Genetic analysis and follow-up of 25 neonatal diabetes mellitus patients in China

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Objectives:

To study the clinical features, genetic and the correlation between phenotype and genotype of neonatal diabetes mellitus (NDM) in Chinese patients.

Methods:

We reviewed the medical records of 25 NDM patients along with their follow-up details. Sanger sequencing of genes KCNJ11 and ABCC8 were performed in all NDM patients within first year after diagnosis, and if the mutations were not within the genes, gene panel-based next-generation sequencing (NGS) was used to detect mutations in PNDM, microarray comparative genomic hybridization was performed in TNDM patients to detect uniparental disomy of chromosome 6 (UPD6) and paternal 6q24 duplication. We called back KATP-PNDM patients and switched insulin injection to oral gluburide, usually it happened within one and half a year after diagnosis. We selected 15 infantile onset T1DM patients who hospitalized in (15 patients had recorded HbA1c in PNDM group) as control group, and HbA1c levels in these controls were compared with PNDM group.

Results:

Of 25 NDM patients, 18 (72.0%) were PNDM and 7 (28.0%) were TNDM. Among 18 PNDM cases, 6 (33.3%) had known KATP channel mutations (KATP-PNDM), including one ABCC8 and five KCNJ11 gene mutations. There were six non-KATP mutations, five novel mutations, including INS, EIF2AK3 (n=2), GLIS3 and SLC19A2, one known EIF2AK3 mutation. There are two ABCC8 mutations in TNDM cases and one paternal UPD6q24. Five of the six KATP-PNDM patients were tried for gluburide transition, 3 were successfully switched to gluburide. Except three PNDM patients without recorded HbA1c, the mean HbA1c was 7.4% in 12 patients on insulin therapy, 6.8% in 3 patients switched to gluburide and 7.2% in 15 PNDM patients. Mean HbA1c of PNDM was not significantly different from infantile onset T1DM (7.2% vs 7.4, P=0.41).

Conclusions:

PNDM accounted for 72% of NDM patients. About one-third of PNDM and TNDM patients had KATP mutations. The genetic etiology could be determined in 50% of PNDM and 43% of TNDM cases. PNDM patients achieved good glycemic control whether on insulin or on gluburide therapy.

References:
