MANTECH Publications

Swasthavritta: Journal on Diet, Hygiene, Yoga & Naturopathy
Volume 1, Issue 2, July-December, 2022

The Role of Diet Therapy in the Treatment of Refractory Epilepsy and its Connection to Dentistry

Veena Malhotra[1], Harika Das[2], Srujan Kumar[3]

Students[1, 2], Professor[3]

Department of Swasthavritta

Dr Krishna Gopal Dwivedi Ayurvedic Medical College

Corresponding Author's E-Mail: *surajnkumar011@gmail.com[3]*

Abstract

Intractable epilepsy is defined as seizures that cannot be controlled with AED one year after onset, despite proper diagnosis and therapy monitoring. Intractable epilepsy is associated with an increased risk of death, unemployment, and cognitive impairment. Dietary therapy has been used to treat refractory epilepsy since prehistoric times. Alternative treatment methods, such as nutrition therapy, have grown in favour over the previous decade. The ketogenic diet (KD) is a non-pharmacological therapy for drug-resistant epilepsy as well as difficult-to-treat epilepsy disorders of infancy and early epileptic encephalopathies. The diet is low in vitamins and minerals, and a number of consequences have emerged in the form of case reports, the majority of which demonstrate oral and systemic difficulties attributable to a specific deficiency condition.

Keywords: *Diet Therapy, Ketogenic Diet, Encephalopathies, Non-Pharmacological Therapy*

INTRODUCTION

The name "Epilepsy" is derived from Latin and Greek roots meaning "seizure" or "to seize upon". 1 A seizure is defined as a change in neurologic function caused by an excessive discharge of neurons in the brain. 2Epilepsy is a brain condition that is one of the most frequent chronic neurological illnesses. 3 It includes the induction of seizures, which is connected with changes in behaviour, perception, and

mental activity. It also causes a brief loss of consciousness and muscle spasms. [4]

"Epilepsy Syndrome" refers to a collection of clinical symptoms that occur in tandem with comparable seizure(s), age of start, electroencephalography (EEG) results, triggering events, genetics, natural history, prognosis, and response to antiepileptic medicines (AEDs). [2]

Epilepsy is mostly diagnosed clinically. According to the International League Against Epilepsy (ILAE), epilepsy is diagnosed when: 1. two unprovoked seizures occur more than 24 hours apart;

1. 1 spontaneous seizure with a 60% likelihood of recurrence (equivalent to 2 unprovoked seizures) during the following 10 years; or
2. The epilepsy syndrome has been discovered.
3. Epilepsy can be caused by a number of reasons, including genetics, developmental problems, infections, traumatic traumas, neoplasia, and degenerative illnesses.

According to the World Health Organization, around 50 million individuals worldwide are afflicted, with the prevalence being higher in underdeveloped nations than in industrialised countries.[6]

A seizure can be partial (when epileptic discharges occur in a single area of the brain) or generalised (when discharges affect the entire brain cortex). Certain diagnostic tools, such as EEG, which records brain waves, and Magnetic Resonance Imaging, are used to make the diagnosis (MRI). [7]

Following a diagnosis of epilepsy, therapy is initiated, with AEDs being the primary pharmacological treatment advised. AEDs only treat the symptoms of epilepsy (seizures), not the illness itself. AEDs are often begun with a tiny single dosage and gradually raised to the lowest effective maintenance dose. Following the initial AED, almost half of the patients have symptom relief. [3]

According to epidemiological research, recurring, spontaneous, unprovoked seizures in epilepsy occur in 1 to 3% of children. Such individuals are effectively treated with AEDs; however, 10-40% of children show no change in seizure activity after medication treatment. [5]

Refractory Epilepsy:

Seizures that are intractable or refractory despite the use of AEDs are referred to be intractable or refractory. 8 The International League against Epilepsy (ILAE) defines refractory epilepsy as the inability to achieve seizure control after two trials with relevantly selected and utilised AEDs, either as monotherapy or in combination with additional medications.[3]

