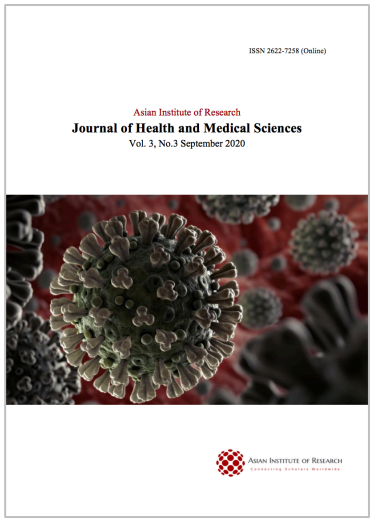

Journal of Health and Medical Sciences

Mubarak, Rabeea, Raza, Izma, Khursheed, Aleena, Mushtaq, Maham, Hanif, Birah, and Majeed, Ayesha Bint. (2020), Therapeutic Effects of Ketogenic Diet in the Treatment of Epilepsy. In: *Journal of Health and Medical Sciences*, Vol.3, No.3, 358-369.

ISSN 2622-7258

DOI: 10.31014/aior.1994.03.03.131

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.3, 2020: 358-369
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.03.131

Therapeutic Effects of Ketogenic Diet in the Treatment of Epilepsy

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Abstract
Epilepsy is characterized by seizures due to abnormal discharge of nerve impulses from the brain. Antiepileptic drugs are used to counter these seizures. However, in some types and severities in epilepsy where seizures are resistant to drugs, ketogenic diet (high in fat and low in carbohydrates) is used. In this review beneficial effects of ketogenic diet have been explored in treating epilepsy. It is used as a standard treatment for refractory epilepsy and has showed positive effects in treating all types of epilepsy, in all ages, especially in children. These findings were supported by previous studies which proved that ketogenic diet optimized the therapeutic effects against epilepsy by decreasing the oxidative stress, neuronal damage and enhancing the function of mitochondria. However, the exact mechanism of ketogenic diet in the treatment of epilepsy is still unknown but it can be used as potential therapy for children. More researches are needed to conclude the same for adults.

Objective: The purpose of the study is to investigate the mechanism and action of the ketogenic diet in the treatment of epilepsy along with the side effects. Through this review, the reader can get a full understanding on how efficient the therapy is practically, the diet's tolerable levels and effectiveness.

Keywords: Ketogenic Diet, Ketogenic Diet Therapy, Epilepsy, Seizures, Ketone Bodies, Amino Acids

1. Introduction

Ketogenic Diet (KD) is referred to as high fat and a very low carbohydrate diet that shares many similarities with the low-carbs diet. Over a century, it is used as a beneficial treatment for epileptic individual (Rho, 2017). Faith Healer introduced a KD diet in 1920's in Greece to help epileptic children (Walczyk & Wick, 2017). KD may increase the effects of fasting leading to the formation of ketones in the liver, the main ones being, Beta-hydroxybutyrate, acetones and acetoacetates (J. M. Freeman & Kossoff, 2010). In the 1940's, the initiation of anti-epileptic drugs started to replace the ketogenic diet, but overtime, the ketogenic therapies got higher consideration in the 1990's. It has now become a standard treatment for epileptic patients along with its uses in many other neurological disorders such as Alzheimer disease, Parkinson's disease, and amyotrophic lateral sclerosis, cerebral injury and also ischemia (Barañano & Hartman, 2008) (Guelpa, 1911; Prins & Matsumoto, 2014; Tefera & Borges, 2017; Zhao et al., 2006).

The efficacy of the KD diet is not linked to the type of seizures/epilepsy, age, sex and etiology (Coppola et al., 2002). Numerous studies have revealed positive results of KD on adolescents, adults and children. KD showed more significant result for the improvement of cognition and social behavior among children 3-8 years of age than gluten and casein free diets (El-Rashidy et al., 2017). Thiele EA observed that children may also take the vitamin and mineral supplements along with Ca supplements when they are on KD diet. Moreover, in ketogenic diet fat necessities are encountered by heavy cream, dietary fats and oils. Children may also encourage consuming specific fruits, vegetables and proteins. In addition, fruits and vegetables which contain starch, simple sugars, pasta and grains should be avoided (Thiele, 2003). Ketogenic diet has exhibited promising results in generalized and partial epilepsy in adults. The diet has manifest to be bearable in the majority of patients (Sirven et al., 1999).

