Detection of the pathogenic genes in the diagnosis and treatment of hyperglycemia infants and children

Objectives To explore the clinical value of common pathogenic gene detection in the diagnosis and treatment in hyperglycemia infants and children.

Subjects and Methods Subjects were in-patients with hyperglycemia, age of onset before 1 year-old，or insulin antibody negative and with family history of diabetes. Gene sequencing for ABCC8, KCNJ11, INS and GCK were performed and potential mutations were analyzed. The patients with ABCC8 and KCNJ11 gene mutations were treated with sulfonylurea, patients with GCK mutations were given the lifestyle intervention and others with insulin.

Results Total 21 patients were enrolled, 15 patients were found with pathogenic gene mutations, 52.4% in ABCC8 gene and KCNJ11 gene (11/21). The patients with KCNJ11 or ABCC8 gene mutation are with average age 2.01±1.62 months or 2.52±2.60 months, respectively. GCK gene mutations were detected in children with age of onset more than or equal to 12 months, at 58.33±43.02 months of age. There existed significant statistical difference among the onset ages of the three genetic variants, P = 0.001. The onset random blood glucose levels were significantly higher in the patients with INS gene mutation (66.70 mmol/L) than those of GCK gene mutation patients (9.73 + 1.97mmol/L, P=0.003). 11 patients with ABCC8 or KCNJ11 gene mutation were treated with sulfonylurea and 9 patients reached euglycemia.

Conclusions Mutations in potassium channel related genes (KCNJ11 and ABCC8) were the most common cause of neonatal diabetes in Chinese. Sulfonylurea therapy was effective and euglycemia were reached in most of the patients with the mutations in KCNJ11 and ABCC8. Patients who were diagnosed hyperglycemia before 1 year-old，or with negative antibody testing and family history of diabetes were referred for gene testing, even by targeted next-generation sequencing of all known related genes. The target therapy based on gene diagnosis is more effective and improvement of life quality.

Age at onset with gene mutation with different age onset

Age at onset	Gene mutation				
	ABCC8	KCNJ11	KCNJ11	GCK	total
<6 months	7	4	4	0	10*
6-12 months	1	0	0	0	2
>1 year	0	0	0	3	3
total	8	4	4	3	15
Positive rate	36%	18%	18%	14%	71%

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