Ketogenic dietary therapy for Neurometabolic disease

Written by:

Elizabeth Neal  MSc PhD RD

Research Dietitian, Matthew’s Friends Clinics
Honorary Research Associate, UCL - Institute of Child Health

The ketogenic diet is a high fat, restricted carbohydrate regime that has been used as a successful treatment for epilepsy since the 1920s. Alternative ketogenic therapies to this strict classical diet are the addition of medium chain triglyceride (MCT) allowing more carbohydrate and protein, or two more relaxed newer variants, the modified Atkins diet and low glycaemic index treatment. Ketogenic therapy is designed to induce a similar metabolic response to starvation, with the ketone bodies acetoacetate and β-hydroxybutyrate becoming the primary brain energy source in absence of adequate glucose supply. This therapy is also treatment of choice in two rare neurometabolic diseases which affect energy metabolism of the brain, glucose transporter type 1 deficiency syndrome (GLUT1DS) and pyruvate dehydrogenase (PDH) deficiency.

GLUT1DS is caused by a defect in the transporter protein responsible for moving glucose across the blood-brain barrier into the brain. It usually presents with seizures early in life; brain growth may be impaired with developmental delay and other neurological problems including a complex movement disorder. It is characterized by a low glucose concentration in the cerebrospinal fluid in the absence of hypoglycaemia, in combination with a low to normal lactate in the cerebrospinal fluid (1). Ketogenic therapy provides ketones which can be used as an alternative energy source for the brain and is therefore the recommended first-line treatment. The classical ketogenic diet will significantly reduce seizure frequency in most patients and improvements in movement disorders, neurological function and cognition have also been reported (2-8) with no significant adverse effects on short term inflammatory and metabolic profiles (9) or longer term body composition or bone mineralization (10). There have been several case reports (7, 11-14) and a retrospective study (15) on successful use of the modified Atkins diet in GLUT1DS. A low glycaemic index diet combined with modified high amylopectin cornstarch has also been tried (16). Although reports have limited patient numbers and there has been caution about use of more liberal ketogenic therapies in GLUT1DS (17), these may be preferred by older children or adolescents. Two GLUT1DS surveys have recently been published. Japanese physicians provided efficacy data on their GLUT1DS patients: 31 were treated with ketogenic therapy including 11 on classical ketogenic diet, 3 MCT ketogenic diet and 17 on modified Atkins diet. The latter was reported as the most palatable with comparable effectiveness to the classical ketogenic diet (18). A survey of 90 parents of GLUT1DS children treated with ketogenic therapy attending a GLUT1DS Foundation meeting in USA found no significant seizure outcome differences between the different diet variants (59 classical ketogenic diet, 29 modified Atkins diet, 4 MCT ketogenic diet and 2 low glycaemic index treatment) with many switching between the types of diet (19).

PDH deficiency is a severe mitochondrial disorder caused by deficiency in one of the enzymes involved in glucose metabolism. It can present with lactic acidosis and variable degrees of neurological degeneration during infancy and childhood including seizures; prognosis is poor. First-line therapy is the ketogenic diet which will bypass the metabolic block by providing ketones as an alternative fuel to glucose. Although it will not fully reverse clinical
symptoms, the progressive loss of neurological function can be slowed, especially if the diet is initiated early in life (20, 21, 22). A classical ketogenic diet is usually recommended as stricter carbohydrate restriction has been associated with greater improvement in clinical outcome (21) although one recent case report suggests a modified diet may also be helpful (23).

International consensus recommendations suggest that the ketogenic diet should be used as a first line therapy for GLUT1DS and PDH deficiency (24). In these neurometabolic disorders the diet will usually be continued well into adolescence and will therefore need regular monitoring and support to ensure the most appropriate dietary prescription with minimal risk of side-effects.

References:

