# Old Drug, New Tricks: Diazoxide Use with Continuous Glucose Monitoring in the Management of Glut1 Deficiency Syndrome

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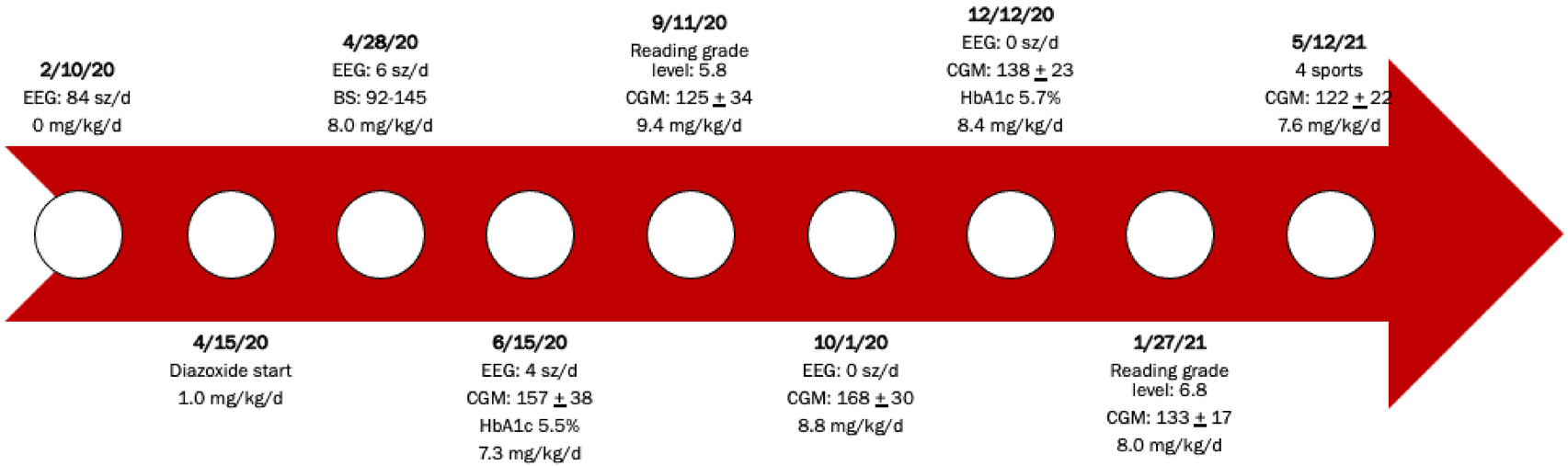
## Background

- Standard of care for Glut1 deficiency syndrome (Glut1DS): ketogenic diet (KD), alternative fuel for brain but not preferred energy source
- Treatment options limited if patients fail KD
- Diazoxide: ↓ insulin ➡ ↑ blood glucose ➡ ↑ cerebral glucose ➡ restoration of brain energy metabolism ➡ ↓ seizure activity
- Previous use of diazoxide complicated by hyperglycemia
- Continuous glucose monitoring (CGM): demonstrated benefit in diabetes, congenital hyperinsulinism
- Can CGM enable diazoxide use in KD-resistant Glut1DS?
- CGM: small sensor inserted under skin, measures interstitial glucose every 5 minutes
- Interstitial glucose correlates well w/ blood glucose, can lag if blood glucose changing rapidly

## Clinical Case

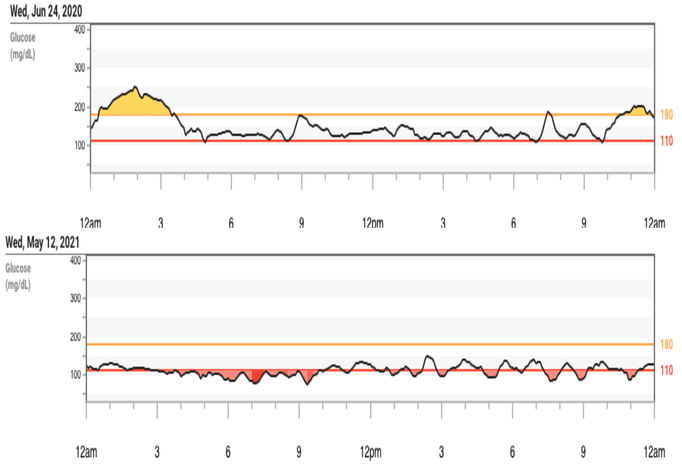
- 14 yo F w/ Glut1DS (c.398_399delGCinsTT:p.Lys133Phe)
- Failed KD and modified Atkins diet due to severe nausea, vomiting, abdominal pain and hypertriglyceridemia
- Before diazoxide: CSF glucose 36 when blood glucose 93 (ratio 0.39)
- After diazoxide: CSF glucose 55 when blood glucose 118 (ratio 0.47)
- Course complicated by fluid retention and weight gain
  - Fluid retention management: hydrochlorothiazide (thiazide diuretic), amiloride (potassium-sparing diuretic), sodium-restricted diet
  - Weight management: ↓ caloric intake, ↓ cornstarch, pairing complex carbohydrates w/ protein, goal interstitial glucose 90-110 mg/dL, treatment threshold <90 mg/dL sustained for 3-4 hours




Timeline: CGM data is reported with average glucose ± SD and diazoxide dose is presented as total daily dose.

| Time Point | Glucose Levels | Diazoxide Dose | EEG Seizure Count |
|---|---|---|---|
| -2 months | - | - | 84 per 24 h (2 day study) |
| 3 weeks | 92-145 mg/dL (blood) | 9.0 mg/kg/day | 6 per 24 h (3 day study) |
| 2 months | 124-190 mg/dL (interstitial) | 7.3 mg/kg/day | 4 per 24 h (3 day study) |
| 6 months | 140-284 mg/dL (interstitial) | 7.9 mg/kg/day | 0 per 24 h (5 day study) |
| 8 months | 80-201 mg/dL (interstitial) | 8.4 mg/kg/day | 0 per 24 h (1 day study) |

Diazoxide initiation data.




Daily CGM reports: First day vs recent day with CGM.

## Learning Points

1. CGM: safe initiation and precise titration of diazoxide
2. Diazoxide addresses neuroglycopenia unlike KD ➡ a new standard of care for Glut1DS?
3. Management of diazoxide-induced fluid retention requires frequent laboratory monitoring for hypokalemia, alkalosis, and renal dysfunction

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