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Pharmacogenetics and diabetes

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Pharmacogenetics is an emerging discipline involving the research for genetic polymorphisms, commonly observed among the general population, which are able to influence drug response. This rising importance has been highlighted also in chronic illnesses such as diabetes mellitus. This illness is characterised by two major forms: type 1 and type 2 diabetes mellitus. From a genetic point of view it is possible to divide diabetes in monogenic and polygenic forms. Monogenic diabetes derives from one or more mutations in a single gene. It should be hypothesized and evaluated in diabetic patients with features inconsistent with their current diagnosis (unspecified neonatal diabetes, type 1 or type 2 diabetes) and clinical features of a specific subtype of monogenic diabetes (such as neonatal diabetes, familial diabetes, mild hyperglycaemia, syndromes). The list of these monogenic forms of diabetes includes MODY, mitochondrial diabetes, permanent neonatal diabetes (PNDM) and transient neonatal diabetes, familial lipodystrophies and some others. The knowledge of the molecular background of these specific forms of diabetes allows to point out the underlying aetiology and optimize therapy and the clinical follow-up. For example, patients with MODY2, caused by glucokinase mutations, show very mild diabetes characterized by modest fasting hyperglycaemia. Diet is frequently sufficient to control their glycol-metabolic balance. Some other forms of monogenic diabetes associated with impaired function of the beta-cell, such as MODY3 and PNDM linked to mutations in Kir6.2 and SUR1 genes, can be successfully managed by sulphonylurea agents. In these cases treatment could be successfully switched from insulin injection to oral sulphonylurea therapy.

These are some examples of pharmacogenetics those patients can also benefit from genetic testing. The challenge for diabetologists is to recognise these monogenic forms whose care will be greatly helped by the treatment changes that follow molecular genetic testing. The list of new putative monogenic forms of diabetes mellitus is increasing in a exponential manner, showing a high interest of the scientific community. Regarding polygenic diabetes, the knowledge obtained from recent genome-wide association studies has been demonstrated to be useful in understanding the pathogenesis and development of type 2 diabetes, but its usefulness is still now uncertain.

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