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Ketogenic diet in treatment of Pediatric Refractory Epilepsy – Efficacy and potential Adverse Effects, A Review

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Abstract

Background. Epilepsy affects 0,5-1% of children. It is more frequently resistant to anti-seizure drugs compared to the adult population. Ketogenic diet is a high-fat, low-carbohydrate nutrition style that has been widely used and researched as treatment for refractory pediatric epilepsy, giving a relatively safe alternative to more hazardous and invasive forms of seizure therapy.

Aim. Discussion of efficacy and potential adverse effects of the ketogenic diet in treatment of pediatric refractory epilepsy, with additional overview of different ketogenic diet forms.

Material and methods. A narrative review of the PubMed database using the following keywords was performed: ketogenic diet, KD, pediatric epilepsy, pediatric refractory epilepsy. The findings were analysed in terms of relevance, studied population and researched outcomes. Studies from the year 2015 or older were excluded.

Results. Ketogenic diet was identified as highly effective in pediatric refractory epilepsy. Examined research shows a significant seizure frequency reduction in studied populations. Comparison between the classic ketogenic diet and its alternatives is inconsistent, but the efficacy seems to be comparable. The diet is reported to have frequent side effects, most commonly gastrointestinal, however they are usually mild and easy to prevent or treat.

Conclusions. Ketogenic diet seems to be a relatively low-risk, effective option for treatment of refractory pediatric epilepsy. Possible adverse effects in majority should not be a reason for withdrawal.

Key words: ketogenic diet, KD, pediatric epilepsy, pediatric refractory epilepsy, MAD, MCT, LGIT

1. INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent epileptic seizures or changes in behavior or movement being a direct effect of a primary change in the electrical activity of the brain (Wells et al., 2020). It affects over 50 million people worldwide with its prevalence estimated to be 0,5-1%. Although the majority of individuals with epilepsy will have seizures controlled with antiepileptic drugs or enter spontaneous remission in their lifetime, up to 35% will suffer from refractory epilepsy (Wells et al., 2020).

The International League Against Epilepsy defines drug-resistant epilepsy as “failure of adequate trials of 2 tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom”. The problem of Drug Resistant Epilepsy (further called DRE) particularly concerns the pediatric population, as some age-specific epileptic syndromes, such as West or Dravet syndrome (Enkhtuy et al., 2019), are predisposed to more frequent pharmacoresistance (Skrobas et al., 2022). Alternative non-drug treatments for epilepsy include vagus nerve stimulation, surgery and dietary approaches.

The Ketogenic Diet is a well-established treatment method for children with pharmacoresistant epilepsy. It is a dietary approach in which dietary composition results in a ketogenic state of human metabolism. It comprises of four major KDTs – the classic Ketogenic Diet (cKD), the Modified Atkins Diet (MAD), the medium-chain triglyceride diet (MCT) and the low glycemic index treatment (LGIT) (Skrobas et al., 2022). The main purpose of this review is to evaluate the efficacy of the Ketogenic Diet Approach in the treatment of childhood epilepsy as well as to analyze its safety and tolerability based on existing research.

Research Objective

To discuss the efficacy and potential adverse effects of the ketogenic diet in treatment of pediatric refractory epilepsy, with an additional overview of different ketogenic diet forms.

2. RESEARCH MATERIALS AND METHODS

2.1. METHODOLOGY

The study was conducted as a narrative literature review. The literature search was performed in the Pubmed database to identify relevant studies on ketogenic diet in treatment of pediatric refractory epilepsy as well as its potential adverse effects. The literature search was conducted using a combination of keywords: “ketogenic diet”, “KD”, “pediatric epilepsy”, “pediatric refractory epilepsy”. Studies from the year 2015 and older were excluded. Studies published in languages other than English were excluded. Only systematic reviews, meta-analyses, original research articles and randomized controlled trials were taken into consideration. Literature selection was performed independently by authors.

2.2. AI

AI was not utilized in any part of the making process of this review.

