Clinical aspects of MODY

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Maturity-onset diabetes of the young (MODY) is a genetic subtype of diabetes mellitus. Clinically, MODY is characterised by an early-onset of diabetes mellitus and an autosomal dominant pattern of inheritance due to single mutations in genes involved in beta-cell function. Two distinct syndromes can be recognised. Mutations in the gene for glucokinase (MODY2) cause mild, stable hyperglycemia. Approximately 20-30% of MODY are caused by glucokinase diabetes. Hyperglycemia during childhood and long-term complications are rare. Despite the fact that many different mutations in the glucokinase gene have been identified, there is a remarkable homogeneous phenotype. Mutations in transcription factors involved in beta-cell development and/or insulin secretion cause a more progressive form of diabetes mellitus. Mutations in the gene for HNF-1α (MODY3) are the most common form of MODY in subjects of european descent (40-60%). Mutation in HNF-α (MODY1), PDX-1 (MODY4), HNF-1β (MODY5) and Neuro-D1/β2 (MODY6) are rare. Age of diagnosis is usually during adolescence but a marked variability in age of diagnosis is present. There is a progressive loss of beta-cell function and insulin treatment is frequently necessary during life. Microvascular complications are often observed during the course of the disease. There is a marked clinical heterogeneity within and between different subtypes of MODY due to mutations in these transcription factors. HNF-1α diabetes shows marked sulphonylurea sensitivity. This pharmacogenetic effect has important implications for patient management. Renal abnormalities are frequently observed in MODY4. Clinical observations and studies in patients with MODY provide important insight in genotype/phenotype relationships in diabetes mellitus.

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