker of exhaustion of the compensatory reserve is an increase in the content of MDA in the blood by 23.3 % and a decrease in SOD by more than 18.2 % relative to the permissible values. Decompensation of adaptation mechanisms in the system «mother-placenta-fetus» leads to antenatal losses.

Prospects for further research aim to prevent reproductive losses and pathological conditions caused by internal radiation.

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ОСОБЛИВОСТІ ФУНКЦІОНУВАННЯ СИСТЕМИ ДЕТОКСИКАЦІЇ ПРИ ЗАГРОЗІ ПЕРЕРИВАННЯ ВАГІТНОСТІ ЯК НАСЛІДОК НАКОПИЧЕННЯ ^{137}CS

А. А. Живецька-Денисова[1], І. І. Воробйова[1], Л. А. Лозова[1], В. Б. Ткаченко[1], О. А. Волошин[2], С. М. Толкач[1], О. В. Шамаєва[1], С. К. Стрижак[1]

ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України»[1], Національний університет охорони здоров'я України імені П. Л. Шупика [2] (м. Київ, Україна)

Резюме.

На сьогоднішній день немає єдиної думки щодо патогенезу невиношування вагітності. У сучасному житті на здоров'я людини істотно впливають фактори зовнішнього середовища. У зв'язку з цим через 37 років після аварії на Чорнобильській АЕС залишається актуальним питання про віддалені цитогенетичні та спадкові ефекти у нащадків батьків, уражених радіацією. Забруднені радіонуклідами екосистеми є джерелом радіації для людини. Внутрішнє опромінення є однією з причин репродуктивних втрат. Радіаційний стрес впливає на перебіг окисно-відновних процесів в організмі. Біохімічні показники є маркерами впливу факторів зовнішнього середовища на людину. Дослідження присвячено визначенню стану перекисного гемостазу при невиношуванні вагітності.

Мета дослідження – визначити особливості функціонування системи детоксикації при невиношуванні вагітності внаслідок накопичення ^{137}Cs.

Матеріал і методи дослідження. До першої (дослідної) групи увійшли жінки з репродуктивними втратами в анамнезі та ознаками переривання поточної вагітності; до другої (контрольної) групи – жінки з неускладненим анамнезом та перебігом вагітності. Додатково перша група була розподілена на підгрупи за результатами вагітності: А – 38 жінок, які народили в 37-40 тижнів, незважаючи на ускладнений перебіг поточної вагітності, В – 13 жінок, які народили в 28-36+ 6 тижнів, С – 9 жінок, які народили в 22-27+ 6 тижнів. Стан перекисного гемостазу у жінок вивчали за допомогою біохімічних досліджень. За допомогою β-спектрометрії в плацентах обстежених жінок обох груп було виявлено накопичення ^{137}Cs з різною активністю. Морфологічне дослідження плацент проводили відповідно до протоколу. Використовуючи мікроскопи Olympus BX51 та Axioskop 40, досліджували ступінь ураження плаценти. Аналіз результатів виявив зв'язок між біохімічними показниками, активністю ^{137}Cs і сценаріями вагітності.

Статистичний аналіз даних проводили за допомогою Microsoft Excel (2016) та кутового перетворення Фішера. Різницю між порівняльними значеннями вважали вірогідною при $p < 0,05$ (індекс вірогідності більше 95 %).

Дозвіл на проведення досліджень отримано від Комісії з медичної етики ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (протокол № 3 від 07.06.2017 р.).

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Результати дослідження. Підтверджено, що стан навколишнього середовища відіграє вирішальну роль у патогенезі невиношування вагітності. Доведено, що дисфункція плаценти, спричинена аномальним окислювальним стресом через дію інкорпорованого ^{137}Cs, призводить до переривання вагітності. В результаті виснаження антиоксидантного резерву знижуються компенсаторні можливості плаценти. Встановлено, що активність у плаценті до 1,0 Бк/кг ^{137}Cs не впливає на перебіг гестації. Компенсаторна здатність плаценти зберігається при накопиченні від 1,1 до 4,4 Бк/кг 137Cs. При цьому можливо пролонгувати вагітність до терміну вчасних пологів. Внутрішнє опромінення з активністю 4,5-10,4 Бк/кг 137Cs викликає пошкодження строми материнської поверхні плаценти і передчасні пологи в терміні 28-36+ 6 тижнів. При цьому новонароджені життєздатні завдяки збереженню компенсаторних реакцій у плаценті. Накопичення понад 10,4 Бк/кг 137Cs спричиняє антенатальну загибель плода та ранні передчасні пологи через пошкодження материнських і плодових структур плаценти. Підвищення вмісту малонового діальдегіду та зниження активності супероксиддисмутази в крові свідчать про тяжкість променевого ураження.

