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Human Genetics & Genome Meet 2019: The role of xenobiotic enzyme genes in predicting fetal loss syndrome in Uzbekistan – NigoraMavlyanova - Ministry of Health of the Republic of Uzbekistan

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Introduction: Fetal growth restriction syndrome (FGRS) is a clinical syndrome caused by morphological and functional changes in the placenta and penetrant by limit of the growth and development of the fetus, its hypoxia that arises as a result of the combined reaction of the fetus and placenta to various disorders of the pregnant woman. This syndrome is based on pathological changes in the fetal and or uterine-placental complexes with a derangement of the compensatory-adaptive mechanisms at the molecular, cellular and tissue levels. In this case, the transport, trophic, endocrine, metabolic, antitoxic functions of the placenta underlying the pathology of the fetus and newborn are disordered. The most significant risk factors of FGRS development include preeclampsia and a combination of pregnancy with extra genital pathology, accompanied by vascular damage.

Various etiological factors, affecting at different stages of the development and functioning of the placenta, are ultimately involved in the general pathogenetic mechanism leading to the development of the fetal growth limit syndrome, one of the main manifestations of which is considered a violation of placental circulation - the main function of the placenta. In this regard, the main direction in the study of the problem of FGLS, is the development of objective methods for prediction, preclinical diagnosis, optimal prevention and treatment, which can significantly reduce the frequency of FGLS, and its complications. Recently, special attention has been paid to studying the genes of xenobiotic biotransformation enzymes (XBEs), which are candidate genes for the formation of a predisposition to these pathologies, since their protein products interact with the environment, detoxifying or toxicizing foreign chemical compounds that enter the body, including also drugs. However, they have not yet been sufficiently studied as genetic predisposition factors in fetal growth limit syndrome.

According to the literature, these genes are a rather complex object of study due to a number of their specific features. These are overlapping substrate specificity, inducibility and participation in the metabolism of endogenous compounds. But it is precisely these features of XBE that make it possible to assume that they can be genetic markers at all stages of the development of the disease from its initiation to the outcome and, accordingly, will make it possible to identify a predisposition, help in the early diagnosis of the disease, knowing the patient's genotype, make a prognosis of the course of the disease, and choose the most suitable therapy

Aim: The goal of our research was to establish the role of the polymorphic variants of the xenobiotic enzymes genes GSTM1 and GSTT1 and IIe 105Val of the gene GSTP1 in the mechanism of formation and development of fetal loss syndrome.

Material & Methods: Molecular genetic studies were conducted in 114 pregnant women aged from 20 to 45 years old. Molecular genetic examination of biomaterials (DNA) was performed at Department of Molecular Medicine and Cellular Technologies of the Research Institute of Hematology and Blood Transfusion of the Ministry of Health of the Republic of Uzbekistan. Statistical analysis of the results was carried out using the statistical software package "OpenEpi 2009, Version 2.3".

Results: The results of molecular genetic studies in pregnant women with Fetal Loss Syndrome (PPS) showed an increased detection rate of combined functionally defective genotypes GSTM10/0+GSTT10/0 - 25.4%, against the control group 4.1% (??2=12.4; P=0.0004; OR=7.8; 95% CI 2.146-28.65). Whereas, with the combined variants - the null and functional genotypes of the polymorphism of the GSTM1 and GSTT1 genes between the studied groups did not reveal statistically significant differences (??2=0.1; P=0.3; OR=1.4; 95% CI 0.697-282; p>0.05). Whereas, the distribution of genotypes IIe 105 Val of the GSTP1 xenobiotic enzyme in pregnant women revealed a high detectability of A/G genotype polymorphism in the pregnant group compared to the control group 56.1% versus 19.4%, which was 2.9 times higher than the control groups. Thus, an analysis of the association of genic combinations of zero polymorphisms of the GSTM1 and GSTT1 genes revealed that in the group of pregnant women with fetal loss syndrome, combinations of the homozygous del/del genotype responsible for the lower level of protein product synthesis are significantly more common.

The chance of developing pathology in the presence of this combination of the genotypic version of the del/ del genes GSTM1 and GSTT1 increases significantly: Up to 7.8 times more than other genotypes (??2=12.4; P=0.0004; OR=7.8; 95% CI 2.146-28.65). Whereas, the functionally unfavorable GSTP1 G allele 2.7 times was statistically significantly predominant in the studied chromosomes of pregnant women with PPS compared with pregnant women without PBS (??2=4.6; P=0.03; OR=4.5; 95% CI 1.061-19.5).

This work is partly presented at Joint Meeting on 6th World Congress on Human Genetics and Genetic Diseases & 12th World Conference on Human Genomics & Genomic Medicine April on 08-09, 2019 held at Abu Dhabi, UAE

Conclusion: Analysis of the results showed that the polymorphism variants of the GSTM10/0+GSTT10/0 genotypes of the GSTM1 and GSTT1 genes, as well as the G/A IIe 105 Val genotypes of the GSTP1 gene are significant predictors of the risk of developing fetal loss syndrome, resulting in disorders of the detoxification process in the body in women during pregnancy.

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