Intractable epilepsy is defined as seizures that cannot be controlled with AED one year after onset, despite proper diagnosis and therapy monitoring.[5]

Intractable epilepsy is associated with an increased risk of death, unemployment, and cognitive impairment.[9]

There is no common criterion for how long the seizures must last in order to be classified as refractory. Although the specific origin of intractable epilepsy is unknown, it has been proven that the majority of individuals with refractory epilepsy are resistant to most or all AEDs. 5 However, neuroinfections were found as a primary source of treatment resistance in a research done in a juvenile population. [8]

A research in North India discovered various markers of refractory epilepsy, including cerebrum anatomical abnormalities, resistance to first AED, a delay in mile stones, a rise in early seizure frequency, partial seizure type, febrile seizures, and beginning before the age of 14 years.[8]

It's linked with excess disability, morbidity and mortality 3 and affects brain in its early stages of development, spatial learning and memory.[5]

When a diagnosis of drug-resistant epilepsy is obtained due to failure of therapy with two AEDs, numerous therapeutic options, including surgery, are considered. 3 However, significant problems such as recurrent bleeding from the Central Nervous System (CNS), post-operative motor impairments, hydrocephalus, and wound infections have been described following temporal lobectomy, callosotomy, and hemispherectomy.[9]

Few novel AEDs for the treatment of drug-resistant epilepsy (such as lamotrigene and vigbatrin) are attempted. Several medication studies on novel medicines have yielded positive results in individuals with refractory epilepsy. Though these medications are intended for adults,

physicians routinely use them to treat refractory epilepsy in children. [9]

Dietary therapy has been used to treat refractory epilepsy since prehistoric times. Alternative treatment methods, such as nutrition therapy, have grown in favour over the previous decade. [9]

Ketogenic Diet and Its Relativity to Dentistry:

The ketogenic diet (KD) is a non-pharmacological therapy for drug-resistant epilepsy as well as difficult-to-treat epilepsy disorders of infancy and early epileptic encephalopathies. 5 It is a high-fat diet that was established in the 1990s and has been linked to specific biochemical alterations associated with times of restricted food supply.[10]

Starvation has been shown to be effective in treating epilepsy since the fifth century BC. It was claimed in the early twentieth century that fasting improved the frequency of seizures. The usefulness of KD in treating epilepsy was documented in 1921. The antiepileptic effect of KD that produces Ketosis without extended fasting times was postulated by Johns Hopkins University researchers.[9]

Wilder created the phrase "ketogenic diet" at the Mayo Clinic, which is defined as a diet that creates high levels of ketones in the blood by consuming extra fat and fewer carbs 5 and proteins, forcing the body to use ketone bodies (KB) as the primary source of fuel.[9]

During a diet, the body's energy consumption shifts from glucose (primary fuel) to the creation and use of KB.[11]

K.D was quite popular in the 1920s and 1930s 10, but with the development of some antiepileptic medications in the late 1930s and 1940s 9, the use of diet treatment faded and the emphasis turned to pharmacological therapy.

10 However, there has been a change in the use of diet therapy in the treatment of refractory epilepsy during the last 15 years.[12]

Classical KD, modified Atkins diet, Low index treatment diet, Medium chain-triglyceride (MCT) diet, and Modified MCT are diet regimens for the treatment of refractory epilepsy.[13]

The traditional diet consists of a 4:1 ratio of fat to protein and carbs combined. Approximately 90% of the calories in the

diet originate from fat 12 since there are 9 calories per gramme of fat compared to 4 calories/g of carbohydrate or protein combined. 14 Initially, calories are restricted to 80-90% of the required daily limit, although this can be progressively increased. 13 Children and young adults are started with a ratio of 3:1 of fat to carbohydrate plus protein, as they are rapidly growing. This provides enough proteins (1-1.5g/kg per day) for development. [14]

The Modified Atkins diet has a similar composition as the classical KD and has a 1:1 ketogenic ratio approximately.15 It does not limit calorie intake and allows for limitless protein and fat consumption. The dietary requirements for modifiedatkins diet consists of a concentration of 60-70% fatty acid, 25-30% proteins, and approximately 5% carbohydrates. [13]

