Congenital Hyperinsulinism in Kosova

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Introduction

Hypoglycemia in infants and children can lead to seizures, developmental delay, and permanent brain damage.

Hyperinsulinaemic hypoglycaemia (HH), refers to a clinically, genetically and morphologically heterogeneous group of disorders associated with dysregulated insulin secretion.

It is the most common cause of persistent hypoketotic hypoglycaemia in neonates and infants with the incidence 1 :50.000 live births, and is associated with a significant risk of permanent brain damage.

Mutations in 12 different key genes (ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, UCP2, HNF4A, HNF1A, HK1, PGM1 and PMM2) that are involved in the regulation of insulin secretion from pancreatic β-cells have been described to be responsible for the underlying molecular mechanisms leading to congenital HH.

Aim of the study:

The aim of the study is to present clinical manifestation, diagnosis , molecular genetics and therapy in children with different forms of Hyperinsulinemic Hypoglycemia(HH), diagnosed in Department of Endocrinology in Pediatric Clinic in Kosova .

Methodology

Retrospective study of CHI patients diagnosed and treated in Pediatric Clinic, Department of Endocrinology in Kosova, their clinical presentation, biochemical markers at diagnose and treatment modalities.

Results

3 cases were diagnosed in neonatal period and 1 case was diagnosed in infancy, in a girl six months old.

None of the mothers had Gestational Diabetes and no consanguinity.

Patients: clinical feature

patient	1	2	3	4
sex	female	male	female	female
Birth weight (kg)	3.8 (+ 1.3 SD)	4.2 (+2.6 SD)	3.7 (+1.1 SD)	3.5 (+1.1SD)
Birth length (cm)	57 (+2.6 SD)	56 (+2.5 SD)	53 (+1.3 SD)	52 cm (+1.2 SD)
Seizures	common	common	common	common
hypotonia	yes	yes	yes	yes
Poor sucking	yes	yes	yes	yes

Biochemical details of patients

patient	1	2	3	4
Age at diagnose	2 days	3 weeks	3 days	6 months
Glucose (mmol/l)	1.4	1.9	1.7	2.5
Insulin (mU/mL)	47.5	39.5	63.2	9.0
C peptide (ng/ml)	4.6	4.5	4.7	2.1
Urine ketones	negative	negative	negative	negative
Glucagon response	inappropriate	inappropriate	inappropriate	inappropriate
Glucose infusion rate (mg/kg/min)	15	20	15	>8
Cortisol	>500 nmol/l	>500 nmol/l	>500 nmol/l	>500 nmol/l

Genetic Testing

patient	1	2	3	4
Mutation details	Heterozygous mutation	Homozygous mutation	Heterozygous mutation	Still not known
gene	ABC88	ABC88	ABC88	Still not known
Inheritance	Splicing mutation from her father	Missense mutation, Autosomal recessive HH	Missense mutation, Autosomal dominant HH	

Treatement Modalities

patient	1	2	3	4
	Octreotide 20 mcg/kg/day, divided in four doses Nifedipin sol. 1.0 mg/kg/day divided into 2 doses	Octreotide 15 mcg/kg/day, divided in four doses	Diazoxide 15 mg/kg/day, three divided doses	Diazoxide 20mg/kg/day, three divided doses, Lanreotide 60 mg, 1 x 28 days
	Subtotal pancreatectomy			

Conclusions

Hyperinsulinemic Hypoglycemia (HH) most commonly presents during the neonatal period, but can also present during infancy.

Newborns with HH may be macrosomic due to intrauterine hyperinsulinemia, however the absence of macrosomia does not exclude HH.

The management of patients with severe CHI is challenging and requires multidisciplinary approach.

Long term and careful monitoring id needed and neurological development should be closely followed up.

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Bone, growth plate and mineral metabolism

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