Clinical Predictors of Transient versus Persistent Neonatal Hyperinsulinism

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Hormone Research inPaediatrics 2020;93:297–303
DOI: 10.1159/000511139

Introduction*:* Hyperinsulinism (HI), the most common neonatal cause of persistent hypoglycemia can be associated with prolonged hospitalizations and risk for long-term neurological sequelae. Rapid identification of transient versus persistent forms of HI is crucial to optimize management.

Objectives*:* The aims of the study were to assess the ability of clinical and biochemical features at presentation to predict transient versus persistent HI, and to evaluate differences in hospital outcomes.

Methods: This study is a retrospective review of 79 infants with HI admitted to the Hospital for Sick Children, Toronto, from 2012 to 2017. Patients were classified into 3 groups: transient and the 2 persistent forms, diazoxide responsive (DR) and diazoxide unresponsive (DU).

•**Transient HI** was defined as subjects diagnosed with HI (an inappropriately elevated or measurable insulin concentration at the time of a serum blood glucose <2.7 mmol/L or 50 mg/dL in babies requiring a glucose infusion of >8 mg/kg/min) that resolved by 4 months of age.

•**Persistent HI** was defined as the need for ongoing therapy after 4 months of age and were associated with K ATP channel mutations (ABCC8/ KCNJ11). It could be Diazoxide responsive (DR) or Diazoxide unresponsive (DU)

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

Can we predict Persistent Hyperinsulinism in Neonate with hypoglycemia?

Results: The cohort of infants diagnosed with HI (n = 79) was divided into 3 groups: transient (n =46) and the 2 persistent sub types: DR (n = 20) and DU (n = 13).

•Infants with birth weight >90th percentile had an 8-fold increased risk of having a persistent form of HI (or 8.8, 95% CI 2.5–30) and a 21-fold increased risk of having a diazoxide unresponsive (DU) form of HI (OR 21.1, 95% CI 4.9–91.8).

•Transient forms of HI were commonly seen in infants who were SGA and majority were born to mothers with gestational diabetes.

•A lower cortisol concentration in the infants with transient HI compared to permanent HI.

•Neither the severity of hypoglycemia, as measured either by glucose levels in the critical sample or glucose infusion requirement (GIR), nor the insulin measured at the time of hypoglycemia was predictive for the type of hyperinsulinism.

•The diazoxide unresponsive (DU) children were more likely to require gastrostomy tube insertion and had an extended length of hospital admission.

Conclusion: In newborns with persistent hypoglycemia, a higher birth weight in the absence of maternal gestational diabetes is highly associated with a persistent form of HI as well as diazoxide unresponsiveness. Given the marked difference in clinical outcomes between groups, expedited genetic testing should be considered in infants with this presentation to inform clinical management.

Key message: Macrosomia in the absence of maternal diabetes can be a predictor of persistent hypoglycemia in hyperinsulinemic newborns. This may also predict diazoxide unresponsiveness. All infants with HI who are LGA, which is not explained by maternal gestational diabetes, should be considered for expedited genetic testing without first assessing for diazoxide responsiveness.

EXPERT COMMENT

“Neonatal hyperinsulinism is a disease with many potential long-term neurological sequelae. Neither the severity of hypoglycemia nor the insulin levels at the time critical sampling are predictive of the transient or permanent nature of the illness. Macrosomia in the absence of maternal diabetes as demonstrated in this Canadian study should make us suspicious about permanent HI and genetic tests should be undertaken early in these babies for optimizing their management.”

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With warm regards,

Reference

Falzone N, Harrington J: Clinical Predictors of Transient versus Persistent Neonatal Hyperinsulinism. Horm Res Paediatr 2020;93:297-303. doi: 10.1159/000511139.