Investigation of Genes That are Defined with New Generation Sequence Analysis in Children/ Adolescents Followed with Maturity Onset Diabetes of the Young

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Maturity onset diabetes of the young (MODY) is an autosomal dominant inherited diabetes type with a distinctive heterogeneity. Although so far 13 genes have been shown as causes of MODY, new genes are being identified each day as a scause of MODY. Verifying the MODY diagnosis genetically is very important in terms of patient-oriented therapy and genetic counseling. Recent genetic tests search for the most appropriate gene for the presenting phenotype in the first step and if it cannot define any mutation, the other genes become the target. This method causes time loss and also increases the cost. In this study, we aimed to detect the genotype of children and adolescents diagnosed with MODY and to evaluate the relationship with the phenotype using the new generation sequence method which can analyze a wide range of genes at a time.

MODY patients followed in four endocrinology center (aged between 1 and 18 years) were included in the study. The laboratory results and clinic reports obtained at the time of diagnosis were recorded from the hospital charts. Isolating the DNA from the peripheral blood and with the new generation sequence analysis method, *GCK, HNF1A, HNF4A, HNF1B, IPF1, NEUROD1, KLF11, CEL, PAX4, INS* and *BLK* genes' sequence analysis was done in these patients. When a new mutation was defined, the pathogenicity of the mutation was decided using computer softwares and segregation studies.

42 children and adolescents (22 male) who were followed with MODY diagnosis were added to the study. Average age at diagnosis was 10.3±4.2 years and mutations were detected in 12 patients (29%). 8 patients had *GCK* and there was one patient each for *HNF1A, HNF1B, IPF1,* and *BLK* mutations. 5 new mutations were detected as a cause of MODY: p.Val338Met, p.Cys252Ser, and p.Val86Ala mutations on the *GCK* gene; p.Cys241Ter mutation on *HNF1A*; and p.Gly55Asp mutation on *IPF1*.

In this study where MODY genotype was investigated in Turkish children, it was shown that (I) the cause of the disease was found genetically in only 29% of patients; (ii) the most frequent mutation was *GCK*; and (iii) there were 5 new mutations in these patients. Regarding the cost and time advantages, this new generation sequence analysis method will provide us more information about genotype and help us to find new mutations and differences that are specific to our country with a broader molecular studies in the Turkish population.

Key words: Children, diabetes, autosomal dominant, MODY, new generation sequence analysis