REVIEW PAPER/*ARTYKUŁ POGLĄDOWY*

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.

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.

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 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