The high fat low carb diet prevents starvation and provides necessary calories to the body by oxidation of fats which surpass the TCA cycle. By the oxidation of fats, production of ketone bodies increased which are used by cells for energy creation including the brain, when glucose is absent. The ketone bodies further undergo oxidation and acetyl-CoA is released which then goes into the TCA cycle as summarized in Fig.1 (Gasior, Rogawski, & Hartman, 2006). The micronutrients present in the KD are in the ratio 4:1 (4 gram of fat for 0.5g proteins and 0.5g carbs – 8% proteins, 2% carbohydrates and 90% fats (McDonald & Cervenka, 2018) (Allen et al., 2014).

An epileptic seizure can be physiologically defined as "a state produced by an abnormal excessive neuronal discharge within the central nervous system" (Penfield & Erickson, 1941). In Europe, the estimated figure of children and adolescents having active epilepsy is 0.9 million. Moreover, an estimated percentage of 20-30% of epileptic populace have >1 seizure/month (Forsgren, Beghi, Oun, & Sillanpää, 2005). According to previous epidemiological studies showed that there was a reduction in 50% seizures in adults who were given 22-25% classic KD treatment (12). In addition, a number of other evidence based studies showed that ketogenic diet is more effective in refractory epilepsy than anticonvulsant medications among children (Acharya, Hattiangady, & Shetty, 2008).

The efficacy of KD has been seen across a diversity of age, types of seizures and the severity of seizures. The role of KD in epilepsy is very evident among a diverse group of studies. Various studies documented that the effectiveness of KD in intractable epilepsy among adults was 13-70%. Previous clinical researches indicated that KD contains some potential procedural limitations, such as improper study designs and sub optimal categorized patients and populace (Neal et al., 2008) . Furthermore, 38% children receiving KDT had a greater than 50% decrease in seizures, 7% had greater than 90% reduction in the amount of seizures (Sampaio, 2016). Clinical researches done till now do contain potential procedural limitations, such as improper study designs and sub optimal categorized patients and populace. To counteract these limitations, a no. of creative, prospective randomized controlled trials (RCT's) have been planned, and executed. The outcomes of these studies will expectantly offer important information to better understand the role of KDT in the treatment procedures in various types of epilepsy (J. Freeman, Veggiotti, Lanzi, Tagliabue, & Perucca, 2006).

