VASCULAR ENDOTHELIAL GROWTH FACTOR A AND POLYMORPHISM OF G634C GENE IN PATIENTS WITH MYOCARDIAL INFARCTION IN ACUTE AND DISTANT PERIODS

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The Vascular endothelial growth factor A (VEGF-A) promotes endothelial cell survival in acute myocardial infarction (AMI), accelerates the development of collateral blood supply to ischemic myocardium, reduces the size of the necrotic area. The difference in the synthesis of the VEGF-A between individuals is genetically determined. The purpose of our work was to study the association of polymorphism of the VEGF-A gene (G634C) with cardiovascular risk factors, complications and the dynamics of structural and functional parameters of the left ventricle (LV) myocardium in patients with AMI with ST segment elevation (STEMI) during 6 months.

Materials and Methods. The study involved 91 patients with STEMI, 70 (76.9%) males and 21 (23.1%) females, with an average age (59.21 ± 8.92) years. Patients were hospitalized during the first three days of STEMI after coronary artery stenting. Control group - 12 practically healthy persons. The diagnosis of STEMI and treatment were established in accordance with the recommendations of the European Society of Cardiology (2017). All patients performed a 6-minute walk test, echocardiography from the 3rd to the 5th day of hospitalization and after 6 months. Investigation of the allelic polymorphism of G634C gene of the VEFRA (rs 2010963) was carried out by real-time polymerase chain reaction. The level of the VEGF-A was determined by the enzyme-linked immunosorbent assay. The data is presented as median, interquartile scale, mean ± standard error of mean.

Results. The distribution of alleles and genotypes according to the polymorphic marker of G634C gene of the VEFRA (rs 2010963) in STEMI patients corresponded to the Hardy-Weinberg principle. The following frequency of alleles was observed: G - 76% and C - 24%. Genotypes GG, GC - 52% and 48%. Homozygotes of the GC genotype were not detected, so further analysis was carried out in two groups - GG (n = 48) and GC genotypes (n = 43). Higher concentrations of the VEGF-A were reliably determined in the acute period of the disease in the GG genotype carriers 194.10 [115.02-398.86] pg / ml compared with the GC genotype carriers 148.44 [68.84-221.28] pg / ml (p = 0.047). A significant increase of the VEFRA is defined in the GC group after 6 months from 148.44 [68.84-221.28] pg / ml to 444.18 [236.42-685.58] pg / ml (p = 0.003). There was a decrease in systolic blood pressure (p = 0.028) and diastolic blood pressure (p = 0.045) at re-examination of the GC genotype carriers and compared with the GG genotype carriers (p = 0.043) and (p = 0.021) respectively. The GC genotype group had differences in the LV end-diastolic volume (P = 0.049), the LV end-systolic volume (P = 0.045), and the LV myocardial mass (LVMM) (P = 0.04) during the acute period of the disease. However, significant differences were not detected in the size of the LV cavity after 6 months. The GC genotype group had LVMM reduction after 6 months from 249.97 ± 87.68 g to 213.96 ± 53.03 g (p = 0.039). At the same time, this indicator increased in the GG group, but not veraciously (from 214.27 ± 75.43 to 262.35 ± 77.92, p = 0.737).

Prospects for further research. We made the following conclusions: the GG genotype carriers have a significantly higher VEGF-A concentration than the GC genotype group (p = 0.047) in the acute period of STEMI. GC genotype patients with STEMI is associated with more pronounced changes in LV geometry during the acute period. The GC genotype is associated with better control of hypertension and LVMM reduction after 6 months of observation. Further investigations of the VEGF-A biological effects are perspective direction in the development of prevention and treatment of STEMI.

Key words: Vascular endothelial growth factor A, acute myocardial infarction with ST segment elevation, polymorphism of the VEGF-A gene (G634C).

