Molecular Genetics, Genomics, Mechanisms of Diseases

AB110. Genotype and phenotype of 107 patients with congenital hyperinsulinism

Dung Chi Vu[1], Ngoc T. B. Can[1], Khanh Ngoc Nguyen[1], Thao Phuong Bui[1], Hai Thanh Le[1], Dat Phu Nguyen[2], Duong Anh Dang[1], Sian Ellard[3]

[1]Department of Medical Genetics, Metabolism and Endocrinology, National Children's Hospital, Hanoi, Vietnam; [2]Department of Pediatrics, Hanoi Medical University, Hanoi, Vietnam; [3]University of Exeter Medical School, Exeter, UK

Background: Hyperinsulinemic hypoglycemia (HH) is a consequence of unregulated insulin secretion by pancreatic β-cell. Congenital HH is caused by mutations in genes involved in regulation of insulin secretion (*ABCC8*, *KCNJ11*, *GLUD1*, *CGK*, *HADH*, *SLC16A1*, *HNF1A*, *HNF4A* and *UCP2*). Severe forms of congenital HH are caused by inactivating mutations in *ABCC8* and *KCNJ11*, which encode the two components of the pancreatic β-cell ATP-sensitive potassium channel. Objectives: Our aim is to identify mutations in the *ABCC8* and *KCNJ11*, *HNF4A* and *GLUD* genes, and to describe genotype and phenotype correlations of Vietnamese children with congenital HH.

Methods: A prospective study was conducted on 107 cases with congenital HH diagnosed and treated at the National Children's Hospital from January 2007 to February 2017. Patients were selected by using inclusion criteria of Hussain K [2008]. All exons of *ABCC8*, *KCNJ11*, *HNF4A* and *GLUD1* were amplified from genomic DNA and directly sequenced.

Results: Mutations were identified in 57 cases (53.3%) including mutations of *ABCC8* gene (51 cases; 47.7%), among them 29 with homozygous/compound heterozygous of *ABCC8* and 22 cases with one paternal/maternal mutation of *ABCC8* gene; mutations of *KCNJ11* (5 cases; 4.7%); and *HNF4A* (1 case; 0.9%). 98.2% of cases with homozygous/compound heterozygous recessive mutations or one paternal dominant mutation of *ABCC8* gene did not respond to diazoxide treatment and required 95% pancreatectomy or octreotide injection. Other cases without identified mutations responded to diazoxide and/or glucose infusion.

Conclusions: Children with congenital HH should be performed mutation analysis which helps in making diagnosis and treatment decision. Families of children with congenital HH should be given genetic counseling. Prenatal diagnosis should be performed as well as follow up and treatment should be given to children with congenital HH immediately after birth.

Keywords: Congenital hyperinsulinism; hypoglycemia; beta cell disorders

doi: 10.21037/atm.2017.s110

Cite this abstract as: Vu DC, Can NT, Nguyen KN, Bui TP, Le HT, Nguyen DP, Dang DA, Ellard S. Genotype and phenotype of 107 patients with congenital hyperinsulinism. Ann Transl Med 2017;5(Suppl 2):AB110. doi: 10.21037/atm.2017.s110