

Health State of Belarusian Children Suffering from the Chernobyl Accident: Sixteen Years after the Catastrophe

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Abstract

A prospective cohort study was carried out to investigate the health state of Belarusian children suffering from the Chernobyl accident. The main group consisted of 133 children permanently residing in the radioactively contaminated territories, while the control group was 186 children permanently residing in the territories with natural radiation background. During the period of observation the constantly increased level of the annual summary effective dose of radiation (0.13-2.24 mSv) were revealed in the children of the main group. All members of both groups were clinically examined at least two times during the follow-up of 1990 - 2001. Heavy metals burden of Pb, Cd and Hg were also measured in urine excretion. The results of clinical examination clearly indicate that the frequency of complaints, as well as the frequency of major clinical syndromes and diagnoses, was increasing in both groups. A growth of the gastrointestinal pathology, as well as an increase in cardiovascular manifestations of the vegetative dysfunction syndrome, was the most important. It should be noted that practically all forms of studied nosology were more prevalent in the main group than in the control both at the first and the second examination. High values of relative risk (RR) of the main group were obtained for arterial hypotension (RR=2.21 and 3.73 at the first and the second examination, respectively) and cardiac metabolic dysfunction (RR=4.66 and 3.33). Aggravating situation of the health state of Belarusian children requires urgent prophylaxis measures for pathologies that are enhanced by environmental factors.

Introduction

Sixteen years passed after the Chernobyl accident, but the problem of radioactive contamination in Belarus is still actual. During the first months after the accident, radioactive iodine was the main dose-forming radionuclide. At present, radioactive cesium-137 holds this place [1-5]. Chronic radiation exposure by this radionuclide presents a great danger for the population living in the contaminated areas.

In the formation of exposure doses to the population, a considerable role belongs to the type of soils, which determines the rate of cesium radionuclide migration through the biological (food) chain. Peaty and swampy soils of Belarusian woodlands are typical in the territory of radiation control. These soils are characterized with high speed of migration in the biological chain [6]. As a consequence, increased radiocesium activity in milk is observed, as well as high radionuclide body burden. Residing in the radioactively contaminated territories leads to the formation of accumulated exposure dose of 80 mSv and greater in separate settlements of Gomel region during the whole period after the accident.

In addition to radioactive contamination, chemical contaminations with heavy metals such as lead (Pb), cadmium (Cd), mercury (Hg) etc. due to various social activities are also playing important roles in the appearance and development of diseases. Increase of lead burden in human body leads to brain malformation, embryonic development disorders, atrophy of mucous membrane of gastrointestinal tract, and impairment of structural and functional properties of erythrocyte membranes [7-10]. Cadmium effects

the state of cell immunity damaging the activity of polymorph nuclear leucocytes and inhibiting the processes of clonal differentiation and activation of mature lymphocytes [7]. Chronic mercury intoxication leads to an increase of goiter prevalence, disturbance of endocrine function of thyroid gland, membranous proteins SH-groups, oxidation, inhibition of activity of a number of enzymes [7,9].

In the territory of Belarus, a considerable amount of xenobiotics penetrates the organism of children. The response of children's organism to the effect of anthropogenic factors differs considerably from that of adult. Intensity of metabolic processes in children is higher than in adults, but the rate of xenobiotics' metabolism is lower. With an increase of concentration of chemical substances in the biosphere, the number of children with deviations of reactivity is growing [11]. The younger the child, the less manifest are specific features of toxic effect [12].

According to our studies, in rural districts of Brest and Gomel regions where the territories were contaminated by the Chernobyl accident, the proportion of the children found to be "contaminated" with lead are 41.1 and 56.7 %, respectively. While, a more favorable situation (15.2%) is observed in rural districts of Vitebsk region (control) where the technogenic effect is rather less.

Considering the aggravated environmental situation in Belarus, it is urgent to study the combined effects of radionuclide and several chemicals in their small concentrations, which are most frequent under the real condition. It should be noted that these effects are not manifested by typical signs of damage with clear-cut clinical pictures, but exist in the form of nonspecific reactions or syndromes of different degree of manifestation [13-18].

This report presents the results of a prospective cohort study we are continuing to investigate the health state of the children suffering from the combined effects of the long-term low-dose radiation and chemical exposure.