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GENETIC MARKERS OF VENTRICULAR DILATION AND HYDROCEPHALUS INDUCED BY INTRAVENTRICULAR HEMORRHAGES IN PREMATURE INFANTS

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Post-hemorrhagic ventriculodilation (VD) and hydrocephalus (GC) in premature infants are the consequences of intraventricular hemorrhages (IVH). About 75-80% of premature infants with low and extremely low body weight with intraventricular hemorrhages have signs of ventriculodilatation[4] or hydrocephalus[1, 5], which subsequently requires surgical correction to prevent the development of neurological deficiency. However, timely and successful ventriculoperitoneal shunting does not guarantee positive prediction and regression of neurological symptoms[2, 6]. The innovative methods for the prevention or restriction of brain damage in preterm infants require searching for factors that influence the course of severe intraventricular hemorrhages, the progression of pathology with the subsequent occurrence of post-hemorrhagic ventriculodilatation, which is a key stage in the evolution of neuronal protection[3,7]. The use of non-invasive laboratory biomarkers has become the main element of clinical practice over the past decades. The studies of new biological markers, that enable early identification of newborns from the
risk groups, allow careful monitoring of the disease and providing information about the prognosis, are the strategic
goal of modern neonatal research. The purpose of the work was to determine genetic markers of ventriculodilation
and hydrocephalus induced by intraventricular hemorrhages in prematurely born children by studying renin-
angiotensin system (RAS) genes.

**Materials and Methods.** A multicentre study was conducted, which included 76 prematurely born children with
severe IVH. The including criteria were: gestational age less than 34 weeks, body weight at birth less than 2000,
excluding criteria respectively: presence of congenital malformations, body weight at birth more than 2000 g.
Among the infants with IVH the frequency and causes of such adverse events were investigated: ventriculodilation
and hydrocephalus, which arose up to 28 days of life. The group of infants with ventriculodilation included those
with IVH, which had the expansion of the ventricles more than 90 percentiles according to the gestational age to 28
days of life according to echoscopy. Thus, 2 groups were formed – a group of children with ventriculodilation (n=38)
and a group of children without ventriculodilation (n=38). The group of infants with IVH-induced hydrocephalus included
those who had the ventricular enlargement of more than 97 percentiles up to 28 days of life and the
presence of a diagnosis confirmed by the neurosurgeon. In the group IVH-induced hydrocephalus were 25 infants,
and in the group without the specified disease – 51 infants with IVH. Genetic methods included the study of the
diagnosis confirmed by the neurosurgeon. In the group IVH-induced hydrocephalus were 25 infants,
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**Results.** The study group included 76 infants: 36 girls (47.4%) and 40 boys (52.6%), average body weight at birth
was $1037.84 \pm 43.72$ g., gestational age $27.07 \pm 0.27$ weeks. In the study group, the ratio of boys and girls had not
statistically significant difference (p=0.364). According to the analysis of genotypes distribution in prematurely born
children with severe IVH, we found that the combination of $ID + DD$ genotype of $ACE$ gene and $AC + CC$ genotype
of $AGTR_1$, was significantly more commonly determined in newborns with VD (p=0.050). The frequency of other
investigated genotypes among the groups of children with VD and without this pathology was almost identical. We
have not found any significant differences in the distribution of the genotypes $ACE$, $AGTR_1$, $eNOS$ genes, as well
as their combination in the groups of children with and without HC. It should be noted that in our study the weight
at birth was not associated with the development of IVH-induced hydrocephalus (OR 1.0; 95% CI 0.999 – 1.000;
p=0.130).

**Conclusion.** The combination of $ID + DD$ genotype of $ACE$ gene and $AC + CC$ genotype of $AGTR_1$, gene is
strongly associated with the emergence of IVH-induced ventriculodilation in premature infants with III-IV stages of
IVH.

**Prospects for further research.** The involvement of molecular genetic research in the future is intended to promote
the use of less invasive diagnostic techniques in neonatology with the receipt of an individual genetic passport of
the newborn, which will allow to emphasize the onset and treatment of premature infants and the prevention of the
disabling pathologies.

**Recommendations.** The results of this study are involved in the working-out of a prognostic model for the
development of the IVH-induced ventriculodilation in premature infants with the inclusion of reliable clinical
variables, namely: congenital infection, glucose and diastolic hypotonia on the 2-nd day of life.

**References:**


Impact of Low-Grade Germinational Matrix-Infraventricular Hemorrhage on Neurodevelopmental Outcome of Very Preterm


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**Keywords:** prematurely born child, intraventricular hemorrhage, ventriculodilation, hydrocephalus, polymorphism
of renin-angiotensin system genes.