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# Pediatric Seizure Management with Ketogenic Diet

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**Abstract**

Seizure disorders can be life altering and debilitating, especially for developing children. Children who have seizure disorders often require social, emotional, educational, and behavioral adjustments for children. Most medication regimes do not achieve complete management of seizure frequency and intensity. For children, seizure disorders can lead to unsuccessful education experiences, low self-esteem, severe injury, and difficulties with social skills and engagement. Discovering that a dietary means can reduce their frequency and intensity is groundbreaking. The ketogenic diet is a high protein, high fat, and almost no carbohydrate diet. The ketogenic diet is an effective non-pharmacological method for treating epilepsy (Karimzadeh, 2019). It is a common treatment method employed by those who experience complications of seizure drugs or those for whom seizure drugs are ineffective. The relationship between the ketogenic diet and seizure disorders is at a cerebral level. Ketogenesis decreases the quantity of cerebral glutamate (Sarlo, 2021). Glutamate, when increased, is what causes decreased concentration of GABA and increased excitability seen in seizure disorders (Sarlo, 2021). Increased use of ketone bodies by the brain as energy sources results in decreased seizure activity. Ketone bodies in the blood elevate when carbohydrates are low (Özata Uyar, 2018). The focus of my honors research will be to determine the effects of a ketogenic diet on the management and trajectory of pediatric seizure disorders. To gain insight into the routines and nutritional needs of children with disabilities, I had the opportunity to intern for 99balloons. I spent one on one time with special needs children and observed the many nutritional requirements and diet plans that were specific to each child. Further, I completed a literature

review of 21 articles that reviewed how effective the ketogenic diet is to decrease frequency and severity of seizures compared with traditional epilepsy medications.

## Reflective Journal

### Introduction

During the first half of 2021, I interned with 99balloons. 99balloons is an organization based in Northwest Arkansas that helps community members engage with persons experiencing disability globally. I have worked and interned with organizations reaching out to persons experiencing disability since 2016. I also have lifelong experience in the disabled community because my older brother who is 29, has a rare neurodegenerative disease called Pontocerebellar Hypoplasia Type 1B. My experience working, living, and interacting with these individuals oriented me to common medications and routines that mitigate the complications of their disabilities or aim to treat the disability itself. Furthermore, those experiences gave me a zeal to research how nutritional interventions can 'cure' or mitigate the symptoms of some diseases. At 99balloons, I gained greater professional insight into the routines and nutritional needs of children with seizure disorders, and more broadly, children with disabilities.

From my experience interning with 99balloons, I have a greater understanding of how efficacious non-pharmacological intervention can be. However, in the United States healthcare system, there may be resistance to emphasizing the importance of non-pharmacological interventions for a multitude of reasons. Some of those reasons are that non-pharmacological interventions may take revenue away from pharmacological corporations, non-pharmacological interventions may be more difficult to implement or comply with consistently, and non-pharmacological treatments can be less objective than simply taking a pill every morning

(Becker, 2017). From my observations, society seems to assume that medications should be able to fix any health issue they are experiencing. Medications are often seen as a quick fix for negative symptoms that lifestyle changes could mitigate. Yet, utilizing only pharmacological interventions limits the potential for achieving better health outcomes. The ketogenic diet can be used to treat the seizure disorders of patients who failed to respond to anti-seizure medications (Kossoff, 2018). It can also be used synergistically with other non-pharmacological interventions (Kossoff, 2018). I hope to enter the work field with the ability to provide information to patients about non-pharmacological interventions that can improve patient outcomes. This was an extremely important take-away because I will be able to provide my future patients with a broad range of education regarding interventions that may aid their journey to achieving their health goals that goes beyond pharmacological interventions.

