Transition from Insulin to Oral Sulfonylurea in 14-year-old Male with Neonatal Diabetes

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Introduction

Neonatal diabetes mellitus caused by activating mutations in the KCNJ11 gene can be mistaken for antibody negative type 1 diabetes mellitus. However, this form of diabetes specifically results from the inability of the ATP sensitive potassium channel to close, which leads to impaired insulin secretion.[1,2] Sulfonylureas (SU) close ATP sensitive potassium channels in an ATP independent process and may therefore serve as an effective treatment option for patients with KCNJ11 neonatal diabetes.[1,2] We present a case of KCNJ11 neonatal diabetes whose treatment was successfully transitioned from insulin to oral SU.

Case Presentation

This 14-year-old male who initially presented with neonatal diabetes at 1 month of age had shown clinical response to SU therapy with discontinuation of insulin therapy by age 4.[3] He returned to our clinic five years later after relapsing on insulin therapy and presenting in diabetic ketoacidosis at an outside hospital. Due to persistent suboptimal glycemic control, with significant hypoglycemic episodes, transition from insulin to oral SU therapy was initiated with literature guidance on dosing. Continuous glucose monitoring sensor (CGMS) was used to closely monitor glucose trends and adjust medication dosing.

Results

Calculated predicted SU dosing per literature review was 32 mg/day with emphasis on slow transition to achieve successful response.[1] Plan for dosing was begun using glyburide at a dose of approximately 0.05 mg/kg/day with anticipated titration up to 0.8 mg/kg/day and decrease in insulin by 25-50 percent each week based on blood glucose trends.[1]

Our patient was very sensitive to small doses of SU. Transition off insulin to oral SU therapy was achieved within 1 week. His initial regimen consisted of glyburide up to a maximum dose of 3.75 mg/day; repaglinide was added for better pre-meal glycemic control. However, he continued to experience overnight hypoglycemia and glycemic fluctuations during the day. Most recently, we modified both the dosing and type of SU therapy (switched to glimepiride and nateglinide) to improve glycemic control.

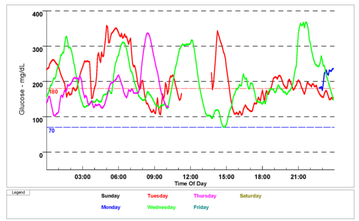

Figure 1. CGMS data documented worrisome hypoglycemia on subcutaneous insulin and initial wide fluctuations on glyburide. His glycemic control progressively improved over the first year of life with repeated adjustments of glyburide requirements of 0.4mg/kg/day which decreased to 0.1 mg/kg/day divided in doses given prior to breast feedings. Glyburide dosing eliminated hypoglycemia and enabled excellent weight gain. (Adapted from Pancratz et al.[3])

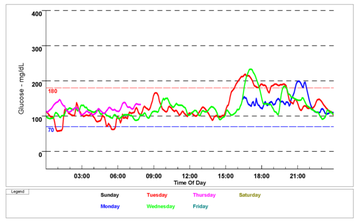

Figure 2. His CGMS at 14 months of age documented markedly improved glycemic control to allow subsequent weaning off glyburide. (Adapted from Pancratz et al.[3])

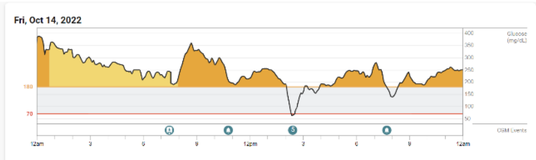

Figure 3. CGMS download on minimal insulin therapy with variability in blood glucose range, both hypo and hyperglycemia. (Insulin degludec 10 units, insulin to carbohydrate ratio of 1 unit insulin aspart for every 20 grams of carbohydrates, no sliding scale)

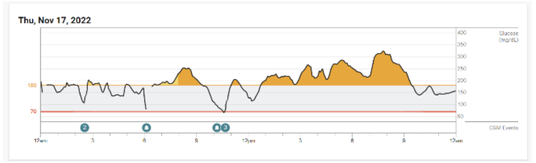

Figure 4. CGMS download on glyburide 3.125 mg/day

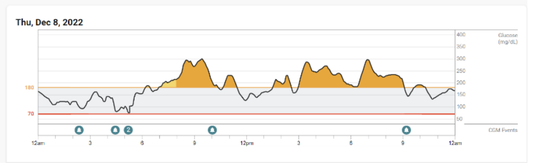

Figure 5. CGMS download on glyburide 2.5 mg/day and repaglinide 0.25 mg/day

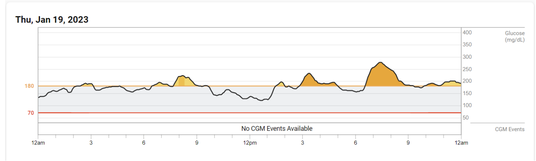

Figure 6. CGMS download on glimepiride 4.5 mg/day and nateglinide 180 mg/day

Discussion

Transition to oral SU therapy is effective in managing KCNJ11 neonatal diabetes. Therapeutic response is reflective of the pharmacogenetics of the activating mutation.

Conclusions

This case highlights the suitability of oral SUs as a treatment option for managing KCNJ11 neonatal diabetes as well as the value of CGMS technology in providing glycemic data to make informed dosing adjustments during the transition to SU therapy.

References

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