PATHOGENETIC CONFIRMATION OF THE USE OF CEREBROLIZINE FOR TREATMENT OF PERIVENTRICULAR LEUCOMALACIA IN PREMATURE INFANTS

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The purpose of this report was summarizing of the results of study in 100 premature infants with preventricular leucomalacia and identification of the gene molecular markers focusing the attention on the population characteristics of the Leiden V factor polymorphisms and mutation of prothrombine G20210A and their effect on the development of intracranial hemorrhages and PVL in the premature infants, and use of preparation cerebrolizine.

Keywords: infants, premature, perinatal lesion of the central nervous system, genes

The different sensitivity to the diseases of children with small birth weight, insufficient of the reliable antenatal prognosis of the unfavourable primary results, for example, development of hemorrhage in the cerebral ventricles and periventricular leucomalacia (PVL) may be witnesses that genetic variants of the blood coagulation factors may be involved in the development of some pathological state in children born with small birth weight. The last investigations showed the effect of the thrombophylia risk factors, such as Leiden V factor and mutation of prothrombin G20210A, on the development of intracranial hemorrhages and PVL in the premature children. However, the genetically confirmed low levels of the blood coagulation factors, such as VII-323del/ins factor stimulator factor polymorphism, may both increase the risk of intracranial hemorrhage (as showed investigations in the adults) and effect on the cerebral circulation disturbances in the premature newborns, for example, on the development of periventricular leucomalacia.

This disease presents serious social and medical problem so the methods of molecular-genetic diagnosis and efficacy of therapy performed acquire the special significance. The cerebrolizine has the required organ-specific efficacy that inhibit effect of Ca 2+-dependent intracellular proteases, such as calpain, and consequently preventing the process of the decomposition of immunoreactivity of sinaptofisin.

The purpose of this work is to summarize the results of study of the gene molecular markers focusing the attention on the populational characteristics of the effect of polymorphism of the Leiden V factor and mutation of prothrombin G20210A on the development of intracranial hemorrhages and PVL in the premature infants and use of preparation cerebrolizine.

Material and Methods

The effect of gene variants participating in the hemostasis was studied in 100 newborns who were born in the Scientific Research Institute of Obstetrics and Gynecology of the Ministry of health of the Republic of Uzbekistan and then observing at the Department of Pathological Neonatology of the Hospital N 5 of Mirobod district during the period from 2007 to 2009 (including criteria: gestation age from 28 to 36 weeks, birth weight < 1500 g). The premature infants who were born at the gestation age 23-26 weeks were excluded from tour investigation because the percent of lethality is very high in this group. The clinical-laboratory methods of investigations included analysis of obstetric-gynecological and somatic medical history of mothers, development of the present pregnancy. The roentgenography of the chest, neurosonography and dopplerography of the cerebral vessels as well as other investigations in association with the traditional methods of examination of newborns. Cerebrolizine was used in dose 1,0 ml during 20 days.

Results

The study included 100 newborns with small birth weight of Uzbek nationality. In this population the genotyping was successful in 53 cases (Leiden factor), 47 (mutation of prothrombin G20210A). Investigation of the infants born with periventricular leucomalacia (PVL) there were found echo-dense lesions which may transfer into porencephalitic cyst and periventricular hemorrhages those were distributed by severity degree: PIVK 1.

Genotyping: all polymophisms were found with use of polymerase chain reaction (PCR) and restriction analysis. Primers and DNA-consequences were selected. PCR was used to study mutation of Leiden V factor and prothrombine G20210A.

On the basis of these data it may be concluded that this will be enough for identification of the total difference 5% of the carriers frequency rate among the children born with small weight and studied healthy children (prothrombin G20210A).

The expected rate of the carriers for Uzbek population of homozygous or heterozygous Leiden V factor was 4.9% and prothrombine G20210A was 3,0%.

This study allowed to reveal mechanisms of the cerebrolizine effect which provide increase in the level of gene expression by postranscriptional mRNA stabilization and improvement of translation efficacy that results in increase of the synthesis of protein – glucose transporter from blood into brain through hematoencephalic barrier.

In order to estimate the changes which were found in the premature infants with PVL after therapy during the study there were used different criteria. The dynamics of recovery was evaluated with use of parameters of clinical-neurological scale.

During clinical trials there was revealed that the earlier beginning treatment with cerebrolizine in the acute phase of PVL the better was functional outcome, and its neuroprotective effect manifested rather quickly and may be detected even on the 5 and 7 day of therapy.

Thus, in the neuropediatrics the therapeutic success was achieved during treatment with cerebrolizine which resulted in significant statistical and clinical improvement of the motional and cognitive functions on the twentieth day, that is, at the moment of the ending acute phase PVL, stopping the process of conversion into organic changes.

References

1. Fogel F., Motulski A. Genetika cheloveka (trns. from Engl.) M.,1990.P.142-149.

2. Harper P. Prakticheskoe medico-geneticheskoe konsultirovanie. M.,1984.

3. Bianchi D.W. Prenatal diagnosis by analysis of fetal cells in maternal blood. // Icl.-1995.-Vol.127, N 6.-P.847-856.

4. Codori A.M., Brandt J. Psychological costs and benefit of predictive tosiin. HtuHingtons disease // Airier J.Med.gen.-1994.-Vol.54,N3.-P.174-174.

5. Roy J.C., Johnsen J., Breese K. Fragile X syndrome which is the impact of diagnosis on families // Dev.Brain.Dis.-1995.-Vol. K, N 4.-P.327-335.

6. Slwag Clu, Anikster T., Christensen E. The molecular basis of canavan (aspartoactlase deficiency) in European newborn patients // M.Hum.Gen.-1995.-Vol. 57.