

Dietary treatment of epilepsy: rebirth of an ancient treatment

Leczenie padaczki dietą: renesans starej terapii

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Abstract

Since its introduction in 1921, the ketogenic diet has been in continuous use for children with difficult-to-control epilepsy. After decades of relative disuse, it is now both extremely popular and well studied, with approximately two-thirds of children demonstrating significant seizure reduction after 6 months. It is being used for less intractable seizures in children as well as recently adults. Modifications that help improve tolerability include the medium chain triglyceride diet, modified Atkins diet, and low glycemic index treatment. Major side effects include acidosis, increased cholesterol, kidney stones, gastroesophageal reflux, and growth disturbance. However, these side effects are usually treatable and nowadays often even preventable. Future non-epilepsy indications such as Alzheimer disease, amyotrophic lateral sclerosis, autism, and brain tumors are under active investigation. This dietary treatment for epilepsy has undergone a rebirth. Its widespread use in Poland and Europe is a welcome additional treatment for those with drug-resistant epilepsy.

Key words: ketogenic diet, epilepsy, treatment.

Introduction

The ketogenic diet (KD) is a high-fat, low-carbohydrate and normal-protein diet which has regained recognition over the past 15 to 20 years due to its

Streszczenie

Dieta ketogenna od jej opracowania w 1921 r. znalazła stałe miejsce w leczeniu lekoopornej padaczki u dzieci. Po kilku dekadach względnego zapomnienia, stała się znowu popularna i szeroko badana – u ok. 2/3 dzieci stwierdza się istotne zmniejszenie częstości napadów w ciągu 6 miesięcy leczenia. Dieta ketogenna coraz częściej jest wykorzystywana w leczeniu mniej opornych padaczek, a ostatnio także u dorosłych. Pojawiają się łatwiej tolerowane odmiany diety: dieta oparta na średniołańcuchowych trójglicerydach, zmodyfikowana dieta Atkinsa czy dieta z niskim wskaźnikiem glikemicznym. Do głównych objawów ubocznych stosowania tego typu diety należą: kwasica, hipercholesterolemia, kamica nerkowa, refluks żołądkowo-przełykowy i zaburzenia wzrostu. Powyższe objawy uboczne poddają się obecnie leczeniu, a nawet można im zapobiegać. Bardzo aktywnie bada się możliwości stosowania diety poza padaczką: w chorobie Alzheimera, stwardnieniu zanikowym bocznym, autyzmie i guzach mózgu. Leczenie padaczki dietą przeżywa swój renesans. Należy się spodziewać jej szerszego zastosowania w Polsce i Europie u chorych na lekooporną padaczkę.

Słowa kluczowe: dieta ketogenna, padaczka, leczenie.

antiepileptic effect. Typically used in children with intractable epilepsy, it has also become studied in adults in the past decade. Recent reports on its beneficial effect for several metabolic and neurodegenerative disorders have also increased the interest in its use in neurology.

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Fasting as a therapy for seizures has been known since biblical times. However, it was not until the early 20th century that the KD was used to mimic the biochemical mechanisms of fasting. The first scientific reports on the value of fasting and water diets in epilepsy were authored by Guelpa and Marie, both French physicians, in 1911 [1], but it was not until the 1921 American Medical Association convention, at which Rawle Geyelin, an eminent American pediatrician declared successful treatment of epilepsy by fasting, that this method of treatment gained the attention of medical professionals. Geyelin reported a case of a 10-year-old boy who had frequent seizures for the last 4 years and was successfully treated by an osteopath, Dr. Hugh Conklin. Repeated 15-day periods of fasting resulted in long-term cessation of seizures [2].

For the next 20 years, mainly due to researchers at the Mayo Clinic in Rochester, the ketogenic diet became a well-recognized method of treatment for patients with epilepsy. Introduction of phenytoin in 1938, at the time a new antiepileptic drug, which could be more easily applied than a diet, hindered the use of the ketogenic diet for more than five decades.

The diet has regained recognition over the past 15 to 20 years, largely due to the Charlie Foundation and their movie *First, do no harm* (1997) depicting a boy with drug-resistant epilepsy successfully treated with KD and starring Meryl Streep. Since then, an enormous growth of interest in the KD has been noted. A PubMed search made on 29th December 2010 indicates a nearly 6-fold increase of the number of peer-reviewed articles on the KD in the last decade compared to the previous one (828 : 144). In 2006, for the first time ever, separate sessions on KD were organized during the International Child Neurology Association and Child Neurology Society annual meetings. In 2008 and 2010, two large conferences dedicated solely to this kind of treatment took place in Phoenix, Arizona and Edinburgh, Scotland, hosting several hundred attendees.

The KD is now available in at least 50 countries worldwide [3]. The growing number of centers working with KD resulted in the first recommendations, written by 26 neurologists and dieticians from 9 countries, which were published in *Epilepsia* in November 2008 [4].

Ketogenic diet and its modifications

The classic KD, also called the long-chain triglyceride diet, is high in fat, adequate for protein (1 g/kg per

day) and low in carbohydrate. The fat calories come not only from butter and mayonnaise, but also from a variety of oils, olives, etc. The diet is traditionally calorie limited and most frequently is started in the hospital after 1 or 2 days of fasting. Fasting is no longer regarded as necessary for starting the KD, but it helps to obtain ketotic status in a shorter time. Also fluid restriction is no longer considered necessary.

The classic KD is calculated in a ratio of grams of fat to grams of protein and carbohydrate combined. The ratio ranges from 2 : 1 to 4 : 1. The most common diet, "4 : 1" (4 grams of fat to 1 gram of protein plus carbohydrate), is regarded as the most restrictive but the most effective. The fat, the main source of calories, is obtained from standard foods. Calories cover initially 80% to 90% of the daily recommendations for age but are frequently adjusted over time to ensure ideal growth.

In the search for better palatability, the medium-chain triglyceride (MCT) diet was developed in 1971 [5]. In the traditional MCT diet 60% of the total calorie prescription was provided by MCT oils. Due to its higher ketogenic effect the MCT diet allowed liberalization of carbohydrate content in the diet.

The high proportion of patients with gastrointestinal discomfort with abdominal cramps, diarrhea and vomiting prompted the researchers to modify the MCT diet and reduce MCTs to 30% of calories, replacing them with 30% long-chain fat ('modified MCT diet'). This kind of diet turned out to be more expensive and less affordable for families. Recent studies have shown both diets to be equivalent [6].

In the past decade two other modifications of KD have been developed for epilepsy treatment: low-glycemic-index treatment (LGIT) and the modified Atkins diet [7,8]. Both diets are high in fat and restrictive in carbohydrate, but unlike the classic KD may be initiated in outpatient settings and do not require precise weighing of food ingredients and portions.

LGIT allows liberalization of carbohydrate intake to approximately 40-60 g/day with glycemic indices < 50 used for the carbohydrates. The modified Atkins diet is very similar to KD with high fat and low carbohydrate and approximately 1:1 ketogenic ratio. The initial carbohydrate intake is approximately 10 g for children (20 g per day for adults), and all carbohydrates (although limited) are allowed. The lack of limitations on protein, fluids and calories helps improve the palatability of the diet [9]. According to the International Ketogenic Diet Study Group both LGIT and the modified Atkins diet may be particularly advantageous for

Table 1. Characteristics of the classic ketogenic diet and its modifications (1000 kcal/d provided) (adapted from [10])

Diet	Fat (g)	Protein (g)	Carbohydrate (g)
Classic 4 : 1	100	17	8
Classic 3 : 1	96	18	14
Classic 2 : 1	92	20	26
Classic 1 : 1	77	37	40
Medium-chain triglyceride oil diet	78	25	50
Low-glycemic-index treatment	67*	40-60*	40-60
Modified Atkins diet	72*	68-78*	10-20

*Approximate values

adolescents and adults [4,10]. The aforementioned diets are characterized in Table 1.

How does the diet work?

Despite nearly 100 years of use, the mechanism of antiepileptogenic action of KD remains unclear [11]. Broad spectrum efficacy of KD against heterogeneous seizure types and epileptic syndromes indicates that the diet must work through a common molecular pathway responsible for neuronal hyperexcitability and hypersynchrony.

Early studies suggested that the suppression of epileptic activity is related to the degree of ketosis, as a consequence of increased fatty acid oxidation. There is no study to show a correlation between urine ketones and seizure control. The only study, by Gilbert *et al.* [12], showed that seizure control correlates better with serum β -hydroxybutyrate than with urine ketones.