After my research and observation at 99balloons, I have a greater understanding of how nutritional interventions are just as important and can even have a greater impact than taking a prescribed medication. Although it may seem like common sense, nutritional health can pave the way of *being* healthy whereas healthcare is a means to *get* healthy (Heluna Health, 2022. The specific non-pharmacological intervention that I researched is the ketogenic diet as a means of treating pediatric seizure disorders. The ketogenic diet and other equally strict low glycemic index diets can be major tools for preventing the complications of seizure disorders and increase quality of life for children.

On a holistic scale, this experience is important because, in my nursing care, I will hold non-pharmacological interventions as having the potential to have similar or greater efficacity as pharmacological interventions. Moreover, interning at 99balloons allowed me to work directly

with my target population that I researched. This experience will allow me to answer questions such as: “What is the significance of diet on the trajectory of the manifestations of cognitive disabilities, specifically seizures?” “What are the benefits of substituting pharmacological intervention with nutritional intervention?” “Should the efficacy of non-pharmacological interventions be considered, if not emphasized, as being equal to or better than pharmacological intervention?”

**Reflection**

I interned specifically in the 99balloons initiative called rEcess. The purpose of rEcess is to provide a night of respite for parents and a night of fun for children experiencing disabilities. The parent’s child or children experiencing disability can attend as well as any siblings of their disabled child or children. My role at 99balloons as a “fellow” was to pair one-on-one with a special needs child for the duration of rEcess. My primary duties as a fellow were to aid the disabled child with mobility, administer medications assisted by the nurse on site, serve and assist giving meals, provide companionship, and cultivate a fun environment for the children.

The primary way that my nursing coursework and clinical experience prepared me for this internship is pharmacology and pathophysiology. The foundation of pathophysiology enables me to understand the processes in the body that create the symptoms of a disease or disability. The pharmacological coursework prepared me by explaining how medications can work to improve symptoms of diseases and disability. I was better equipped to assist and provide therapeutic fun and companionship by understanding the pathophysiological components of disabilities and how medications and interventions affect them. My therapeutic communication course was also greatly employed during the internship. Communicating with disabled

individuals can feel different because oftentimes, the individual has communication needs that differ from the average. All people should be treated equitably with respect, patience, and consideration of their needs.

Some challenges were that not all children I was a fellow for had seizure disorders. So, although broadly helpful to my research, my time was not always used working with individuals who were included in my research topic. Additionally, due to the Covid-19 pandemic, the number of families able to attend rEcess was limited. Many families with disabled children also chose to take a break from attending rEcess to protect their child from potentially contracting Covid-19.

As I spent time with disabled children, I observed the many nutritional requirements and diet plans that were specific to each child. The internship provided an organic space to document the importance of the nutritional regimes of children with differing disabilities. The hope is that that documentation will confirm that diet may be of even greater importance than prescription medications when it comes to the side effects and trajectory of certain disabilities. Proper nutrition and intake of vitamins is essential to the effective development of children. Specific nutrients, components of food, or allergies may alleviate or prevent exacerbation of their disability's symptoms. Seizure disorders can be disabling and lead to significant injury, but it has been found that dietary adjustments can be used as treatment for those disorders in children. Thus, determining a dietary means to reduce their frequency and intensity would be groundbreaking.

## Introduction

Seizure disorders have been found to correlate with learning disabilities. One in three children who experience a learning disability also experience seizures (Epilepsy Society, 2021). Proper nutrition and intake of vitamins is essential to the effective development of children. Many children may struggle to consume the appropriate amounts of necessary nutrients daily. This can be attributed to having finicky eating habits, lack of access to foods, or consuming nutrient-poor foods. Adding disability to the clinical picture of nutrition can present innumerably more obstacles. There are two primary reasons children with disabilities often have requirements for their diet. First, their diet may depend on what eating mechanics they are able to do and how they process food. For example, dysphagia is a common struggle for many people with disabilities and may require an individual to only consume soft foods or at an extreme, receive alternative, non-oral forms of nutrition. Second, specific nutrients, components of food, or allergies may alleviate or prevent exacerbation of their disability's symptoms. For my research, I will focus on this second variable of how the ketogenic diet has shown to alleviate the intensity, frequency, and symptoms of seizure disorders. Primarily, the experience allowed me to have extended time observing the nutritional requirements of children with differing disabilities. I was able to observe how children experiencing disability can depend on a particular diet to work as treatment for symptoms of their disability and how an average diet for a child can be adapted to meet their individual needs.

Seizure disorders have been recorded from the beginning of human documentation of disease. A Babylonian text written in 1000 B.C. called the "Sakikku (meaning "all diseases")" details common manifestations of seizures (Karimzadeh, 2019, p. 2). One of the first effective dietary treatments for epileptic and seizure disorders was starvation. (Karimzadeh, 2019, p. 6)

Doctors noted that starvation induced ketonemia which nearly cured patients' seizures. From there, the ketogenic diet was developed and used for treatment of seizure disorders by limiting the quantity of cerebral glutamate.

Ictogenesis and epileptogenesis are the processes that lead to the generation of spontaneous and recurring seizures. One of the primary biological components of ictogenesis and epileptogenesis is increased extracellular glutamate combined with a reduction of GABA concentrations. GABA is inhibitory whereas glutamate is excitatory. This combination can lead to "excitotoxicity, seizures, and cell death" (Sarlo and Holton, 2021). High glucose levels cause an increase in cerebral glutamate release. Thus, diets that emphasize a reduction of circulating glucose and reducing chemical processes that use glucose work to ultimately decrease glutamate levels (Xiao-Ting Huang). Decreasing glutamate and directly increasing concentrations of GABA through diets with a low glycemic index has been shown to significantly reduce seizure events or symptoms secondary to seizure disorders.

There are multiple diets that function by decreasing glycemic carbohydrate quantities. The three most common diets used as treatment for seizure disorders are the ketogenic diet, the modified Atkins diet, and the low glycemic index diet. The ketogenic diet has a restriction of up to 10-20 g of carbohydrates per day. This extremely low level of carbohydrates forces the body to utilize stored fat as a means of energy rather than glucose. Ultimately, the body uses ketones for energy rather than carbohydrates. The modified Atkins diet parameters include limiting carbohydrate intake to 15-20 grams per day. The limit for daily carbohydrate intake on a low glycemic index diet is 50g.

## Methods

**Study Design**

A literature review was performed to answer the question, "For pediatric patients with seizure disorders, how effective is the ketogenic diet to decrease frequency and severity of seizures compared with traditional epilepsy medications?" To begin my search, I accessed the University of Arkansas Nursing Libraries webpage where databases of nursing journals are located. Two databases, CINAHL Complete and Medline Complete were utilized to answer this research question. The Boolean phrases "pediatric patients" "ketogenic diet" "seizure disorders" "management" were used.

**Inclusion/Exclusion Criteria**

Articles must have met the following criteria to be considered for inclusion in the evidence table; (A) the journal must have been about pediatric patients with seizure disorders; (B) the journal must have talked about the ketogenic diet as a treatment mechanism for seizure disorders; (C) must be published in the last 6 years; (D) full text was available. Articles were excluded from the literature review if (A) the participants were adults, and (B) if all participants in the study groups did not have seizure disorders.

**Search Results**

Twenty-one articles were found through a search of Medline Complete and CINAHL complete. The first search using the phrases "ketogenic diet," "management of seizure disorders," and "low glycemic index diet."

## Results

***Efficacy and Benefits of Ketogenic Diet for Epileptic Patients***

The biochemical mechanisms involved in the ketogenic diets anti-seizure properties were explained and showed that although there are differing diet plans, they all have similar efficacy (Barzegar, 2021). Participants in a 2021 case study demonstrated improved ataxic gait, language skills, and decreased behavioral disturbances (Yıldırım, 2021). Aside from a decrease in seizures and their severity, some other benefits were experienced by study participants including "higher productivity, reduced tension/anxiety/hostility, and better cognitive functioning" (Sourbron, 2020, p. 43). The quantity of adverse seizure events correlated directly with the achieved level on the glycemic index. The most common adverse effects of the ketogenic diet for pediatric patients who had refractory seizures were gastrointestinal effects such as constipation, diarrhea, and vomiting. (Sourbron, 2020) Long term severe potential adverse effects of the ketogenic diet are fatty liver, kidney stones, gallstones, and acute pancreatitis. Adverse events were the least frequent for children with the lowest glycemic index therapy diet. One adverse event may be avoided for every 4.3 children treated with the low glycemic index therapy diet (Sondhi, 2020).

Liquid anti-seizure medications had approximately eight times higher carbohydrate content than solid dosage forms. The significant difference of ketogenic fat: non-fat gram ratios was found when prescribed carbohydrate content in medications was higher than 2 g/day (Sawangrit, 2020).

Full adherence to a ketogenic diet produces more effective brain use of protein for fuel instead of carbohydrates (Özata Uyar, 2018). Children who strictly adhered to the nutrient guidelines saw a decrease in symptoms and seizures. The more ketones circulating in the body, the fewer seizures a child had.

### *Historical and Worldwide Context for Ketogenic Diet as Seizure Treatment*

Documentation of seizures and their various treatment modalities have been documented in Iran for centuries. In Iran today, there has been increased implementation of the ketogenic diet as a means to treat epilepsy and seizure disorders. Researchers concluded that the ketogenic diet and its variants are an effective means to treat seizures with minimal side effects (Karimzadeh, 2019) Implementation of the ketogenic diet has successfully reduced treatment gaps, social and physical burdens, and has given the community a means to treat seizure disorders with minimal side effects. A meta-analysis of 19 studies including a total of 1084 children showed more than 90% seizure reduction in one third of patients and more than 50% seizure reduction in half of patients (Karimzadeh, 2019).

***Benefits of Ketogenic Diet for Pediatric Patients***

In children with symptoms secondary to their primary diagnoses, the ketogenic diet was more or only effective at treating seizures rather than ataxia and language skills (Yildirim, 2021). Time trajectory for the ketogenic diet is that children were seizure-free in the sixth month of the diet. Despite its primary benefit being a decrease in seizure quantity and severity, the ketogenic diet participants demonstrated improved ataxic gait, language skills, and decreased behavioral disturbances (Yildirim, 2021).

***Biological Factors to Consider***

Differential ketogenic diet-induced shift in CSF (Cerebrospinal fluid) lipid/carbohydrate metabolome of pediatric epilepsy patients with optimal anticonvulsant response. Metabolomic analysis of cerebrospinal fluid samples taken before and during ketogenic diet treatment in patients with optimal response (100% seizure remission) and patients with no response (no seizure improvement). Response to ketogenic diet in epileptic pediatric patients is based on

biologic markers. Age and gender play a role in response to diet. This study considered that one gender may benefit more than another and that age has an impact on the effect of ketone body uptake by the brain (Masino, 2021). The Ketogenic diet is recommended for children under two years of age (Kossoff, 2018). The low glycemic index treatment and modified Atkins diet were more recommended for adolescent patients (Kossoff, 2018). The primary outcome of reducing the frequency of seizures was attained in 35-56.1% of the participants in the intervention group (Kossoff, 2018).

### *Rational for Using Non-Pharmacological Seizure Treatment*

There is a high rate of hypovitaminosis D in pediatric epilepsy patients who take anti-seizure medications (Likasitthananon, 2021, p. 6). Children are at higher risk of complication from hypovitaminosis D because it can cause loss of bone density. The key risk factors for hypovitaminosis of vitamin D are pediatric patients who are in puberty and patients who take anti-seizure medications that are non-enzyme inhibiting. Demographic data, seizure types, puberty status, physical activity, duration, and types of anti-seizure medications were analyzed to characterize common vitamin and mineral imbalances for pediatric patients that may correlate with their seizures (Likasitthananon, 2021).

