Editorial

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Neonatal Diabetes Mellitus: A Genetic and Clinical Approach

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Insulin exerts a pivotal role in the glucose homeostasis of the human body, while its deficits are related to complete inadequacies, such as Type 1 diabetes mellitus or related deficiencies such as Type 2 diabetes mellitus [1-4]. It has been identified that these deficiencies have a genetic background and can arise either from mutations in a single gene (monogenic forms of diabetes) or by a combination of rare genetic mutations the action of environmental factors (polygenic forms of diabetes) [4-7]. Although the exact aetiology of diabetes remains unknown, it appears to follow a polygenic inheritance pattern, and it is believed that the genetic and environmental factors associated with it have the potential to affect its appearance and development in most cases [8].

However, monogenic forms have been observed during neonatal and early infancy, resulting in the occurrence of permanent and transient neonatal diabetes mellitus [1,9-13]. The former is diagnosed before the first 6 months of life and persists for the rest of life [1,10]. The latter is characterized by transient symptoms, which disappear during the first year of age, but may return during adolescence and it is estimated that neonatal diabetes occurs in a ratio 1 in 300,000 births or 1 in 400,000 births [1,9-12]. For the transient form, long-term treatment is not required, but lifetime monitoring is vital [1,9-11].

From a genetic point of view, mutations in the human insulin gene are a major cause of permanent neonatal diabetes mellitus and this type has a developmental potential during adolescence and maturation (type 1b diabetes) [4]. Diabetes occurring in childhood and adolescence is caused by mutations in the glucokinase gene (GCK), but ABCC8 gene mutations (ATP-Binding Cassette Transporter Subfamily C Member 8) lead to the transient or permanent form of neonatal diabetes, while mutations in the Potassium Voltage-Gated Channel Subfamily J Member 11 lead exclusively to permanent neonatal diabetes [8,10,13]. The gene encodes the ATP-dependent potassium channel Kir6.2 subunit on pancreatic islets, indicating the treatment of sulfonylureas suitable for these patients [6,8,14]. Of note, Kir6.2 is expressed in parallel to the brain, leading to epilepsy phenomena in neonatal diabetes or other brain lesions [6,8,14]. Importantly, mutations in miscellaneous genes, including NEUROD1, NEUROG3, FOXP3, FACX6, PDX1, PLAGL1, SLC19A2, SLC2A2, RFX6, PTF1A, IER3IP1, EIF2AK3, WFS1, ZFP57, HNF1B, INS and GLIS3, have been linked with the onset of neonatal diabetes [2-4,8,10,13-16].

Neonatal diabetes presents with dehydration, persistent thirst and the need for frequent urination [12]. Diagnosis rests on measurement of blood glucose levels. Typically, neonatal diabetes is diagnosed before the first 6 months [12]. However, it may also develop after this period [12].

Currently, treatments for neonatal diabetes include insulin, the sulphonylurea glibenclamide or both [14-16]. There are several data supporting the use of Glibenclamide (Glyburide) for the treatment of neonatal diabetes. [14-16]. Other sulfonylureas have also been used for the treatment of neonatal diabetes, but there is currently less experience with them than with glibenclamide [14-16].

Conflict of Interest

None

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