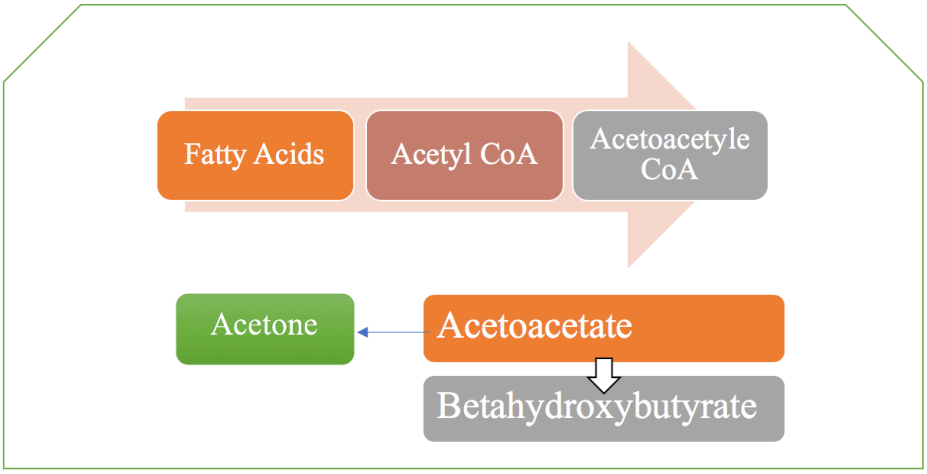

Fig 1. Production of ketone bodies by oxidation of fats

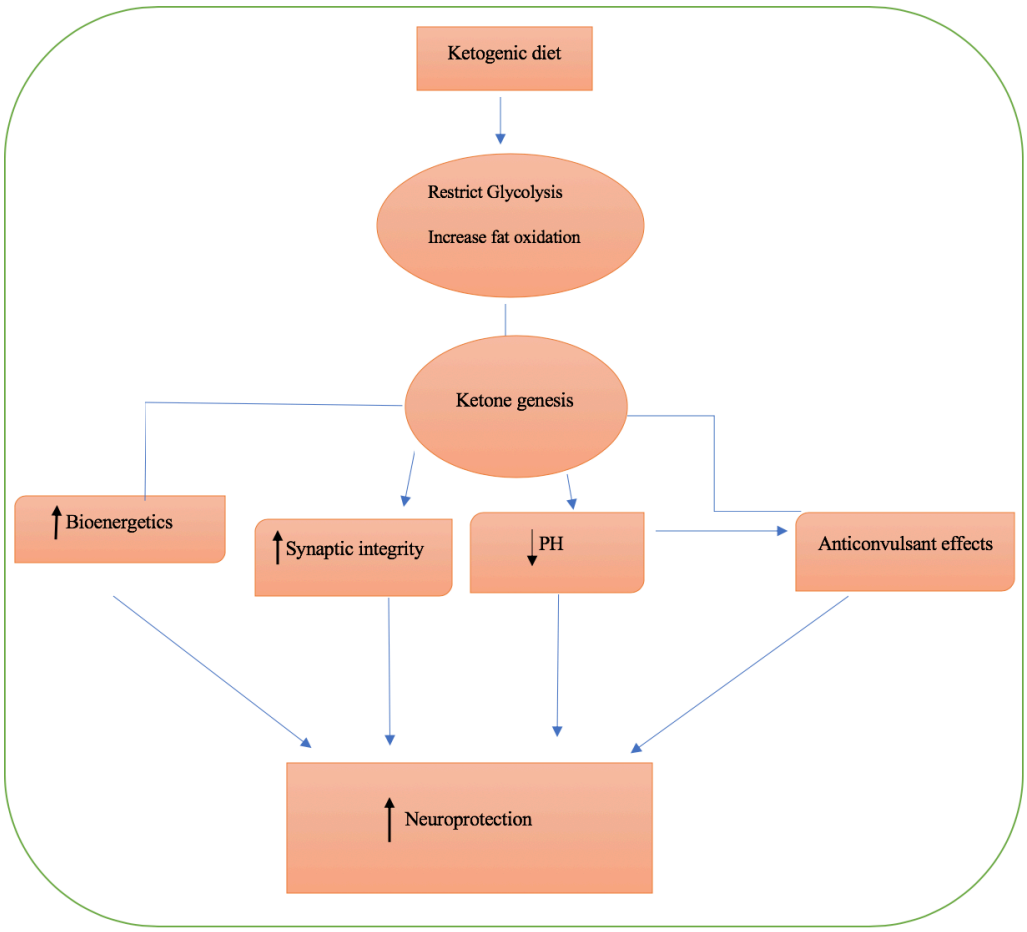

Fig 2. Basic mechanism of the role of KD in decreasing convulsions in epilepsy

2. Literature Review

KD is the oldest and the most effective therapy used for treating epilepsy. It is shown to be most beneficial in treating interactable epilepsy in children (Thiele, 2003). In 1921, Wilder initiated ketogenic diet comprised of high fat and low carbohydrates for the treatment of epilepsy and its effectiveness was analyzed by clinical trial performed by Peterman, Helmholtz, Keith and Livingston (MILLICHAP, JONES, & RUDIS, 1964). During KDT, the consumption of carbs is decreased to almost 50g/day or 10% of total calories. Consumption of protein increases to 1.2-1.5g/kg/day and the remaining ingestion of energy is from fats (60-80%)(Aragon et al., 2017).

Epilepsy is considered as the most common disorder of the brain, can befall at any age and is diagnosed through clinical and neurophysiological investigations (Duncan, Sander, Sisodiya, & Walker, 2006). It is too multifaceted to be considered a disease. In fact, it can better be called as a syndrome categorized by seizures that can occur due to a variety of conditions. Different types of epilepsy occur due to dysfunctions in potentially different biological pathways. Drugs used to target one pathway will only treat a specific no. of epileptic patients because the mechanism of the medication is specific to specific type of epilepsy. Potential pathways which are responsible for causing seizures include: glucose/amino acid transport, mitochondrial dysfunction and neuronal myelination. Present studies do not have the ability to test every person to detect the actual etiology of epilepsy which leads to an increased number of misdiagnosis. So the usage of ketogenic diet is suggested as a primary long term treatment in terms of effectiveness and efficiency (Clanton, Wu, Akabani, & Aramayo, 2017).

2.1 Mechanism

The 2 circumstances should be considered when KDT is to be used before the failure of 2-3 anti-convulsant medications. The first one is the glucose transporter deficiency syndrome, when transportation of glucose to the BBB (blood brain barrier) is weakened. The second is the loss of pyruvate dehydrogenase when pyruvate isn't metabolized to acetyl co-A (Kossoff et al., 2009). Researches also suggest that many other causes may benefit from KDT. For example, epilepsies caused by genes (ex: juvenile myoclonic and absence epilepsy) and epilepsies caused by catastrophes such as those due to deformities (ex: lissencephaly, hypoxic-ischemic injury, migrating focal seizures of infancy, and febrile infection-related epilepsy syndrome) (Thammongkol et al., 2012).

