

KETOGENIC DIET IN ADULT OBESITY: SAFETY, LIMITATIONS, AND EVIDENCE FROM VARIOUS CLINICAL APPLICATIONS

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ABSTRACT

The aim of this study was to present the current state of knowledge regarding the use of the ketogenic diet in the treatment of obesity in adults, with particular emphasis on its safety, indications, and contraindications, and to relate these findings to its established use in drug-resistant epilepsy and other clinical conditions. Despite growing interest in its clinical application, the effectiveness and safety of this intervention remain a matter of debate. A narrative review of the literature available in PubMed and Google Scholar from 2021 to 2024 was conducted using the keywords “ketogenic diet,” “obesity,” “epilepsy,” “type 2 diabetes,” “cardiovascular diseases,” “PCOS,” “neurological diseases,” and “psychiatric disorders,” as well as their combinations with AND/OR operators. Meta-analyses, randomized controlled trials, systematic reviews, and selected clinical trials evaluating the effectiveness and safety of the ketogenic diet were included in the analysis. The ketogenic diet demonstrates effectiveness in short-term weight loss and improvement of selected metabolic parameters in patients with obesity. However, its long-term effects remain equivocal and do not appear to offer significant advantages over other dietary strategies. The diet is associated with a risk of adverse effects and requires appropriate clinical monitoring. While it is a recognized and effective therapeutic option for drug-resistant epilepsy, its use in other conditions has not been established as a standard therapeutic approach. The ketogenic diet may be considered as part of obesity treatment in carefully selected patients, provided that potential benefits and risks are individually assessed. Further high-quality studies are needed to determine its long-term effectiveness and safety.

Keywords: *ketogenic diet, adult obesity, safety, limitations, evidence from various clinical applications*

INTRODUCTION

Obesity is a lifestyle disease that poses one of the most serious challenges to modern medicine. Its prevalence is increasing in many countries around the world [1, 2]. This disease is associated with an increased risk of numerous complications, including cardiovascular disease, type 2 diabetes, and certain cancers, which translates into a significant burden on healthcare systems [2]. The basic recommendation for people with obesity in the doctor's office is lifestyle changes, primarily related to dietary modifications and increased physical activity [2].

One nutritional model that has gained significant popularity in recent years is the ketogenic diet [1]. It is characterized by a significant reduction in carbohydrate intake while simultaneously increasing

fat consumption, leading to the induction of ketosis. Not every low-carbohydrate diet is a ketogenic diet. Nutritional ketosis is achieved only when carbohydrate intake is sufficiently restricted, whereas less restrictive low-carbohydrate dietary patterns may provide metabolic benefits without inducing ketosis. Therefore, distinguishing between these dietary models is essential when interpreting clinical evidence. The mechanism of action of ketosis is associated with, among other things, changes in energy metabolism, reduced insulin levels, and an impact on appetite regulation. Numerous studies have shown that the ketogenic diet can lead to significant weight loss in the short term, but its long-term effectiveness and safety remain controversial [2].

Despite the growing popularity of the ketogenic diet in the treatment of obesity, significant doubts remain

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regarding its impact on lipid profiles, kidney function, the risk of nutritional deficiencies, and the long-term maintenance of therapeutic effects. At the same time, this diet is well-established in the treatment of drug-resistant epilepsy, where its effectiveness has been confirmed in numerous clinical trials, making it an interesting example of a nutritional intervention with documented therapeutic effects [3, 4]. In recent years, there has also been growing interest in the potential use of the ketogenic diet in other conditions, including metabolic, neurological, and cancer diseases. However, for most of these indications, available data remain limited and require further research [2, 5].

The aim of this paper is to present the current state of knowledge on the use of the ketogenic diet in the treatment of obesity in adults, with particular emphasis on indications, contraindications and safety of its use in clinical practice, as well as to relate these data to its role in the treatment of drug-resistant epilepsy, cancer and other disease states in which the ketogenic diet is considered as a therapy or its component.