Yet, in 1933 Keith [13] reported in normal rabbits a protective effect of acetoacetate in seizures induced by thujone, a GABA_A receptor antagonist. More recently Likhodii *et al.* [14] proved that acute administration of acetoacetate and acetone blocked seizure activity induced by maximal electroshock and pentylenetetrazole in normal rats. However, there is no direct effect, even if some experimental studies may justify such an assumption.

It has also been shown that the KD can increase levels of ATP and other bioenergetic substrates through enhanced mitochondrial respiration [15]. Still, as high ATP levels block surface ATP-sensitive potassium channels, it remains unclear how the infusion of ketone bodies in the substantia nigra pars reticulata may result in their opening.

Masino *et al.* [16] stress the role of adenosine, the core molecule of ATP, in antiepileptic mechanism of KD. According to the authors such metabolic and dietary strategies as KD may increase regional or global adenosine and increase the overall seizure threshold.

Also some other agents have been studied as potential factors influencing KD effectiveness. 2-deoxyglucose, an inhibitor of phosphoglucose isomerase, an enzyme converting glucose-6-phosphate to fructose-6-phosphate, has been shown to be effective in multiple types of animal models of seizures and in kindling models of temporal lobe epilepsy [17,18].

Despite the multiple working hypotheses the underlying mechanisms of antiepileptic effect of the KD remain to be confirmed.

Efficacy of ketogenic diet in childhood epilepsy

The KD is an effective nonpharmacological treatment for patients, particularly children, with drug-resistant epilepsy, both partial and generalized. In comparison to vagus nerve stimulation (VNS), another major nonpharmacological treatment for intractable epilepsy, the KD appears to work faster, usually within 2 to 4 weeks, compared to several months when on VNS [19]. Both treatments are typically used after 2-3 drugs have failed and if surgery is not a straightforward option.

Some epileptologists believe that the KD may be one of the most effective therapies in childhood epilepsy [20]. Its effectiveness has been documented in infantile spasms [21,22], Lennox-Gastaut syndrome [23], Dravet syndrome [24] myoclonic-astatic epilepsy of early childhood [25,26], and absence epilepsy [27].

It should be noted that during its history the KD has been used almost exclusively for intractable epilepsy after multiple anticonvulsants have been tried unsuccessfully. It is commonly recognized that in such patients the probability of successful treatment is often extremely low. Even in these patients the KD is highly effective, resulting in greater than 50% improvement in seizure frequency in two-thirds of those treated, and complete cessation of seizures in 7-23% [28-30]. Therefore, it seems to be well justified that the KD should be considered after no more than two anticonvulsants have been tried, not five or more as is frequently the case. Such a recommendation has been recently issued by the International Ketogenic Diet Study Group [4].

Until 2008 there existed only open label cohort studies on the efficacy of the KD in intractable epilepsies. A Cochrane review in 2003 reviewed 14 studies, but reported a lack of reliable randomized controlled trials which might support the use of the KD [31]. The authors concluded that 'for those with a difficult epilepsy on multiple antiepileptic drugs, we consider the ketogenic diet a possible option'.

There are 3 other major meta-analyses of the efficacy of the KD, all of which conclude that despite the lack of controlled, randomized studies, there is clear evidence of KD efficacy [32-34]. The first meta-analysis, performed by Lefevre and Aronson, systematically reviewed 11 studies (9 from a single institution), all observational and only two prospective. Fifty-six percent of patients had >50% reduction in seizures and 32% had >90% seizure reduction [32]. In 2006, two meta-analyses were published. In his review, Keene [33] included 14 studies with at least 6 months follow-up since KD initiation. In the total cohort of 972 patients at 6-month follow-up 15.6% were seizure-free and 33% of children had more than 50% reduction of seizures. Similarly, Henderson *et al.* [34] reviewed 19 studies with a follow-up of at least 6 months, providing a total of 1084 patients. The authors confirmed that the KD reduced seizures by >90% in a third of the patients and by >50% in half. All authors of the meta-analyses stressed the lack of class I and class II data.

In 2008 Neal *et al.* conducted at the Institute for Child Health in London the first randomized controlled trial on efficacy of KD in childhood epilepsy [35]. One hundred forty-five patients aged between 2 and 16 years who had at least daily seizures and had failed to respond to at least 2 antiepileptic drugs participated in the study. Children were randomly assigned to receive the KD, either immediately or after a 3-month delay, with no other changes to treatment (control group). The obtained data documented responder rates (>50% improvement in seizure frequency) on an intention-to-treat basis of 38% when compared with 6% of the control group. Moreover, 7% of the patients in the diet group had greater than 90% seizure reduction compared with none in the control group. The KD group was further randomized to receive either MCT or the classical KD. No difference was seen in efficacy between the classical and MCT diets [6].