Various studies demonstrated that KD as an adjunct treatment in children and adults with refractory epilepsy, is considered as a first-choice treatment in some explicit metabolic disorders. For example, in glucose transporter type 1 and pyruvate dehydrogenase deficiencies, and mitochondrial complex I defects. Papers also suggest that KDT is significantly effective in West syndrome, severe myoclonic epilepsy of infancy, myoclonic-astatic epilepsy, febrile infection related epileptic syndrome, and drug-resistant idiopathic generalized epilepsies or refractory status epilepticus (Elia, Klepper, Leiendecker, & Hartmann, 2017; McDonald & Cervenka, 2017).

Epilepsy is brought by phenotypic alterations in endothelium of brain which bring seizure reactions due to changes in blood brain barrier and they have abnormal expression of glucose transporter molecule (GLUT1).I t is also characterized by hypo metabolism in seizure foci and altered properties of non-excitable CNS cells which lead to decreased uptake of ions from channels. Glucose uptake is hindered but ketone bodies generated by ketogenic diet can be used as an alternative to glucose and can cross Blood Brain Barrier easily as depicted by the flow diagram Fig.3 (Janigro, 1999).

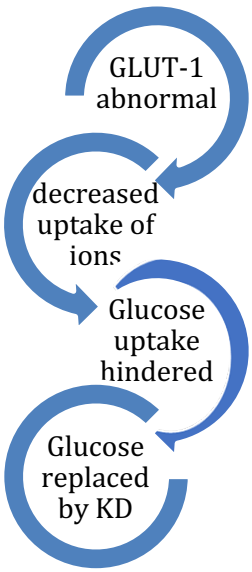

Fig 3. Glucose uptake hindered by brain cells

Many researches have been focused on how the ketone bodies show anti-convulsant effects. There have been discrepancies in researches trying to associate guarding against seizures with the amount of ketone bodies. This proposes the fact that some other processes can be involved in KDT's positive outcomes on seizures. Many mechanisms have been suggested (Fig 4) such as; the production of ATP's causing the neurons to become resistant when the demand of metabolism is high during seizures; changes in the pH of the brain altering the excitation of neurons; the inhibition of fatty acid/ion channels by ketone bodies (KB); and changes in the metabolism of AA (amino acids) that lead to the production of Gamma aminobutyric acid (GABA), a neurotransmitter of the brain (Barañano & Hartman, 2008).

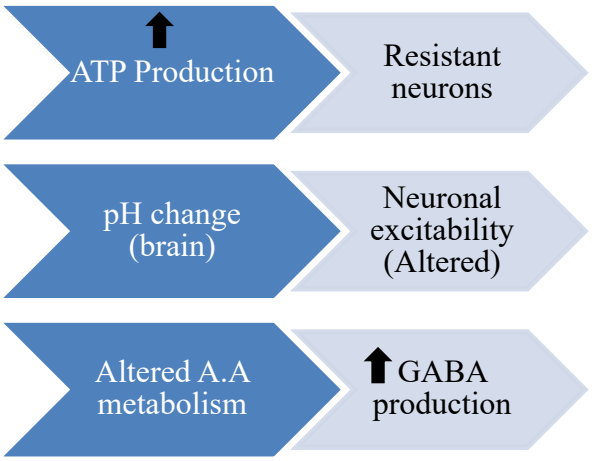

Fig 4. Positive Effects of KD on seizure reduction

GABA signaling is the best studied goal of study. Epilepsy was induced by GABA antagonists in mice and they were seen to exhibit an extraordinary response to KD (Bough, Gudi, Han, Rathod, & Eagles, 2002). Aspartate is an amino acid. The role of aspartate is to stop the action of glutamate decarboxylase. Glutamate decarboxylase catalyzes alpha-ketoglutarate to GABA. If the level of aspartate is decreased by KD, it would indorse the production of GABA. The excitatory neurotransmitter glutamate would then be converted to glutamine in astrocytes (the glial cells of the nervous system). Neurons take up glutamine which is converted to GABA, which hinders neuron action (Fig 5) (Zhang, Xu, Zhang, Yang, & Li, 2018).

