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Possibilities of molecular genetic research in the diagnosis of MODY diabetes

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Motivation and Aim: Most young patients with hyperglycemia are diagnosed with type 1 diabetes mellitus and type 2 diabetes mellitus but up to 10 % of all cases of the disease occur in MODY (Maturity-Onset Diabetes of the Young) diabetes [1]. Diagnosis of the correct type of diabetes mellitus (DM) leads to the appointment of pathogenetic effective therapy, adequate management of pregnancy and the prevention of specific complications. Currently 14 types of MODY are known which differ in clinical manifestations and therapy, so it is very important to understand which phenotypic manifestations correspond to a certain type of monogenic form of diabetes. The aim of the study was to explore the possibility of molecular genetic testing in determining the type of diabetes mellitus in young people.

Materials and methods: The Research Institute of Internal and Preventive Medicine – branch of the Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences examined 421 patients with diagnosed diabetes mellitus under the age of 45 years. Of these patients 387 met the inclusion criteria for targeted sequencing of genes associated with the development of MODY 1-14 diabetes: absence of antibodies to GAD, b-cells, insulin, normal or slightly reduced C-peptide level, normal body mass index.

Results: Different types of MODY were verified in 135 (34.9 %) patients out of 387. In the majority of patients as in the Russian Federation [2], GCK-MODY (MODY2) prevails (85 patients, 63.0 %). Also, many patients were diagnosed with HNF1A-MODY (MODY3) (30 people, 22.2 %) and ABCC8-MODY (MODY12) (10 people, 7.4 %). The following types of MODY were also identified: HNF4A-MODY (MODY1), NEUROD1-MODY (MODY6), CEL-MODY (MODY8), APPL1-MODY (MODY14) – each of the types for 1 patient (0.7 %); HNF1B-MODY (MODY5) – in 4 patients (3.0 %), PAX4-MODY (MODY9) – in 2 patients (1.5 %).

The digenic type of inheritance was verified in some patients, mutations were identified in two genes associated with MODY at once: in one patient in the genes associated with HNF1A-MODY and ABCC8-MODY and in one patient – in the HNF1B genes and predisposing to the development of diabetes mellitus type 1. The course of diabetes was more aggressive in patients with this type of inheritance, there was decompensation of carbohydrate metabolism for several months and insulin therapy was prescribed. Thus, if a patient is diagnosed with a mutation in a gene associated with MODY this does not exclude the presence of other types of diabetes mellitus. If a pathogenic mutation associated with MODY is detected and clinical manifestations are uncharacteristic for this type of MODY including a rapidly progressive course of DM, it is necessary to study other genes predisposing to diabetes.

Conclusions: 1. The frequency of mutations in MODY-associated genes among individuals with phenotypic features of this type of diabetes is 35 %.
2. In case of decompensated progressive course of carbohydrate metabolism in MODY it is necessary to examine other genes that predispose to the development of other types of DM.
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