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EDITORIAL OPEN ACCESS

Importance of ketogenic diet in refractory epilepsy

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The ketogenic diet, introduced by Wilder in 1921, and is used in the treatment of children with pharmacotherapy-resistant epilepsy [1]. Seizure management with dietary therapies was documented as far back as Hippocrates, who described body 'purification' with fasting to treat patients with seizure disorders [2]. Despite its long history of clinical use, it is still not clear how the diet affects the brain and what the mechanisms are which underlie its seizure-suppressive action [3, 4]. Fifty million people in the world have epilepsy, and there are between 16 and 51 cases of new-onset epilepsy per 100, 000 people every year [5]. Approximately, 22.5% of patients with epilepsy have drug resistant epilepsy in a community-based study in southern France [6]. Patients with drug resistant epilepsy have increased risks of premature death, [7] injuries, psychosocial dysfunction and reduced quality of life [8, 9]. The International League against Epilepsy (ILAE) had developed a global consensus definition of drug-resistant epilepsy [10]. This definition is based on the observation that if complete seizure control is not achieved with trials of appropriate antiepileptic drugs (AEDs), the likelihood of success with subsequent regimens is much reduced [11, 12]. Most individuals who develop epilepsy will respond to pharmacologic treatment, however, approximately 20–30% will develop medically refractory epilepsy [13]. For this population, 'alternative or non-pharmacologic treatments such as dietary therapy can be highly efficacious and should be seriously considered.

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The ketogenic diet is a non-pharmacologic treatment used for children with intractable epilepsy [14–16]. Dietary therapies are designed to mimic the starvation state but provide a long-term treatment plan for patients with intractable epilepsy. When deprived of glucose through restriction of carbohydrate intake, the human body begins metabolizing fat. In doing so, ketone bodies (acetoacetate, acetone and β-hydroxybutyrate) are produced and can be measured in the serum and the urine. Diets that produce a state of ketosis are referred to as ketogenic. The classic ketogenic diet remains the most widely utilized dietary treatment and is effective in children with a variety of epilepsy syndromes. The classic ketogenic diet is traditionally started as a 3:1 or 4:1 ratio of fat to carbohydrates and proteins in grams, of which 90% of caloric intake of the patient is obtained from consumption of fat. The children usually stay on the diet for a trial of 3–6 months, and if the efficacy is considered to be 'satisfactory', they usually remain on it for two years [17].

Research in animal models of epilepsy suggest that the mechanisms of action are much more complicated than the assumption that seizure reduction resulted from starvation and direct correlation with the degree of either acidosis or ketosis achieved [18]. One speculation is that the antiepileptic effect is exerted via neuroprotection, but the mechanism for this is unclear. Ketogenic diet has been shown to be beneficial in treating a variety of epilepsy syndromes in children with frequent, medically resistant seizures. It has been reported to be effective in the treatment of seizures associated with glucose transporter 1 deficiency, pyruvate dehydrogenase deficiency, infantile spasms (West syndrome), absence epilepsy, myoclonic astatic epilepsy (Doose syndrome), severe myoclonic epilepsy of infancy (Dravet syndrome), tuberous sclerosis complex, mitochondrial disorders, Lennox–Gastaut syndrome, Sturge–Weber syndrome and Rett syndrome. In addition, dietary therapies are a consideration in developing counties where anticonvulsants are less available or more costly [19]. Adverse effects of ketogenic diet only infrequently requires the diet to be discontinued but are important for neurologists and pediatricians to recognize. Early-onset adverse effects associated

with diet initiation include acidosis, hypoglycemia, gastrointestinal distress, dehydration and lethargy. They are typically transient and early managed and are minimized if patients are not on fasting. Later adverse effects include dyslipidemia, kidney stones and slowing of growth. Deaths have been reported in patients on the diet. Albeit it is unclear that any of the deaths have been a result of the diet. The ketogenic diet cannot be a successful treatment for seizures without the cooperation of a dedicated group of physicians, nurse, dietitians, and pharmacists. Additionally, the patients and their families must be committed to the strict nature of the diet and be willing to follow the instructions of the ketogenic diet team.

Despite its use primarily in children, the ketogenic diet has been used successfully in adults with epilepsy, demonstrating that adults with partial epilepsy can achieve ketosis and seizure control [20]. This is in contrast to earlier studies suggesting greater efficacy of a ketogenic diet in younger rather than older children and adults [21, 22].

The ketogenic diet continues to compare favorably with other new treatments that have been introduced to treat epilepsy in children. The renewed interest in ketogenic diet has once again raised several research questions that if answered, have the potential to improve our understanding of the neurochemistry of epilepsy and would allow better treatment of all patients with epilepsy. The ketogenic diet, a therapy that started at the beginning of the 20th century, appears to have a definitive role in the treatment of both childhood and adult epilepsy well into, and perhaps beyond the 21st century.

Keywords: Antiepileptic drug, Intractable epilepsy, Ketogenic diet, Pharmacoresistant epilepsy

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Authors declare no conflict of interest.

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