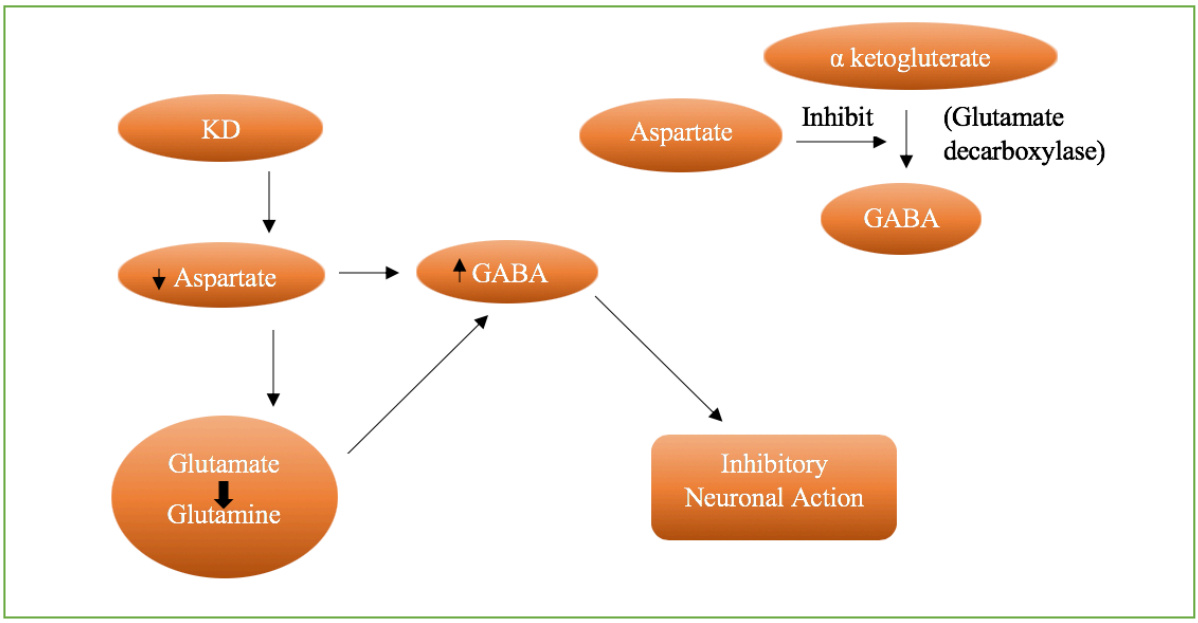

Fig 5. Role of KD in inhibition of neuron action

Levels of Poly unsaturated fatty acids are also increased along with ketone bodies in epileptic individuals who were given KD. Studies show that both ketones and PUFA show neuroprotective action in neurodegenerative disorders which are related to improper functioning of the mitochondria. Mechanisms of neuroprotective actions include decreased free radicals in the mitochondria. This would lead to decreased oxidative stress and reduced neuron damage (Fig 6). It is still not clear as to how KD specifically causes an anti-convulsant reaction. But the positive effects of KD do propose the fact that if synthesis of ATP is heightened and reactive oxygen species are suppressed, it can cause a remarkable decrease in epileptic seizures (Masino & Rho, 2012).

2.2 Previous Studies

To validate the effect of KD on refractive epilepsy, another study was done, in which diet, seizure and adverse effects history were taken during a 36-month period. Out of the 29 children who were given KD, 75.8% showed less seizure after 4 weeks and 48.3% of children showed a 90% reduction in the frequency of seizures. At 1 year, 8 epileptic patients continuously presented constructive results. No effective changes were seen in levels of triglycerides, albumin, total protein, creatinine, glycemia, AST's and ALT's. Levels of serum cholesterol were shown to increase in the first 4 weeks, reduced in the next 6 months and had come to normal after that. The overall results concluded that almost $1/3^{rd}$ patients had accomplished a potential decrease in the frequency of seizures, and a few of them were totally cured with no seizures at all (Martins et al., 2012).

The effectiveness and tolerable levels of KD were further proved when a study on 48 children and adults with refractory epilepsy was conducted. Patients were randomly selected in the KD group and the care as usual (CAU) group. The results indicated that mean frequency of seizures was potentially lower in the KD group than in the CAU group and a two-fold decrease was seen in the score of the severity of seizures in the KD group. Gastrointestinal side effects were also higher in the KD group. The results concluded that this RCT trial was a Class 1 proof that KD diet was effective in the treatment of refractory epilepsy in children and adolescents but patients frequently reported gastrointestinal symptoms (Lambrechts et al., 2017).

Another type of epilepsy, Lafora Body Disease (worsened myoclonus epilepsy) was studied in 2006. This type of epilepsy cannot be treated by a specific therapy. In LBD patients the accumulation of polyglucan occurs due to the mutation in the protein that is involved in glycogen metabolism. This study provided KD to such patients and assessed its effectiveness on them. The study involved 5 LBD patients who remained under observation for 10-30 months. The KD brought effective changes in the first 16 months and the nutritional and clinical findings of the patients remained stable during this period. KD therapy was not able to stop the disease progression instead it slowed down the progression rate. However further investigations should be done on a larger case series (Cardinali et al., 2006).

