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THE CONTRIBUTION OF GENETIC DETERMINANTS TO THE DEVELOPMENT OF SIGNIFICANT DELAY IN PHYSICAL DEVELOPMENT OF EXTREMELY LOW-BIRTH-WEIGHT INFANTS

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Abstract. We conducted a molecular genetic study using polymerase chain reaction methods with isolation of DNA samples from peripheral blood. A reliable relationship was established between the dominant model (GG + AG vs. AA) of the glutathione-S-transferase genes family and a significant delay in the physical development of premature infants.

The introduction of genetic research to determine the GG + AG genetic model of GSTP1 gene in premature infants will allow to identify the group at risk for significant delay in physical development and to approach its correction individually.

Keywords: genetic determinants, physical development, very low body weight, extremely low body weight, premature infants.

Introduction. Improvements in obstetric and neonatal care both in the world and in Ukraine have led to an increase in the survival rates of small premature infants, but the number of pathological conditions that accompany their adaptation does not decrease, and the proportion of healthy children does not exceed 10-25% [1, p. 139]. The frequency of the development of disorders in physical development in a given cohort of children is also increasing [2, p. 97]. Our previous studies have investigated the contribution of glutathione-S-transferase genes polymorphism to the development of speech disorders in extremely preterm infants and to the development of impaired physical development in this cohort of children with bronchopulmonary dysplasia [3, p. 36; 4, p. 110]. Therefore, we hypothesized that polymorphism of these genes may also have an effect of significantly delaying the physical development in preterm infants, which may serve as a basis for creating a comprehensive prophylactic program of early intervention.

The aim of the research was to determine the genetic determinants for the formation of a significant delay in the physical development of infants born with very and extremely low small body weight.

Object and methods of the research. A prospective cohort study was conducted, which included 155 children who were observed at the Development Center at Poltava Regional Clinical Hospital for 2 years of life.

Physical development assessments were performed according to the WHO charts, scales by Fenton T.R. [5, p. 3], Order No 149 of Ministry of Public Health of Ukraine at 6, 12, 18, 24 months of adjusted age [6, p. 20]. A significant delay in postnatal physical development (DPPD) was identified if body weight, body length, or head circumference were less than 3 ‰. Two groups of infants were formed. The first group included infants with significant DPPD at 24 months (n = 24), when at least at 24 months of adjusted age at least one of the curves of growth, body weight, head circumference was within <3 percentile. The second group included infants who had normal physical development (n = 131) if these indicators were found to be ≥3 percentile.

To investigate the role of genetic determinant in significant DPPD of the examined infants, we examined the associations between glutathione-S-transferase genes polymorphism, dominant models of ACE gene; AGT2R1, eNOS, and significant DPPD at 24 months of age.

Peripheral venous blood served as the material for genetic research. The sampling was performed for the first three days after birth in the amount of 0.25 ml in tubes of the “Monovette” closed system. To determine polymorphic variants after the procedure of DNA samples isolation from the obtained material, which was performed using the commercial set of reagents "DNA-sorb-B", we conducted the molecular genetic study using methods of polymerase chain reaction [7, p. 184].

Results of the research and their discussion. We have investigated the contribution of genetic models to significant DPPD: the “+” vs. "-" of GSTT1 and GSTM1 genes; dominant models: (GG + AG vs. AA) of GSTP1 gene, (DD + DI vs. II) of ACE gene; (CA + AA vs. AA) of AGT2R1 gene (aa + ab vs. bb) of eNOS gene. The results of the study indicated that there was no reliable relationship between the deletion polymorphism of GSTT1 gene or GSTM1 gene and significant DPPD, between the deletion polymorphism of ACE gene; (CA + AA vs. AA) of AGT2R1 gene (aa + ab vs. bb) or eNOS gene and significant DPPD at 24 months. However, we found that the dominant genetic model (GG + AG vs. AA) of GSTP1 gene increases the likelihood of significant DPPD in preterm infants by more than fourfold (Table 1).

Table 1

Associations between significant delay in physical development, glutathione-S-transferase genes polymorphism and renin angiotensin system

Genetic models	OR	95 % CI	P
GSTP1 GG+AG vs. AA	4.2	0.85-413.4	0.044
GSTT1 «-»	0.75	0.58-9.62	0.825
GSTM1 «-»	0.5	0.04-6.08	0.587
ACE DD+ ID	14.0	0.42-88.2	0.09
AGT2R1 AC+CC	3.3	0.11-235.2	0.424
eNOS 4ab+bb	1.5	0.02-36.15	0.624

Conclusion. The introduction of genetic research to determine the GG + AG genetic model of GSTP1 gene in premature infants born with very low and extremely low body weight will identify the group at risk for the significant delay in physical development and will allow to approach its correction individually.

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