COMMENTS AND RESPONSES

Blunted Counterregulatory Hormone Responses to Hypoglycemia in Young Children and Adolescents With Well-Controlled Type 1 Diabetes

Response to Graveling, Warren, and Frier

We thank Graveling et al. (1) for their thoughtful comments regarding our article (2). In their letter, they argue that our conclusion was not supported by the study data because the achieved level of hypoglycemia was not adequate. They point out that the mean nadir plasma glucose level in our subjects was ~60 mg/dl, whereas plasma glucose concentrations <60 mg/dl are often required to elicit a counterregulatory hormone response in healthy, nondiabetic adults. This comment overlooks the fact that the nadir plasma glucose level in 16 of the 28 subjects in our study was <60 mg/dl, and it was between 60 and 69 mg/dl in 10 of the others. The latter observation is important because in 16 healthy, nondiabetic children, Jones et al. (3) demonstrated that the mean plasma glucose threshold that stimulated a plasma epinephrine response to hypoglycemia was ~70 mg/dl or ~10 mg/dl higher than in healthy adults. In addition, the magnitude of the plasma epinephrine in the nondiabetic and poorly controlled diabetic children in the study of Jones et al. was much greater than in the diabetic children in both age-groups in our study. The characterization that the plasma epinephrine responses in our relatively well-controlled diabetic subjects were abnormally blunted and delayed is supported further by the brisk plasma epinephrine responses to mild hypoglycemia in nondiabetic children in the Pittsburgh study. We can argue whether these changes are sufficient to classify our patients as having frank hypoglycemia-associated autonomic failure, but we would point out that recent continuous glucose monitoring studies indicate that children with type 1 diabetes who have an A1C level between 7.0 and 8.0% spend 4–5% of the day with a glucose level <70 mg/dl (4,5).

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