3. BACKGROUND

The groundwork for modern ketogenic diets was laid by ancient fasting practices in the treatment of seizures, first mentioned in the Hippocratic Collection, dating back to 5th century BC (Borowicz-Reutt et al., 2024). In modern times, fasting as a remedy for epilepsy has appeared in 1911, where it was found to improve the control of seizures in 20 children and adults. It was later discovered that the benefits of fasting can be replaced by inducing ketosis through a high-fat diet. In the 1920s, in order to avoid malnutrition tied to prolonged fasting, work on the ketogenic diet began (Ko et al., 2022). Its efficacy has been confirmed in a 1928 Barborka study, where it was proven to improve seizure control in 56 out of 100 patients. It has been widely applied throughout the 1920s and 1930s, however the introduction of anticonvulsant drugs has downgraded the KDT’s position as a treatment, so that by the 1980s it was rarely used (Youngson et al., 2017). The development of 2nd and 3rd generation antiepileptic drugs, although having fewer side effects than the previous ones, did not improve response rates in patients with refractory epilepsy (Borowicz-Reutt et al., 2024). The ketogenic diet gained attention again in the 1990s, with research published by the Charlie Foundation describing a 2-year-old patient who had been cured from his epilepsy using the KDT (Wells et

al., 2020). From then on, the diet had been used and studied as therapy for drug-resistant seizures in children and adults. Due to some patients' and their families' difficulty to adhere to the diet and complaints of some adverse effects, new modifications of the KDT have emerged, resulting in the development of MAD, MCT and LGIT (Sondhi et al., 2020).

4. THE KETOGENIC DIET (and its modifications)

The ketogenic diet is a high-fat low-carbohydrate diet, in which the main energy source for the body comes from fat instead of glucose (Ko et al., 2022). This method of nutrition leads to an increased production of ketone bodies (β -hydroxybutyrate, acetoacetate and acetone) in the organism leading to a state of ketosis. The condition of ketosis can also be obtained through fasting or a very low calorie diet. The usual share of macronutrients in the diet is as follows: fats 60-90%, carbohydrates below 50g daily (5-10%) and proteins 1.0-1.7 g per kilogram body weight (about 20%). The diet imitates the condition of fasting leading however to no negative effects of starvation (Dyńska et al., 2022).

4.1. The classic ketogenic diet

It is a high fat, low carbohydrate and adequate protein diet. When implemented, a specific ratio of fats, carbohydrates and proteins is established.. In most cases a 4:1 ratio is used, however when dealing with infants and adolescents in order to improve tolerability, a lower ketogenic ratio of 3:1 can be utilized (Haridas et al., 2025). The diet has to be implemented in a hospital setting, with careful monitoring of ketosis, acid-base balance, hydration and glucose levels as well as the diet's tolerability. Two different approaches of implementing cKD can be used; the first requires a period of fasting until reaching ketosis with a subsequent diet introduction; the second gradually increases the ketogenic ratio in patient nutrition without the requirement for abstaining from food causing a slower ketosis progression however also less adverse effects for the patient (Verrotti et al., 2020).

4.2. The modified Atkins diet

The Atkins diet was first introduced in the 1960s by an American cardiologist Robert C. Atkins as a way to loose body weight. The Modified Atkins Diet, with the use of the word 'modified' to emphasise its separation from AD associated with weight loss, has been used since the early

2000s. It usually consists of a lower, 1:1 to 1.5:1 ketogenic ratio. Differently from cKD, patients do not have to measure and calculate using a scale (Haridas et al., 2025). Moreover, it has no protein, fluid, or calory limit which facilitates meal planning and also increases diet tolerance (Ko et al., 2022). The restriction of carbohydrates varies from 10 to 20g per day in children. The diet can be implemented in an outpatient setting (Verrotti et al., 2020).

4.3. Medium-chain triglyceride diet

In the cKD the main source of fat is long-chain glycerides. The MCT diet, as the name suggests, uses more medium-chain triglycerides, which provide a larger amount of ketones per kilocalorie of energy than the long-chain. Often, the main component of the diet are MCT oils. This allows for a reduction in the amount of total fat consumed and an increase in the amount of carbohydrates and proteins in the diet. It permits both for an easier implementation of the diet as well as its better tolerability (Haridas et al., 2025). Surprisingly, the ketone bodies concentration in the blood plasma are usually low and do not correspond with seizure control (Enkhtuy et al., 2019). This suggests that the antiseizure mechanism in the MCT diet lies more with the medium-chain triglycerides instead of the ketone bodies as it is with the cKD.

4.4. Low glycemic index treatment

With the same intention of improving tolerability and allowing more carbohydrate consumption, the LGIT was developed. The carbohydrates have to have a low glycemic index (usually <50) (Haridas et al., 2025). The glycemic index (GI) is the tendency of food to increase blood glucose levels compared to an equivalent amount of reference carbohydrate such as glucose (Enkhtuy et al., 2019). Examples of the low GI foods are meat, dairy, vegetables and unprocessed whole-grain foods, while refined carbohydrates are an example of high GI foods. Therefore, by incorporating low GI produce, the patients are allowed to live a more flexible lifestyle with a more liberal intake of carbohydrates compared to the cKD. While LGIT does not itself cause ketosis, the decreased glucose metabolism and its stable levels contribute to the antiepileptic mechanism of ketogenic diets.

5. WHERE IT IS RECOMMENDED TO BE USED

Ketogenic diet as a valuable treatment option is mostly used in pharmacoresistant pediatric epilepsy. This includes generalized epilepsy as well as pediatric epileptic syndromes such as Doose syndrome, Dravet syndrome, Lennox-Gastaut syndrome, Infantile Spasms (West syndrome), Febrile infection related epilepsy syndrome (Verrotti et al., 2020). The diet at first was not recommended in infants under 2 years of age due to the uncertainty of it providing the correct amount and ratio of nutrients. However, this problem seems to be resolved with supplementation and recent research shows that infants seem to have an even higher response rate to this form of treatment than older patients. It is suggested that this may be a result of increased compliance or biological factors (Lyons et al., 2020). Recently the interest in KD has expanded from pediatrics to adults and seems to also be proven effective with a substantial number of patients having a reduction in seizure frequency, however further research is required (Verrotti et al., 2020)

6. MECHANISM OF ACTION

The exact antiepileptic mechanisms of action of the ketogenic diet are still unknown. However, many theories have been proposed and researchers seem to agree that the mechanism may be multifactorial. One of the proposed explanations is a change in neurotransmitter function; KD interferes with GABA, norepinephrine, serotonin and dopamine levels which in turn modifies neuronal excitability and results in a decrease in seizure frequency (Wang et al., 2024). Other possible hypotheses suggest, among others, that the diet induces a change in neuronal metabolism, has a modifying effect on ion channels and even causes a decrease in insulin-like growth factor-1 concentration which could all positively affect seizure control in the brain (D'Andrea Meira et al., 2019) (Murakami & Tognini, 2022). More research on the mechanisms of action of the ketogenic diet and its anticonvulsant effects is required.

7. FUTURE POSSIBILITIES FOR THE DIET

Although, as previously mentioned, the mechanisms of the anticonvulsive effects of the ketogenic diet are not yet fully understood, research aims to identify the possibility of reproducing the same benefits of the diet with a drug or a supplement. The multitude of proposed mechanisms as well as efficacy of the diet in various types of epileptic syndromes

might suggest that the potential drugs should focus more on the promotion of ketogenesis in the liver rather than on the end-stage effect of, for example, neurotransmitter level manipulation (Youngson et al., 2017). Ketogenesis is primarily a response to starvation – with decreased carbohydrate intake, lipid stores in the liver and adipose tissue are mobilized, metabolized to ketone bodies in the liver, released into the blood and used as an energy source (Youngson et al., 2017). This process is regulated by multiple regulatory pathways possibly presenting an opportunity for the starvation signals to be mimicked by pharmaceuticals. Studies name several potential mechanisms and drugs that could promote liver ketogenesis. These include hepatic beta-oxidation activation (Resveratrol), hepatic lipogenesis inhibition (Acetyl-CoA Carboxylase inhibitor), hepatic glycolysis inhibition (Stripentol), mitochondrial pyruvate carrier inhibition (Pioglitazone) and liver mitochondrial complex 1 to favour fat metabolisms inhibition (Metformin) (Youngson et al., 2017). So far however, all those remain in the area of theory - not practice - and require further research.

8. LITERATURE REVIEW

8.1. EFFICACY

The efficacy of the ketogenic diet in therapy of epilepsy has been widely analyzed in scientific research. There is a significant variability between studies in terms of the criteria used to define seizure frequency outcomes. Moreover, available research emphasizes the diversity in participant groups, low group size, as well as low-quality methodology which all account for a difficult analysis. For the purpose of this review the proportion of subjects achieving a $\geq 50\%$ reduction in seizures and the number of patients achieving complete seizure freedom are analyzed as these seem to be most frequently used to measure as outcomes and also most objective. Additionally, it is important to note that the studies differed in follow-up length which has a substantial impact on long-term reported results. Analyzed studies have had a 1-36 month follow-up period. A 50% SFR was reported in 17-73% (Skrobas et al., 2022), 38-70% (Verrotti et al., 2020), 38-57,4% (Lyons et al., 2020), 38-72% (Borowicz-Reutt et al., 2024). 1-23,5% (Skrobas et al., 2022), 1-15% (Lyons et al., 2020) of children achieved complete seizure freedom. As previously stated, data majorly varies between studies. A common phenomenon was also described in children on the classic KD diet. A study described 82% of seizure-free patients experiencing some seizures at 1 month post diet implementation. The continuation of diet treatment stopped the seizures, which should suggest not withdrawing

from the diet even if seizures reappear in hope for returning to seizure freedom. (Borowicz-Reutt et al., 2024)

When it comes to other childhood epilepsies, the diet has been analysed as treatment for among others: Dravet syndrome, Doose syndrome, Infantile Spasms and Lennox-Gastaut syndrome. These epileptic syndromes are known to have a relatively lower response to anti-seizure medication. The KD seems to be an effective alternative for patients after multiple drug combinations did not have a sufficient effect. 51% of children diagnosed with Lennox-Gastaut syndrome were reported to have a >50% seizure reduction (Kossoff et al., 2018). Its efficacy in Infantile Epileptic Spasm Syndrome (IESS) was described as >50% SFR in 90,9% of patients after 12 months of KD therapy (Wang et al., 2024). It has also been described as useful in Doose syndrome, with a 50-99% SFR in more than one third of children (Verrotti et al., 2020). These outcomes create hope for an improvement in seizure management in otherwise unresponsive to treatment patients.

Some studies have analyzed the effectiveness of different KD dietary approaches. Alternative KD types were usually compared against cKD or against traditional treatment. Most studies found all KD models more effective than traditional treatment., with some pointing to cKD as the most successful. The effects of MAD are usually similar or mildly inferior to cKD, however some authors suggest cKD being more effective in children younger than two years old as they require faster intervention due to potential development of epileptic encephalopathy. One of the studies comparing the effectiveness of MAD and cKD described a 33.8% for cKD and 44.6% for MAD baseline seizure frequency at 6 months of follow-up, proving the cKD to be more effective (Kim et al., 2016); majority of authors described similar results. A randomized clinical trial described the median difference in seizure reduction between cKD and MAD to be 21 percentage points in favour of cKD. Same study compared the efficacy of cKD and LGIT, with a median difference in SFR to be 12 percentage points in favor of cKD (Sondhi et al., 2020). In another study, the number of patients with a >50% SFR in the LGIT group compared to the MAD group was significantly higher (73.3% vs 43.3%) (Borowicz-Reutt et al., 2024). Overall, all ketogenic dietary approaches seem to be effective with the classic ketogenic diet being proven the most. It is important to note, that alternative ketogenic diets usually have higher retention rates due to their better tolerability, which provides a higher probability for potential positive outcomes.

8.2. ADVERSE EFFECTS

The ketogenic diet is generally considered to be a safe treatment option for epilepsy in children, however all reviewed studies have found this diet intervention to be associated with some adverse effects. Studies suggest incidence of adverse effects in patients ranging from on average 30-50%, with approximately 10% of patients choosing to discontinue the diet because of both its unpalatability and the below mentioned side effects, being a cause for concern for both the patient and the physician.

8.2.1. Gastrointestinal

Gastrointestinal disturbances are among the most commonly reported. They are often noted in the period of diet introduction (especially first 3 months) (Kim et al., 2016) and can lead to nonadherence or even withdrawal from treatment (Haridas et al., 2025) (Parveen et al., 2024). Among them most frequent are constipation, diarrhea and vomiting. Studies suggest their prevalence of 4-46% for constipation (Wells et al., 2020), (Sourbron et al., 2020), (Lyons et al., 2020); 6-50.9% for vomiting (Wells et al., 2020), (Lyons et al., 2020), (Sondhi et al., 2020); only one study (Lyons et al., 2020) depicts the prevalence of diarrhea (at 4%) while others only mention it as a frequent adverse effect. The total percentage of patients presenting with gastrointestinal symptoms in the reviewed research ranges from 30% to over 50% (Sourbron et al., 2020), (Borowicz-Reutt et al., 2024), (Verrotti et al., 2020), (Kossoff et al., 2018).

Although common, these are usually mild and transient and should not be a reason for discontinuation. If persistent or particularly unpleasant for the patient, GI side effects can often be successfully treated. Constipation can be resolved with an enema, polyethylene glycol or modified intake of dietary fibers. Nausea and vomiting can be treated with anti-emetics (Wells et al., 2020), (Sourbron et al., 2020). Other reported GI side effects include gastroesophageal reflux, abdominal pain, fatty diarrhea, hunger, dysphagia (Lyons et al., 2020), (Verrotti et al., 2020), (Martin-McGill et al., 2020). The varying KD types and different ages of the studied population of patients - from infants to adults - can be an explanation for the split of prevalence of gastrointestinal side effects in the studies.

8.2.2. Dyslipidemia

High amount of fats in KD can result in high serum lipid profiles (hyperlipidemia, hypercholesterolemia and hypertriglyceridemia). Highest risk of their development occurs in the first 6-12 months since KD initiation (Haridas et al., 2025). Overall, dyslipidemia incidence varied from 3,2% to 16% (Wells et al., 2020) (Lyons et al., 2020) with one study describing the precise incidence of the following: hyperlipidemia 4,6% hypercholesterolemia 3,8% and hypertriglyceridemia 3,2% (Wells et al., 2020). However, research is inconsistent, and some results remain insignificant.

Abnormal lipid levels are a significant factor for increased cardiovascular risk. Therefore, lipid levels should be regularly monitored, especially in instance of prolonged exposure to KD. Some studies suggest however that those values stabilize overtime and present no increased risk for atherosclerotic change (Haridas et al., 2025), (Kossoff et al., 2018). Dyslipidemia can frequently be prevented by modifying the KD ratio, excluding high amounts of trans and saturated fats and instead increasing olive oil, omega-3 fatty acid and MCT consumption. Research also points to formula-based KD as being less prone to cause dyslipidemia in comparison to solids (Kossoff et al., 2018).

8.2.3 Skeletal and growth

The use of the classic KD in children has been linked to possible growth retardation (Borowicz-Reutt et al., 2024). The reasons for this include both insufficient protein and calorie intake as well as the effect of accompanying treatments and the underlying condition (Wells et al., 2020). It is a rare adverse effect of the treatment, with studies linking it more with the calorie restriction and lack of adequate vitamin and mineral supplementation than the diet itself (Wells et al., 2020). Results across studies are inconsistent and insufficient especially due to different follow up periods potentially being too short to observe this long-term side effect. Studies with a follow-up period of more than 12 month usually point to negative effects of KD on growth (Verrotti et al., 2020). Impact on growth is cited between 6-9% when the diet is not calorie restricted and 75-85% with an energy restriction in order to achieve ketosis (Haridas et al., 2025) (Wells et al., 2020). Both the impact on growth and the skeletal system should be particularly taken into consideration when implementing the diet in infants and young children as it can result in height deceleration.