MATERIALS AND METHODS

This work is a narrative review of the literature. The analysis was based on scientific publications available in the PubMed and Google Scholar databases, published primarily between 2021 and 2024. The following keywords were used in the search: “ketogenic diet,” “obesity,” “weight loss,” “epilepsy,” “type 2 diabetes,” “cardiovascular diseases,” “PCOS,” “neurological diseases,” and “psychiatric disorders.” Meta-analyses, systematic reviews, randomized controlled trials, and selected clinical trials on the efficacy, safety, and clinical applications of the ketogenic diet were included in the analysis. Publications that did not meet the criteria for thematic relevance, publications with limited data availability, and articles duplicating previously analyzed results were excluded. After a preliminary review of titles and abstracts, publications that most closely matched the topic of the study were selected, with particular emphasis on studies concerning the treatment

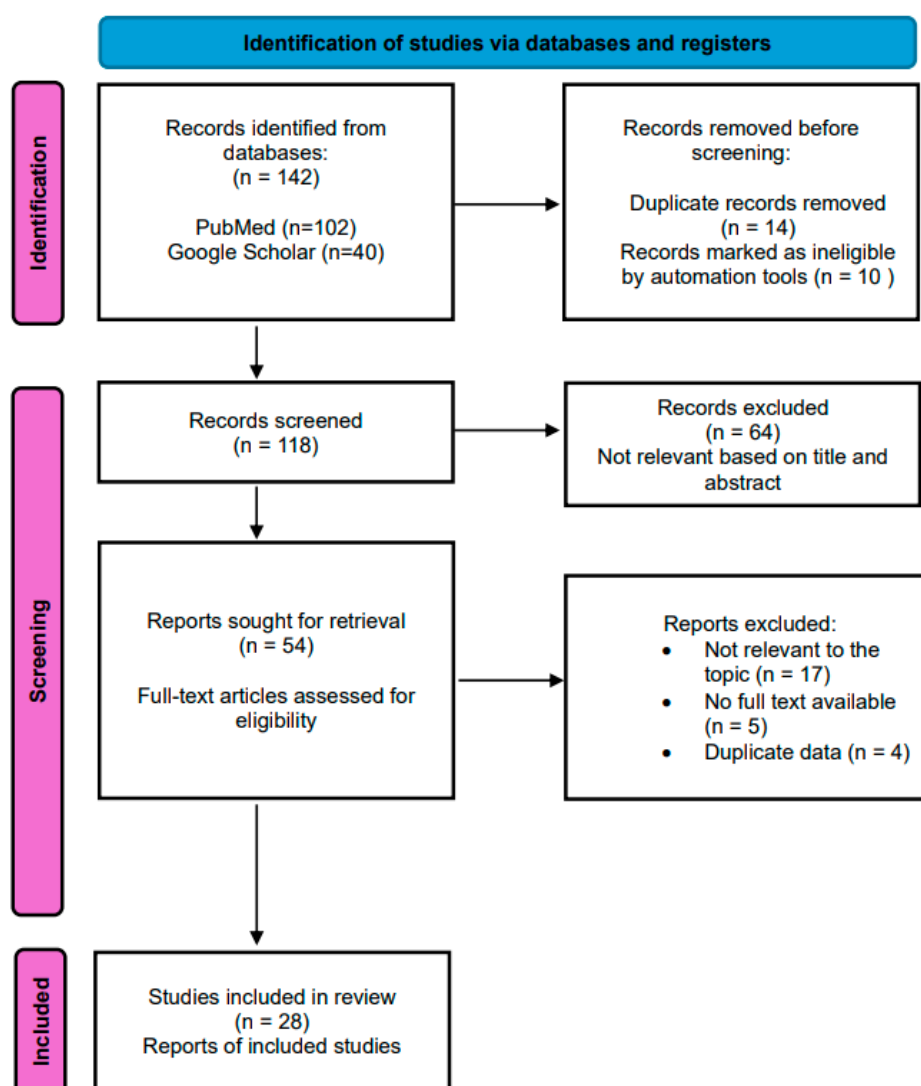


Figure 1. Flow diagram of study selection based on the PRISMA framework

of obesity in adults. The publication selection process is presented schematically in Figure 1, based on the PRISMA framework.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Mechanism of action of the ketogenic diet