## Discussion

Overall, care plans for pediatric patients must be individualized. The pediatric patient's provider should be consulted before deciding on the best treatment regime. Diets with a low glycemic index, specifically the ketogenic diet, have been shown to decrease seizures and the symptoms of seizures. Age and gender should be considered when choosing which diet to prescribe. The ketogenic diet is a cost-effective alternative to seizure medications and can be

equally and sometime more effective than seizure medications. Anti-seizure medications can lead to adverse cognitive and systemic effects (Garcia-Penas, 2018). Pediatric patients on the ketogenic diet can experience a greater percentage of mood stabilization, improved cognition, sustained attention, and more effective social interactions when compared with epileptic patients not on the ketogenic diet. The limitations of the ketogenic diet are that it can cause nutritional deficiencies and can be hard on the kidneys. The most common adverse effects of the ketogenic diet and its variants are gastrointestinal issues such as constipation and vomiting. Cultural considerations must also be taken when prescribing the ketogenic diet. Food can be a major component of cultural and religious identity, and the ketogenic diet might not be a feasible option while continuing to adhere to their religious and cultural needs. In addition, many cultures and religions have diets that are more carbohydrate heavy and thus a nutritional lifestyle change would be a bigger adjustment.

**Conclusion**

There are multiple barriers to using pharmacological treatment for seizure disorders. Those barriers include finances, accessibility, and the fact that 20-30% of children with seizure disorders are resistant to anti-seizure medications (Özata Uyar and Şanlıer, 2018, p. 8). The ketogenic diet is an effective non-pharmacological treatment for pediatric seizure disorders. The stricter adherence to the diet, meaning <20 grams of carbohydrates per day, leads to a direct decrease of adverse seizure events (Özata Uyar and Şanlıer, 2018, p. 8). Studies showed a statistically significant decrease in seizure events when pediatric patients adhered to the diet guidelines (Sondhi, 2020). In my internship with 99balloons, I was able to observe the efficacy of non-pharmacological interventions, especially those pertaining to nutrition. The

literature review proves how non-pharmacological interventions can have outcomes that are just as effective, if not more effective, than medications. Additionally, seizure disorders are the perfect example of how the same medications do not work for everyone with the same disorder. Healthcare teams should be prepared to individualize care and be knowledgeable about information to provide their patients about alternative treatments on top of their patient's medication regimes. Further studies should be completed about the long-term efficacy of the ketogenic diet for pediatric seizure patients. Additionally, management techniques for the adverse effects of the ketogenic diet such as constipation, should be provided to improve long-term adherence to the diet.

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## Appendix A: Table of Evidence

| First Author (Year) | Sample and Setting | Title | Major Variables Studied | Measurement | Results | Relevance to Research |
|---|---|---|---|---|---|---|
| Barzegar, Mohammad (2021) | Tabriz, Iran; Literature Review and Nutritional Overview | Ketogenic diet: overview, types, and possible anti-seizure mechanisms. | classic KD (Ketogenic Diet), medium-chain triglyceride diet (MCTD), modified Atkins diet (MAD), and low glycemic index treatment (LGIT) | classic KD, medium-chain triglyceride diet, modified Atkins diet, and low glycemic index treatment. | Several types of ketogenetic diet were explained. The biochemical mechanisms involved in the ketogenic diets anti-seizure properties were explained and showed that although there are differing diet plans, they all have similar efficacy. | Have definitions and components of various kinds of ketogenic diets and implications for specific symptoms that epileptic patients experience. |
| Sondhi, Vishal (2020) | Randomized clinical trial. 158 children subjects with drug resistant epilepsy | Efficacy of Ketogenic Diet, Modified Atkins Diet, and Low Glycemic Index Therapy Diet Among Children With Drug-Resistant Epilepsy: A Randomized Clinical Trial. | Number of Seizures; Type of diet: Ketogenic, modified Atkins diet (MAD) and low glycemic index therapy (LGIT) | Percentage change in frequency of seizures | Adverse events were the least frequent for children with the lowest glycemic index therapy diet. 1 adverse event may be avoided for every 4.3 children treated with the low glycemic index therapy diet. | Supports evidence that low carbohydrate, ketogenic diet, Atkins, or low glycemic index diets may be used to reduce adverse events in those with seizure disorders. |
| Sawangrit, Thanarat (2020) | Retrospective study<br>King Chulalongkorn Memorial Hospital, a tertiary referral teaching hospital in Thailand, from 2009 to 2017. 169 subjects and their ketogenic diet order forms | The carbohydrate content of medications prescribed to children treated with a ketogenic diet. | Background: Carbohydrate excipients include starches, dextrin, maltodextrin, sugar, and sugar alcohols.<br><br>Carbohydrate content of medications prescribed to children with epilepsy. | Review of ketogenic diet order forms of children under 18.<br>Cross sectional medical records.<br>Grams of carbohydrate in ketogenic ratio | Liquid medications had approximately eight times higher carbohydrate content than solid dosage forms. The significant difference of ketogenic fat: non-fat gram ratios was found when | Relevant because it determines what specifications for medications are required if patients combine the ketogenic diet with seizure medications. |

