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The Induction of Diabetes by High-Sugar and High-Fat Diets and Potential Applications of Healthy Eating

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Abstract:

The rising prevalence of diabetes has intensified research in this field. Among the various causes of diabetes, insulin resistance plays a crucial role. High-sugar, high-fat diets are known to induce hyperglycemia and obesity, which significantly affect the progression of insulin resistance. It should be noted that obesity can significantly increase insulin resistance, thereby inducing prediabetes and aggravating diabetic symptoms. Additionally, such diets disturb the balance of intestinal flora. Controlling carbohydrate intake through low-carb or ketogenic diets can effectively improve glucose and lipid metabolism, improving insulin sensitivity, reducing insulin resistance, and lowering insulin levels. Adjustments to diet can also help shape a healthy gut flora composition. Furthermore, consuming natural products like flavonoids can also contribute to the improvement of diabetic symptoms. This article summarizes the impact of high-sugar, high-fat diets on the progression of diabetes, their effects on insulin resistance and intestinal flora, and the regulatory benefits of a healthy diet in managing diabetes.

Keywords: Diabetes; Insulin resistance; High-sugar and high-fat diets; Obesity; Diet

1. Introduction

Type 2 diabetes mellitus (T2DM) is primarily characterized by hyperglycemia, which results from a relative deficiency in insulin secretion and insulin resistance. Prolonged hyperglycemia can lead to acute complications such as ketoacidosis and chronic complications. Insulin resistance (IR) is a key factor contributing to hyperglycemia. Extended consumption of high-sugar and high-fat diets can seriously affect blood glucose levels and impair the pancreas' ability to secrete compensatory insulin, thereby causing insulin resistance [1]. Additionally, obesity is a major trigger for T2DM. Overweight and obese individuals are more prone to insulin resistance and compensatory hyperinsulinemia [2]. The prevalence of diabetes is higher among overweight and obese individuals and is increasingly affecting younger populations. Thus, it is essential to study the impacts of high sugar and high fat diets on diabetes. This paper explores how these diets trigger hyperglycemia and obesity, subsequently leading to diabetes and the associated disruption of intestinal flora, as well as strategies to improve diets structure. Regarding nutritional management for diabetes, ketogenic diets (KD) and low-carb diets are commonly used to reduce weight, improve blood glucose levels, and regulate energy metabolism.

2. Insulin resistance and T2DM

Studies have found that a high-sugar and high-fat diet can trigger insulin resistance. The mechanism by which such a diet induces insulin resistance may involve an increase in plasma triglyceride and free fatty acid levels, which inhibit glucose storage and reduce insulin sensitivity through various pathways, including the glucose-fatty acid cycle and insulin signaling, ultimately leading to insulin resistance [3]. In mouse and rat models, hyperinsulinemia and insulin resistance can be induced by high-sugar and high-fat intake. If pancreatic function is impaired, for instance by the injection of streptozotocin (STZ), it can lead to the dysfunction of compensatory insulin secretion by the pancreas, resulting in hyperglycemia [4].

When insulin resistance occurs, as long as the pancreas can maintain a high enough level of insulin secretion to overcome insulin resistance, glucose tolerance remains normal or only mildly impaired. Once pancreatic β-cells start to fail, glucose tolerance rapidly deteriorates, leading to the development of T2DM. Recent advances in endocrinology have highlighted the endocrine function of adipocytes, with tumor necrosis factor (TNF-α) being closely linked to IR. TNF-α impedes the phosphorylation of tyrosine, a substrate of the insulin receptor, and promotes the phosphorylation of serine and threonine, thus interfering

with the insulin receptor and its downstream signaling in the PI-3K pathway. It also down-regulates the expression of glucose transporter-4 (GLUT4) and inhibits GLUT4 translocation from intracellular compartments to the cell membrane. Additionally, TNF-α activates macrophages in pancreatic islets, releases IL-1, induces the expression of NO synthase, and increases NO levels, thereby inhibiting insulin action [5].

3. Unhealthy diets and obesity and T2DM

The effect of a high-sugar, high-fat diet on glucose-lipid metabolism plays an important role in the perception, uptake, and utilization of glucose in adipocytes and muscle cells through the activation of peroxisome proliferator-activated receptors [6]. A high-sugar diet has a linear effect on blood glucose levels, and prolonged intake of high-sugar foods can lead to persistently high blood glucose levels. This can trigger insulin resistance and significant weight gain, further increasing insulin resistance. Prolonged consumption of high-sugar foods results in 100 percent insulin resistance. This is accompanied by symptoms such as increased appetite and thirst, frequent urination, and typical signs of diabetes such as slow healing wounds and body infections [7].

Obesity is one of the major triggers of diabetes mellitus, and a high-fat diet affects insulin sensitivity and secretion, thus interfering with the mechanism of blood glucose regulation. In obese individuals with type 2 diabetes, the number and affinity of insulin receptors on adipocyte membranes are reduced, leading to insulin resistance and a compensatory increase in insulin β-cell secretion, resulting in hyperinsulinemia. Elevated blood insulin levels reduce the number of receptors through down-regulation, creating a vicious cycle, and ultimately causing insulin β-cell function to decline, leading to elevated blood glucose levels [8].

