Comparing the Intervention Effects of the Low-carbohydrate Diet and the Ketogenic Diet on Type 2 Diabetes

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Abstract. Diabetes is a serious issue in human society, and over 90 percent of all cases are type 2 diabetes. Type 2 diabetes is caused by multiple factors such as genetic factors, dietary factors, and metabolic factors. Since dietary factors are one of the causes of type 2 diabetes, scientists and doctors consider food therapy to be a feasible method to intervene in diabetes. Low-carbohydrate and ketogenic diets are applied by many people who want to lower their carbohydrate intake, reduce their blood glucose level, and lose weight. These two dietary patterns are often applied to patients with type 2 diabetes, too. This paper will describe about the causes and pathophysiology of type 2 diabetes, introduce the low-carbohydrate diet and the ketogenic diet respectively, and then compare their intervening effects on type 2 diabetes. Neither dietary pattern is the most suitable for type 2 diabetes treatment as the intervening effects are limited. Also, the side effects of the two dietary patterns must be considered when applying them to patients with type 2 diabetes.

Keywords: Type 2 diabetes; Dietary patterns; Low-carbohydrate diet; Ketogenic diet; Intervening effects.

1. Introduction

Diabetes Mellitus is a common disease in modern society, with an estimated 422 million patients worldwide [1]. Type 2 diabetes (T2D) accounts for over 90% of patients and is more common in older adults compared with type 1 diabetes. Although T2D is not a fatal disease, it will bring various problems to the patients: they are more likely to get cardiovascular diseases; they tend to have problems with cut recovery; they often experience headaches and fatigue; and, with a long-term high blood glucose level, their eyesight may also be damaged. Scientists have found that T2D patients are often overweighed or experience obesity. Thus, diet is often taken into consideration when concerning on intervening in T2D. In the early years, T2D patients were recommended a high-carbohydrate, low-protein, and low-fat diet, which aimed a weight loss [2]. However, later research has found that carbohydrates contribute the most to blood glucose regulation, thus taking in excess carbohydrates will have side effects on controlling blood glucose levels.

For this reason, dietary patterns with low carbohydrate intake were created to help regulate the blood glucose level. These dietary patterns have a mutual name as the low-carbohydrate diet (LD). The LD contains fewer carbohydrates and tends to have more proteins and fat to fill the gap left by reducing carbohydrate intake. The LD does show efficacy in blood glucose control and weight loss. Meanwhile, another similar but slightly different dietary pattern, the ketogenic diet (KD), was created also for losing weight. The KD generally has even less carbohydrate content than the LD. This dietary pattern is a very efficient method for fat burning.

Both dietary patterns may have effects on weight control, and blood glucose control. However, risks are also found for each that side effects might occur as a result of inadequate usage of the LD and the KD. Appropriate usage of these two diets is very crucial to a person's health.

In this paper, both the side effects of the LD and of the KD will be provided, and the comparison of the two diets will show which one is more suitable for which case. Moreover, their intervention effects on T2D will be given.

2. Causes and Pathophysiology of Type 2 Diabetes

T2D is often triggered by multiple factors, which include a complex combination of genetic, environmental, and metabolic factors. Among all those factors, genetics play a very strong role in causing T2D, and the incidence of T2D tends to increase in families with more members having T2D. Other factors such as obesity, lack of physical activities, unhealthy diets, and abnormity in insulin secretion could also lead to T2D. Although T2D is strongly inheritable, it can be intervened, which means avoiding or delaying the time of onset, by following appropriate dietary patterns.

T2D is the result of abnormal insulin levels caused by pancreatic β-cell dysfunction and the inability of insulin-sensitive organs (mostly in muscles, liver, and fat tissue) to respond correctly to insulin regulation [3]. Insulin is a peptide hormone that regulates blood glucose homeostasis. In normal cells, there are insulin receptors and glucose channels on the surface. Once insulin binds the receptor, a signaling cascade will be triggered and the glucose channel is opened (Fig. 1). Glucose will be able to go into the cell and the glucose concentration in the blood vessel will be controlled to a normal level. However, the insulin-resistance organs will fail to transport glucose into the cell, so the glucose will be mistakenly left in the blood vessel and the circulatory system.

