

## Efficacy of Ketogenic Diet in Seizure Reduction in Epileptic Patients-A Review

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Epilepsy is a neurological disorder characterized by unprovoked seizures of varying frequencies and intensity. Several pharmacological treatments had been used previously for its treatment. However ketogenic diet has gained importance as non-pharmacological therapy to epilepsy in recent years. This review aims to discuss the efficacy of ketogenic diet in epilepsy. Key words used for search include "ketogenic diet", "epilepsy", "childhood epilepsy" and "ketogenic diet side effects". Studies conclude that ketogenic diet is an effective remedy in seizure reduction. It comprises of very high fat, low protein and very low carbohydrates. Seizure reduction is due to decrease in the amount of reactive oxygen species which is a result of high ketone bodies and low glucose levels achieved by the use ketogenic diet, hence improving the condition of epileptic patients. It has proven efficacy in patients with epilepsy resistance to pharmacological treatment. In children it has positive or no impact on cognition, mood and behavior of children along with its antiepileptic properties. However further researches must be carried out to highlight the impact of ketogenic diet on cognition and mood of children. As ketogenic diet is high in fats, its long-term use may alter the lipid profile of patients. Moreover, gastrointestinal disturbances, insulin resistance has also been observed. Studies also show that there still need of clinical trials and researches in adult epileptic patients.

**Keywords:** Ketogenic Diet; Epilepsy; Childhood Epilepsy; Ketogenic Diet Side Effects**Abbreviations**

DHA: Docosahexaenoic Acid; AA: Arachidonic Acid; ROS: Reactive Oxygen Species

**Introduction**

Epilepsy is a neurological disorder. It is characterized by  $\geq 2$  unprovoked seizures, which occur by a difference of at least 24 hours [1]. Seizure refers to uncontrolled disordered electrical discharge in cerebral neurons [2]. Cannabis based treatment has been used as pharmacological treatment since ages [3].

Ketogenic diet comprises of very high fat, low protein and very low carbohydrates [4]. It consists of macronutrients in 4:1 ratio, with more grams of fats as compared to proteins and carbohydrates [5-7]. A high fat, low protein, low starch ketogenic diet has been utilized effectively to treat obstinate epilepsy. Ketogenic diet was formulated in 1921 and was used as an effective non-pharmacological treatment for childhood epilepsy [5].

Ketogenic diet increases the level of ketones in body, inhibiting the production of glucose. In this way it affects the level on neurotransmitter in the body which reduces seizures [7-9]. Ketogenic diet increases the level of ketone bodies effecting the metabolic

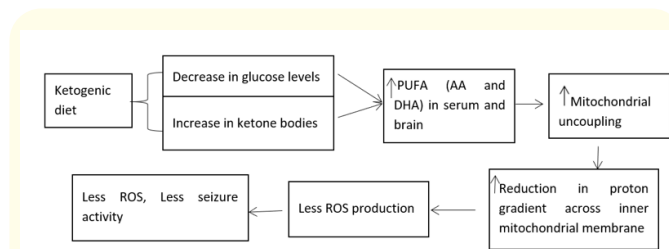
changes such as increase of adenosine levels which in turn decreases the seizures as compared to glucose. However ketogenic diet may increase the levels of medium chain triglycerides, which are more effective than ketones in blocking the seizure and increasing its threshold [6].

The use of ketogenic diet for the treatment of epilepsy has gained importance in recent years as an effective non-pharmacological treatment along with medications. This study aims to evaluate the efficacy of this high fat diet in seizure reduction in epileptic patients. Also, to review the proposed mechanism by which ketogenic diet helps to reduce seizure.

**Literature Review**

Ketogenic diet in epilepsy helps to maintain a constant level of ketone bodies in body helping in seizure reduction [9]. It has been assumed that the ‘high-fat’ part of the KD has anticonvulsant properties. Several exploratory investigations have proposed the anticonvulsant properties of PUFA [10].

**Proposed mechanism of action of ketogenic diet [7,11]**



**Figure**

**The effect of ketogenic diet in seizure reduction in epileptic patients**

Following table shows the results of few experiments carried out on epileptic patients. The results show seizure reduction after the use of ketogenic diet for a considerable time period.

