OBSERVATIONS

Early Glibenclamide Treatment in a Clinical Newborn With *KCNJ11* Gene Mutation

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Activating mutations in the *KCNJ11* gene, which code for the ATP-sensitive K^+ channel subunit Kir6.2, are the most common cause of permanent neonatal diabetes. Recently, a switch from insulin treatment to oral sulfonylurea has been proposed if genetic testing reveals sulfonylurea-sensitive *KCNJ11* mutations (1). Until now, hurdles for early treatment were *1*) the time until the mutation analysis is finished and *2*) the lack of knowledge about adverse effects of glibenclamide in small infants.

We report on a boy with neonatal diabetes and the heterozygous *KCNJ11* mutation R201H who was successfully switched from insulin pump treatment (continuous subcutaneous insulin infusion [CSII]) to glibenclamide at 12 weeks of age. The boy was born small for gestational age (40 weeks, 2,660 g) as the first child to healthy, German parents. Until day 3 of age, poor feeding, weight loss, and a blood glucose level of 240 mg/dl was noticed. Hyperglycemia persisted, and intravenous insulin treatment was started, followed by CSII. Genetic testing for *KCNJ11* and *ABCC8* mutations revealed a de novo heterozygous *KCNJ11* mutation (R201H) that has been recently reported (1) to respond well to glibenclamide treatment. Based on the experience in older children and the positive clinical prognosis in R201H mutation carriers, the child was switched from CSII to oral glibenclamide treatment in an in-hospital setting under monitoring with a continuous glucose monitoring system.

At present, glibenclamide is given at a dose of 0.15 $mg \cdot kg^{-1} \cdot day^{-1}$ three times daily (maximum 0.2 $\cdot kg^{-1} \cdot day^{-1}$), and within a follow-up time of 8 weeks, no adverse effects had been observed. Continuous glucose monitoring system evaluation of two representative days on glibenclamide versus CSII showed decreased 24-h glucose levels (93 vs. 126 mg/dl) and lowered glucose variability (>180 mg/dl: zero vs. two and a half times per day; <70 mg/dl: zero vs. two times per day).

In summary, genetic testing enabled successful glibenclamide treatment as early as 3 months of age. Glibenclamide was superior to CSII in terms of glucose control and variability, without any short-term adverse effects. Further clinical trials are necessary to document the safety and efficacy of sulfonylurea treatment in children <12 months of age carrying sulfonylurea-sensitive *KCNJ11* mutations.

References

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