The premise of the ketogenic diet is to achieve ketosis, a metabolic state in which ketone bodies, formed in the liver from fatty acids, become the body's primary energy source. To achieve this state, carbohydrate intake must be significantly reduced while simultaneously increasing fat consumption, whereas protein intake should be adjusted to individual requirements rather than deliberately increased. The classic ketogenic diet is based on a 4:1 lipid to nonlipid weight ratio, meaning 80% of energy comes from fat, 15% from protein, and 5% from carbohydrates. However, these ratios are sometimes adjusted to 3:1 or 2:1 to tailor the diet to the individual patient [3, 6-8].

In the human body, conditions of limited glucose availability result in decreased insulin levels and increased glucagon secretion, which promotes increased lipolysis in adipose tissue. The released fatty acids are transported to the liver, where they are converted through β -oxidation into ketone bodies, such as β -hydroxybutyrate, acetoacetate, and acetone [1, 2, 6, 7, 9]. These compounds constitute an alternative energy source for many tissues, including the central nervous system [5, 8, 9].

Appetite regulation is a significant mechanism responsible for weight loss during a ketogenic diet. It has been shown that ketosis can reduce the feeling of hunger by affecting the satiety centers in the hypothalamus and modulating appetite-regulating hormones such as ghrelin and leptin [6]. Furthermore, increased protein and fat consumption may promote prolonged satiety after a meal [1, 6]. An additional factor in weight loss may also be increased metabolic energy expenditure associated with gluconeogenesis [1, 6].

A ketogenic diet also affects the functioning of the nervous system, as ketone bodies are an efficient energy source for neurons and exhibit neuroprotective effects, including by reducing oxidative stress, modulating neurotransmission, and influencing mitochondrial function [3, 7, 8, 10]. These properties form the basis for using a ketogenic nutritional model in the treatment of drug-resistant epilepsy, which has led to a reduction in the frequency of seizures in some patients [3].

Due to its multifaceted effects on cellular metabolism, oxidative stress, and mitochondrial function, the ketogenic diet is also being studied in the context of other conditions, including

neurodegenerative, metabolic, and cancer diseases [3, 5, 7-10]. These mechanisms may potentially play a therapeutic role, but their clinical significance in most of these conditions has not yet been clearly confirmed.

The ketogenic diet in the treatment of obesity

Due to its growing popularity in recent years, the ketogenic diet is one of the most frequently analyzed nutritional models in the treatment of obesity in adults. Numerous randomized controlled trials and meta-analyses have been published assessing its effectiveness in weight loss and its impact on metabolic parameters.

Clinical studies suggest that the ketogenic diet results in significant weight loss, often greater than that of low-fat diets. A meta-analysis demonstrated that very-low-carbohydrate ketogenic diets were associated with an additional mean weight loss of 0.91 kg compared with low-fat dietary interventions [6, 11]. These findings are particularly favorable in the short term (up to 6 months), and the mechanism of this effect is multifactorial and includes both decreased appetite associated with ketosis and hormonal and metabolic changes favoring the use of adipose tissue as the primary energy source [1, 6, 11, 12].

However, the long-term effectiveness of the ketogenic diet is less clear and beneficial. Some studies indicate that after 12 months, the differences in weight loss between the ketogenic diet and other nutritional strategies diminish or disappear. The reasons are attributed, among others, to increased water loss in the initial stages of this dietary pattern and the difficulty of maintaining a restrictive diet long-term [1, 13].

The effectiveness of a ketogenic diet is assessed not only based on weight loss but also on its impact on cardiovascular risk factors. It has been shown that ketosis can lead to improved glycemic control, reduced triglyceride levels, and increased HDL cholesterol levels [1, 6, 10, 11, 13]. On the other hand, some studies report an ambiguous or even negative effect on LDL cholesterol levels, raising questions about the long-term safety of this diet [1, 10]. The advantage of the ketogenic diet over other dietary patterns in generating muscle mass growth has also been considered, which would also be a positive indicator of the positive impact of ketosis on individuals with obesity. However, the study results did not reveal significant differences between groups using different diets [14].

