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Genes Involved in Vascular Homeostasis are Responsible for Alterations in Erythrocyte Membrane Proteins in Patients with Essential Hypertension

A. POLONIKOV¹, D. USHACHEV², V. IVANOV¹, I. KRIVOSHEI³, S. SIROTINA³, M. FREIDIN⁴, M. BYKANOVA¹, O. BUSHUEVA¹, O. KOLESNIKOVA², M. CHURNOSOV³, M. SOLODILOVA¹

¹Kursk State Medical University, Russia, ²Kursk Regional Clinical Hospital, Russia, ³Belgorod State University, Russia, ⁴Research Institute for Medical Genetics, Russia

Background & Hypothesis:

Alterations in structural and functional properties of the cell membrane may represent disease-associated intermediate phenotypes reflecting the mechanisms of essential hypertension (EH). The study was designed to assess the effects of polymorphisms in genes associated with EH on the variation of erythrocyte membrane proteins (EMPs) in hypertensive patients.

Methods:

Major EMPs content was analysed in blood from 1162 unrelated Russians (235 hypertensive patients, 176 healthy controls and 751 random individuals from the Central Russia population). EH patients were genotyped for 11 polymorphisms of EH susceptibility genes including *ADD1* (*rs4961*), *GNB3* (*rs5443*, *rs16932941*), *NOS3* (*rs1799983*, *rs2070744*), *ACE* (*rs5186*), *AGTR1* (*rs5186*), *AGT* (*rs699*, *rs4762*), *MR* (*rs5534*), and *TGFBI* (*rs1800471*).

Results:

Gender-specific differences in EMP contents between the cases and controls were observed. Regardless of gender, hypertensives exhibited mainly decreased levels of alpha- (SPTA1) and beta-spectrin (SPTB) and increased levels of glucose transporter (GLUT1) as compared with healthy subjects ($P \leq 0.001$). The EH susceptibility genes showed considerable effects on the levels of spectrins and glucose transporter. A joint variation of the genes explained about half the total polygenic variance in the GLUT1, SPTA1 and SPTB levels in hypertensives.

Discussion & Conclusion:

The study showed that EH susceptibility genes are the important factors of the inherited EMP variation, and their pleiotropic effects may be mirrored in the altered expression of genes encoding cytoskeletal proteins and those related to intracellular glucose metabolism. The study was supported by the Russian Research Foundation (No.-15-15-10010).