KETOGENIC DIET IN CHILDREN WITH EPILEPTIC ENCEPHALOPATHY

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Uncontrolled epileptic activity could lead to progression of cerebral dysfunction, resulting in a group of disorders called epileptic encephalopathy (EE). Lennox-Gastaut Syndrome (LGS) is a severe form of EE. It usually happens in children between 1-8 years old. Individuals with LGS could experience multiple types of seizures. LGS can be caused by a variety of conditions, including brain malformations and severe head injury. Most people with LGS experience some degree of impaired intellectual functioning/information processing, with developmental delays and behavioural disturbances.

The management of children with LGS includes antiepileptic drugs, with valproate and clobazam as the preferred drugs. These children were also prescribed a ketogenic diet (KD).[1] KD is hailed as one of the managements of seizure in children with EE. The classic KD consists of a high-fat, low-protein and carbohydrate diet, with restricted calories and fluids. The diet is similar to fasting, whereby the metabolism is altered by using fats as a primary fuel source. Urinary ketosis is also induced by the production of ketone bodies from fatty acid catabolism in the liver. [2]

Recent studies have found a significantly positive outcome with the use of KD for the treatment of refractory epilepsy in children and adults.

Theories about the roles of KD

1. Glucose metabolism produces rapidly available energy that is necessary for seizure activity. In patients on KD, blood glucose energy level is low, and the brain begins to use ketone bodies for energy. This anaerobic metabolism slows the energy availability, which reduces seizures.[3]
2. Chronic ketosis elevates the brain's energy reserve through stabilization and reduction of synapses excitability.[4] There was an increase in mitochondria production in an experimental model of rats fed with KD, indicating an increase in energy stores.[5] This leads to an increase in ATP production, which activates KATP, eventually reduces neuronal excitability.
3. KD interferes with the concentration of gamma-aminobutyric acid (GABA), a major inhibitory neurotransmitter. In clinical practice, there is an increased GABA levels in the CSF of patients on the KD diet.[6] The decrease in aspartate levels promoted by KB leads to the synthesis of GABA.[7]
4. KD modifies the gut microbiota, causing an increase in the reputedly beneficial bacteria Akkermansia muciniphila and Parabacteroides spp. This leads to a decrease in gamma-glutamyl amino acids. The decreasing level of gamma-glutamyl amino acids in the blood increases the GABA/glutamate content in the brain.[8]

Paediatric patients are usually prescribed syrups or suspensions, which often contain sucrose to improve palatability. For paediatric patients on a ketogenic diet, the pharmacists should suggest alternative medications that could be crushed and are stable when diluted in water or other non-sucrose vehicles.

In conclusion, the mechanisms described can lead to changes in the seizure threshold and hyperexcitability, contributing to the final antiseizure mechanism of KD. Pharmacists play an important role in the optimal management of EE patients with KD.

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