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| | | | | | prescribed carbohydrate content in medications was higher than 2 g/day | |
| Yıldırım, Miraç (2021) | Case Study 3 subjects. | Glucose Transporter Type 1 Deficiency Syndrome: A Single-Center Case Series. | Glucose transporter type 1 deficiency syndrome symptoms and the effect of the ketogenic diet on the severity of movement disorders, intractable seizures, and acquired microcephaly, behavior disturbances, gait, ataxia, and language issues. | Electroencephalographic measurement, cerebrospinal fluid to blood glucose ratio, and number of seizures in a month period. | Seizure-free in the sixth month of the diet. KD also improved ataxic gait, language skills, and behavioral disturbances. | Explains what symptoms secondary to seizure disorders are resolved by ketogenic diet. In children with symptoms secondary to their primary diagnoses, the ketogenic diet was only effective at treating seizures rather than behavior disturbances, ataxia, and language skills |
| Özata Uyar, Gizem (2018) | Practice Guidelines; Review<br><br>Ankara, Turkey | The Effect of Ketogenic Diet Treatment in Drug-resistant Epilepsies of Childhood. | Ketone bodies, seizures, full or partial adherence to ketogenic diet | Quantity of ketone bodies; children who were resistant to 2-3 or more anticonvulsant drugs | Increased use of ketone bodies by the brain as energy sources results in decreased seizure activity. Ketone bodies in the blood elevate when carbohydrates are low. | Importance of full adherence to ketogenic diet to produce effectiveness of brain using protein as fuel instead of carbohydrates. |
| Masino, SA (2021) | Pilot Study | Differential ketogenic diet-induced shift in CSF (Cerebrospinal fluid) lipid/carbohydrate metabolome of pediatric epilepsy patients with optimal vs. no anticonvulsant response: a pilot study. | Cerebrospinal fluid composition; Metabolic therapy. | Metabolomic analysis of cerebrospinal fluid samples taken before and during ketogenic diet treatment in patients with optimal response (100% seizure remission) and patients with no response (no seizure improvement) | Response to ketogenic diet in epileptic pediatric patients is based on biologic markers. Age and gender play a role in response to diet. | Consider that one gender may benefit more than another and that age has an impact on the effect of ketone body uptake by the brain. |

