of group «4», the ARA of Bax expression was 5.93±0.1%. Expression of Bax was identified predominantly in the cytoplasm of tumor cells and in single cells of immune infiltrate. As regards the anti-apoptosis marker bcl-2, it was detected only in single tumors: in one of five observations in the group «2», in one of three observations in the group «3» and in a single case of group «4». Immunopositive staining was detected only in the cytoplasm of single cells of the immune infiltrate. Expression of bcl-2 was absent in tumor cells. Expression of p53 was absent in all observations of the group «1» and in two of five cases of the group «2» (respectively, in three, there was a positive staining of single tumor cells). In groups «3» and «4», all observations were characterized by a positive reaction with p53, but only in single tumor cells. Statistical analysis showed a high positive correlation between the relative area of Ki-67 and relative area of Bax and p-53 expression (r=+0.83 and r=+0,70 respectively). Also moderate positive correlation between the relative area of Bax and p-53 expression (r=+0.62) was identified. Valid correlation between the relative area of Bcl-2 and other investigated markers was absent. Prospects for further research. Further investigation of proliferative-apoptotic processes in other germ cell tumors is planned with the detection of differences between them.

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GENETIC PROFILE OF THE RISK OF DEVELOPING FATAL CASES IN PREMATURE NEWBORNS WITH SEVERE INTRAVENTRICULAR HEMORRHAGES

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Intraventricular hemorrhage (IVH) is one of the main causes of infant mortality. According to data from the University of Southern California, the mortality rate of newborns with intraventricular hemorrhage III and IV degrees is 18-40% [4], initial studies indicated that mortality in premature newborns with intraventricular hemorrhage III degree of severity till 30% and till 60% in children with intraventricular hemorrhage IV degree [2, 3], the same data are confirmed by Ahn S.Y. from et al. [1]. According to the analysis of the mortality rate of prematurely born children with severe IVH in the Poltava region for 2009- 2016 years, we found that the mortality rate remains constant [5]. In our opinion, this situation can be explained by an increase in the survival of newborns with body weight at birth <1000 g, due to improved diagnostic protocols, the presence of combined pathology in premature infants. The purpose of the work was to determine the profile of the risk of developing fatal cases in premature newborns with severe IVH, taking into account the impact statement of polymorphous variants of the *PAC* and *eNOS* genes.

Materials and Methods. To study the effect of the polymorphism of the studied genes on the development of severe IVH and their negative effects, the following genetic models were used: the dominant model (DD DI vs. II) of the *ACE* gene, the dominant model (CA AA vs. AA) of the *AGT2R1* gene, the dominant model (aa ab vs. bb) *eNOS* gene and their combinations. The material for conducting genetic studies was 0.25 ml of blood of newborns, which was taken on the 6^{th}-10^{th} day of life after

diagnosis. To determine the polymorphic variants of the *ACE, AGT2R1* and *eNOS* genes, a polymerase chain reaction was conducted followed by a restriction analysis of the amplification reaction products.

Results. We studied two groups of newborns: I group - 40 infants (birth weight 903.72 ± 56.61 g, GA 26.15 ± 0.34 weeks, girls 19 / 47.5%), who died, and II group - 36 infants (birth weight 1187,3 ± 58,0 g, GA 28,09 ± 0,37 weeks; girls 17/47,22%) who did not die. With simple logistic regression, the association between child death and gestational age (p=0.01) is proved; intubation of the trachea (p = 0.055); introduction of surfactant in the delivery room (p = 0.025); sepsis (p = 0,027), severe respiratory distress syndrome (p = 0,001), acquired by infection, as evidenced by the association with the level of CRP (p = 0.072), the number of leukocytes (p = 0,01) and platelets (p = 0,007) on the 6th day of life. An analysis of the Kaplan-Meier Lean Case study revealed increased risk of infant mortality with a combination of dominant models of ID & DD *ACE* gene + 4ab & 4aa *eNOS* gene after correction for gestational age, compared with infants from II *ACE* and 4bb *eNOS* models. The study of the distribution of polymorphic genotypes of *eNOS* genes and renin-angiotensin system in the infants with severe IVH revealed a lack of significant differences in the frequency of detection of the genetic model of ID + DD of the *ACE* gene (83.3% and 73.53%) and the genetic model of the AC + CC gene of the *AGTR1* gene (37.5% and 58.82%) between surviving children and children who died. Instead, the difference between the frequency of the genetic model 4ab + 4aa of the *eNOS* gene among the children of the two groups was on the verge of statistical significance The obtained results indicate that premature infants with a combination of the dominant models of the + 4ab & 4aa *eNOS* gene + 4ab & 4aa *eNOS* gene have increased risk and prognostic fatal time for the Kaplan-Meier method (p = 0.05) compared with infants with a combination of genotypes of the second *ACE* gene + 4bb *eNOS*. Regarding the frequency of detection of the combination of the studied genes, among the children who died, *ACE* gene D allele was significantly more likely to be identified with the 4a allele of the eNOS gene than in surviving children. Also, there is a reliable association between the occurrence of lethal effects in premature newborns with severe IVH and the combination of the AC & CC gene of the *AGTR1* gene and the 4ab & 4aa genotype of the *eNOS* gene. Conclusions: We determined that premature infants with a combination of the dominant models of the ID4D and DD ACE gene + 4ab & 4aa eNOS gene had increased risk of mortality and the predictive mortality rate for the Kaplan-Meier method (HR 1.02; p = 0.05) compared with infants with a combination of genotypes II ACE gene + 4bb eNOS.

Prospects for further research. The molecular genetic research in the future is intended to promote the use of low-invasive diagnostic techniques in neonatology with the obtaining of an individual genetic passport of the newborn, which will help to treat premature newborns with minimal risk of fatal cases.

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Key words: *premature newborn, intraventricular hemorrhage, polymorphism of renin-angiotensin system genes.*