A significant limitation of the ketogenic diet's effectiveness is its dependence on patients' adherence to dietary recommendations. The limited variety of products may lead to long-term non-adherence to the diet. This dietary model is characterized by a high degree of restriction; a single deviation from the diet

may result in a state of ketosis and, consequently, a lack of interventional effectiveness [1, 3].

In summary, the ketogenic diet can be an effective treatment for obesity in adult patients, but its effects are most noticeable in the short term, and in the long term, it has no observed advantage over other dietary strategies. It is necessary to individualize recommendations, consider potential benefits and risks, and assess the likelihood of adherence to the diet before implementing this form of therapy [6].

Ketogenic diet in the treatment of drug-resistant epilepsy

One of the first and best-described applications of the ketogenic diet in the scientific literature is the treatment of drug-resistant epilepsy. Unlike the treatment of obesity, where scientific data is ambiguous and sometimes contradictory, the effectiveness of the ketogenic diet in reducing the frequency of seizures has been confirmed by numerous clinical studies [4, 5, 15].

Drug-resistant epilepsy is characterized by a failure to achieve seizure control despite the use of at least two appropriately selected antiepileptic drugs [3, 4]. In this group of patients, the ketogenic diet is an important therapeutic option, used as a standalone treatment or as part of a combined therapy [3, 5]. Studies have shown that in some patients, the diet leads to a reduction in seizure frequency by over 50%, and in some cases even to their complete cessation [3, 5].

The effectiveness of the ketogenic diet in epilepsy is mediated by a number of complex biochemical and neurophysiological processes. The mechanism of action of this nutritional model is not yet fully understood, but it is hypothesized that ketone bodies, such as β -hydroxybutyrate, may stabilize neuronal cell membranes, modulate neurotransmission, and increase gamma-aminobutyric acid synthesis, leading to reduced neuronal excitability. Furthermore, ketosis may reduce oxidative stress and positively impact mitochondrial function, which may also play a role in antiepileptic effects [3, 5, 6, 8].

Unlike obesity treatment, the use of a ketogenic diet as a treatment for drug-resistant epilepsy requires close supervision by a team of specialists, including a physician and a clinical dietitian, as well as careful monitoring of the patient's condition, metabolic parameters, and potential adverse effects [5, 8]. Long-term use of the ketogenic diet may result in side effects such as gastrointestinal disturbances, hyperlipidemia, or kidney stones. However, the balance of benefits and risks in this group of patients often favors its use, sometimes in a modified form to ensure patient adherence [3, 5, 8].

Comparing the use of the ketogenic diet in the treatment of obesity and drug-resistant epilepsy

highlights significant differences in the reliability of scientific evidence and clinical approach. In the case of epilepsy, the diet is a recognized therapeutic method with documented effectiveness, while in the treatment of obesity, its role remains supportive and requires further research, particularly in the context of long-term safety and durability of effects.

In summary, the ketogenic diet is an effective and recognized treatment method for drug-resistant epilepsy, the use of which is based on a reliable scientific basis. The different nature of the evidence for obesity and epilepsy emphasizes the need for cautious interpretation of research results and individualized therapeutic decisions in the treatment of obesity.

The ketogenic diet in the treatment of other diseases

Besides its use in the treatment of obesity and drug-resistant epilepsy, the ketogenic diet is being studied in many other conditions. In most of these cases, the observed therapeutic effects may be partially related to weight loss and improved metabolic parameters, making it difficult to clearly assess the direct impact of the ketogenic diet. As a therapeutic element, its use is being considered in the treatment of cancer, cardiovascular diseases, type 2 diabetes, polycystic ovary syndrome, and certain neurological and psychiatric conditions, among others.

In the case of cancer, it has been suggested that limiting glucose availability may affect cancer cell metabolism, slowing tumor growth [6, 12, 16]. Some studies also indicate the potential sensitization of some cancer cells to chemotherapy or radiotherapy when using a ketogenic diet [6, 12, 16, 17]. Clinical trial results to date are limited and do not allow for clear recommendations, but it appears that the ketogenic diet may be a potential candidate for adjuvant cancer therapy [6, 12, 18]. However, due to their restrictive nature and the frequent presence of cancer cachexia, ketogenic diets may increase the risk of malnutrition and should only be implemented under close medical and nutritional supervision.