The initial daily carbohydrate consumption is estimated to be 10gms with a gradual increase to 15-20g/day after a period of 1-3months.15 Though, modified atkins diet has several advantages, it is very restrictive for Indians, specially vegetarians.[12]

The Low-glycaemic index(low-GI) diet restricts the carbohydrate intake of the patient.[13]

The low-GI carbohydrates produce comparatively small changes in the blood glucose. It allows intake of total daily carbohydrate of 40- 60g/day. [15]

Medium chain triglyceride (MCT) diet contains MCT's (decanoic acid and octanoic acid) which has better absorbability and produces more ketones per unity energy during metabolization. Less fat is needed which allows addition of a greater concentration of other substances such as carbs and proteins.

The MCT contains 60% energy which is derived from MCT oil, such high levels of MCT can cause Gastro-intestinal discomfort in children, because of this, Modified MCT diet was introduced.[15]

It consists of 40-50% long chain fatty acid, 18-20% protein, 5-10% carbohydrates and 30% MCT oil.[13]

K.D should be considered when there is failure in seizure control following treatment with two or three appropriate AEDs.

12 The diet is initiated in a hospital set up so as to allow careful monitoring of patient's glucose and urinary levels of ketone bodies. It is usually started following fasting of approximately twenty-four to forty-eight hours (fasting initiation) 13 or till the presence of ketones is confirmed in the urine. [12]

The patient is given one-third of the targeted calorie intake on the first day of feeding, two-thirds on the second, and full caloric intake on the third day before being released on the fifth. [12]

Fasting start has various advantages, including a shorter time for the beginning of ketosis, the ability to check for any underlying metabolic abnormalities, and the ability to properly monitor ketosis.[12]

Non-fasting beginning is similarly successful and begins with a 1:1 ration of fat to carbohydrate plus protein by weight, full calorie meals, and then progresses to a 2:1, 3:1, and eventually 4:1 ration on a daily basis. The procedure can be started in an outpatient environment. [12]

K.D is not dangerous and is often well accepted by Indians.

12 A research done in AIIMS, New Delhi, India, in 2009 to test acceptability of KD in young Indian paediatric patients with intractable epilepsy reported that 14 patients withdrew out of the trial because the diet was too restrictive for the youngsters. Despite the fact that Indian diets are cereal-based and include less fat than Western diets, KD was shown to be well accepted by the remaining youngsters. Unpalatability was cited as the most common reason for youngsters discontinuing their diet. [16]

Problems encountered during the implementation of KD in the Indian population include a lack of packaged foods, interference from relatives, which results in a modification of the original diet plan, a large percentage of Indians being vegetarians, and religious customs resulting in the prohibition of several foods.[17]

Table 1: - Sample Diet for Vegetarians

Non-starchy vegetables: spinach, brocolli, mushrooms, bell peppers.
Healthy fats: olive oil, coconut oil, mct oil.
Coconut products: full-fat coconut milk, coconut scream, unsweetened coconut.

Nut and seed butter: almonds, walnuts, cashew butter.
Berries: blueberries, blackberries and strawberries.
Protein: tofu, nutritional yeast
Herbs and seasonings: basil, salt, pepper, paprika, turmeric.

The precise mechanism of action by which K.D suppresses epilepsy is unknown 12; however, several theories have been proposed that suggest that there is a direct stabilising effect of ketone bodies on the Central Nervous System, acidosis that occurs after ketosis has been shown to modify seizure threshold, changes in fluid and electrolyte balance, and changes in lipid concentration induced by diet, has an antiseizure effect. 9

Both acetone and acetoacetate have been proven in animal models to have anticonvulsant effects. 12 Incomplete fat oxidation in the absence of carbs results in ketosis, which plays a significant role in diet success. 14