Material and Methods

Cohort selection

At the Pediatric Department of the Research Clinical Institute for Radiation Medicine and Endocrinology, during 1990 – 2001, a cohort prospective examination of children (individual examination in age dynamics) residing in the territory of the Republic of Belarus has been conducted. All the randomly selected children were divided into 2 groups: the main and the control. The main group included 133 children (73 boys and 60 girls) permanently residing in the radioactively contaminated territories of Gomel (Yelsk, Narovlya, Bragin districts), Mogilev (Cherikov) and Brest (Stolin, Luninets) regions. The control group consisted of 186 children (101 boys and 85 girls) permanently residing in the territories with natural radiation background (Braslav district of Vitebsk region).

Medical examination

Standardized protocol of clinical examination included the children's complaints and case history, pediatric examination, laboratory findings, ECG, ultrasound examination, fibrogastroscopy with gastric biopsy and morphological examination of gastric biopsies.

Clinical examinations of the selected children were performed at least two times: the first examination was 1995 - 1998 and the second - in 1998 – 2001. Average time interval between the examinations in the main group was 2.1 years (within the range from 1.5 to 2.5 years) and in the control group – 2.5 years (from 2 year to 3 years). Mean age of the children at the time of the first examination was 10.6 years (6 - 15 years) in the main group and in the control group – 9.5 years (6 - 14 years).

Dose assessment and heavy metals determination

Annual summary effective dose of radiation (ASED) was calculated as a result of both individual whole body counting for internal dose and gamma rate measurements on the ground for external dose [19]. All children underwent whole-body counting based on registration of gamma quantum in a scintillation detector with a sodium iodine crystal activated with thallium. The whole body counters used in this study

were permanently located at the regional centres and calibrated on a regular basis as part of a national programme for calculating annual internal dose to the population of Belarus. The calculation of external dose was based on the annual gamma rate measurements in the villages of Belarus and performed by the Belarus state committee for the control of radiological situation.

The urine level of lead (Pb), cadmium (Cd) and mercury (Hg) was determined with the method of roentgen spectral analysis, using a roentgen fluorescent spectrofluorimeter “Spectrace-5000” (“Trackor X-ray”, Netherlands).

Erythrocyte membranes state

Physical-chemical state in membrane lipids were estimated using luminescence of lipophylic fluorescent probe 1,6-diphenyl-1,3,5-hexatriene (DPH) and coefficient of pyren excimerization (CEP), included into the erythrocytes ghosts. Fluorescent parameters of erythrocytes membranes were measured using luminescent spectrophotometer LSF 222 (“Solar”, Belarus).

Data processing

Results of examination were input into a database (Paradox 4.0) and processed with methods of parametric and nonparametric statistics using SPSS 9.0 statistical package. Epidemiological analysis of data was performed with the help of EPIINFO6 (version 6.04 b). Relative risk (RR) with confidential intervals (CI) was calculated and relationships of two variables were determined using χ^2 -criteria. Results of the first and the second clinical and laboratory examination of children are analyzed in this article.

Results and discussion

Radio-ecological status

Radio-ecological parameters of both examined groups are shown in Table 1. The data given in Table 1 testify to a non-significant increase in ASED in the children of the main group during the time period of two observations. ASED in the exposed children (main group) is characterized with a permanently higher values compared to the unexposed group (control). Lead, cadmium and mercury urine levels were significantly lower in the control group compared to the main at the time of the first examination. Further, changes in heavy metals urine contents were characterized by a decrease of lead, cadmium and mercury levels in urine in the children of the main group and by an increase of urine lead concentration in the children from the control group (Table 1).

Table 1. Radio-ecological parameters in children of observed groups.

Parameters	Groups			
	Main		Control	
	1 st examination a	2 nd examination b	1 st examination c	2 nd examination d
ASED, mSv	0.770 (0.13-1.297)	0.810 (0.13-2.24)	0.024** (0.017-0.037)	0.034*** (0.017-0.320)
Pb urine excretion, mg/l	0.040 (0-0.359)	0.020* (0-0.076)	0.0172** (0-0.069)	0.028* (0-0.082)
Cd urine excretion, mg/l	0.035 (0-0.159)	0.025 (0-0.053)	0.02** (0-0.08)	0.015 (0-0.041)
Hg urine excretion, mg/l	0.031 (0-0.078)	0.021* (0-0.063)	0.022** (0-0.102)	0.019 (0-0.069)

Note: Minimal and maximal values are shown in brackets.

*- ^{b-a}; ^{d-c} (P<0.05) **- ^{c-a} (P<0.05) ***- ^{d-b} (P<0.05)

Clinical findings

Complaints of the examined children

Contents of complaints observed in the examined children are shown in Table 2. The frequency of the children with some kinds of complaints is larger in the main group than in the control both at the first and the second examinations. There is observed a growing tendency of complaints for both groups between the first and the second examinations.