In type 2 diabetes, the ketogenic diet has been shown to have beneficial effects on glycemic control, improved insulin sensitivity, and weight loss. However, its long-term safety remains controversial, primarily due to its adverse effects on LDL levels and the observed increased risk of hypoglycemia and ketoacidosis. For these reasons, ketogenic diets are not routinely recommended for patients with type 1 diabetes and their use is limited to highly selected clinical situations, such as patients with concomitant drug-resistant epilepsy, under specialist supervision [1, 6, 11, 19]. Some studies have shown that despite improved patient outcomes in the short term, there is no significant difference in long-term weight loss, glycemic control, or insulin sensitivity [1, 20].

Furthermore, a randomized controlled trial from 2024 showed that a 10-day ketogenic diet did not improve glucose tolerance, insulin sensitivity, plasma lipid profile, or blood pressure in obese patients with type 2 diabetes unless accompanied by weight loss [21]. Current American Diabetes Association (ADA) and Polish Diabetes Association (PDA) recommendations support individualized low-carbohydrate dietary patterns for selected adults with type 2 diabetes but do not specifically recommend ketogenic diets over less restrictive low-carbohydrate interventions [22, 23].

In cardiovascular diseases, both potential metabolic benefits and adverse effects on LDL cholesterol levels are observed, and consequently, on the risk of developing atherosclerosis and its associated complications [1]. The ketogenic diet may affect the cardiovascular system at various levels. Its anti-inflammatory effects, the positive effect of ketone bodies on the vascular endothelium, lowering triglyceride levels, increasing HDL levels, and potential weight loss may have a cardioprotective effect [24]. On the other hand, some studies report that the ketogenic diet leads to cardiomyocyte apoptosis and cardiac fibrosis, which may suggest its harmful effects [6].

The literature also indicates the potential impact of the ketogenic diet on the hormonal system, which, combined with its positive effect on certain metabolic parameters, may be used in the short-term treatment of polycystic ovary syndrome (PCOS) [6, 25]. Due to the proven effectiveness of other nutritional models in this condition, it is particularly important that the person prescribing dietary intervention is a specialist who will select an individualized treatment, assess contraindications, and assess the risk of adverse effects [25].

In neurology, the ketogenic diet is being studied in conditions such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis, citing its pleiotropic effects on the body and neuroprotective nature [5, 6, 8, 26]. Available scientific data indicates the potential benefits of using a ketogenic diet in neurological diseases, but the limited number of studies prevents clear confirmation of the therapeutic effects of this nutritional model [5, 6]. The exceptions with confirmed therapeutic effects are the previously described drug-resistant epilepsy and drug-resistant migraine. Current clinical recommendations indicate that ketogenic dietary therapies may reduce the frequency and severity of migraine attacks and can be considered in selected patients with chronic or drug-resistant migraine [15, 27].

In psychiatry, the ketogenic diet is also beginning to be studied; its potential impact on mood disorders and cognitive functioning may contribute to the treatment of conditions such as depression and schizophrenia

[6, 28]. A 2024 study demonstrated increased life satisfaction, improved overall functioning, and improved sleep quality in patients with schizophrenia and bipolar disorder who received a ketogenic diet in combination with pharmacotherapy [28]. However, it should be emphasized that for most of these indications, the available data are preliminary, and the use of a ketogenic diet requires further research, particularly with large cohorts and longer durations, and cautious interpretation of results.

There are also isolated reports of the use of a ketogenic diet in the treatment of lipodema, but the scientific data in this area is very limited and does not allow for the formulation of clear conclusions [29].

In summary, despite growing interest in the use of the ketogenic diet in various disease entities, its effectiveness has only been unequivocally confirmed in selected indications. In most cases, the available data are preliminary, emphasizing the need for further research and a cautious approach to its use in clinical practice.