Another randomized controlled and also a double blind study specific for Lennox-Gastaut syndrome was published in 2009 by researchers from Johns Hopkins Hospital [23]. The children, aged 1 to 10 years, were

initially fasted and subsequently clinical and electroencephalographic events were documented. Half of them received a saccharin drink and another half a glucose drink, those with the latter assumed to break ketosis. Parents and physicians were blinded, both to the solution composition and level of ketosis. On the 6th day the children were reexamined. Seizure count and control EEG were performed and children were crossed over to receive the alternative drink. The study was finished after another 6 days with seizure control and EEG reevaluation. Comparing baseline seizure frequency to day 12, there was a significant reduction in seizures with a median decrease of -34 seizures per day ($p = 0.003$). Sixty-five percent of patients experienced >50% reduction in seizures over the study period. Unfortunately, for multiple reasons, the difference between the saccharin (treatment) and glucose (placebo) groups only neared statistical significance ($p = 0.07$).

There are only a few papers analyzing the efficacy of the KD in different seizure types. The KD seems to be more efficient in focal than in generalized epilepsies [36].

The KD is also helpful for many children in medication reduction, improving cognitive function, and often alertness. Kossoff *et al.* [37] recommend reducing medications after the first month to ensure the diet is being effective, then choosing one medication at a time and reducing it slowly.

Some reports have described improvement in the EEG, but this has never been fully demonstrated prospectively. The majority of children will continue the KD for approximately 2 years if successful, and 3-6 months if it is not. [38]. The KD is typically weaned over a 2-4 month period. [4].

Efficacy of ketogenic diet in adulthood epilepsy

The history of the KD for adults is also not a new idea, despite the recent interest. The first study, in 100 adults, was performed in 1930 by Barborka [39]. After one year of treatment with KD monotherapy 12% of patients became seizure-free, 44% improved and 44% remained unchanged. Recently, four reports have been published on classical KD treatment of epilepsy in adolescents and adults [40-43].

The efficacy of KD in these studies is similar to that observed in pediatric cohorts. These data suggest that the KD may be very effective in a proportion of adults. The reason why the KD was rarely used in adults was

Table 2. Indications for the ketogenic diet (adapted with modifications from [4])

Evidenced benefit/probable benefit
Epileptic syndromes
Infantile spasms
Severe myoclonic epilepsy of infants (Dravet syndrome)
Myoclonic-astatic epilepsy (Doose syndrome)
Lennox-Gastaut syndrome
Metabolic conditions
Glucose transporter protein 1 (GLUT-1) deficiency
Pyruvate dehydrogenase deficiency (PDHD)
Neurodegenerative disorders
Rett syndrome
Tuberous sclerosis
Children receiving only formula (infants or enterally fed patients)
Suggestion of benefit
Selected mitochondrial disorders
Glycogenosis type V
Landau-Kleffner syndrome
Lafora body disease
Subacute sclerosing panencephalitis (SSPE)
Angelman syndrome
Sturge-Weber syndrome
Phosphofructokinase deficiency
Undetermined benefit
Schizophrenia
Brain tumors
Amyotrophic lateral sclerosis
Parkinson disease
Alzheimer disease
Migraine

a general opinion that the diet is restrictive and unpalatable and its preparation is complex and time-consuming. In addition, many adults will tend to be noncompliant if they are not seizure-free (and likely not driving). Therefore non-compliance may be a major problem in adult patients.

Looking for a more palatable and less restrictive diet for adult patients, three groups of investigators studied the effectiveness of the modified Atkins diet in epilepsy

[44-46]. In one study of 30 patients 33% of them achieved a 50% seizure reduction at 6 months, one patient was seizure-free, and 33% stopped treatment after a 3-month period [44]. In another small series of 8 patients, 3 continued a diet for 6 months with the following seizure reduction: > 50%, > 30% and < 30% [45]. A recent study from Toronto reported 4/18 (22%) with > 50% seizure reduction after 6 months [46].

Ketogenic diet in other indications

Except for epileptic syndromes there is a growing list of conditions in which the KD was found to have a beneficial effect (Table 2).