The frequency of astenoneurotic complaints was significantly higher in the main group than in the control during the first examination. In the children of the main group a growing tendency of such complaints was observed with time. In the control group an increased incidence of astenoneurotic complaints was also ascertained at the moment of the second investigation, though it did not get the values observed in the main group.

It should be noted that there were high frequencies of complaints of headaches among the examined children. A significantly higher prevalence with this complaint in the main group was observed as compared with the control, while the incidence of headaches increased in both groups with time.

The number of complaints of heart disturbance significantly increased at the second examination in both groups with a higher prevalence in the main group.

Gastroenterological complaints prevailed among the total structure of complaints. At the time of the second examination, significant increases were observed in the frequency complaints such as belch, heartburn and decreased appetite in both groups. Stomachache was the most frequent complaint.

Clinical syndromes and diagnoses

The data shown in Table 3 give the distribution of major clinical syndromes and diagnoses in the examined children during the both periods of observation.

Table 2. Frequency of complaints in examined children, (%).

Complaints	Groups			
	Main		Control	
	1 st examination a	2 nd examination b	1 st examination c	2 nd examination d
Complaints present	72.2	78.9	45.7**	66.1****
Complaints absent	27.8	21.1	54.3**	33.9****
Weakness	31.6	28.6	11.9**	24.7*
Dizziness	12.8	17.3	4.9**	5.8***
Headache	37.6	45.1	20.7**	25.9****
Syncope	0.8	2.3	0	0
Nasal bleeding	2.3	3.8	0.5	1.2
Fatigability	27.1	23.3	8.2**	17.2*
Irritability	3.0	4.5	1.1	2.9
Troubled sleep	3.0	1.5	0.5	0
Uracrasia	0.8	1.5	0.5	1.7
Heartache	6.8	9.0	13.0	11.5
Heart disturbance (arrhythmia)	1.5	18.8*	0	5.8****
Stomachache	51.9	64.7*	21.2**	44.3****
Belching	9.8	15.8	2.2**	12.6*
Heartburn	1.5	7.5*	1.6	5.8*
Decreased appetite	9.0	14.3	1.1**	10.3*
Diarrhea	2.3	0.8	0.5	0
Constipation	0.8	0.8	1.1	0.6
Allergic eruptions	1.5	3.0	0.5	5.8*

Note : * - b-a; d-c (P<0.05) ** - c-a (P<0.05) *** - d-b (P<0.05)

In the structure of diseases and clinical syndromes, the most prevalent were cardiovascular manifestation of the vegetative dysfunction (vegetovascular syndrome), chronic pathology of the gastrointestinal tract (chronic gastritis, duodenitis and gastroduodenitis), caries, asthenoneurotic syndrome, tonsilla hypertrophy and chronic tonsillitis. A significant increase in the incidence of the combined form of chronic gastrointestinal pathology (chronic gastrodoudenitis) was observed in both groups with its higher prevalence in the main group.

Cardiovascular syndromes and diagnoses are presented in the form of mitral valve prolapse and vegetovascular syndrome including arterial hypertension, arterial hypotension and cardiac syndrome (arrhythmia, metabolic dysfunction, isolated heart murmur). For the arterial hypertension syndrome, the children of both groups were distributed approximately equally. A special attention should be paid to the distribution of children with the arterial hypotension syndrome: during the first examination, the frequency of hypotension in the main group exceeded significantly than in the control group; later on, with age a tendency to a decreased frequency of hypotension was observed only in the control group. An opposite picture was revealed in the main group: the arterial hypotension syndrome increased at the second examination.

In the children suffering from the combined radio-chemical influence the main hemodynamic mechanism of arterial pressure decrease is the insufficiency of the arterial blood vessels tonus. The so-called syndrome of arterial hypotension is caused by the disturbances in the mechanisms of neurohormonal regulation of vascular tonus as a decrease in the catecholamine activity combined with a decrease in the hormonal activity of thyroid gland as a result of iodine deficiency observed in Belarus [20] and the impact of radioiodine released after the Chernobyl accident. Besides, a decrease of serum cAPM level as well as predominance in prostacyclin depressive activity was revealed in the children with

Table 3. Frequency of clinical syndromes and diagnoses in examined children (%).