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|---|---|---|---|---|---|---|
| Sourbron, J (2020) | 472 subjects; Meta analysis. Literature review of randomized controlled trials. | Ketogenic diet for the treatment of pediatric epilepsy: review and meta-analysis. | Patients not eligible for epilepsy surgeries. Biomarkers that are favorable with ketogenic diet. | Percentage of seizure frequency reduction | The primary outcome (seizure frequency reduction (SFR) ≥ 50%) was attained in 35-56.1% of the participants in the intervention group | The meta-analysis gives objective values for the quantity of seizures that are reduced for epileptic pediatric patients on the ketogenic diet. |
| Likasitthananon, N (2021) | Bangkok, Thailand A cross-sectional retrospective cohort study.<br><br>138 subjects | Hypovitaminosis D and risk factors in pediatric epilepsy children. | Demographic data, seizure types, puberty status, physical activity, duration, and types of anti-seizure medications were analyzed. | Serum vitamin D level, percentage of vitamin D deficiency and insufficiency. | There is a high rate of hypovitaminosis D in pediatric epilepsy patients. | Characterizes common vitamin and mineral imbalances for the selected population. |
| Karimzadeh, P (2019) | Tehran, Iran<br><br>Double Blind Peer Reviewed Article meta-analysis and systematic review study.<br><br>215 subjects | A Journey of Dietary Therapies for Epilepsy in Iran: Diet Restriction in the Ancient Era to the Ketogenic Diet in the Modern Period. | Epilepsy in the ancient and modern world. Ketogenic diet, Modified Atkins Diet, and | Ketogenic diet rates of adherence, low glycemic index diet rates of adherence, and modified Atkins diet rates of adherence by percentage. | Ketogenic diet is an effective non-pharmacological method for treating epilepsy. It is a common treatment method employed by those who experience complications of seizure drugs or those for whom seizure drugs are ineffective. | Historic context and use of the ketogenic diet to treat epilepsy. Origins and development of the ketogenic diet are given. Explores implications of the diet on a global scale since the study takes place in Iran. |
| Kossoff, EH (2018) | Randomized controlled trial | Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. | Patient selection, pre-KDT counseling and evaluation, diet choice and attributes, implementation, supplementation, follow-up, side events, and KDT | Quantity of failed epilepsy medications, number of disorders of brain energy metabolism, | The study results showed that the ketogenic diet should be a last resort treatment when at least 2 antiepileptic drugs are ineffective at reducing seizure quantity and severity. The ketogenic diet | The study results show what criteria must be met prior to a patient being prescribed to the ketogenic diet. |

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| | | | discontinuation | | is most effective for Glucose transporter protein 1 (Glut1DS) and Pyruvate dehydrogenase deficiency (PDHD). | |
| Barbanti, P (2017) | 150 subjects Case reports and prospective studies Rome, Italy | Ketogenic diet in migraine: rationale, findings, and perspectives. | Cortical spreading depression, glutamate, and GABA neuroinflammation, oxidative stress, mitochondrial free radicals, and brain metabolism were all considered. | Days per month that patient experienced a migraine. | Ketogenic diet may be rapid onset prophylactic treatment for migraines. | Gives specific information about what processes in the brain are affected by the ketogenic diet. In theory, treatments for migraines may help manage epilepsy because migraines and epilepsy disorders are often comorbid. |
| Elliot, Jesse (2019) | Systematic review. 9 subjects | Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. | Weight gain over time, switching or discontinuation of treatments, effectiveness of interventions and comparators, and long-term effectiveness | Economic Evaluation and quantity of time using specific treatment methods. | Ketogenic diet is a cost-effective means to treat pediatric epilepsy. | Evaluates the economic implications of multiple modalities of seizure treatment including cannabis, ketogenic diet, and antiepileptic drugs. |
| Udani V 2015 | Literature review | Pediatric epilepsy -- an Indian perspective. | Neurocysticercosis and neonatal hypoglycemic brain injury | Prevalence of pediatric seizure disorders per 1000. | Ketogenic diet reduces the complications of seizure disorders and prevents further injury. | Classifies seizure disorders and shows which diets are more beneficial to specific disorders. |
| Garcia-Penas, JJ (2018) | Randomized controlled trial, animal subjects | Epilepsy, Cognition, and Ketogenic Diet | Behavior and cognitive abnormalities, ketogenic diet vs normal diet. | Quantity of positive mood activation on the ketogenic diet vs quantity not on | Subjects on the ketogenic diet experienced a greater percentage of mood stabilization, | Contributes information about how the ketogenic diet not only reduces seizures, but also provides |

