The Impact of The Ketogenic Diet on Disease Management and Long-Term Health

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Abstract. The ketogenic diet (KD) is a diet that helps lose weight and manage blood sugar by reducing the intake of carbohydrates and making the body rely on fat for energy. It has a certain effect on people with obesity, type 2 diabetes and epilepsy, especially in weight loss and control of seizures is significantly helpful. However, long-term adherence to this diet can lead to nutritional imbalances, such as insufficient mineral and fiber intake, and may also increase the risk of intestinal health. This article focuses on the effects of the ketogenic diet (KD) in the treatment of diseases such as obesity, type 2 diabetes (T2DM), and epilepsy. The article analyzes existing literature to explain how KD forces the body to use fat as an energy source by reducing carbohydrate intake, thereby aiding in fat burning and ketone body production. This can help with the management of these diseases, while also analyzing the metabolic processes of KD and the potential long-term risks it may bring.

Keywords: Ketogenic diet, obesity, type 2 diabetes, epilepsy.

1. Introduction

In recent years, the effects of the ketogenic diet (KD) have become a matter of concern. With the change of lifestyle and the emergence of metabolic diseases, the ketogenic diet has gradually entered the public's vision as an extremely low-carbohydrate, high-fat diet. People usually associate "weight loss", "cure disease" and "radical diet" with it naturally. According to research, the ketogenic diet was originally designed in the 1930s for the treatment of childhood epilepsy, and studies in recent years have further demonstrated its effectiveness in a variety of conditions, including potential benefits in asthma, polycystic ovary syndrome, obesity, and more [1].

Most people only pay attention to the effect of KD on weight loss and health improvement, but there is a lack of in-depth understanding of its basic principle and applicability. First of all, an incomplete understanding of KD will produce cognitive blind spots and neglect of potential risks in practical applications. Secondly, not everyone is suitable for KD, and individual differences will also affect the effect of KD. People need to be determined according to different health conditions, age groups and lifestyles. Following this diet without proper supervision can lead to serious risks, such as malnutrition, chemical imbalances, vitamin deficiencies, and potentially even death [2]. It makes sense to help people scientifically and objectively assess whether KD is right for them, so as to avoid the potential health risks of blindly following dietary trends, and to ensure that dietary choices can achieve the desired results while safeguarding long-term health.

The purpose of this study was to explore the use of KD in different health problems and its safety and potential risks. This study will focus on analyzing the metabolic mechanisms of KD and its role in diseases such as obesity, diabetes, and polycystic ovary syndrome (which will be modified later in the main part of the study), as well as evaluating the safety of long-term use. The research method is mainly to sort out the biological principle, clinical application and possible side effects of KD by screening and analyzing the existing literature. The ultimate goal is to help better understand KD, especially its applicability, in order to make more informed dietary choices.

2. Mechanism and metabolic effects of KD

KD works primarily by changing the body's energy source. The basic principle of KD can be summarized as changing the body's energy source from glucose oxidation to relying on fat oxidation to produce ketone bodies for energy. Normally, fat is mainly used as an energy reserve in the body, while carbohydrates become the body's preferred energy source due to their faster metabolic rate. In the course of biological evolution, the body preferentially selects carbohydrates to meet rapid energy needs. However, when there is a surplus of carbohydrates, the excess is converted into fat and stored under the action of insulin. KD alters this metabolic pattern by significantly reducing carbohydrate intake, making the body dependent on ketone bodies as its primary energy source. Through the breakdown of fat and the production of ketone bodies, the body realizes the energy supply based on fat rather than carbohydrates, thus promoting fat burning.

It is worth noting that in KD, when the intake of carbohydrates is less than 10% of the total calories, the body is forced into a state called "ketosis". In ketosis, a type of fuel called ketone bodies is produced. Beta-hydroxybutyric acid, as the primary energy fuel, plays an important role in providing energy and reducing inflammation. KD activates T and gamma cells in adipose tissue, and through the activation of these cells, reduces inflammation in adipose tissue, thereby promoting health. Research has shown that ketone bodies have a potential therapeutic effect on neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, etc., as they can replace glucose, act as an energy source for the brain, and provide neuroprotective effects [3].

Effects on the gut microbiota: Studies have shown that this diet reduces the abundance of some beneficial bacteria, such as bifidobacteria and E. rectale, while increasing the abundance of harmful bacteria, such as E. coli and other potentially pathogenic bacteria. A recent study on children with epilepsy discovered a decrease in Bifidobacteria, E. rectale, and Dialister. These microorganisms are linked to health benefits such preventing colon cancer, IBS, and necrotizing entercolitis [4]. Actinobacteria and Escherichia coli were found in relatively high abundance; this finding may be related to the VLCKD's restriction on carbs. It is important to emphasize that scientists have discovered a depletion of the pathways causing the breakdown of carbohydrates through their investigation of the 29SEED subsystem [5].

