HYPERINSULINEMIC HYPOGLYCAEMIA SYNDROME IN SMALL-FOR-GESTATIONAL AGE NEWBORNS: CLINICAL CHARACTERISTICS AND GENETIC STUDY

Pamela Yesquen, María Clemente, Ariadna Campos, Mónica Fernández, Félix Castillo, Diego Yeste.
Vall d'Hebron University Hospital, Barcelona, Spain.

INTRODUCTION AND OBJECTIVE

Hyperinsulinemic hypoglycaemia (HH) is a common cause of severe and persistent hypoglycaemia during the neonatal period. Risk factors for neonatal transient HH are small-for-gestational age (SGA), perinatal asphyxia and maternal diabetes mellitus. This state of HH in SGA newborns could persist from weeks to years, resulting in an important comorbidity; its pathogenesis remains unknown.

In this research we describe the clinical-genetic characteristics of SGA newborns with HH, under care of the Pediatric Endocrinology department at Vall d'Hebron Hospital, Barcelona, Spain.

METHODS

Review of our HH patient database and selection of SGA patients who presented hypoglicaemia during neonatal period for more than 3 weeks.

SGA was defined as birth weight and/or length ≤-2 SD.

HH was defined as insulin and/or C-peptide detectable during hypoglycaemia and/or suppressed or low concentrations of free fatty acids during hypoglycaemia, in patients with carbohydrate requirements >12mg/kg/min.

Genetic study included *ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, HNF4A, HNF1A, UCP2, HK1* and *PGM1* genes.

Patients with history of maternal diabetes mellitus, perinatal asphyxia and clinical-biochemical markers of infections were excluded.

RESULTS

N°	Gestational age (weeks)	Hypoglycaemia started at (days of life)	Maximum carbohydrate requirements	**Diazoxide / maximum dose** (mg/kg/day)	Occurrences during treatment	End of diazoxide a/o nutritional treatment (months)	Genetic study
1.	boy 39	1	20 mg/kg/min	**yes** / 10		24	**negative**
2.	girl 30	4	18 mg/kg/min	**yes** / 10	PH, required intubation	24	**negative**
3.	boy 34 3/7	1	17.3 mg/kg/min	no		7	wasn't carried out
4.	boy 39	1	16 mg/kg/min	no		28	**negative**
5.	boy 35 2/7	1	18 mg/kg/min	no		0.9	wasn't carried out
6.	girl 37 1/7	1	16.6 mg/kg/min	**yes** / 15	Ductus arteriosus reopening	Still in treatment[1]	**negative**
7.	girl 37 1/7	1	14 mg/kg/min	no		2.63	wasn't carried out
8.	boy 34	1	17.4 mg/kg/min	**yes** / 5		3.3	***UCP2 mutation***
9.	boy 36 2/7	1	21 mg/kg/min	**yes** / 15		Still in treatment[2]	**negative**

PH: Pulmonary hypertension. [1] current age is 16 months. [2]current age is 8 months.

Mean Z-score of weight at birth was -2.45 SD (range −1.23 to −3.38) and of length −2.2 SD (range 0.78 to −3.02).

Pre-treatment echocardiographic study found patent ductus arteriosus (PDA) in patients 2, 6 and 9; patient 2 had PDA ligation at 7 days of life.

Diazoxide was suspended in patient 2 after 6 days due to pulmonary hypertension.

In patient 6 the dosage was decreased due to reopening of the ductus arteriosus with subsequent spontaneous closure.

All patients who received diazoxide had a good response to treatment.

Average nutritional and/or diazoxide treatment duration was 12.8 months (range 0.9 – 28 months).

CONCLUSIONS

- SGA newborns have a risk of presenting long-term transitory HH.
- Diazoxide was effective in all patients who received it. Two complications were attributed to the treatment: reopening of the ductus arteriosus and pulmonary hypertension.
- The genetic study showed positive results for only 1 of 6 patients (16.6%) in contrast to the 60% in non-SGA patients from our database.

BIBLIOGRAPHIC REFERENCES
- Arya VB, Flanagan S, Kumaran A, Shield J, Ellard S, Hussain K, et al. Clinical and molecular characterisation of hyperinsulinaemic hypoglycaemia in infants born small-for-gestational age. Arch Dis Child Fetal Neonatal Ed. 2013;98:F356-F358.
- Stanley Ch.A, Perspective on the Genetics and Diagnosis of Congenital Hyperinsulinism Disorders. J Clin Endocrinol Metab. March 2016;101(3):815-826
- Carrascosa A, Fernández JM, Ferrández A, López-Siguero JP, López D, Sánchez E, et al. Estudios Españoles de Crecimiento 2010. An Pediatric (Barc). 2008;68:544-51.