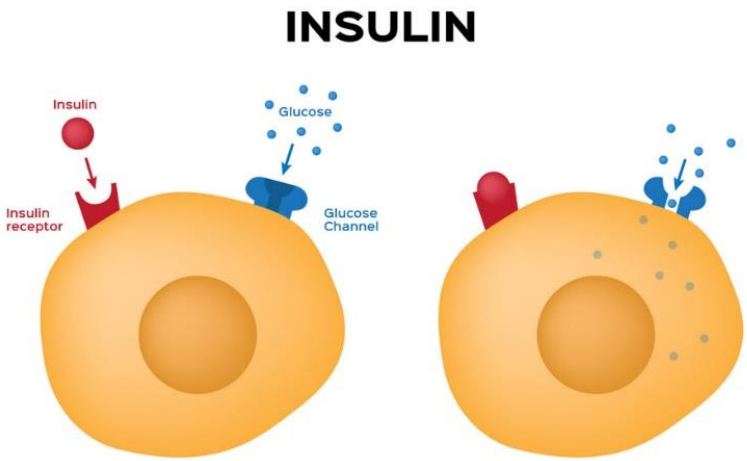

Fig 1. How insulin functions in an insulin-sensitive cell [3]

This will eventually result in long-term high blood glucose levels and can lead to disorders of the urinary, circulatory, nervous, and immune systems. The urinary system, for example, will be affected by the high glucose concentration in the blood. Excess glucose enters the urine, which the phenomenon is known as glycosuria, as the blood glucose level in the kidney exceeds the threshold of reabsorption. The high concentration of glucose in the urine will produce a hypertonic environment in the kidney so that reabsorption will be inhibited, and urine production will be promoted. As a result, the loss of water in the body will be increased, so the body compartments will undergo dehydration, and the patient will be more likely to feel thirsty.

So far, insulin injection is the most applied therapy for T2D patients with severe symptoms. Those patients need to inject insulin every day after meals to control their blood glucose levels.

3. Role of the Low-carbohydrate Diet on Type 2 Diabetes

The concept of a LD was first held out by Dr. Irwin Stillman in the late 1960s, as he was trying to find out a method that can quickly help a person lose weight. The Stillman diet, a high-protein and LD, was considered the first prototype of the LD. In the 1970s, another well-known LD, named the Atkins diet, was created by Dr. Robert Atkins [2]. This dietary pattern was created in the background when scientists considered excessive protein and fat to be dangerous, thus the Atkins diet was initially held out. In later generations, more and more similar dietary patterns were created, which all follow a basis to have low carbohydrate content and adequate protein and fat content.

3.1. Characteristics

A LD is a general group of diets that generally restricts the average carbohydrate intake in the overall diet. Carbohydrate-rich food such as bread, rice, and sugar contents are replaced by food with plenty of fat, fiber, and proteins, such as meat, seafood, mushroom, and fibrous vegetables.

Given the pre-condition of carbohydrate restriction, scientists came up with a new concept called the glycemic index (GI). GI assigns numbers 0 to 100 to food to indicate the rise in blood glucose level 2 hours after consuming that food. Food with a high GI means it is rapidly digested and absorbed, and vice versa. The higher level of the GI is, the higher the blood glucose level would rise in the time interval. Glycemic load (GL) is an extension of the concept of GI, which is GI times the grams of carbohydrate in a serving divided by 100. GL gives a more accurate measurement of the real-life postprandial rise of blood glucose levels. In LD, food with low GL is recommended to reduce carbohydrate intake, thus lowering the rise of blood glucose levels.

3.2. Intervention Effects on Type 2 Diabetes

It is a challenging process for the treatment of T2D since it is often caused by a combination of genetics, diets, body weight, living habits, etc. Although there isn't a clear view of a specific dietary pattern that can most effectively intervene in T2D so far, recent studies suggest a LD shows decent effects on T2D. A LD shows great improvements in short-term glycemic control, weight loss, and cardiovascular disease risk [4, 5].

In studies on T2D, a certain type of hemoglobin called glycated hemoglobin (HbA1c) was measured for patients with T2D. HbA1c is an indicator that its reduction indicates the intervening effect on T2D. The higher the reduction the greater the intervening effect is. According to research in 2013, a group of researchers tested the intervening effect of a LD on 146 patients with T2D [6]. The results show that a 48-week application of the LD can reduce the HbA1c level, body weight, and sugar contents in the body (Table 1.). However, this improvement cannot be long-term sustained. The results of the research above indicate a LD is a feasible way to intervene in T2D in the short term, but the treatment effect of diabetes over a long period is insufficient.

Table 1. The contents of BMI, Body Weight, HbA1c, and Fasting Glucose in the T2D patients' bodies After a 48-week LD Treatment [6].

Measurement	Week 0	Week 48	Net change after 48 weeks	P Value
BMI (kg/m2)	38.7	36.3	2.4	0.7
Body weight (kg)	116.9	109.4	7.5	0.8
Hemoglobin A1c %	7.6	6.9	0.7	0.045
Fasting glucose, mg/dl	152.6	133.7	18.9	0.2

Although a LD cannot bring the long-term blood glucose level back to a normal level, it brings a basic direction to the treatment of T2D. The ideal dietary pattern for T2D treatment can be nearly confirmed to have a relatively low carbohydrate content.

3.3. Side Effects

Despite a LD can intervene in T2D in a short time, there are also some non-negligible disadvantages. Carbohydrates are the main source of energy in the body, so they are essential for the organs and the central nervous system. Reducing carbohydrate intake may result in headaches, fatigue, difficulty concentrating, nausea, constipation, etc. [7]. Low carbohydrate content in the body may be also harmful to children's brain development, Therefore, a LD is especially not suitable for people in the growth periods of childhood or adolescence.

Furthermore, having a LD may also be risky for urinary calcium loss and bone mineral loss [7]. Urinary calcium level indicates whether the kidney is under stone formation and other medical issues. One study shows that reducing the carbohydrate intake for rats can result in urinary calcium loss and bone mineral loss. Although another study group found no significant effect of a LD on the rats' bone

mineral density, the problem is still worth considering. Further studies are expected to test for the effects on urinary calcium levels and bone mineral content after having a long-term LD.

4. Role of the Ketogenic Diet on Type 2 Diabetes

Society has become more concerned about the popularity of the KD's potential role in weight loss, improved metabolic health, and as a potential therapeutic approach for various conditions, including T2D. This dietary pattern has a century of history in which the concept was first held out in 1921 when Woodyatt and Dr. Wilder concurrently discovered the benefit of fasting and the chemical produced by the body during fasting [8]. Since a series of chemicals called the ketone bodies will be produced during this diet, the dietary pattern was named the KD.

4.1. Characteristics

The KD has high fat, moderate protein, and very low carbohydrate content. The reduction in carbohydrates leads to a metabolic state called ketosis, in which the body breaks down fats into ketone bodies for energy instead of carbohydrates. When the carbohydrate intake is extremely low, the body doesn't have enough carbohydrates to burn for energy. In this case, fats become a substitution for energy synthesis. As the body breaks down fats, it produces chemicals called ketone bodies. These ketone bodies then serve as the main energy source for the body [9].

Since the body requires a large amount of fat to produce ketone bodies, they burn the fat intake from the food and the fat previously stored in the body. Therefore, the KD can effectively help the body lose weight, as well as lowering the risk of some cardiovascular diseases caused by obesity.

4.2. Intervention Effects on Type 2 Diabetes

Since the KD has a very low carbohydrate intake, it can naturally lower blood glucose levels. This reduction in blood glucose level may then reduce the demand for insulin. Lowering the demand for insulin can help mitigate the disadvantage for T2D patients whose bodies cannot secrete sufficient insulin to normalize their blood glucose levels. This can lead to better glycemic control and help patients with T2D reduce or eliminate the need for insulin medications [9].

Table 2. The HbA1c and FBG content in the T2D patients' bodies before and after a 3-month KD treatment [10].

Parameter	Sample size (n)	Mean value (before)	Mean value (after)	P value
HbA1c (%)	8	10.5	5.99	0.001
FBG (mmol/L)	8	13.99	6.63	0.021

Recent research focused on a group of people with diabetes issues after a 3-month KD treatment. The researchers focused on the index HbA1c. Patients with more severe diabetes tend to have higher HbA1c levels. Compared to the mean value of HbA1c level before the treatment, the mean value after the treatment has a significant decrease of almost half that before (Table 2). The results reflect a positive intervening effect on T2D after a 3-month KD treatment (Fig. 2) [10].