Osteopenia and osteomalacia are also listed as side effects of KD. Disorders of bone mineralization are an effect of biochemical disturbances such as inadequate calcium levels. Research once more is inconclusive in this matter. Some studies registered a decline in BMC despite calcium and vitamin D supplementation while in others no negative effects in bone composition were detected (Wells et al., 2020) (Verrotti et al., 2020). One study found the decrease in BMD in lumbar DXA (Dual energy X-ray absorptiometry) scans to be decreasing by 0,22 Z-score/year, yet the results were not statistically significant. However, a positive significant correlation in BMD values while implementing cKD along with bisphosphonates was found, highlighting a possible preventative method. DXA as well as serum levels are advised by some to be incorporated periodically to assess bone health and prevent potential pathologic fractures (Wells et al., 2020) (Haridas et al., 2025). It is also important to supplement vitamin D (Haridas et al., 2025).

8.2.4. Renal

Ketogenic diet can lead to increased calcium and acid urine levels as well as low citrate excretion, all being risk factors of developing kidney stones. Incidence varies between 0,05% (Verrotti et al., 2020) to 7% (Kossoff et al., 2018). One study reported 43% (cKD) and 23% (MAD) of patients developed hypercalcuria. Oral intake of sodium or potassium citrate seems to prevent the formation of renal stones as well as reduce acidosis (Kossoff et al., 2018) (Haridas et al., 2025). Kidney stone formation is exacerbated by insufficient fluid intake, which should be closely monitored for the duration of KD therapy. Patients were found to have three main types of stones – uric acid, calcium oxalate or calcium phosphate. Incidence may increase with prolonged KD treatment (Wells et al., 2020).

8.2.5 Other

Among other reported side effects of KD dehydration is mentioned to occur in 46,5% (Borowicz-Reutt et al., 2024). A metaanalysis by Lyons found the incidence to only be 1%, however many studies did not include dehydration as a possible adverse effect which explains the low percentage (Lyons et al., 2020). QTc interval prolongation was observed in 0-3% which could be a result of metabolic derangement (Wells et al., 2020). The initiation of the ketogenic diet sometimes presents itself with an elevation in liver enzymes (Borowicz-Reutt et al., 2024).

Gallstone formation is also mentioned and occurs usually after 12 months of therapy (Borowicz-Reutt et al., 2024).

Authors also mention metabolic acidosis, serum selenium deficiency, lower respiratory tract infections, body mass loss, lethargy, abdominal pain, hypoglycaemia and other laboratory abnormalities, behavioral problems, change in appetite and/or taste (Sondhi et al., 2020) (Dyńska et al., 2022) (Martin-McGill et al., 2020) (Borowicz-Reutt et al., 2024) (Lyons et al., 2020).

8.2.6 Diet types

Importantly, frequency of these side effects majorly differs depending on the type of ketogenic diet in place and seems to increase with the diet's restrictiveness. Across research cKD has proven to be least tolerated and associated with the most frequent adverse effects. The MAD, MCT and LGIT were evaluated as more palatable and satisfactory (Borowicz-Reutt et al., 2024). This affects adherence to the diet and should be a factor in choosing the optimal treatment. Comparison of the cKD and MCT revealed incidence of constipation ranging from 45-48% for cKD and 33-41% for MCT (Wells et al., 2020). Frequency of vomiting also differed between different diet types ranging from cKD 50,9%, MAD 44,8% to LGIT 31,6% (Sondhi et al., 2020). For the MAD, MCT and LGIT the undesired effects were in majority of gastrointestinal nature (constipation, vomiting, diarrhea), were transient, did not require additional pharmacological interference and did not result in discontinuation. Serious adverse effects were noted less frequently than in patients following the cKD. Importantly, initiation of diets other than cKD can be done in an outpatient setting (Borowicz-Reutt et al., 2024).