Additional study was conducted in 2014 by Maromi Nei on ketogenic diet as an alternative treatment for epilepsy. Sample size of 29 including adults and adolescents with the mean age of 32 years and range of 11-51 years was collected and were initiated keto-diet for 9 months. Results showed that 52% of them demonstrated improvements by a reduction of 50% of seizure frequencies. 31% showed no improvement, 7% were not able to follow up and frequency of seizures increases in 10% of patients. The study concluded that the diet could be used for the treatment in adults and adolescents with epilepsy, and patients who had a generalized epilepsy who show symptoms can be good choice of applicants for KDT (Nei, Ngo, Sirven, & Sperling, 2014).

An experimental study conducted on mice showed that KD can decrease the episodes of seizures in mice by increasing activation of adenosine A_1 receptors (A_1Rs). KD reduced adenosine kinase, the major adenosine-metabolizing enzyme. Importantly, hippocampal tissue resected from patients with medically intractable epilepsy demonstrated increased adenosine kinase concluding that can reduce seizures by increasing A_1R-mediated inhibition (Masino et al., 2011).

A study conducted on 168 epileptic patients aged ≥ 18 years showed that the effectiveness of KDT varied from 13-70% with the total effectivity rate of 52% for the classic ketogenic diet (Ye, Li, Jiang, Sun, & Liu, 2015). A study on 27 subjects given KD for a duration of 2-118 months showed an 33% complaint rate ≥ 90% seizure reduction in 52% patients and ≥ 50% reduction in 70% patients (Cervenka & Kossoff, 2013). To offer additional

proof for the tolerable levels of KD in adults, another study was conducted. 23 subjects given KD in the ratio of 2-2.5:1 for a duration of 1 year showed a 39% complaint rate ≥ 90% seizure reduction in 8% patients and ≥ 50% reduction in 39% patients. These results concluded that epileptic adults can tolerate KD in the long-term reducing frequency of seizures (Schoeler et al., 2014).

To evaluate the limitations of KD is equally important as its benefits. A study was conducted to calculate the management and prevention of KDT. 129 epileptic patients on 129 on KDT were assessed to review the early and late onset complications. Results exhibited complications of dehydration, nausea, vomiting, diarrhea, constipation, gastritis and fat intolerance. Hypertriglyceridemia, transient hyperuricemia, Increased cholesterol levels, numerous infectious diseases, symptomatic low blood glucose levels, hypoproteinemia, decreased magnesium levels, repetitive decreased sodium levels, low concentrations of high-density lipoprotein, lipoid pneumonia because of aspiration, hepatitis, acute pancreatitis, and persistent metabolic acidosis were also noted. Late-onset complications consisted of osteopenia, renal stones, cardiomyopathy, secondary hypocarnitinemia, and iron-deficiency anemia. Most of these adverse effects were effectively controlled. At the same time 17.1% stopped KDT because of serious side effects, and 3.1% died during KD treatment, 2 deaths were reported due to sepsis, 1 due to cardiomyopathy and 1 due to lipoid pneumonia. The study concluded the basic fact that complications during KD are temporary but should be monitored carefully at the same time (Kang, Chung, Kim, & Kim, 2004). Randomized studies of the ketogenic diet in Cochrane Epilepsy Group's Specialised Register (June 2011), the Cochrane Central Register of Controlled Trials (CENTRAL 2011, Issue 2 of 4), MEDLINE (1948 to May week 4, 2011) and EMBASE (1980 to March 2003) suggest that the KD results in short to medium term benefits in seizure control in children. However, one study of long term outcome report poor tolerance and GIT issues. It was not possible to meta-analyze data from these randomized trials due to heterogeneity. However, all studies showed 30-40% reduction in seizures compared to comparative controls (Levy, Cooper, Giri, & Weston, 2012).

A retrospective case study was reviewed in 29 infants aged two and a half weeks and 23 months given KDT. Results showed that 2 of them showed no signs of seizures after 4 weeks of KDT, 7 showed >50% decrease in seizures and 8 demonstrated a reduction in the severity and frequency of seizures. 45% had no side-effects of the treatment and KDT was stopped in 2 because they could not tolerate the diet. The review came to a conclusion that infants can tolerate KD well even when the intensity of the seizures is high. The results also concluded that 50% reduction is possible with KDT without adverse effects (Ismayilova, Leung, Kumar, Smith, & Williams, 2018).