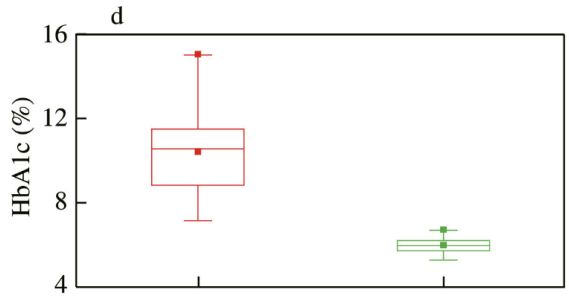

Fig 2. The box plot of the percent HbA1c. The red box represents that before the treatment, and the green box represents that after the treatment [10].

Moreover, the KD may also be used as an insulin-sensitizing medication. Since the KD can reduce the amount of glucose and insulin circulating in the bloodstream, insulin sensitivity may be increased. This can in some ways reduce insulin resistance, one of the primary causes of T2D.

4.3. Side Effects

Like the LD, the KD also has potential side effects. The most common side effect caused by a KD is called the "keto flu". In the keto flu, patients often experience symptoms like nausea and vomiting, headache, extended tiredness, dizziness, insomnia, and constipation [11]. Although the keto flu is only considered a minor short-term side effect, optimal use of the KD is very necessary.

Since the KD has very low carbohydrate intake and high fat intake, low bone mineral density, kidney stones, and high cholesterol are also possible risks for the KD. These issues are all worth concerning in future studies.

5. Comparison

One of the most common characteristics between the LD and the KD is they both have low carbohydrate intake. Low carbohydrate intake can effectively reduce the blood glucose level and the need for insulin. Thus, both dietary patterns can improve glycemic control. They also share similar shortages such as bringing headaches, fatigue, dizziness, insomnia, nausea, difficulty in exercise tolerance, and constipation to the patients. What's more, the low carbohydrate intake may also result in kidney stones and bone mineral loss.

Besides the similarities, the two dietary patterns have differences in some ways. Although the LD sounds to be having a very low carbohydrate intake, at about 50-150 grams per day, the KD restricts carbohydrate intake even more to less than 50 grams per day. Only the KD is able to induce ketosis since its carbohydrate intake has been decreased to an extremely low level. For this reason, the KD also has a slightly higher risk of kidney stones than the LD. Also, although both dietary patterns consume fat as a primary source of energy, the KD requires a higher fat intake, typically around 70-80% of total daily calories. This higher fat intake is required for ketosis.

As for sustainability, the LD can be sustained for a relatively longer time, as they allow for a wider variety of foods and the restrictions are less than the KD. The KD can be more challenging to maintain, as it requires strict conditions to force the body into ketosis. This process requires accurate tracking of macronutrient intake and will restrict the range of food available.

Neither the LD nor the KD is the best dietary pattern for intervening in T2D. The side effects are non-negligible considering factors of choosing the method for treatment, so applying the two dietary patterns should be under the guidance of experts. Also, the most ideal dietary pattern still remains undiscovered yet.

6. Conclusion

According to the research, both the low-carbohydrate and the KD can intervene in T2D that they can reduce blood glucose levels to a normal level in a short period. The KD can more effectively reduce the HbA1c level in patients' bodies, which means the KD can reduce the blood glucose more significantly Lowering the blood glucose level reduces the essential need for insulin rejection and other insulin treatments. Also, the KD can be further used as an insulin-sensitivity therapy that can assist in the recovery of insulin sensitivity of the patient's organs. However, both dietary patterns have their limitations in that neither is sufficient for the treatment of T2D. Since T2D is caused by multiple factors, the treatment should be a combination of food therapy, medical treatment, and a change in unhealthy lifestyles. Moreover, both dietary patterns have potential side effects that might harm the patient's body, so they are not suitable for long-term usage.

Since both the low-carbohydrate and the KD have side effects, nor can they intervene in T2D in the long term, they are not the most suitable dietary pattern for food therapy for T2D. They bring an

idea for food therapy for T2D that the dietary pattern should have a relatively low carbohydrate content, a moderate protein intake, and a reasonable fat intake. Future studies should look for a dietary pattern that can maximize its intervening effects in T2D and minimize the limitations concurrently. Also, merely applying food therapy is insufficient for treating T2D. Therefore, combining medical treatment and the ideal dietary pattern will probably be one of the future solutions to T2D.

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