MEDICAL SCIENCES

GENDER DIFFERENCES IN THE PROCESSES OF REGULATION OF THE FUNCTIONING OF THE FOLATE CYCLE AND THE PITUITARY-THYROID AXIS IN CHILDREN LIVING NEAR THE CHERNOBYL EXCLUSION ZONE

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The long-term humanitarian consequences of the accident at the Chernobyl nuclear power plant (ChNPP) are a serious problem for the medical community.

The emergence of previously unknown forms of pathological conditions among the child population forces us to reconsider the methodology of etiopathogenetic studies.

This applies, in particular, to the condition of hyperhomocysteinemia, which was first registered in 2015 in a large number of children living near the Chernobyl Exclusion Zone (ChEZ) [1, p. 29].

The wide range of reference values of the studied biochemical parameters does not allow for an objective assessment of the metabolic status of children living in the territory affected by the Chernobyl accident.

In these children, with a pronounced increase in the content of homocysteine (H_{cy}) in the blood, the values of most indicators associated with the metabolism of this amino acid did not go beyond the reference range.

In this regard, when assessing the metabolic processes in the body of children under conditions of constant radiation exposure due to the Chernobyl accident, it is advisable to use the results of an analysis of correlations of the determined indicators, taking into account the state of the genetic system that controls H_{cy} methylation and the formation of internal methionine.

At the same time, attention should be paid to gender characteristics, since hyperhomocysteinemia is more common among boys than among girls [2, p. 33].

Studying the correlations between H_{cy}, pituitary thyroid-stimulating hormone (TSH), thyroxine (T_4), triiodothyronine (T_3) will provide objective information about the regulation of the functioning of the thyroid gland

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(thyroid) and the occurrence of pathological processes associated with this organ.

The material for the analytical study was the results of a laboratory genetic examination of 379 children aged 12-17 years (187 boys and 192 girls) from Polessky and Ivankovsky districts of the Kyiv region, carried out in 2015 within the framework of projects of the European Commission and the Regional Council of Rhone-Alpes (France).

In the course of the study, direct and inverse correlations were identified between the analyzed indicators in genetic subgroups. A direct correlation between H_{cy}-T_4 was found in subgroups of boys in the Polessky district (main genotypes A/A MTR:2756, A/C, C/C MTHFR:1298, C/C MTHFR:677 and A/A MTRR:66), with blood H_{cy} levels ≤ 10.0 μmol/l.

It indicates physiological parity between the folate cycle (FC) and the pituitary-thyroid axis.

In the same subgroups, when the level of H_{cy} in the blood > 10.0 μmol/l, an inverse correlation between TSH and T_4 was determined, indicating the influence of TSH on the process of T_4 deiodination. Moreover, in some of these subgroups, the proportion of cases with the T allele MTHFR:677 was greater than those with H_{cy} levels in the blood ≤ 10.0 μmol/L (Table 1).

Table 1

Proportion of genotypes C/T, T/T MTHFR:677 in genetic subgroups of boys

Main genotype	Level H_{cy}, μmol/l	Correlations	Proportion of genotypes C/T, T/T MTHFR:677, %
A/A MTR:2756	≤ 10.0	+H_{cy}-T_4	28.6
	> 10.0	-TSH-T_4	60.0
A/C, C/C MTHFR:1298	≤ 10.0	+H_{cy}-T_4	7.1
	> 10.0	-TSH-T_4	39.3
A/A MTRR:66	≤ 10.0	+H_{cy}-T_4	25.0
	> 10.0	-	37.5

Note. «+» - direct correlation; «-» - inverse correlation.

In the general group and subgroups of girls from the Polessky district (main genotypes A/A MTR:2756, A/A MTHFR:1298, C/T, T/T MTHFR:677, A/A MTRR:66, A/G, G/G MTRR:66), with blood H_{cy} levels ≤ 10.0 μmol/L, inverse associations between H_{cy}-T_3 and H_{cy}-T_3/T_4 were identified. These connections indicate the influence of T_3 on the process of H_{cy} methylation.

After forest fires in the ChEZ [3, p. 10] in subgroups of girls from the Ivankovsky district, when the level of H_{cy} in the blood was >10.0 μmol/l, direct

correlations of TSH-T_3 and TSH-T_3/T_4 were most often detected, illustrating the stimulating effect of TSH process of T_3 formation.

In the subgroups of girls and boys, with the main genotype C/C MTHFR:677, with the level of H_{cy} in the blood > 10.0 μmol/l, correlations were revealed - direct TSH-T_3/T_4 (in the subgroup of girls r = 0.629, p = 0.002, n = 21; in the boys subgroup r = 0.428, p = 0.010, n = 35) and reverse TSH-T_4 (in the girls subgroup r = - 0.673, p = 0.001, n = 21; in the boys subgroup r = - 0.403, p = 0.016, n = 35), reflecting the influence of TSH on the process of T_4 deiodination and T_3 formation.

In the same genetic subgroup of girls, with a blood H_{cy} level of ≤ 10.0 μmol/l, an inverse correlation between H_{cy}-T_3/T_4 was recorded (r = - 0.632, p = 0.011, n = 15), which was absent in the similar subgroup of boys.

Considering the absence in the genome of children of this subgroup of the T MTHFR:677 allele, which contributes to an increase in the level of H_{cy} in the blood [4, p. 12], it can be reasonably stated that the identified effects of the interaction of H_{cy} and hormones of the pituitary-thyroid axis are due, to a greater extent, to external environmental radiation exposure.

The results obtained indicate that in the bodies of children living near the ChEZ, with appropriate combinations of FC genes, including the T allele MTHFR:677, environmental radiation exposure causes a disruption in the process of H_{cy} methylation and activation of TSH, which affects the metabolism of thyroid hormones.

At the same time, there is an intensification of the process of deiodination of T_4 and an increase in the formation of T_3, which can influence FC enzymes, stimulating the process of H_{cy} methylation.

This is also evidenced by direct correlations between T_3 and the active form of vitamin B_9 [5, p. 382].

The effects of T_3 on FC enzymes, in particular methylenetetrahydrofolate reductase, are more pronounced in girls compared to boys.

This may be the reason why girls' blood contains less H_{cy} than boys' blood.

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