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| | | | | the ketogenic diet. | improved cognition, sustained attention, and more effect social interactions when compared with epileptic subjects not on the ketogenic diet. | beneficial outcomes for mood stabilization and cognition. |
| Kim, JA (2016) | 104 subjects | Efficacy of the classic ketogenic and the modified Atkins diets in refractory childhood epilepsy. | Seizure frequency on the ketogenic diet compared to baseline seizure frequency per day. | Mean percentage of seizures for patients on each diet. | The Modified Atkins ketogenic diet is suitable for children 3-18, whereas the ketogenic diet is suitable for children <2 years of age. | Gives a basis for the relationship between age group and diet that is most conducive to seizure cessation. |
| Baby, N (2018) | Pragmatic Study<br>70 subjects | A pragmatic study on efficacy, tolerability, and long term acceptance of ketogenic diet therapy in 74 South Indian children with pharmacoresistant epilepsy | Diet efficacy: Length of time that patients continued diet | Reduction in the seizure frequency and reduction in the number of antiepileptic drugs taken by the patient. | Baseline seizure frequency per day.<br>Percentage on antiepileptic drugs. | Stresses importance of cultural considerations of prescribing certain diet regimes. The south Indian diet is very carbohydrate heavy, but the ketogenic diet was still effective for these patients. |
| Bjorn Bjurulf (2020) | Prospective controlled study<br>55 subjects | Potassium citrate and metabolic acidosis in children with epilepsy on the ketogenic diet: a prospective controlled study | Potassium citrate supplementation vs no supplementation. | Measure metabolic acidosis.<br>Measure percentage of seizure reduction. | After introducing the ketogenic diet and providing potassium citrate supplementation, seizures were reduced by 50% in 9 of the subjects with supplementation. | Study could show how to prevent metabolic acidosis while still giving the antiepileptic effects of the ketogenic diet when children are supplemented with potassium citrate. |

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| McDonald, Tonya (2018) | Randomized trial | Improving compliance in adults with epilepsy on a modified Atkins diet: A randomized trial | 20 g/day net carbohydrate limit MAD; Patients were randomized to receive one 8-ounce (237 mL) tetrapak of Keto Cal®, a 4:1 ketogenic ratio formula, daily in combination with MAD during the first month (treatment arm) or second month (control/cross-over arm) | Patients recorded urine ketones, weight, and seizure frequency and followed up at 1 and 2 months | Long term adherence to modified Atkins produced the most reduction in epileptic disorder symptoms including seizures. | How to improve compliance of dietary modifications for epileptic pediatric patients. |
| Su, Ting-Yu (2021) | Graph Theory Clinical Trial | Graph Theory-Based Electroenceph alographic Connectivity and Its Association with Ketogenic Diet Effectiveness in Epileptic Children | Responder vs non-responder to ketogenic diet. | Brain activity in specific areas for responders and non-responders to the ketogenic diet. | Brain activity is associated with symptoms and complications of epilepsy. | Shows specific visual of where brain activity changes as a result of ketogenic diet treatment. |
| Surbi, Gupta 2021 | Randomized, open labelled, controlled clinical trial | Modified Atkins Diet vs Low Glycemic Index Treatment for Drug-Resistant Epilepsy in Children: An Open Label, Randomized Controlled T**rial** | Percentage cessation of seizures, Modified Atkins diet or Low Glycemic Index Diet | The proportion of children who achieved seizure freedom as defined by complete cessation of seizure at 12 weeks as the primary outcome measure. Secondary outcome measures were proportion of children who achieved >50% and >90% seizure reduction at 12 | The best long-term success for seizure success was found in the low glycemic index diet. | Gives a quantifiable period for when benefits of ketogenic diet begin to manifest. |

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