KETOGENIC DIET AS ANTIEPILEPTIC THERAPY: HISTORICAL PERSPECTIVE

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ABSTRACT

Ketogenic diet (KD) is a high-lipid diet, adequate for protein content but low in carbohydrates content. Caloric intake is calculated on the basis of the ideal patient's needs, reduced by about 20%, and is about 90% of lipids present in 3: 1 or 4: 1 ratio with proteins and carbohydrates. KD is considered the most ancient antiepileptic therapy, actually proposed also for migraine therapy.

Keywords*: ketogenic diet, epilepsy, cholesterol, free fatty acids.*

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Ketogenic diet: background and theory

Ketogenic diet (KD) is a high-lipid diet, adequate for protein content but low in carbohydrates content. Caloric intake is calculated on the basis of the ideal patient's needs, reduced by about 20%, and is about 90% of lipids present in 3: 1 or 4: 1 ratio with proteins and carbohydrates. Along with surgical exeresis of epileptogenic outbreaks, vascular stimulation, transcranial magnetic stimulation (TMS), immunomodulation and deep brain stimulation, KD is one of the possible alternative therapeutic approaches, non-pharmacological, KD can be used both as a single therapy and in association with pharmacological therapy, depending on the patient's clinical features.

Most effective at the age of development, but equally useful at other ages, it is currently used in most of the world for the treatment of selected forms of focal and generalized refractory epilepsy and early childhood epileptic encephalopathies (i.e. West syndrome).

On the other hand, KD is the first choice treatment for epilepsy related to the deficiency of the Glut-1.

The purpose of KD is to reproduce the metabolic fasting condition in which the body, in the absence of glucose, catabolizes free fatty acids producing ultimately the ketone bodies responsible for anti-commodity action. Despite the clinical efficacy experienced by numerous experimental studies and the therapeutic benefits it offers in the treatment of non-epileptic diseases including migraine headache and Parkinson's disease, its use presents some contraindications, difficulties and side effects. Diet is contraindicated, for example, in patients with beta-

oxidation deficiency, primary carnitine deficiency, pyruvate dexabosilase deficiency, and in patients with porphyria. One of the most felt limits lies in the reduced palatability of foods that you need to ingest to maintain adequate levels of ketosis. Although this problem does not exist in diets given to patients with gastrostomy or infants using balanced liquid formula, many authors continue to propose numerous variations in menu composition, and in the type of macronutrients to improve this aspect, while not affecting the achievement of therapeutic values of ketoneemia (modified Atkins diet), a diet containing medium chain polyunsaturated fatty acids (MCT), low glycemic index diet and many more. Side effects are distinguished in early (i.es drowsiness, fever, constipation, irritability) and late (i.e vomiting, gastroesophageal reflux and weight loss). There are effects that appear even later, including kidney stones, more frequently in patients with familiarity to this disorder, hypercholesterolemia and hypertriglyceridemia with increased LDL that appear a few months after the introduction of the diet and sometimes They increase progressively during the KD continuation. In any case, the most common side effects are monitored during patient follow-up by frequent checkups and laboratory examinations[1-25].

KD brief history

Dietary control is one of the oldest and most common forms of medical treatment. Before pharmacological presets gained the prestige and spread of the last 50 years, changing the style of nutrition was a method used for a variety. Huge of pathologies. from the dawn of Western Medicine there are written observations and clinical reports of more or less refined forms of ketogenic diet, but many of them have disappeared due to their apparent uselessness or lack of theoretical support. But the basics of such therapy are far more remote, dating back to ancient Greece, during which Hippocrates faced the treatment of natural epilepsy, giving particular importance to the diet associated with regular lifestyle. Even in the Bible there are references to fasting as a means of purification to avert the emergence of crises. The reasons why the ancients perceived the possible antiepileptic effect of fasting and ketogenic diet should be sought in the meaning they attribute to the illness itself. Over the millennia, there have been many "beliefs" about the aetiology of epilepsy.

It was regarded as a sign of demonic possession, but also as an expression of divine will, so to be described as "Sacred Morbid". Even today, with Vietnamese Hmong tribes, people with epilepsy are considered to have divinatory abilities. Parallel to this superstitious view of the epileptic phenomenon - which is periodically found in various historical periods - there were numerous hypotheses on the causes that could trigger an accessory episode based on the observation of natural phenomena, which would open the way for modern scientific studies. It was thought that some toxins, "moods", infections could be responsible. Therefore, in addition to "magical" remedies based on prayer or on exorcism, empirical remedies were considered including the ingestion of particular organs of animals or even humans, abstinence from certain foods, until fasting[26-36].

The first scientific evidence of the efficacy of dietary manipulations dates back to 1911, when Guelpa and Marie experienced that during the absolute fast the epileptic seizures disappeared. In 1920, Hugh Conklin stated that epilepsy was the result of brain intoxication by toxins from the intestines. He introduced the "water care" whose purpose was to put the gut into rest by 20 fasting days during which only water was given to the patient. In a time when there were not many effective antiepileptic treatments, this therapy was considered valid. The first scientific article where it was stated that a diet rich in fat and poor in carbohydrates could stimulate the same metabolic pathways of fasting, retaining the beneficial effects on crisis control, was published in 1921 by Wilder, Majo Clinic. In a revised and corrected form this would then become the modern chenogenic diet. In the decades that followed, numerous evidence of the efficacy of the ketogenic diet was reported. The latter, in fact, became the main anti-comic therapeutic garrison until the discovery of the first antiepileptic drug in 1938, Fenitoina, followed by the introduction of Valproic acid in the 1960s. Thanks to the ease of prescription and the best patient compliance, less restrictive and more practical pharmacological therapy captured the interest of clinicians and researchers who gradually shifted their attention from the study of the mechanisms of action of the diet to the pharmacodynamics of new anticonvulsant agents. From the '70s onward, dietary therapy was progressively set aside, supplanted by the discovery of increasingly innovative and effective drugs.

However, about 25-30% patients are non-negligible (25-30%), especially in infancy, or are non-responders to such therapy. On the other hand, the large-scale use of drugs, while highlighting its therapeutic properties, offered clinicians considerable concern over the side effects they caused. There was, therefore, a renewed interest in diet therapy, especially in children with poorly controlled drug-related crises. Therefore, KD was progressively reintroduced in Europe as it was considered a valid alternative in selected cases of epilepsy. Although only recently, it was possible to carry out Phase I and II clinical trials, the scientific basis of diet has always been considered solid. Current research is aimed at further improving the tolerability of the treatment by limiting its side effects, delineating the characteristics of ideal candidates, and controlling the efficacy of the diet in a controlled manner. They then offer the added benefit of widening our knowledge of the aetiology of epilepsy and therapeutic appendage. Thanks to this evidence, this "old" diet is still at the forefront of epilepsy treatment and remains one of the most powerful weapons available to the neuropediatric and infantile neuropsychiatrists who deal with this pathology[37-100].

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