Indications and contraindications

The basis for qualifying a patient for a ketogenic diet should be an individual clinical assessment, taking into account the potential benefits and risks associated with its implementation and the patient's likelihood of compliance. This dietary model is not a universal method for treating obesity, but it is one of the possible dietary interventions in appropriately selected patients.

The main applications of the ketogenic diet are drug-resistant epilepsy and obesity in adult patients with co-occurring metabolic disorders such as insulin resistance or type 2 diabetes [30]. This nutritional model has been shown to improve glycemic control and weight loss, making it a potentially beneficial therapeutic option in patients with obesity [30]. Furthermore, the ketogenic diet may be considered in patients who fail to achieve clinically significant results with other dietary models.

However, there are contraindications to the ketogenic diet. The most important include kidney disease, liver disease, lipid metabolism disorders, concomitant propofol therapy, which increases the risk of propofol infusion syndrome, and congenital metabolic diseases that impair the utilization of fatty acids as an energy source [3, 12]. Furthermore, special caution should be exercised in patients with cardiovascular disease, nutritional disorders, malnourished individuals, and those with poor ability to adhere to restrictive dietary recommendations [3]. Pregnancy and breastfeeding are additional contraindications due to the lack of sufficient safety data.

In clinical practice, proper patient qualification and monitoring of the treatment course are crucial. Before

initiating a ketogenic diet, it is recommended to assess the patient's general condition, including laboratory tests such as lipid profile, renal and liver function, and carbohydrate metabolism. Regular monitoring of metabolic parameters and assessment of treatment tolerance are necessary during the diet [30].

Safety

Introducing a ketogenic diet is associated with the risk of adverse effects, which are most often short-term, but some may also be long-term, especially during chronic use. The earliest observed early adverse effects are a series of symptoms collectively referred to as “keto flu,” which include weakness, headaches, dizziness, nausea, and impaired concentration [3, 5, 8]. These are usually transient and subside within a few days to weeks, and their occurrence is associated with the body's adaptation to using ketone bodies as its primary energy source [5, 6]. During the initial period of the diet, special attention should be paid to disturbances in water and electrolyte metabolism, including increased sodium and potassium loss, which requires appropriate monitoring [3, 6, 8].

The literature highlights the potential adverse effects of the ketogenic diet on lipid profiles, particularly increased LDL cholesterol in some patients, which could potentially be a long-term side effect of this dietary model. At the same time, beneficial changes in

triglyceride and HDL cholesterol levels are observed, suggesting a complex and individually variable effect of this diet on cardiovascular risk [8, 18, 31, 32].

Adoption of a ketogenic diet may also be associated with the development of kidney stones and a high burden on the kidneys due to increased protein intake and metabolic changes [5, 6, 8]. Individuals with pre-existing kidney disease are particularly susceptible to this adverse effect, and in their case, special caution or even complete elimination of this dietary model is recommended. Moreover, prolonged ketogenic diets may accelerate the progression of renal insufficiency in susceptible individuals, highlighting the need for careful patient selection and renal function monitoring.

Another important safety aspect of the ketogenic diet is the possible occurrence of nutritional deficiencies, including those in the B vitamin group, vitamin C, minerals, and dietary fiber, resulting from the limited consumption of grain products, fruits, and some vegetables [8]. Supplementation of these dietary components is important, especially with long-term adherence to the diet, as their deficiency can result in constipation, osteopenia, or even osteoporosis, which can develop not only due to deficiencies but also due to acid-base disturbances [15].