KD has both positive and potentially negative effects on the gut microbiota. On the plus side, KD can promote weight loss by reducing carbohydrate intake. Improving metabolic health in some cases, such as epilepsy and certain neurodegenerative diseases, has potential therapeutic effects. In addition, intake of polyunsaturated fatty acids (PUFAs) can help maintain intestinal function.

However, there are also negative effects, such as a reduction in the number of some beneficial bacteria, such as bifidobacterium and E. rectale, which may not be good for long-term gut health. In addition, the high-fat characteristics of KD may also trigger some intestinal flora imbalances, leading to inflammation or other potential health problems. Therefore, the effect of KD is twofold, and the specific effect varies from person to person. Overall, KD has a significant impact on metabolic health while regulating the gut microbiome.

3. Application of KD in specific diseases

The earliest application of KD is in the treatment of refractory epilepsy, especially in children with epilepsy. KD reduces the frequency of seizures by changing the metabolic environment in the brain and reducing the abnormal firing of neurons. Studies have shown that there are three mechanisms that are considered to be key factors affecting seizures, namely the ketone body regulation mechanism, glucose restriction and energy regulation, and the neuroprotective effect of PUFAs.

First, ketone bodies act as anticonvulsants. KD increases the concentration of ketone bodies in the blood, especially beta-hydroxybutyric acid (BHB). BHB is often used as an anticonvulsant marker for epilepsy. However, although the effect of KD can be tested clinically by BHB, there is no direct significant association between BHB and epilepsy protection. Despite the rapid rise in BHB concentrations, the best epileptic protective effects usually take several weeks to achieve. In addition,

other ketone bodies, such as acetoacetic acid (ACA) and acetone, have shown more direct antiepileptic effects in some animal studies [6].

In addition, glucose restriction is also one of the key mechanisms of KD. By reducing the supply of glucose, ATP-sensitive potassium channels (KATP channels) are activated, leading to hyperpolarization of the cell membrane, thereby reducing neuronal excitability. This mechanism may help control seizures. In addition, after glucose reduction, the energy production of neurons is reduced, inhibiting high levels of synaptic activity, thus reducing the risk of seizures [6].

PUFAs were also strongly associated with a reduction in seizures. For example, docosahexaenoic acid (DHA) and eicosatetraenoic acid (AA) are increased in KD. PUFAs can reduce the overexcitation of neurons in a number of ways, including directly inhibiting sodium and calcium channels, activating potassium channels, and enhancing the function of the sodium pump, thereby reducing the likelihood of seizures. In addition, PUFAs can reduce oxidative stress and protect neurons [6].

Obesity and diabetes: Obesity is an important risk factor for chronic diseases, including type 2 diabetes (T2DM), cardiovascular disease, metabolic syndrome, chronic kidney disease, and cancer, which are associated with increased morbidity and mortality [7]. Given the growing emphasis being paid to obesity, KD is undoubtedly the preferred option for treating diabetes. Its primary method of weight loss is cutting insulin, which aids in the transition of fat metabolism from synthesis and storage to breakdown and oxidation. This leads to nutritional ketosis, which mimics a state of metabolic starvation in the body and uses ketone bodies as a substitute energy source [8].

T2DM is characterized by insulin resistance, which makes the cells unable to effectively absorb glucose. Since glucose is the primary source of energy for cells, insulin resistance weakens the production of ATP, causing dietary carbohydrates to be transported to the liver and converted into fat [9]. This mechanism also increases the risk of complications. The study found that KD significantly reduced glycosylated hemoglobin (HbA1c) and homeostasis model assessment index (HOMA), suggesting a significant role for KD in improving insulin sensitivity. Therefore, KD can effectively help T2DM patients improve blood glucose control and insulin sensitivity [10].

In a study on the effects of KD in patients with diabetes, the main focus was to explore how KD affects body weight, blood sugar and lipid levels in patients with T2DM. The study by Li et al. shows that KD has a good control effect in newly diagnosed T2DM patients, especially those who are overweight or obese. In these studies, KD was found to help reduce weight, reduce waist circumference and improve insulin resistance, ultimately leading to better blood sugar control in patients. Some patients can effectively control blood sugar through KD even without taking drugs [11].