Clinical syndromes and diagnosis	Groups			
	Main		Control	
	1 st	2 nd	1 st	2 nd
	examination a	examination b	examination c	examination d
Chronic gastritis	44.2	36.4	31.9	32.9
Chronic duodenitis	6.2	4.7	1.5	1.4
Chronic gastroduodenitis	17.1	39.5*	11.6	28.7*
Bilious dyskinesia	43.4	34.1	17.4**	12.6***
Mitral valve prolapse	2.9	4.5	5.4	4.8
Vegetovascular and cardiac syndrome (total):	67.9	73.7	40.3**	52.2*, ***
incl. arterial hypertension	5.9	3.8	5.9	3.2
arterial hypotension	14.2	18.1	6.5**	4.8***
metabolic cardiac dysfunction	14.9	23.3	3.2**	6.9***
arrhythmia	2.2	2.3	0.5	0.5
isolated heart murmur	40.4	33.8	23.1**	35.5*
Asthenoneurotic syndrome	20.2	16.9	7.5**	11.3
Uracrasia	3.2	1.5	1.2	4.2
Tonsilla hypertrophy	19.8	20.0	21.2	16.7
Chronic sinusitis	0	1.5	0	0.6
Adenoiditis	2.4	0	0	3.5
Chronic tonsillitis	11.1	9.2	13.6	17.2***
Caries	58.9	59.4	42.6**	37.3***
Chronic periodontitis	6.8	2.4	0**	0.6
Iron deficient anemia	6.6	3.2	6.9	3.5
Allergic eruptions	2.5	0.8	4.6	1.8

Note *_ b-a; d-c (P<0.05) **_ c-a (P<0.05) ***_ d-b (P<0.05)

hypotension of the main group [21]. Study of the blood vessels functional reactivity in the suffering children confirms a significant decrease of arterial blood vessels tonus and shows the insufficiency in the normal arterial pressure supply. Also significant disturbance of peripheral, cerebral and systemic tonus of arterial vessels has been ascertained on the level of intra systemic relations [22].

During the first examination, the frequency of children with vegetative dysfunction manifestations in the form of cardiac syndrome was significantly lower in the control group as compared with the main one. During clinical follow-up this syndrome increased in both groups, which caused an increased number of complaints of heart disturbances. It should be noted that this increase was mainly due to metabolic cardiac dysfunction both in the main and control groups, as well as due to the isolated systolic murmur in the control group. Metabolic cardiac dysfunction is characterized by a disorder in the phase of ventricle myocardium repolarization of different degree of manifestation [23].

Distribution of the psycho neurological syndromes and diagnoses was characterized by the fact that asthenoneurotic syndrome prevailed in the main group both during the first and second examination, the distinctions being statistically significant in the first case (Table 3).

Relative risk analysis

Epidemiological analysis of the obtained data with the calculation of the relative risk (RR) of the development of the diseases is performed in Table 4.

The obtained data show that both during the first and second examination, the RR values of the development of the diseases were higher in the children from the main group as compared with the control. It mostly concerns arterial hypotension and metabolic form of cardiac syndrome. An increase in the RR of the development of arterial hypotension points the relationship between the observed pathology and its age dynamics, on the one hand, and environmental impact on the children's organism, on the other hand.

Chronic small doses radiation and chemical exposure causes nonspecific disorders in the organism (changes in oxidative processes, decrease in cell membrane stability, attenuation of protective and adaptive mechanisms). The effect of some of them leads to the development of ecological disadaptation syndrome [24] and appearance of clinically signed syndromes and diseases.

According to published data, the effect of environmental pollutants on the health of children makes about 20%, therefore, the health of the population is considered at present as an integral index of the quality of the environment [3-5].

Erythrocyte membranes structural and functional state

Cell membranes are considered to be the initial target of the environmental exposure and pathologic effect of xenobiotics is mediated, first of all, by membranous effects. Universal property of biological

Table 4. Relative risk (RR) of some clinical syndromes and diseases in observed children.

Clinical syndrome and diagnosis	1 st examination	2 nd examination
Chronic gastroduodenitis	1.46 (0.85-2.51) $\chi^2 = 1.49, P < 0.223$	1.40 (1.03-1.90) $\chi^2 = 4.01, P < 0.045$
Arterial hypotension	2.21 (1.11-4.40) $\chi^2 = 4.57, P < 0.03$	3.73 (1.79-7.76) $\chi^2 = 13.19, P < 0.0002$
Cardiac metabolic dysfunction	4.66 (1.92-11.92) $\chi^2 = 12.92, P < 0.0003$	3.33 (1.82-6.13) $\chi^2 = 16.02, P < 0.00006$
Vegetovascular syndrome	1.68 (1.36-2.07) $\chi^2 = 22.14, P < 0.000003$	1.41 (1.19-1.68) $\chi^2 = 14.24, P < 0.0002$

Note: Confidential Interval (CI) is shown in brackets.

membranes is their high sensitivity to the environmental influences. Structural changes in erythrocyte membranes may be indicated both in the lipid bilayer and proteins. At present, it has been ascertained that proteins and lipids jointly participate in structural reformation of biological membranes. Investigation of membranes with the help of lipophilic fluorescent probes makes it possible to judge about the changes in micro viscosity of membrane lipids.

