

NEONATAL HYPO-KETOTIC HYPOGLYCEMIA SECONDARY TO TRANSIENT HYPERINSULINISM. DIAZOXIDE RESPONSIVENESS AND EXPERIENCE WITH FASTING TEST AFTER TREATMENT WITHDRAWAL

L. Salamanca Fresno*; N. Itza Martin*; C. Mora Palma*; J. Domínguez Riscart*; M. Sáez de Pipaón**; A. Campos Barros***; I. González Casado*.

*Pediatric Endocrinology. ** Neonatology Unit. ***Institute of Medical and Molecular Genetics (INGEMM), IdiPAZ, CIBERER U753, ISCII.

La Paz University Hospital. Madrid. SPAIN



58TH MEETING 19-21 SEPTEMBER 2019



Introduction:

- Transient hyperinsulinism is described in neonates with stress factors (intrauterine growth restriction (IUGR), large for gestational age (LGA), perinatal asphyxia, infants of diabetic mother etc.).
- Recognition and early treatment is priority to avoid neurological morbidity related with recurrent hypoglycemia.

Objetives:

- Describe the incidence of transient hyperinsulinism.
- Clinical characterization and treatment response in neonates with hypoglycemia due to hyperinsulinism (monogenic forms excluded) admitted to a tertiary hospital NICU from January 2015 to April 2019.

Materials

- Prospective cohort study.
- Newborns > 7 days of age, with diagnostic criteria for hyperinsulinism: non ketotic hypoglycemia with detectable insulin levels, reduced free fatty acids, glucose infusion rate > 10mg/kg/min, and positive response to glucagon test).

Results (1):

- 3918 patients admitted, 0.76% (N = 33) presented hypoglycemia secondary to transient hyperinsulinism.
- The median diagnosis age was 23 days (IQR 10-29 days), with enteral feeding exclusively.
- 3 patients (10%) were infants of diabetic mother and 40% presented acidosis with cord blood pH<7.20.



- 87,9% received diazoxide treatment (dose ranged between 5-10mg/kg/day), presenting as most prevalent side effects hypertrichosis (81,8%) and edema (18,2%).
- Diazoxide median treatment duration was 83 days (IQE 41-110). The response was positive in 100%, with a fasting test performed on an outpatient basis, with glycemia > 60mg / dl after 10 hours of fasting after treatment withdrawal.
- Comparing preterm with term neonates, no significant differences were found regarding diazoxide treatment duration, maximum carbohydrate intake or resolution age.
- Molecular study was carried out through guided NGS in 70% of patients. No mutations were found so far in genes involving monogenic hyperinsulinism (*ABCC8*, *KCNJ11*, *HNF4A*, *GLUD1*, *HADH*, *SLC16A1*, *GCK*, *UCP2*, *HNF1A*, *AKT2*, *INSR*, *CACNA1D*), however, probably pathogenic variants were found in other candidate genes: *G6PC2*, *TH*, *PMM2* and *APPL1*.

Conclusions:

- Transient hyperinsulinism is a prevalent entity to be considered in neonates with risk factors.
- In our series, term newborns presented transient hyperinsulinism (21% of patients) and newborns with weight and/or height appropriate for gestational age (28%).
- Low dose diazoxide treatment is effective. The fasting test could be useful for safe treatment withdrawal when resolution is suspected.