4. Safety and potential risks of KD

Short-term and long-term safety: Although KD has shown significant effects in the management of some health problems, its safety and potential risks still need to be carefully considered. KD is helpful in the short term for people with epilepsy. The short-term effects of KD are not only seen in helping people with epilepsy, but also in potential benefits for weight loss and T2DM management. Many studies have shown that KD is able to rapidly promote fat burning and significantly reduce weight in the short term, so some people use it to lose weight quickly. KD may also help control blood sugar by reducing blood sugar and insulin levels, making it a management option for people with T2DM. In addition to losing weight and treating diabetes, studies have shown that about half of children have a 50% reduction in seizures after 6 months, and about one-third of these patients have a more than 90% reduction in seizures [12]. But while patients benefit, there are also side effects, such as gastrointestinal discomfort, low blood sugar, dehydration and fatigue. Even some patients have reported symptoms of "ketogenic flu." Ketogenic flu refers to symptoms such as headaches, nausea, fatigue and trouble concentrating that can occur early in a diet as the body adjusts to low carbohydrate intake [13].

Although KD shows some efficacy in the short term, especially positive effects on weight management and blood sugar control, it may pose some metabolic risks in long-term use. These risks include dehydration, hypoglycemia, ketoacidosis, and lipid metabolism disorders such as elevated triglycerides and low-density lipoprotein (LDL) cholesterol. While there may be improvements in some aspects, such as HDL cholesterol levels, the long-term effects on cardiovascular diseases such as arteriosclerosis are less clear. Therefore, while short-term benefits may be seen, the long-term health risks are worth treating with caution [14].

Risk of nutritional imbalance: KD is also at risk of nutritional imbalance. Because of its high-fat, extremely low-carbohydrate nature, this nutrient ratio can lead to multiple micronutrient deficiencies, especially in the case of long-term implementation. KD may lead to deficiency of vitamins and minerals, especially important trace elements such as folate, calcium and magnesium. Even with multivitamin supplementation, levels of certain micronutrients remain inadequate, especially as observed in patients maintaining long-term KD [14]. In addition to vitamin deficiency, insufficient intake of minerals and fiber is also the main cause of nutritional imbalance. Early KD due to water loss, often accompanied by the loss of sodium and potassium, resulting in electrolyte imbalance. It follows that societies without fiber-rich foods, such as fruits and beans, are at risk of constipation and indigestion.

Suitability for specific populations: KD is not suitable for everyone, and some populations need to be extra careful when starting this diet, or may not be suitable for it at all. For example, for children and adolescents, especially those who use KD to treat epilepsy, they must always pay attention to their nutrition and growth. For some metabolic diseases such as glucose transporter 1 deficiency (GLUT-1 deficiency), pyruvate dehydrogenase deficiency (PDHD), and some refractory epilepsy children, KD has been used and proved to have a certain effect. However, for autistic people with food selectivity disorder, strict dietary restrictions can lead to implementation difficulties [14]. KD may affect the normal development of the children and can also cause nutritional imbalance. Therefore, this diet must be carried out under the guidance of a doctor, and regular nutritional checks are required.

While KD can be helpful for some adults, it is not suitable for all adults. In particular, those with kidney problems or metabolic disorders may not be able to maintain KD for long. When considering long-term use, their health must be carefully evaluated to ensure that they will not cause harm to the body in the process of burning fat. Overall, although KD works well for some health problems, its short - and long-term risks need to be carefully considered.

5. Conclusion

KD has shown promising results in the treatment of obesity, T2DM and epilepsy. It reduces the intake of carbohydrates, forcing the body to rely on fat and ketone bodies for energy. This helps promote fat burning and weight loss, while also improving insulin sensitivity and blood sugar control. Especially for patients with refractory epilepsy, KD has been shown to be effective in reducing the frequency and severity of seizures.

However, KD is not without risks. Long-term adherence may lead to nutritional imbalances, especially insufficient mineral and fiber intake. In addition, due to high fat intake, it may lead to high triglycerides and elevated LDL cholesterol, increasing the risk of cardiovascular disease. It is also important to note that although there may be some positive effects in the short term, the number of beneficial bacteria may decrease in the long term, affecting gut health. Therefore, when considering KD, both security and personalization need special attention. In the early stages of KD, electrolyte imbalances (such as the loss of sodium and potassium) are a common problem, which can make people feel tired and uncomfortable. In addition, the symptoms of "ketogenic flu" can also cause headaches, fatigue and lack of concentration. Therefore, it is recommended to consult a doctor before starting KD, regularly monitor electrolyte levels, and supplement with necessary nutrients.

KD is not suitable for everyone, especially patients with kidney problems or metabolic disorders, and long-term use may be avoided. A personalized diet is important, especially for children with epilepsy, people with diabetes, and those who want to lose weight, and should be tailored to the individual's health and goals. Therefore, before making a choice, it is best to discuss with a doctor or dietitian to ensure that KD is right for you and to reduce possible side effects.

Future studies should focus on the long-term safety of KD, especially on its effects on the gut microbiota. At the same time, it is also important to explore how to alleviate the potential nutritional imbalance by supplementing vitamins, minerals and fiber. An improved KD may require more personalized guidance to ensure it balances effectiveness with safety.

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