Clinical case of family neonatal diabetes with KCNJ11 gene mutation

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Background: Neonatal diabetes is a rare pathology occurring in around 1 in every 200,000-400,000 live births. The most common cause of permanent neonatal diabetes (PNDM) is heterozygous activating mutations in the KCNJ11 gene encoding the pore-forming Kir6.2 subunit of the pancreatic beta cell KATP channel.

Objective and hypotheses: To determine the dynamic of carbohydrate metabolism in family transferred from insulin to sulphonylureas (SU).

Method: We studied a family (mother and child) with PNDM diagnosed within the first 6 months of life. Carbohydrate metabolism was studied by iPro-2 monitoring, HbA1c, C-peptide and insulin levels during 8 months of SU therapy. The KCNJ11 gene was sequenced by Sanger.

CLINICAL CASE

Results: A mutation in KCNJ11, R201H was identified in both patients. Transfer from insulin to SU tablets was done in child and mother at the age of 2 months and 28 y.o. accordingly. At the start of transfer process in child the daily dose of SU was divided into 6 doses (0.27 mg/kg/day), every feeding, but after 8 months of SU treatment frequency of dosing is reduced to 4 doses with decreasing of SU daily dose (0.17 mg/kg/day). The child's mother at 28 y.o. stopped insulin (45 units/day) and went on to SU in dose 15 mg/day. After 8 months of SU treatment HbA1c improved in both patients (in child 5.15% vs 13.9%, in mother 6.5% vs 8.9%, accordingly). Daily monitoring (iPro-2) in child showed a marked reduction in the fluctuations as well as an overall lower level of glycaemic control (13.8 [2.6-26.6] mmol/l before SU treatment to 6.0 [3.3-10.2] mmol/l – after). C-peptide level increased from 0.09 ng/ml to 0.5 ng/ml in child, and from 0.009 ng/ml to 0.35 ng/ml in mother after 8 months of SU treatment accordingly.

Conclusion: Patients with diabetes, manifested within the first 6 months of life have to perform genetic testing for determination of the pathogenetic treatment. Daily dose of SU given for child during 8 months decreased by 37% on a background of improving of carbohydrate metabolism, HbA1c. A good response on SU treatment was observed even after 28 years of insulin therapy.