8.2.7 Retention

One of the limitations of the diet that must be considered is that it is often difficult to adhere to, especially regarding the pediatric population. This is due to its restrictiveness, less pleasurable taste and the abovementioned side effects (Youngson et al., 2017). Retention rates for the classic ketogenic diet were reported at 45.7% and 29.2% for the classic ketogenic diet at 1 and 2 year follow up respectively. (Sondhi et al., 2020)

Efforts to create alternative ketogenic diet forms such as the MCT, MAD or LGIT, which are less restrictive and allow for more carbohydrate intake have partially resolved the problem. However, when implementing a specific form of the diet, one must take into consideration the

benefit to risk ratio; as previously established, each of the types of the KD establish a different efficacy in particular age groups and specific epileptic syndromes.

9. DISCUSSION

The KD appears to be a highly effective form of anti-seizure treatment in the pediatric population. Most analyzed studies describe a significant increase in seizure frequency reduction as well as an increase in complete seizure freedom. A >50% SFR is described being as high as 50-70%. Seizure freedom is also achieved as often as in 25% according to some research. The data differs between the studies which can be a result of varying seizure severity, different follow-up periods as well as different study populations. Low retention rates are also a significant problem which can disturb the results. The effects of cKD seem to be most prominent, however alternative ketogenic diets show a similar or mildly inferior effect and should be treated as a well-established method of treatment as well. This diet has a significant effect in general epilepsy; however, it seems particularly useful in pediatric epileptic syndromes such as Doose, Dravet or West syndromes, which are often drug-resistant and the ketogenic diet can be a last, but effective resort. Overall, KD appears to be an effective option for refractory pediatric epilepsy which often allows for a reduction in drug doses or overall drug substitution.

Ketogenic diet is becoming an increasingly implemented and favored form of treatment due to its relatively mild side effect profile. Studies point to gastrointestinal effects, including vomiting, diarrhea and constipation, being the most common with incidence varying from 30-50% among studies. These typically appear when the diet is first introduced and usually are bearable for the patient. Other less frequently reported adverse effects include dyslipidemia, dehydration and kidney stones. Particularly concerning among the pediatric population are the inconsistent data on growth and bone health. Although rare, they can have a long-lasting effect on the developing human body and can be cause for concern for parents. Some research suggests a negative impact of KD on growth while other found no link between the two. This, as well as potential development of osteopenia or osteomalacia should be taken into consideration when implementing the diet, especially in the younger pediatric population. Most adverse effects, as previously mentioned, are mild and should not be a reason for withdrawal. For the majority of them there are methods of monitoring, prevention and treatment; this

includes measurement of BMD using DXA, oral intake of potassium citrate to prevent kidney stones and anti-emetics as treatment for vomiting.

10. CONCLUSIONS

The ketogenic diet is widely proven to have a high efficacy in refractory pediatric epilepsy as well as some epileptic syndromes which have low pharmacological response rates. It seems to be a good alternative when anticonvulsive drugs are ineffective. The precise antiepileptic mechanism of action of KD is unknown, with many theories being a potential explanation for the diet's antiseizure effect. There are four main ketogenic diet subtypes, which differ in the lipid, carbohydrate and protein intake. Although all of them do have a proven effect in the treatment of epilepsy, cKD seems to be the most researched and the most effective throughout. The ketogenic diet is generally considered to be a safe treatment option, however when implementing the diet, it is important to weigh the potential benefits to risks as the diet is reported to have adverse effects. Studies suggest though that these are mostly mild, in some cases easy to prevent and in majority should not be a reason for diet withdrawal.

Further research is required, as the low-quality methodology, lack of blinding, short follow-up periods, small study populations as well as a wide range of disease severity analyzed results in a difficulty to objectively analyze and compare the studies.

Supplementary Materials

Not applicable.

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Conflicts of Interest

The authors report no conflict of interest.

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