Adult Experiences with Glucose Transporter Type 1 Deficiency Syndrome (Glut1DS)

AND

Deep Dive: Adulthood- Long Term Keto and Best Practices

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Clinical characteristics of Glut1DS in adults

Children initially diagnosed with Glut1DS in the 1990s are now all adults. Adults that began having mild or unrecognized symptoms as children are now being diagnosed as adults as clinicians are becoming better educated to recognize the symptoms and as genetic testing becomes more widely utilized. Symptomatic and asymptomatic adults are being diagnosed once offspring or other family members are diagnosed with Glut1DS .

According to the recent *Epilepsia Open* guidelines published in 2020, epilepsy tends to be the major clinical symptom in infants and young children with Glut1DS. Seizures tend to decline in frequency or resolve in later childhood, adolescence, and adulthood. Developmental impairment becomes increasingly apparent as well as movement disorders such as ataxia, paroxysmal exertion-induced dystonia and often become the major symptoms in adolescents and adults with Glut1DS. Gradual clinical improvement, decreased frequency, and decreased severity of paroxysmal events are typical in adult life.

However, studies have emerged describing adults with Glut1DS with ongoing seizures and worsening paroxysmal exercised-induced movement disorders during adulthood. Fatigue has been described as a major symptom as well as dysarthria, migraine and neuropsychiatric symptoms. Other symptoms that have been reported such as transient focal neurologic deficits are not well studied or understood. Intelligence quotients can range dramatically and many adults with Glut1DS have normal intelligence and no difference in quality of life measures compared to healthy controls. Some adults with Glut1DS are asymptomatic. Adults with Glut1DS may show improvement in cognitive dysfunction, movement disorders, seizures and dysarthria with treatment.

Treatment options for adults with Glu1DS

Educational support may improve long term cognitive function. Physical and occupational therapy services may lessen the impact of movement disorders on mobility. A targeted speech assessment and speech therapy with a trained specialist may improve dysarthria symptoms.

The standard of care remains ketogenic diet therapy although which ketogenic diet therapy is optimal for reducing symptoms in adults with Glut1DS is unknown. The classic ketogenic diet (CKD) used in children may be an option, particularly in adults who are already on and have seen benefit from CKD without significant side effects and are being transitioned to adult care. A more liberal diet such as the modified Atkins diet (MAD) may be more successful for individuals being introduced to ketogenic diet

therapy as an adult. Low glycemic index diets (LGID) are not recommended at this time because they do not consistently produce ketone bodies. Medium chain triglyceride (MCT) oil can be used to supplement ketogenic diet therapies and increase ketone body production while allowing for more liberal carbohydrate intake and have also been used prophylactically when triggers for paroxysmal events can be anticipated. Acetazolamide and piracetam have also been reported as beneficial in limited studies.

Side effects of ketogenic diet therapies in adults with Glut1DS

Side effects most often reported shortly after starting a KDT are typically gastrointestinal including constipation, nausea and/or vomiting, gastroesphageal reflux and weight loss. Metabolic changes such as hypoglycemia or metabolic acidosis related to excessive ketone body production can also occur as well as fatigue.

As ketogenic diet therapies remain the gold standard for treatment in individuals with Glut1DS, this treatment may be life-long. Most common long-term side effects include nephrolithiasis, vitamin D3 deficiency, bone loss, dyslipidemia and secondary carnitine deficiency. Risks of using KDT during pregnancy and lactation and long-term risks of cardiovascular and cerebrovascular disease on KDT are unknown.

Best practices for use of ketogenic diet therapies in adults with Glut1DS

Best practices while starting and continuing a KDT include remaining well-hydrated and using daily calcium, vitamin D3 and multivitamin supplements. Potassium citrate can prevent kidney stones in individuals on KDT and carnitine supplementation may be required if an individual is carnitine deficient. Stool softeners and antacids may be necessary to address gastrointestinal side effects. Baseline and routine follow up (annually) laboratory studies and bone mineral density scans (at least every 5 years) are recommended to detect and address any long-term side effects. Ketone monitoring is recommended, either measuring blood or urine ketones. The major focus of KDT use is to address symptoms and to improve quality of life.