Correlation between Genotype and Phenotype characteristics in Children with Congenital Hyperinsulinism (CHI) in a specialist centre.

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Introduction and Aim:

Congenital hyperinsulinism (CHI) is the most common cause of hypoglycaemia in early infancy and represents a heterogeneous disorder with respect to clinical presentation, histology and genetics. The aim of our study is to review correlation between genotype and phenotypic characteristics of children with CHI.

Methods:

Retrospective review of CHI patients with positive genetics during the last 8 years in a specialist referral centre.

Results:

Total of 71 children have so far been identified with positive genetic mutation (40 males).

- The median age of presentation with hypoglycaemia was 0-2 days in all mutations except *GLUD1* (259.5 days).
- The median birthweight was significantly higher in children with K_{ATP} channel mutations than in *GLUD1* and *GCK*.

GENETICS

- The majority had K_{ATP} channel (*ABCC8/KCNJ11*) mutation (n=55).
  - 15 had compound heterozygous/homozygous K_{ATP} channel mutation.
  - 30 had paternal inherited K_{ATP} mutation.
  - 10 had maternal inherited K_{ATP} mutation
- The rest were 9 *HNF4a*, 4 *PMM2*, 2 *GLUD1* and 1 *GCK* mutation respectively.

DIAZOXIDE RESPONSIVENESS

- 4 (26.7%) compound heterozygous K_{ATP}
- 7 (23.3%) paternal inherited
- 7 (70%) maternal inherited K_{ATP} channel mutation.
- 9 (88.9%) with *HNF4a*
- 2 (100%) with *GLUD1*
- 1 (25%) with *PMM2*

PARTIAL RESPONSE TO DIAZOXIDE

- 2 (13.3%) compound heterozygous
- 3 (10%) paternal inherited
- 1 (10%) with maternal inherited K_{ATP} channel.

OTHER MEDICAL THERAPIES

- 3 (75%) with *PMM2* mutation had good response to Nifedipine when used in conjunction with Diazoxide.
- 12 children with K_{ATP} channel mutation were managed on octreotide, sirolimus and Lanreotide.

NATURAL REMISSION

- 1 compound K_{ATP} (1.56 years)
- 5 (18.5%) in paternal K_{ATP} (median age 2.19 years)
- 5 (50%) in maternal K_{ATP} (median age 0.33 years)
- 1 in *HNF4a* (0.66 years)

PANCREATECTOMY

- 21 patients (29.6%) underwent pancreatectomy:
  - 16 partial pancreatectomy for focal CHI
  - 5 subtotal pancreatectomy for diffuse form of CHI.

Conclusion:

There is no no significant difference noted in age of presentation amongst all except *GLUD1* mutation which presents much later in life. Most children with K_{ATP} channel mutation require frequent feeds with multiple medications to manage severe form of CHI. Knowledge of genotype might help to determine pharmacotherapy. The odds of being fully responsive to diazoxide was greater in patients with maternal K_{ATP} channel than in homozygous, compound heterozygous and paternal inherited K_{ATP} channel mutation respectively.

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