Nowadays, the KD is a recognized treatment of choice in two distinct disorders of brain energy metabolism: glucose transporter protein type 1 (GLUT-1) deficiency syndrome and pyruvate dehydrogenase deficiency (PDHD) [4].

GLUT-1 deficiency syndrome is characterized by impaired glucose transport across the blood-brain barrier resulting in seizures, developmental delay and complex movement disorders observed in infants and small children [47,48].

In PDHD pyruvate cannot be metabolized into acetyl-CoA, leading to a heterogeneous clinical picture, usually characterized by hypotonia, lethargy, apnea and seizures [49,50]. The diagnosis is made by documenting an elevation of lactate and pyruvate in cerebrospinal fluid. In both conditions the KD provides ketones that bypass the metabolic defect and serve as an alternative fuel to the brain [4].

There is an increasing number of reports on the use of KDs in different neurological conditions with symptomatic epilepsy, such as Lafora body disease [51], Angelman syndrome [52], Landau-Kleffner syndrome [53], Sturge-Weber syndrome [54], subacute sclerosing panencephalitis (SSPE) [55], Rett syndrome [56, 57], and tuberous sclerosis [58].

There are single reports describing the use of KDs in some rare metabolic conditions: glycogenosis type V [59,60], phosphofructokinase deficiency [61], and mitochondrial respiratory chain complex disorders [62]. The beneficial effect of the KD has also been reported in schizophrenia. The authors suggested a possible role of a gluten-free diet in ameliorating schizophrenic symptoms [63].

In 2010 there appeared in the medical literature reports indicating a role of KDs in the regression of brain tumors. The study of Stafford *et al.* [64] demon-

strated that the KD improves survivability in a mouse model of glioma. Zuccoli *et al.* [65] reported of an adult patient with glioblastoma multiforme who experienced regression of the tumor after a two-month restrictive KD with vitamin and mineral supplementation. MRI evidence of tumor recurrence was found 10 weeks after suspension of strict diet therapy. The concept of this application of KD is to shift the prime substrate for energy metabolism from glucose to ketone bodies in order to disrupt tumor metabolism while maintaining the nutritional status of patients [66].

There are several animal model studies and uncontrolled trials suggesting the potential benefits of the KD in amyotrophic lateral sclerosis, Parkinson disease, migraine, autism, and narcolepsy [2]. However, due to a lack of sufficient evidence of efficacy, at this time, the use of KD in these indications cannot currently be recommended [4].

Henderson *et al.* [67] reported significant improvement of cognitive performance in patients with Alzheimer disease treated with the ketogenic agent AC 1202 in a randomized, double blind, placebo-controlled trial [67]. Currently available in the United States is a product called "Axona" that is MCT oil based as a treatment for Alzheimer disease.

Contraindications and safety measures

The KD is contraindicated in several specific disorders (Table 3). The shift of the primary energy source from carbohydrates to ketones may result in severe catabolic crisis in patients with impaired fat metabolism. Therefore clinical suspicion of an inborn error of metabolism (developmental delay, hypotonia, exercise intolerance, myoglobinuria, cardiomyopathy) requires additional testing to exclude the metabolic condition prior to initiation of the KD. Laboratory tests and additional investigations required for pre-KD evaluation are presented in Table 4.

Admission to the hospital is recommended at the beginning of the diet for monitoring in case of metabolic problems, handling acidosis, vomiting or hypoglycemia. It is also helpful to carry out intensive educative work with parents or caregivers.

Patients who start the KD may present early or late onset side effects. The first may be observed during the initiation of the diet. Dehydration, frequently caused by fluid restriction, hypoglycemia, acidosis, vomiting, diarrhea or refusal to eat may be secondary to either the fast

or the diet itself. Gastrointestinal symptoms (e.g. reflux) occur in 12-50% of children [68,69].

