THE ROLE OF KCNJ11 GENE IN NEONATAL DIABETES

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OBJECTIVE

We are aiming to identify mutations in the KCNJ11 gene encoding kir6.2 as a cause of PND in order to identify patients with this mutation and modify their treatment regimen since those patients show better glycemic control on oral hypoglycemics than on insulin.

METHODS

It is a prospective cross sectional observational study done after obtaining approval from the ethical committee. Written informed consent was obtained from patients or their parents after full discussion about the aim of the study
Seventeen patients (age ranged from 1- 16 years) were enrolled in this study, from the Diabetes Pediatric clinic of National Research Centre. They were previously diagnosed to have diabetes mellitus (DM) before the age of 2 years.
Exclusion criteria including: patients with transient neonatal diabetes, patients with syndromic diabetes.
-All patients were subjected to full history tacking, general and neurological examination.
-Three ml of blood were collected from each subject in a sterile EDTA vaccutainer for the genotyping technique. All samples were subjected to DNA extraction, purification and sequencing of KCNJ11 gene. DNA was extracted from fresh samples or samples were stored at – 80 ºC till DNA extraction.
Sequences were compared to the published sequence (NM_000525.3) using **BLAST** [**B**asic **L**ocal **A**lignment **S**earch **T**ool] (www.ncbi.nlm.nih.gov) with nucleotide +1 corresponding to A of the ATG translation initiation codon of the reference sequence.

Table 1: Demographic data of the patients

Data		N	Percent
Sex	**Males**	9	53
	Females	8	47
Permanent versus transient neonatal diabetes	**PNDM**	17	100
	TNDM	0	0
DKA at diagnosis		5	29.4
Family history of diabetes mellitus	**Positive**	9	53
	Negative	8	47

PNDM: permanent neonatal diabetes mellitus, TNDM: transient neonatal diabetes mellitus, DKA: diabetic ketoacidosis. Qualitative data expressed as frequency and percentage

Table 2: R201H mutation distribution among study group

	N	Percent
Wild type (RR)	16	94.1
Heterozygous mutation (RH)	1	5.9
Homozygous mutation (HH)	0	0

Table 3: E23K, I337V, L270V and A190A variant distribution among study group

Variant	N	Percent
E23K		
Wild type (EE)	3	17.6
Heterozygous polymorphism (EK)	9	53
Homozygous polymorphism (KK)	5	29.4
I337V		
Wild type (AA)	2	11.8
Heterozygous polymorphism (AG)	9	53
Homozygous polymorphism (GG)	6	35.2
L270V		
Wild type (CC)	16	94.1
Heterozygous mutation (CG)	0	0
Homozygous mutation (GG)	1	5.9
A190A		
Wild type (CC)	16	94.1
Heterozygous mutation (CT)	0	0
Homozygous mutation (TT)	1	5.9

RESULTS

All of patients that got the E23EK polymorphism (total no. is 14) also got the I337V polymorphism.
The sequence result of PCR products of KCNJ11, E23K polymorphism G>A (67), *I337V polymorphism* G>A(1009), *L270V polymorphism* C>G(808), *A190A mutation* C>T(570).

CONCLUSIONS

In conclusion, our study identified a heterozygous activating KCNJ11 mutation (p.R201H) in a subject who was clinically misdiagnosed as type 1 diabetes diagnosed at the age of 1.5 months. Sulfonylurea therapy proved to be effective in patients with activating KCNJ11 mutations. We recommend to screen patients presenting with diabetes in the first six months of life for mutation in KCNJ11. Long-term studies are needed to ensure the long-term safety and effectiveness of sulfonylureas.

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