

Effect of High-fat Low-carbohydrate Diet on the Structure of Intestinal Flora in T2DM Patients: A Narrative Review

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Abstract: High-fat low-carbohydrate diets are currently popular as one of the methods of weight loss, and the influence of this diet on the structure of intestinal flora in T2DM is a topical issue in the field of research. Despite the controversial result of the studies published so far in patients with type 2 diabetes. As one of the important microbial symbiotic systems in the human body, the intestinal flora is considered to be closely related to the development of type 2 diabetes. The intestinal flora structure abundance of type 2 diabetes patients is different from that of the general healthy population, and alterations in the structure of the intestinal flora can affect intestinal hormone secretion, which in turn affects the blood glucose level in type 2 diabetic patients. It is feasible to treat type 2 diabetes by altering the intestinal flora. Therefore, this narrative review proposes that the possible reason for the treatment of T2DM by high-fat low-carbohydrate diet is that the method of high-fat low-carbohydrate diet alters the intestinal flora structure of patients with T2DM, and treats patients with T2DM by altering their intestinal flora structure, which provides some new ideas and methods for the treatment and prevention of T2DM.

Keywords: High-fat Low-carbohydrate Diet; T2DM; Intestinal Flora.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic disease caused by a pathological state of insulin deficiency and insulin resistance, characterized by high blood sugar, relative insulin deficiency, and insulin resistance. Insulin resistance is generally understood as a condition in which the pancreas does not produce insulin properly, resulting in a rise in blood sugar. Previously, T2DM was more common in older people, but now more and more young people, and even children, are being diagnosed with the disease and are facing increasing numbers of cases worldwide, making it one of the most serious current health problems. At present, there are many treatments for T2DM. Studies have shown that weight control is of great significance for the treatment of type 2 diabetes, and the remission of T2DM can be largely explained by weight loss.[1]

A high-fat low-carbohydrate diet, also known as a ketogenic diet, is an approach to eating that is high in protein, fat, and low in carbohydrates, or understood to be a dietary pattern that is predominantly fat, moderately high in protein, and low in carbohydrates. Typical the diet is structured to contain less than 30 per cent of energy from carbohydrates and more than 50 per cent from fats and varying types of quantities of proteins, with a high intake of animal and/or vegetable proteins and usually a high intake of fats. The principle of a high-fat low-carbohydrate diet is to force the body to rely on fat as its primary source of energy by reducing carbohydrate intake. When carbohydrate intake is reduced, the body's insulin levels drop, prompting adipose tissue to release fatty acids and convert them into energy for use by other tissues. At the same time, ketone bodies are also produced as an alternative energy source to meet the body's energy need.

A high-fat low-carbohydrate diet positively affects type 2 diabetes by modifying the body's energy metabolic pathways.

Firstly, due to reduced carbohydrate intake, blood glucose concentrations are effectively controlled, helping to lower blood glucose levels in type 2 diabetes. Secondly, a high-fat low-carbohydrate diet can also promote the oxidative metabolism of body fat and reduce fat accumulation, achieving weight loss and improving insulin resistance. The main reason why most researchers have advocated low-carb diets in recent years is to balance blood sugar, as blood sugar shock can bring about the dangers of inattention, diabetes, obesity, cardiovascular disease and so on. Only meat and fats in the daily diet do not cause shocks to blood sugar (where shocks refer to blood sugar going up and down quickly, as well as exceeding normal range values). High-fat low-carbohydrate diet is one of the new breakthroughs in nutrition research at present. Many studies have been carried out around high-fat low-carbohydrate diet or ketogenic diet at domestic and international. By exploring the effects of high-fat low-carbohydrate diets on the intestinal flora of T2DM patients, people can better understand the mechanism of action and provide a scientific basis for clinical practice.

The intestinal flora in the human body depends on the host's intestinal environment, and also helps the host perform many physiological and biochemical functions. The intestinal microbiota lives and replicates on the intestinal surface, forming a stable system that protects invasion by pathogenic microorganisms. The majority of the intestinal flora in the structure of the human body belongs to four main families (phylum): Firmicutes, Bacteroides, Proteobacteria, and Actinomycetes.[2]

In recent years, many studies have found that there is an inseparable relationship between intestinal flora and human metabolic diseases. One of the reasons for many metabolic abnormalities such as obesity may be the imbalance of intestinal flora. The main principle of abnormal metabolism is that lipopolysaccharide and other endotoxins produced by the imbalance of intestinal flora enter the human body and are

"caught" by immune cells, producing a variety of inflammatory factors, making the body enter a low-degree inflammation state. For example, a long-term high-fat and high-carbohydrate diet will increase the proportion of opportunistic bacteria in the gut flora and reduce the proportion of symbiotic bacteria, making it easier for the energy consumed in food to be converted into fat and accumulate under the skin, leading to obesity. Moreover, low-grade inflammation can reduce the body's response to insulin and lead to insulin resistance.