In summary, the ketogenic diet can be used in selected patients with obesity, but requires appropriate qualification, monitoring of metabolic parameters,

Table 1. Application of the ketogenic diet in selected medical conditions

Medical condition	Effectiveness	Level of evidence	Main benefits	Limitations/risks
Obesity	moderate	moderate	weight loss	low adherence, lack of long-term studies
Drug-resistant epilepsy	high	high	reduction in seizure frequency	low adherence
Type 2 diabetes	moderate	moderate	improved glycemic control, weight loss	risk of hypoglycemia, unclear long-term effects
Cardiovascular diseases	uncertain	low/moderate	decreased triglycerides (TAG), increased HDL	increased LDL
Cancer	uncertain	low	enhanced response to primary cancer treatment	limited number of studies
PCOS	moderate	low/moderate	improvement in metabolic and hormonal parameters	lack of long-term studies
Neurodegenerative diseases	uncertain	low	neuroprotective effects	limited number of studies
Psychiatric disorders	uncertain	low	improved well-being and cognitive function	limited number of studies
Lipedema	uncertain	low	reduction in symptom severity	limited number of studies

TAG – triglycerides; HDL – high-density lipoproteins; LDL – low-density lipoproteins.

individualization of recommendations and special caution in people with comorbidities. A summary of current applications of the ketogenic diet in selected disease entities is presented in Table 1.

DISCUSSION

The ketogenic diet is currently one of the most popular nutritional models, and its effectiveness and therapeutic potential are being studied in numerous disease entities. However, the level of scientific evidence regarding its effectiveness and safety varies significantly depending on the clinical indication. A review of the scientific literature indicates that in the treatment of obesity, this diet may be effective in short-term weight loss and improving selected metabolic parameters, but its long-term advantages over other dietary strategies remain inconclusive [1, 11].

One of the main limitations of the available studies is the relatively short follow-up period and the significant heterogeneity of the analyzed populations. Data on the long-term effects of the ketogenic diet are lacking, which is particularly important in the context of the chronic nature of obesity. Furthermore, the restrictive nature of the diet makes it difficult for patients to maintain it, especially with long-term use, which reduces its actual effectiveness in clinical practice [1].

The impact of the ketogenic diet on cardiovascular risk is also controversial. Although beneficial changes in triglyceride and HDL cholesterol levels are observed, a simultaneous potential increase in LDL cholesterol levels in some patients requires cautious interpretation and individualized treatment recommendations [1, 20]. This indicates the need to monitor metabolic parameters during the diet and consider the patient's risk profile.

Among the ambiguous data on obesity treatment, the use of the ketogenic diet in the treatment of drug-resistant epilepsy stands out, as its effectiveness has been confirmed in clinical trials and is reflected in recommendations from scientific societies [3]. This difference emphasizes that the ketogenic diet should not be considered a universal therapeutic tool, but rather an intervention with varying clinical value depending on the disease entity.

In recent years, there has been growing interest in the potential use of the ketogenic diet in other conditions, such as cancer, metabolic, neurological, and psychiatric disorders. However, in most of these cases, the available data are preliminary, and their interpretation is limited by the small number of clinical trials and the lack of standardized interventions. Therefore, the use of a ketogenic diet for these indications should be considered experimental [6, 12].

From a clinical perspective, individualizing the approach to each patient is crucial. A ketogenic diet can be an effective tool supporting the treatment of obesity in selected patients, but its implementation should be preceded by an assessment of the potential benefits and risks and should take into account the patient's preferences and the possibility of long-term compliance. This also requires appropriate monitoring and interdisciplinary collaboration between a diabetologist, dietitian, and family physician.

CONCLUSION

The ketogenic diet can be an effective method for short-term weight loss in adult patients with obesity and lead to improvements in selected metabolic parameters. The long-term effectiveness of the ketogenic diet in the treatment of obesity remains ambiguous, and its advantages over other dietary models have not been clearly confirmed. Its use is associated with the risk of adverse effects, therefore, it requires appropriate patient qualification and monitoring of metabolic parameters during use. The ketogenic diet has proven use in the treatment of drug-resistant epilepsy, where its effectiveness has been confirmed in clinical trials and recommendations from scientific societies. However, in most other conditions, such as cancer, metabolic, neurological, and psychiatric diseases, the use of this dietary model remains in the research phase and is not currently standard of care. Implementation of the ketogenic diet should be considered taking into account the patient's clinical condition, potential benefits and risks, and the likelihood of patient compliance. Further studies, particularly long-term studies, are necessary to clearly assess safety and effectiveness in the treatment of obesity and other chronic diseases.

Conflict of interest

The authors declare no conflict of interest.

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