KD is an effective approach in treating drug-resistant epilepsy in young children. It also provides positive results when given to adults with epilepsy. Researches conducted on KD's effectiveness in adults are few and its treatment usage is limited in adults with intractable epilepsy. A meta-analysis gathered information from a few published researches on treating epilepsy with KD in adults from different sources like PubMed, Embase and Conchrane Library for up to 10th January 2017. The main outcome included a 50% reduction in seizures; the methodology reviewed by the New castle-Ottawa scale. There were 402 articles out of which 16 studies predominantly met the inclusion criteria including 338 patients. The results of the meta-analysis showed the following percentages; 13% adults showed effective symptoms of no seizures, 53% adults had a 50% decrease in seizures and 27% adults with intractable epilepsy decrease in seizure presented seizure drop under 50%. KDT showed less harmful effects like weight loss, high level LDL and raised total cholesterol while on the other hand low glycemic index diet (LGID) and low dose fish oil diet (LFOD) has shown fewer side effects. Thus the meta-analysis concluded that KD is an effective approach to treat intractable epilepsy in adults and also its side effects are well tolerated. Further studies are required to make KD more of an effective treatment approach for intractable epilepsy (Liu et al., 2018).

The acceptance, Tolerance and effectiveness was further evaluated in another study. KDT (formula-based) was given to 10 refractory epileptic children. Results suggested only mild side effects and satisfactory adherence, 50% decrease in seizures were observed in 60% patients and 10% patients became seizure free on KDT (Sampaio, Takakura, & Manreza, 2017), which is also supported by other studies (Martin-McGill, Jenkinson, Smith, & Marson, 2017).

A multi-center research pursued to look into the advantaged of KD in seizure reduction in 50 children with myoclonic-astatic epilepsy (MAE). The reduction in seizures were monitored before during and after treatment.

Results indicated a seizure free outcome in 54% patients and >70% decrease in seizures were seen in 86% patients. 50% children had normal development and cognitive outcomes. Introducing KD earlier did not prove to be effective in a greater decrease in seizures, but potentially lead to remission. The significance of the study was the fact that introducing KDT early in MAE has a robust tenacious anti-convulsant effect with remission in the long term (Stenger et al., 2017).

A study was conducted to govern the effect of KD diet on the action of seizures, anthropometric measurements and biochemical markers, along with GI symptoms. 15-50g CHO modified KD was given for a period of 3 months. Participants included 67.7% white, 50% females 39 years of age, with a BMI of 32.6 kg/m^2. The results again showed a significant effect on seizure reduction. LDL increased from 131 mg/dl to 144 mg/dl and HDL from 57-69 mg/dl. Triglycerides elevated from 96-91mg/dl. GI scores were not affected with modified KD in epileptic adults. Significant reductions in seizure frequency were also noted, concluding the fact that KDT may be a valuable option in the treatment of seizures and weight gain in epileptic adults (Schuchmann et al., 2017).

The total evidence of these studies show that KD and its variants are a good alternative for non-surgical pharmaco-resistant patients with epilepsy of any age, taking into account that the type of diet should be designed individually and that less-restrictive and more-palatable diets are usually better options for adults and adolescents (D'Andrea-Meira et al., 2019).

3. Results

#	Source	Study Design	Condition	Population	Main Outcomes
1.	Martins et al., 2012	Experimental Study	Questionnaire and Diet Evaluation – (CHO-3-5%) Dietary Fat – 70% Protein – Not Restricted	A total of 102 respondents 102 completed the questionnaire 17 commenced the diet	Constipation (n = 6) and loose stools (n = 3), shown as adverse effects. No other complication Increase in seizures (n=1)
2.	Lambrechts et al., 2017	Randomized Clinical Trials	Randomized to KD or Care as Usual	Refractory epilepsy patients of 1-18 years of age.	Primary Results - 50% decrease in seizures after a 4-month period. Mean Seizure frequency in KD (56%) compared to control (99%) The group treated with KD showed a higher rate of GI symptoms.
3.	Cardinali et al., 2006	Pilot Study	LBD patients treated with KD	5-Lafora body Disease patients	KD well tolerable in 1st 16 mos. Didn't stop the progression of the disease in the long term.
4.	Nei, Ngo, Sirven, & Sperling, 2014	Long term results report on epileptic adults treated with KD	Started KD and follow up until discontinuation of the diet	29 adults and adolescents with refractory epilepsy (11-51 years of age) (16 women, 13 men)	52% decrease in the frequency of seizures 45% with greater than 50% decrease in the frequency of seizures, 31% - no improvement 10% with greater than 50% rise in frequency of seizures.
5.	Schoeler et al., 2014	A review on the feasibility of KD	KDT – with follow-ups for 1-10 years	23 epileptic adults	1 – experienced psychosis GI symptoms most common Decrease in the frequency of seizures Increased alertness and concentration
6.	(Kang, Chung, Kim, & Kim, 2004	Review on early and late -onset complications of KD	KDT – followed for greater than a year.	Results of 129 epileptic patients on KD	Early onset complications – dehydration, nausea, vomiting, diarrhea, constipation, fat intolerance and gastritis,