K.D ratios and caloric restrict (CR) are two important factors which help in seizure protection. Higher K.D ratios ($\geqslant$ 3:1) have shown to increase anticonvulsant efficacy in clinical and experimental models.18 K.D has neuroprotective ability i.e., in a state of metabolic stress, K.Bs including β-hydroxy butyrate serves as an alternative source of energy. A study by Bough et.al. in 2006 revealed that coordinated upregulation of genes present in the hippocampus (which codes for energy metabolism) is seen with K.D.10

Neurons withstand metabolic stress during K.D intake by acting as a more efficient energy source and carrying a greater mitochondrial load. This leads in an increase in neurons' capacity to endure metabolic stress, which would normally result in cell death and drain neurons' resilience. 10

Chronic ketosis alters the Tricarboxylic Acid (TCA) Cycle, increasing GABA production, limiting the regeneration of Reactive Oxygen Species (ROS), and improving energy synthesis in the brain. These modifications stabilise synaptic function and boost resilience to seizures.

K.D, like other treatment methods, is linked with problems such as dehydration and vomiting (often during the start phase), as well as a drop in blood glucose levels in certain children. Constipation is the most prevalent adverse effect observed

during the maintenance period. 12 Renal stones have been found in 3-7% of children on K.D. 15

The diet is low in vitamins and minerals12, and a number of consequences have emerged in the form of case reports, the majority of which demonstrate oral and systemic issues attributable to a specific deficiency condition. 5

Scurvy has been observed as a result of a Vitamin C deficit, which causes prolonged bleeding from the gums, alterations in platelet function, and severe bruising. Bone mass loss, Vitamin D insufficiency osteomalacia, and fracture risk have also been described. 5

Children with chronic conditions, such as epilepsy, are on long-term drugs that may contain sugar, putting them at a higher risk of tooth decay. Maintaining dental hygiene may be challenging in such instances. 5

Complete or partial ketosis loss can decrease seizure control. 19 As a result, it is critical to maintain a ketotic state by limiting carbohydrate consumption. 5

The label "sugar-free" is mainly reserved for diabetics, and the medications may contain carbohydrate, which might result in ketosis failure. Carbohydrate content is stated to be higher in medication solution, moderate in chewable tablets, and lower in intact capsules. 13

The K.D is a non-cariogenic diet since all cariogenic substances are avoided. It induces ketosis, which reduces the production of ROS (an active biomarker in periodontal disease), which have a short half-life and can cause significant damage to tissues and biological components. 20

The diet's safety during pregnancy must be assessed. "Fetal hydantoin syndrome" is a condition characterised by a variety of defects caused by foetal exposure to teratogenic AEDs such as phenytoin during pregnancy. 21

However, in 2016, Louw E et al reported examples of two pregnant women with epilepsy who were treated with K.D as the only treatment method (monotherapy) or in conjunction with other treatment alternatives (adjunctive treatment). In both cases, K.D was proven to be a successful treatment for epilepsy in pregnancy, allowing for normal foetal development. 22

The dental staff must carefully examine and prescribe sugar-free pills, capsules, or liquid medicines. 5

When feasible, the dentist should choose a drug that will not interfere with ketosis. 19

CONCLUSION

The treatment of refractory epilepsy is a challenge to the physician due to the disease's resistance. It is critical to choose a treatment strategy that effectively regulates seizures in children while also maintaining quality of life. The oral health team must closely monitor the disease condition, be aware of the adverse responses caused by long-term use of AEDs and the present therapy the kid is receiving, and administer a treatment that does not interfere with the treatment in any manner. According to the data, food treatment has a direct or indirect effect on dental health owing to vitamin and mineral deficiencies.

