RESULTS OF SULPHONYLUREAS TREATMENT IN PATIENTS WITH NEONATAL DIABETES MELLITUS DUE TO *KCNJ11/ABCC8* GENE MUTATIONS IN VIETNAM

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Introduction

• Neonatal diabetes mellitus (NDM) may be defined as hyperglycemia diagnosed within the first 6 months of life which is permanent NDM or transient NDM. In there, the most common cause of NDM is associated with activating mutations in the *KCNJ11* gene, which encodes Kir6.2-a subunit of the ATP-sensitive potassium channel (KATP) of the beta cell and *ABCC8*, which encodes the sulfonylurea receptor (SUR1)-the other subunit of the beta-cell KATP channel. *ABCC8* and *KCNJ11* are located on chr 11.

• Patients with *ABCC8/KCNJ11* mutation can be treated with sulfonylurea replacing insulin injection.

• NDM is rare, variously quoted as one case per 300,000 to 500,000 live births.

Objectives

To identify mutations of *KCNJ11* and *ABCC8* in patients with NDM; and to assess the results of oral sulfonylureas therapy replacing insulin injection.

Patients & Methods

• Descriptive study, case series study, collection of the symptoms and investigations, DNA was extracted from peripheral lymphocyte and analysed mutation using PCR and direct sequencing of *KCNJ11, ABCC8*. The patients include of 11 NDM patients with *ABCC8* or *KCNJ11* gene mutations are treated in National Hospital of Pediatrics

Results

- 11 probands from 11 unrelated families were diagnosed NDM and were identified mutation in above mentioned genes.

Demographics :

Age of diagnosis was 52.9 ± 42 days (23 – 180 days)

Gender: 6 males, 5 females

Gestation age was 39.3 ± 1.3 weeks

BW: 2718.2± 451.2 grams (2000 – 3900 g)

Results

Results of Switch to Sulfonylurea Therapy:

Table 1. Baseline characteristics of the Patients when transferring to SU

Characteristics	*KCNJ11* mutation	*ABCC8* mutation
Mutations	R201H, R201C (2 patients), R50Q, E229K, E292G,	R1183W, E747X, E747X &E128K, A1153G, c.3403-1G>A/E1507Q
Neurologic features	1 (R201C)	1 (E747X)
Male sex	3	3
Birth weight (g)	2683.3 ±608	2740 ±433.5
Age at diagnosis (day)	33.16± 10.24	47.2± 29.8
Ketoacidosis at diagnosis	5	2
Age at initiation of SU treatment	1.8± 1.9 (median 0.95)	2.81± 2.89
Weight at time of switch SU Treatment	10.7 ±5.6	12.2± 9.3
Insulin dose — U/kg/day	0.68± 0.35	0.46 ±0.42
HbA1C	6.88± 1.75	6.9 ±1.7
Equivalent dose of glybenclamide (mg/kg/day)	0.92± 0.56	0.84± 0.69
Time transfer (day)	6.3± 4.3	3.4± 2.3

11/11 patients successful switching from Insulin to oral Sulfonylureas. There are 2 patients have not required the drug at 52 months and 9 months of age. Their blood glucose and HbA1C are normal

Duration of insulin treatment: 28,6±32 months (2-86, median: 10,5); HbA1C: 8,5 ±2,7%, glucose 3-17 mmol/l

Duration of SU treatment: 30 ± 16 months (7-51), HbA1C: 6.05 ± 0.8 (%), blood glucose 4-10 mmol/l

9 patients are normal mental development: DQ 80-85%, 2 patients with DEND syndrome have improved of speech and movement

Conclusions

Mutation analysis for neonatal diabetic mellitus helps to understand the pathology, diagnosis and to chose a suitable therapy. The major causes of NDM in Vietnam are mutations in *ABCC8* and *KCNJ11* and treatment was successful with SU.

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Conflicts of interest: None declared; Email address: ngocctb@nhp.org.vn