There is an intense association between the intestinal flora and T2DM. The structure of the intestinal flora in T2DM differs from that of healthy human, and this difference may be relevant to the onset and progression of the disease. Specific species vary. Some experiments have shown that circulating short-chain fatty acids (SCFAs) and bile acids (BAs) are increased, and the decrease of SCFA level may destroy the host metabolic homeostasis. BA metabolic disorders can affect intestinal BA receptor expression, thus damage related to glucose metabolic pathways.[3]

2. Domestic and International to Diet Intervention or Regulating Intestinal Flora Research Progress for the Treatment of T2DM

2.1. Dietary Interventions

The most studied is the Mediterranean-style diet. The Mediterranean diet is a traditional dietary habit and lifestyle in the countries bordering the Mediterranean. The Mediterranean diet has many factors: eat more fruits, vegetables, whole grains, beans and nuts, use extra virgin olive oil instead of butter or oil, other limitations to dairy and red meat, sweets, added sugar, sodium (salt) and highly processed foods.

2.2. Intestinal Flora Regulation

The possible mechanisms of intestinal flora in the occurrence and development of T2DM include affecting glucose and lipid metabolism, intestinal barrier function, the level of short-chain fatty acids (SCFAs), the level of bile acids (BAs), and regulating the level of intestinal peptide hormones. Some studies have shown that the regulation of intestinal flora is related to the mechanism of berberine (BBR) in the treatment of T2DM. Berberine (BBR) can significantly improve the richness and diversity of intestinal flora, and relieve the symptoms of type 2 diabetic rats by affecting the composition of intestinal flora and reducing the concentration of serum aromatic amino acids (AAAs). [4] Also studies show that hyaluronic acid (HA) in patients with diabetes has a great impact on the intestinal flora and its metabolites, HA has beneficial effects on intestinal flora, changing the structure of the diabetes mice intestinal flora and metabolites belong to spend. At the same time, the intestinal flora of patients with T2DM will be affected by taking drugs during the treatment. Dimethyl guanidine, for example, is a widely used drug, on glucose metabolism and diabetes complications associated with obvious benefits. But it also altered the composition of the microbiota: it increased the abundance of *Mucorophilus*, *Lactobacillus*, and *Escherichia*, and decreased the abundance of some pathogens. In the gut, metformin not only can improve glucose uptake, also can promote the production of short chain fatty acids (SCFAs), protect the intestinal barrier,

regulating the secretion of intestinal peptide.[5] In the study of Lutong Shang et al., found that black tea by activating PI3K/Akt pathway regulating insulin resistance and glucose metabolism, have fall blood sugar function. [6]

3. Current Research Progress on High-fat and Low-carbon Water Diets at Home and Abroad:

High-fat low-carbohydrate diets are used to treat epilepsy, autism and Alzheimer's disease. It also has a beneficial effect, and has been widely used in the treatment of diseases of the nervous system, has become a popular way to lose weight.

The use of low-carbohydrate diets for T2DM is controversial. However, current studies at home and abroad have shown that high-fat diet can not directly play a good therapeutic effect on T2DM patients, and even lead to excessive lipid intake and acidosis, resulting in aggravated disease. Here are some case studies showing that low-carbohydrate water diets, such as ketogenic diets, when patients are taking sodium-glucose cotransporter-2 inhibitors (SGLT2i), patients are at risk for ketoacidosis, which is associated with this drug, and patients taking SGLT2i should do so when asking their doctor if they can incorporate a ketogenic diet into your life. With respect to low-carbohydrate diets and all-cause and cause-specific mortality, studies have shown that both high-carbohydrate diets are associated with a higher risk of death. Meanwhile, low-carbohydrate diets (LCD) rich in plant-based protein and fat sources were associated with lower total and cardiovascular mortality.[7]

Existing scientific literature suggests that the LCHF diet on the control of the studies of obesity and diabetes (weeks < 2 years) do to lose weight, blood sugar and insulin has a favorable effect, also have some not too ideal, such as increasing the low density lipoprotein cholesterol, reduce blood vessel reactivity, and so on.[8]

Studies have shown that a very low-calorie ketogenic diet can also improve blood sugar, glycated hemoglobin, insulin resistance index, and triglyceride levels in overweight or obese people with diabetes. However, there was no significant effect on insulin levels, total cholesterol, urea, creatinine, and uric acid levels in overweight or obese people.