While studying the changes of physical-chemical state of erythrocyte membranes with the help of lipophilic fluorescent probes, it has been shown that fluorescent intensity of the lipophilic probe DPH included into the erythrocyte ghosts was 0.84 ± 0.07 relative units in the children of the main group, which was significantly higher than in the control one (0.66 ± 0.02) ($P < 0.05$) (Figure 1).

A decrease by 18.5% in the value of pyren excimerization coefficient (CEP) included into the erythrocytes ghosts of the children from the main group has been ascertained as compared with the group of children living in the Vitebsk region (control group) (Figure 1).

Stability and rheological properties of plasmatic erythrocyte membranes and parameters of hemoglobin reactions determine the supply of body tissue with oxygen. Erythrocyte membrane provides integration and conformation of red blood cell, controls the flow of metabolites inside the cell and outside, and participates in different intercellular interactions and reactions of the erythrocyte cytoplasm to the outside effects. There exist a large number of biochemical and biophysical mechanisms which determine the relation between the state of plasmatic membranes and components of cytoplasm, and regulate the transmission of signal lengthwise through membrane. Changes in the structural organization, properties and stability of erythrocyte membrane in response to environmental effects plays a regulatory role controlling the state of intra erythrocyte components and acting as a means of erythrocyte adaptation to the changing situation in serum. The obtained data show that physical and chemical state of erythrocyte membranes in children from the main group was characterized by changes in micro viscosity of membranous lipids, which may result from the effect of environmental impact. These changes could be estimated as general biological response of cell membranes of all types for the environmental exposure and play significant unified role in development of disadaptation syndrome and different health disorders and diseases.

Conclusions

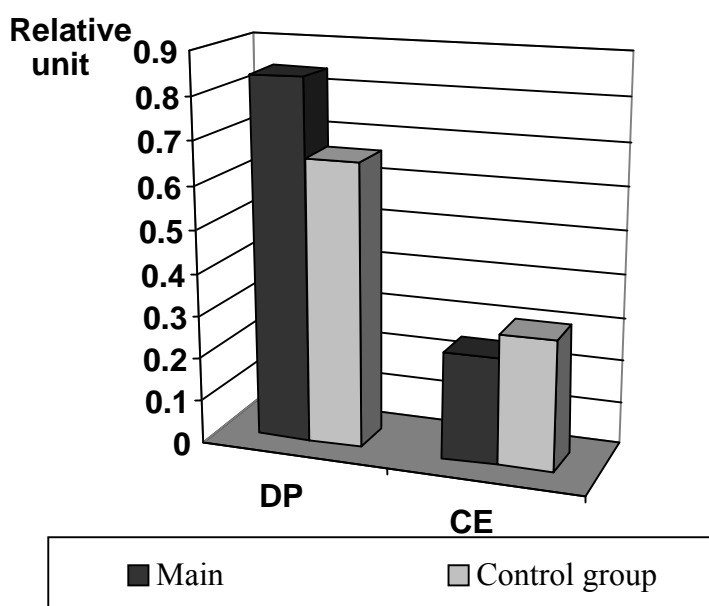


Figure 1. Mean values of lipophilic fluorescent probe 1,6-diphenyl-1,3,5-hexatriene (DPH) and coefficient of excimerization of pyren (CEP) in examined children.

Clinical follow-up of two groups of Belarusian children (the main and the control) clearly indicates an aggravating situation of their health state by both the number of complaints and the number of major clinical syndromes and diagnoses. The most important is the growth of the gastrointestinal pathology, as well as an increase in cardiovascular manifestations of the vegetative dysfunction syndrome.

Practically all forms of studied nosology are more prevalent in the main group compared to the control both at the first and the second examinations. High values of relative risk (RR) are obtained for arterial hypotension (RR=2.21 and 3.73 at the first and the second examination, respectively) and cardiac metabolic dysfunction (RR=4.66 and 3.33).

The present situation requires that measures for correction and prophylaxis of environmental depending pathology should be conducted. These measures should cover all aspects of etiopathogenesis and be directed to restoration of the impaired resistance of the children's organisms using first of all, medication free (medicines free or non medicament) means and methods.

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