Висновки. Внутрішнє опромінення ^{137}Cs порушує архітектоніку та функціональну спроможність плаценти. Екстремальні ефекти залежать від активності ^{137}Cs, компенсаторних можливостей плаценти і організму вагітної. Морфо-функціональний стан клітинних мембран тісно пов'язаний з перекисним окисленням ліпідів. Збільшення в крові вмісту малонового діальдегіду, дієнових кон'югатів та вільних SH-груп корелює із тяжкістю променевого ураження. Декомпенсація адаптаційних механізмів системи «мати-плацента-плід» викликає антенатальну загибель плода. Біохімічним підсилювачем радіаційного впливу є активація перекисного окислення ліпідів.

Ключові слова: невиношування вагітності; плацента; ^{137}Cs; перекисне окислення ліпідів; глутатіон; система антиоксидантного захисту.

Contact information:
Alla Zhyvetska-Denysova – MD, PhD, Leading Researcher of the Department of Scientific Problems of Miscarriage, State Institution «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).
e-mail: alla.zhivetskaya.denisova@gmail.com
ORCID: https://orcid.org/0000-0001-8418-5740

Iryna Vorobiova – MD, DSc, Head of the Department of Scientific Problems of Miscarriage, State Institution «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).
e-mail: doctor.irina.v@gmail.com
ORCID: https://orcid.org/0000-0002-6836-5845

Liliia Lozova – Junior Researcher of the Department of Introduction and Research of Modern Medical Technologies Effectiveness in Obstetrics and Perinatology, State Institution «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).
e-mail: lilya.lozova@gmail.com
ORCID: https://orcid.org/ 0000-0002-7118-6899

Viktoriia Tkachenko – MD, PhD, Leading Researcher of the Department of Scientific Problems of Miscarriage, State Institution «Institute of Pediatrics, Obstetrics and Gynecology named academic Elena M. Lukyanova National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).
e-mail: mdviktoriiatkachenko@gmail.com
ORCID: https://orcid.org/ 0000-0001-6622-9324

Oleksandr Voloshyn – MD, PhD, DSc, Associate Professor, Department of Obstetrics and Gynecology № 1, Shupyk National Healthcare University of Ukraine (Kyiv, Ukraine).
e-mail: alexvolua@gmail.com
ORCID: https://orcid.org/ 0000-0002-6586-5449

Sergij Tolkach – MD, PhD, Leading Researcher of the Department of Scientific Problems of Miscarriage, State Institution «Institute of Pediatrics, Obstetrics and Gynecology named academic Elena M. Lukyanova National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).
e-mail: sergij.tolkach@gmail.com
ORCID: https://orcid.org/ 0000-0003-0753-8869

Olena Shamaieva – MD, PhD, Senior Researcher of the Department of Introduction and Research of Modern Medical Technologies Effectiveness in Obstetrics and Perinatology, State Institution «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).

Svitlana Stryzhak – Researcher, Laboratory of Endocrinology and Biochemistry, State Institution «Institute of Pediatrics, Obstetrics, and Gynecology named academic Elena M. Lukyanova of the National Academy of Medical Sciences of Ukraine» (Kyiv, Ukraine).
e-mail: llanalana1@gmail.com
ORCID ID: https://orcid.org/0000-0002-8331-4050

Контактна інформація:
Живецька-Денисова Алла Антонівна – кандидат медичних наук, провідний науковий співробітник відділення наукових проблем невиношування вагітності, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).
e-mail: alla.zhivetskaya.denisova@gmail.com
ORCID: https://orcid.org/0000-0001-8418-5740

Воробйова Ірина Іванівна – доктор медичних наук, керівник відділення наукових проблем невиношування вагітності, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).
e-mail: doctor.irina.v@gmail.com
ORCID: https://orcid.org/0000-0002-6836-5845

Лозова Лілія Анатоліївна – молодший науковий співробітник відділення впровадження та вивчення ефективності сучасних медичних технологій в акушерстві та перинатології, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).
e-mail: lilya.lozova@gmail.com
ORCID: https://orcid.org/ 0000-0002-7118-6899

Ткаченко Вікторія Борисівна – кандидат медичних наук, провідний науковий співробітник відділення наукових проблем невиношування вагітності, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).
e-mail: mdviktoriiatkachenko@gmail.com
ORCID: https://orcid.org/ 0000-0001-6622-9324

Волошин Олександр Анатолійович – доктор медичних наук, доцент кафедри акушерства і гінекології № 1, Національний університет охорони здоров'я України імені П. Л. Шупика (м. Київ, Україна).
e-mail: alexvolua@gmail.com
ORCID: https://orcid.org/ 0000-0002-6586-5449

Толкач Сергій Миколайович – кандидат медичних наук, провідний науковий співробітник відділення наукових проблем невиношування вагітності ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).
e-mail: sergij.tolkach@gmail.com
ORCID: https://orcid.org/ 0000-0003-0753-8869

Шамаєва Олена Володимирівна – кандидат медичних наук, старший науковий співробітник відділення впровадження та вивчення ефективності сучасних медичних технологій в акушерстві та перинатології, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).

Стрижак Світлана Костянтинівна – науковий співробітник, лабораторія ендокринології та біохімії, ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна).
e-mail: llanalana1@gmail.com
ORCID ID: https://orcid.org/0000-0002-8331-4050

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