Some studies indicate significant increase of LDL, VLDL and non-HDL cholesterol and decrease of HDL cholesterol after 6 months of treatment. It should be noted that significant but less marked changes were

Table 3. Definite contraindications to the ketogenic diet (adapted from [4])

Primary carnitine deficiency
Carnitine palmitoyltransferase I or II deficiency
Carnitine translocase deficiency
Pyruvate carboxylase deficiency
β -oxidation defects :
Medium-chain acyl dehydrogenase deficiency (MCHAD)
Long-chain acyl dehydrogenase deficiency (LCHAD)
Short-chain acyl dehydrogenase deficiency (SCHAD)
Long-chain 3-hydroxyacyl-CoA deficiency
Medium chain 3-hydroxyacyl-CoA deficiency
Porphyria

Table 4. Laboratory tests and additional investigations required for pre-ketogenic diet evaluation (adapted with modifications from [4])

Laboratory tests
Complete blood count with platelets
Electrolytes to include serum bicarbonate, total protein, calcium, zinc, selenium, magnesium, and phosphate
Serum liver and kidney tests (including albumin, AST, ALT, blood urea nitrogen, creatinine)
Fasting lipid profile
Serum acylcarnitine profile
Urinalysis
Urine calcium and creatinine
Anticonvulsant drug levels (if applicable)
Urine organic acids
Serum amino acids
Ancillary investigations (optional)
Renal ultrasound and nephrology consultation (if a history of kidney stones)
Electroencephalography
Magnetic resonance imaging
Cerebrospinal fluid analysis (if no clear etiology identified)
Electrocardiogram, if history of heart disease

Table 5. Supplementation recommended by International Ketogenic Diet Study Group for patients on ketogenic diet (adapted from [4])

Universal recommendations
Multivitamin with minerals (and trace minerals)
Calcium with vitamin D
Optional extra supplementation
Oral citrates
Laxatives: mineral oil, glycerin suppository
Additional selenium, magnesium, zinc, phosphorus, vitamin D
Carnitine
Medium-chain triglyceride oil or coconut oil (source of medium-chain triglycerides)
Salt (sodium to add to modular formulas if used for greater than age 1 year)
All supplements listed should be provided as carbohydrate-free preparations whenever possible.

observed in these children after 12 and 24 months of the diet [70].

The KD does not influence the blood level of antiepileptic drugs [71].

During the maintenance phase particular attention should be paid to renal stones, delayed somatic growth with hypoproteinemia, increased infections or cardiac complications. Kidney stones have been reported in 3-7% of children on KD. Their formation may be related to hypercalciuria and hypocitraturia, which may also result from the KD. Fluid restriction is an additional promoting factor. Oral potassium citrate is an effective preventive supplement against kidney stones, reducing the risk 7-fold [72].

Alimentary restrictions of the KD may also lead to delayed somatic growth particularly expressed in small children. Neal *et al.* [73] assessed in up to 12 months follow-up 75 children on the KD and MCT diet and confirmed that both weight and height z scores decreased during the diet. There was no difference in outcome between classical and medium-chain triglyceride protocols despite the increased protein in the latter diet. Growth appears to improve after the KD is discontinued [74].

In order to prevent the delay of somatic growth while on KD, strict nutritional monitoring has been proposed by the International Ketogenic Diet Study Group with the assessment of protein intake [4]. Some vitamins and minerals which are lacking in the KD should also be supplemented. This is particularly important with re-

spect to vitamins D and B and calcium [75]. There is no evidence to recommend extra supplementation of zinc, selenium, magnesium or phosphorus, but routine vitamins need to be ensured [4] (Table 5).

Increased infections have been reported in 2-4% of children on the KD. While on the diet, the patients may demonstrate abnormal neutrophil functions with impaired bacterial phagocytosis and killing [76].

Cardiomyopathy and prolonged QT interval have been reported in a few children on the KD. Selenium deficiency was disclosed as their potential cause, but was not confirmed in other studies. Best *et al.* [77] postulated that a greater degree of acidosis and a higher β -hydroxybutyrate level might lead to the cardiac abnormalities.

Conclusions

The KD is an effective treatment for refractory epilepsy, particularly in childhood. The efforts to make it more palatable led to several modifications. The increasing interest in KD observed in the last 2 decades led to many new indications.

However, as with many other medical therapies, the KD also has its side effects. Their recognition is very important for proper monitoring of children for development of these complications.

In the era of the internet the dietetic services, supported by such charity organizations as Matthew's Friends, The Charlie Foundation, or the Daisy Garland Trust, are a source of new diets and advice for parents or caregivers. Culture-specific diets have been designed to meet the needs of a wide variety of cultures and nations. The KDs have proven to be an effective treatment in epilepsy and should be considered in all cases of drug-resistant seizures. The establishment of specialized KD centers would help to conduct this kind of treatment in a more efficient and safe way.

Disclosure

Dr. Kossoff is on the Scientific Advisory Board for Atkins Nutritionals, Inc.

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