Author	Year	Study type	Sample size	Duration (months)	Compliant patient %	Results	
						Seizure reduction %	No effect %
Maromi., et al. [12]	2014	Prospective	29	0.13 - 39	100	52	31
Pavel., et al. [13]	2010	Prospective	12	26	58.3	85	NA
Sook., et al. [14]	2011	Retrospective	5	60	5	75 - 100	NA
Danielle., et al. [15]	2012	Prospective	15	12	26.6	≥ 50	NA
Dengna., et al. [16]	2016	Prospective	42	1	100	≥ 50	NA
Lambrechts., et al. [17]	2012	Prospective	15	6	73.3	50	NA

**Table**

It is one of the most effective therapies for intractable epilepsy [18, 19]. Moreover, a study shows its established efficacy in treatment of epilepsy, worldwide too [16]. It has its proven effects in treatment of drug resistant childhood epilepsy [20]. However cognitive activation has been observed in patients treated with ketogenic diet [21]. It was concluded that effective implementation of ketogenic diet has strong neuro-protective effect relative to cognition and social behavior [22]. In 2012, Lambrechts conducted a study to evaluate the possible negative outcomes of ketogenic diet on cognition, psychosocial adjustment and behavior of epileptic patients. 15 participants including adolescents and school going children were assessed before introduction of ketogenic diet. After

6 months 11 of them were re-assessed using a questionnaire and psychosocial test. Results showed that this diet has no adverse effect on cognition. However, it impacts mood negatively [17]. Contrary to this, some studies conclude that ketogenic diet has positive impact on cognition, behavior and mood [23].

A prospective open label pilot study was conducted in 2010. 12 adults with epilepsy were enrolled among which only 7 were compliant to ketogenic diet, 4 were partially compliant and 1 was non-compliant. Participants were followed for a period of 26 months and their serum/urine ketone bodies were monitored. Results showed that there is a significant reduction in seizures among

25% of the subject when followed for a time period of more than 4 months. Its tolerability and palatability was good but this diet does not give long term effects [13].

Studies suggest that along with reduction in seizures in epileptic patients, ketogenic diet poses some harmful effects in terms of hypertriglyceridemia and hypercholesterolemia [24, 25]. Some short-term effects include GIT disturbance [26] leading to some long term side effects such as cardiovascular issues and nutrient deficiencies [19]. This low carbohydrates and high fat diet can induce potentially harmful metabolic effects including insulin resistance and glucose intolerance in the body [27]. Another study showed that growth problems, dehydration, constipation and kidney stones can be produced in individuals using ketogenic diet [7]. Some other adverse effects include weight loss and gastrointestinal effects such as vomiting, nausea, diarrhea and constipation [13].

#### Future/research needs on ketogenic diet

At present there are many hypothesis regarding the mechanisms by which ketogenic diet produces the anti-seizures effects [28, 29]. Studies suggest the need of further research on ketogenic diet and its mechanism of action in reducing seizures [30]. A study showed that patients with young age respond to the ketogenic diet more than adults but further studies are required [9].

A study suggests the need of ketogenic diet in epilepsy as there is a lack of evidence in adults [19]. Use of ketogenic diet in adults is increasing worldwide. Clinical improvements in adult patients are seen with this diet, but its use among adults needs to be supported by extensive researches [31, 32]. The efficacy of ketogenic diet in various epileptic syndromes need further researches so that various alternative practical strategies can be made to improve the impact of diet [33].

#### Material and Methods

Data and information used for this review was collected from different primary and secondary sources including experimental studies, review articles, peer review, randomized control trials and related books. Search engines which were used include Google Scholar, NCBI and Scihub. All the data have been compiled systematically.

#### Discussion

Epilepsy is characterized by involuntary seizure of varying frequencies and intensity. Previously cannabis based pharmacological treatment has been used. However, ketogenic diet has also gained importance for its treatment along with medication. It helps in seizure reduction to a great extent due to its high fat and very low carbohydrate content. This fat and carbohydrates ratio leads to less glucose and more ketone bodies production in the body leading to decrease in reactive oxygen species (ROS). Proposed mechanisms suggest that seizures can be due to increased ROS in body. Hence by decrease in the amount of ROS in the body, this diet effectively helps in seizure reduction. Studies support the effect of this diet in epileptic children also. Ketogenic diet positively impacts mood, behavior and cognition, while few studies show its negative or no impact on mood of epileptic children. Long term use of high fat diet may derange lipid profile, gastrointestinal issues, insulin resistance and kidney stones.

Use of ketogenic diet in epileptic children is effective. However in adults, there is still a need of extensive research and experimentation.

#### Conclusion

Ketogenic diet is an effective non-pharmacological therapy in epilepsy. Specifically, in patients who show resistance to pharmacological treatment, ketogenic diet can be effective in seizure reduction. In children along with seizure reduction it shows little or no impact on their cognition, mood and behavior. However, there is a need of further research in children to know the impact of ketogenic diet upon cognition. In adult epileptic patients, its efficacy still needs further research. As the diet is high in fat, it may pose some adverse effects by altering the blood lipid profile, GIT functions, kidney issues and insulin resistance in body.

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#### Conflict of Interest

There is no potential risk of interest.

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