					hypertriglyceridemia, transient hyperuricemia, hypercholesterolemia, symptomatic hypoglycemia, hypoproteinemia, hypomagnesemia, repetitive hyponatremia, low concentrations of high-density lipoprotein, lipoid pneumonia due to aspiration, hepatitis, acute pancreatitis, and persistent metabolic acidosis Late-onset complications - osteopenia, renal stones, cardiomyopathy, secondary hypocarnitinemia, and iron-deficiency anemia.
8.	Ismayilova, Leung, Kumar, Smith, & Williams, 2018	Retrospective case-note review (2006-2016)	KDT for more than 4 weeks.	29 Children <2years	2/29 – seizure free 7 - >50% decrease in seizures 8 – reduction in the frequency of seizures
9.	Liu et al., 2018	Meta-analysis of observational studies	Effect of KDT	402 articles studied, out of which, 16 studies including 338 patients met the inclusion criteria	13% adults showed effective symptoms of no seizures, 53% adults had a 50% decrease in seizures and 27% adults with intractable epilepsy decrease in seizure presented seizure drop under 50%
10.	Sampaio, Takakura, & Manreza, 2017	Experimental Study	KDT; - CHO to Fat ratio for 3 mos. Orally Fed – 2:1 in 1st week 3:1 in 2nd week 4:1 in 3rd week Enterally Fed:-3:1 – at initiation 4:1 after 2 weeks	10 children with refractory epilepsy (9mos-16 yrs of age)	60% patients showed >50% decrease in the frequency of seizures. 10%- eizure-free
11.	Stenger et al., 2017	Retrospective Study	KDT	50 epileptic children treated by KDT	54% seizure free after 6 mos Earlier KDT – better cognitive outcome and significant results in remission
12.	Schuchmann et al., 2017	Experimental Study	15–50 net g of CHO/d for 3 mos.	31 enrolled patients Follow up of 12 patients at 3 mos. 67.7% white, 50.0% female, aged 39	Seizure frequency (n=9) reduced with KDT Two subjects reduction in frequency of seizures by ≥ 50%, 3 participants -decrease in frequency of seizures by < 50% Low-density lipoprotein cholesterol from 131 mg/dL to 144 mg/dL. High-density lipoprotein 57mg/dL to 69mg/dL, Triglycerides down from 96 mg/dL to 91 mg/dL baseline GI scores (n=4) low, did not change with alterations in KDT

4. Conclusion

KD, thus supports seizure control and inhibits progression of epilepsy. The ratio of fats to protein is 4:1 and fats to carbohydrates are 3:1. It shifts the energy metabolism of the body from carbs to fats which is the leading cause of generating ketone bodies. It is used as standard treatment for the patients of epilepsy particularly the refractory

epilepsy where medication is failed to prove positive effects. Positive results were seen in treating generalized and partial epilepsy with ketogenic diet.

KD is rapidly gaining popularity in almost all fields in the health sector. KD can be and is also used in a variety of other neurological disorders, such as Alzheimer's, Parkinson's and brain tumors, along with brain injuries, and weight management. It is being used for many years, and it's benefits in epilepsy outweigh the side effects. It should be kept in mind that both medicines and restricted diets do have some consequences but can be stabilized if given in the right proportions and monitored strictly with proper follow-ups. RD's who prescribe the diet need to be well acquainted on the basics of KD and how to manage the diet according to the patient. Many randomized control trials with an increase in the number of case-studies still need to be done in order to extensively investigate its mechanisms and effects on epileptic patients, and its mechanisms when given with anticonvulsant medications.

5. Recommendations

KD is a recommendable treatment approach towards intractable epilepsy in the children. The drugs that treat epilepsy target only one of its specific kind and therefore isn't functional and desirably beneficial in treating all kinds of epilepsy. KD has helped in reduction of epileptic seizures by 50% in children and adults in most studies conducted till date. It will be beneficial to conduct more class 1 researches to define the role of ketogenic diet in treating epilepsy in children and adults in a better way.

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