REFERENCES

1. World Health Organization, Global Campaign against Epilepsy, Programme for Neurological Diseases, Neuroscience (World Health Organization), International Bureau for Epilepsy, World Health Organization. Department of Mental Health, Substance Abuse, International Bureau of Epilepsy, International League against Epilepsy. Atlas: epilepsy care in the world. World Health Organization; 2005.
2. Stafstrom CE, Carmant L. Seizures and epilepsy: an overview for neuroscientists. Cold Spring Harbor perspectives in medicine. 2015 Jun 1;5(6):a022426.
3. Perucca P, Scheffer IE, Kiley M. The management of epilepsy in children and adults. Medical Journal of Australia. 2018 Mar;208(5):226-33.
4. Mehmet Y, Senem O, Sulun T, Humeyra K. Management of epileptic patients in dentistry. Scientific Research. 2012 Oct 3(1);47-52.
5. Sharma A, Mathur VP. Refractory epilepsy and the ketogenic diet: pathophysiological aspects and possible implications in dental practice. JISPPD. 2011 Jul 1;29(3):188.
6. Del Rosario Cruz-Cruz M, Gallardo-Elías J, Paredes-Solís S, Legorreta-Soberanis J, Flores-Moreno M, Andersson N. Factors associated with epilepsy in children in Mexico: A case-control study.

Boletin medico del Hospital Infantil de Mexico. 2017 Sep 1;74(5):334-40.

7. Aragon CE, Burneo JG. Understanding the patient with epilepsy and seizures in the dental practice. Journal of the Canadian Dental Association. 2007 Feb 1;73(1).
8. Amudhan S, Gururaj G, Satishchandra P. Epilepsy in India I: Epidemiology and public health. Annals of Indian Academy of Neurology. 2015 Jul;18(3):263.
9. Lefevre F, Aronson N. Ketogenic diet for the treatment of refractory epilepsy in children: a systematic review of efficacy. Pediatrics. 2000 Apr 1;105(4):46-53.
10. Gasior M, Rogawski MA, Hartman AL. Neuroprotective and disease-modifying effects of the ketogenic diet. Behavioural pharmacology. 2006 Sep;17(5-6):431.
11. Güntner AT, Kompalla JF, Landis H, Theodore SJ, Geidl B, Sievi NA, Kohler M, Pratsinis SE, Gerber PA. Guiding ketogenic diet with breath acetone sensors. Sensors. 2018 Nov;18(11):3655.
12. Sharma S, Jain P. The ketogenic diet and other dietary treatments for refractory epilepsy in children. Annals of Indian Academy of Neurology. 2014 Jul;17(3):253.13.
13. Misiewicz Runyon A, So TY. The use of ketogenic diet in pediatric patients with epilepsy. ISRN pediatrics. 2012 Aug 28;2012.
14. Kwiterovich Jr PO, Vining EP, Pyzik P, Skolasky Jr R, Freeman JM. Effect of a high-fat ketogenic diet on plasma levels of lipids, lipoproteins, and apolipoproteins in children. Jama. 2003 Aug 20;290(7):912-20.
15. Kossoff EH, Zupec‐Kania BA, Amark PE, Ballaban‐Gil KR, Christina Bergqvist AG, Blackford R, Buchhalter JR, Caraballo RH, Helen Cross J, Dahlin MG, Donner EJ. Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. Epilepsia. 2009 Feb;50(2):304-17.
16. Sharma S, Gulati S, Kalra V, Agarwala A, Kabra M. Seizure control and biochemical profile on the ketogenic diet in young children with refractory epilepsy—Indian experience. Seizure. 2009 Jul 1;18(6):446-9.
17. Nathan JK, Purandare AS, Parekh ZB, Manohar HV. Ketogenic diet

in Indian children with uncontrolled epilepsy. Indian pediatrics. 2009 Aug 1;46(8).

18. Bough KJ, Rho JM. Anticonvulsant mechanisms of the ketogenic diet. Epilepsia. 2007 Jan;48(1):43-58.
19. Lebel D, Morin C, Achim N, Laberge M, Carmant L. The carbohydrate and caloric content of concomitant medications for children with epilepsy on the ketogenic diet. Canadian journal of neurological sciences. 2001 Nov;28(4):322-40.
20. Dahiya P, Kamal R, Gupta R, Bhardwaj R, Chaudhary K, Kaur S. Reactive oxygen species in periodontitis. Journal of Indian Society of Periodontology. 2013 Jul;17(4):411.