4. Current Domestic and International Studies Related to the Structure of Intestinal Flora

The structure and function of the intestinal flora changes directly affect human body health, play an important role in the occurrence of various diseases. Studies have shown that the facial SCFAs content, especially the acetic acid and butyric acid content, and the expressions of GPR41 and GPR43 are significantly decreased in rats with different stages of T2DM. The cfasegpr41/GPR43 network of intestinal flora may play an important role in the occurrence and development of T2DM.

All in all, intestinal flora and has a strong link between T2DM. Intestine flora imbalance may be an important factor in the development of T2DM, by adjusting the composition and function of intestinal flora, is expected to provide new strategies for prevention and control of T2DM, is helpful to further reveal the pathogenesis of T2DM, which will provide a scientific basis for individualized treatment and nutritional

intervention.

5. The Relationship between High-fat low-carbohydrate Diet and Microbiota

In recent years, high-fat low-carbohydrate diet as an emerging dietary pattern has attracted much attention. This dietary pattern changes the nutritional status of the body mainly by restricting carbohydrate intake and increasing fat intake. Many studies have shown that there is a close correlation between high-fat low-carbohydrate diets and intestinal flora.

First, the high-fat low-carbohydrate diet can change the composition of the intestinal flora. Studies have pointed out that the high fat diet can make certain bacteria of the genus number increased significantly, especially rich in fatty acids generated bacteria number. At the same time, due to the decrease in carbohydrate intake, the number of other genera may decrease accordingly. This compositional adjustment may lead to an imbalance in the flora, which in turn affects the function of the gut microbe. Secondly, high-fat low-carbohydrate diet can also alter the metabolic activity of gut microbiota. A high-fat diet has been found to promote the production of more short-chain fatty acids, such as propionate and butyrate, in certain bacteria. The short chain fatty acids metabolism plays an important role to the human body, can be used to provide energy, adjust the intestinal peristalsis, and have anti-inflammatory and immune regulation, and other functions. However, a high-fat diet may also cause certain bacteria to produce large amounts of harmful metabolites such as cholesterol and oxalic acid, which can negatively affect human health. In addition, the high-fat low-carbohydrate diet may also change the intestinal environment, affecting the survival and proliferation of intestinal flora. Due to increased fat intake, a better redox balance may develop in the gut. At the same time, the reduction of carbohydrates may change the pH and mucus layer structure in the intestine, which in turn affects the colonization and reproduction of different bacterial genera. This change can lead to a shift in the flora, which affects its function and health for the human body. In conclusion, there is a complex correlation between high-fat low-carbohydrate diets and intestinal flora. Although there is still some controversy about the effect of high-fat low-carbohydrate diet on the intestinal flora, the impact of this dietary pattern on the microbiota can be further studied to better understand its impact mechanism on human health. At the same time, it can also help to provide scientific basis for nutrition regulation and related disease treatment, and promote the development of personalized nutrition intervention strategies.

It has been demonstrated that a consistently unbalanced diet impairs the stability of bacterial communities to environmental perturbations. Some articles have pointed out that dietary adjustment can change the structure of human intestinal flora, control glucose metabolism, and cause obesity. There are also some research has shown that by high-fat low-carbohydrate diet, reduce body fat, reach the purpose of reducing weight, reduce the probability of the metabolic syndrome, thus reducing insulin resistance, achieve the goal of control blood glucose levels.[9]

6. Conclusion and Outlook: The Way Forward

At present, the research and discussion on high-fat low-carbohydrate diet and T2DM show a tendency to be reversible. When recommending this diet for T2DM patients, it is necessary to strictly control the drugs and dosage of patients, so as to better avoid the negative effects. Considering the high fat, low carbohydrate diet effects on patients with T2DM, it should be noted that so far there is no conclusive results show that the effect of the unidirectional nutritional mode. Therefore, patients with T2DM nutrition model components should be unique to compensate for the need of the blood sugar levels and diabetes other parameters as the instruction, but must pay attention to the use of individual diet, pay attention to current health, according to the patients used in the treatment of pharmacological methods, and the patient's individual characteristics, have regular meals and appropriate physical activity.

The dysregulation of intestinal flora may be an important factor in the occurrence and development of T2DM. Regulating the composition and function of intestinal flora may provide a new strategy for the prevention and treatment of T2DM. In the near future, structural changes in the intestinal flora could be considered in microbiome-specific dietary interventions developed for the prevention or treatment of T2DM, and intestinal flora characteristics may be related to observed different responses to dietary interventions or pharmacotherapy, so there are interpersonal differences at the phylum level that should be considered when studying the role of a certain intestinal flora phylum in disease development.

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