Discontinuation of Diazoxide therapy in children with Hyperinsulinaemic Hypoglycaemia with no identified genetic aetiology. A long-term follow-up study.

Mouza AlYahyaeei 1,2, Pratik Shah 2,3, Maria Guemes 2,3, Clare Gilbert 2, Kate Morgan 2, Sian Ellard 4, Sarah Flanagan 4, Khalid Hussain 2,3

1 Department of Paediatric Endocrinology, Royal Hospital, Moscow.
2 Department of Paediatric Endocrinology, Great Ormond Street Hospital for Children, London.
3 Department of Developmental Endocrinology Research Group, Clinical and Molecular Genetics Unit, Institute of Child Health, University College London, London.
4 Institute of Biomedical and Clinical Science, University of Exeter Medical School, Exeter EX2 5DW.

Background

Congenital hyperinsulinism (CHI) is a cause of severe persistent hypoglycaemia in children. Diazoxide is the first line medical therapy for CHI; however diazoxide is usually ineffective in CHI with K_ATP channel gene mutations. Patients with no mutations in the K_ATP channel genes do respond to therapy with diazoxide. There are no previous studies assessing how long diazoxide therapy is needed in those patients with no genetic aetiology identified for the CHI.

Aims

To describe the clinical, biochemical, genetic aspects and duration of therapy in a cohort of CHI patients who no longer required diazoxide

Methods

Retrospective review of diazoxide-responsive CHI patients admitted to Great Ormond Street Hospital. Data on gestation age, birth weight, maternal risks, age of diagnosis, biochemical and genetic studies on ABCC8 and KCNJ11 were obtained. Follow up data on glycaemic profile, fasting studies, dose of diazoxide and duration of therapy were recorded.

Results

Twelve diazoxide-responsive CHI patients with no known genetic aetiology were identified. Diagnosed between 9days and 23months old, three presented as neonates. Nine were male and all were born at term with median birth weight of 3.793kg (2.99-4.99kg). Three had pregnancy induced hypertension; none had gestational diabetes. All responded to diazoxide, with median maximum dose of 11.5mg/kg/day (5-20). All were negative for ABCC8 and KCNJ11 mutations. In all patients diazoxide was stopped at a median age of 8.5 years (4-15); the median duration of diazoxide therapy was 7.25years (2.9-14.6). Fasting studies done after stopping diazoxide showed resolution of CHI.

Conclusion

CHI children with no known genetic aetiology may be able to come off diazoxide at some stage during follow up. These children need regular assessments for continuing diazoxide therapy. The molecular mechanism(s) that lead to the gradual improvement in CHI over time are not known.

Authors have nothing to disclose.