Obesity can exacerbate the development of diabetes mellitus through dysregulated adipocytokine secretion, ectopic lipid deposition, fatty acid lipotoxicity, peroxidase-activated receptor dysfunction, impaired endothelial diastolic function, social and psychological stress, abdominal fat accumulation, and elevated cortisol levels [9]. Adipocytokines are not only coagulation factors but also anti-inflammatory markers and acute-phase proteins synthesized in the liver in response to the IL-6 cycle. Blood coagulation factor I is the main substance involved in bleeding and thrombosis, and its elevated levels can exacerbate coagulation [10].

Prediabetes mellitus (PDM) is a condition where blood glucose levels are intermediate between those of normal subjects and people with diabetes mellitus (DM), usually characterized by impaired fasting glucose (IFG) and abnormal glucose tolerance (IGT). The prevalence of PDM in a community population in Chongqing showed that the prevalence was 16.5%, 16.0%, and 28.7% in 2003, 2008, and 2013, respectively [9]. This indicates not only a high prevalence rate but also an alarming growth rate. PDM not only has a high prevalence among the elderly, but also shows a younger trend [11]. Li Zhi and Wang Wenxi et al. found that the BMI, waist circumference, body fat percentage, and lipid accumulation index of PDM individuals were different from those of the control population, and the specificity of setting a threshold for the diagnosis of PDM was higher than 70% [12]. The prevalence of PDM is relatively high in large cities due to the fast pace of life, work pressure, and dietary irregularities. The prevalence of PDM in the normal BMI population is only 15.8%, while the prevalence of PDM in the overweight and obese population rises to 35.1% and 49.1%, respectively [13].

4. Gut microbiome and T2DM

The microbial populations hosted in the human intestine are collectively known as the intestinal flora, often referred to as the “second largest human genome” due to their vast number and diversity. The balance of the intestinal flora plays a crucial role in human health, and type II diabetes is closely related to this balance. A decrease in beneficial bacteria or an increase in conditionally pathogenic bacteria in the intestinal tract can cause chronic inflammation, leading to the development of type II diabetes. Studies have shown that the intestinal flora of patients with type II diabetes is disturbed to varying degrees, primarily by a decrease in the abundance of some butyrate-producing bacteria and an increase in the abundance of some conditionally pathogenic bacteria [14].

The composition and function of the gut microbiome are linked to host energy absorption and storage, adipose tissue inflammation, and insulin sensitivity. The gut flora of obese individuals tends to differ significantly from that of healthy individuals, with an increase in certain bacterial species and a relative decrease in beneficial bacterial species. This imbalance leads to increased energy intake from food, while promoting the production of short-chain fatty acids, further affecting fat storage and energy metabolism [13]. Diabetes mellitus is one of the consequences of gut microbial dysbiosis caused by nutritional imbalance, which severely disrupts the diversity and stability of the gut flora, reducing the number of beneficial microbiota and increasing the number of conditionally pathogenic microbiota. This triggers chronic low-grade inflammation in the gut, leading to diabetes mellitus [15, 16]. Dysbiosis

also leads to decreased fluctuation of biochemical factors, lower levels of short-chain fatty acids, bile acids, and endocrine-regulating peptides (e.g., glucagon, GLP-1, GLP-2), and increased levels of endotoxins, which further predispose to diabetes mellitus [17].

The intestinal flora in the body can play nutritional, anti-tumour, anti-aging, detoxification, and antagonistic roles. Changes in the quantity and species of intestinal flora can disrupt the intestinal microecological balance and trigger the body's immune response, highlighting the close relationship between intestinal flora and diabetes [18]. Studies have shown that patients with diabetic kidney disease have intestinal flora disorders and decreased immune function. In these patients, the number of Escherichia coli increases while the numbers of bifidobacteria and eubacteria decrease, indicating intestinal flora disorders and bacterial dysbiosis. This is mainly because the glomerular filtration function of patients with diabetic kidney disease is reduced, leading to the accumulation of metabolic wastes and subsequent intestinal flora dysbiosis [19]. Furthermore, in diabetic patients and their animal models, intestinal barrier function is impaired, manifested by morphological changes and increased permeability of the intestinal mucosa. The lactulose-mannose permeation assay has shown that the intestinal mucosal permeability of diabetic patients is significantly higher than that of the normal population, which can impact the gut microbiome [20].

5. Healthy eating and T2DM

T2DM is a metabolic disease that progresses slowly and is difficult to cure. If long-term glycemic control is ineffective, it can lead to multiple organ damage and significantly impact health. This is particularly true for obese T2DM patients, who often have more severe metabolic abnormalities and more significant blood glucose fluctuations. Therefore, clinical management for these patients should focus on both blood glucose and body weight to slow disease progression [20]. Standardized dietary care is crucial for the health management of obese T2DM patients. Formulating dietary plans based on optimal dietary ratios can help reduce glucose absorption and body fat, thus promoting lower blood glucose levels and weight loss.

Studies have shown that adherence to a healthy diet in people with T2DM is closely related to long-term glycemic control. However, patients are often influenced by their natural eating habits and may not follow dietitian-prescribed recipes, continuing to consume large amounts of staple foods like rice and pasta, leading to poor glycemic control [21]. Additionally, the dietary structure affects the composition of the intestinal flora, further influencing the progression of T2DM.

Natural products in the diet, such as flavonoids, can play a significant role in regulating T2DM. The mechanisms include lowering blood sugar, reducing blood lipids, providing anti-oxidation benefits, improving insulin sensitivity, and regulating intestinal flora.

5.1 Controlling blood glucose and lipids

Fluctuations in blood glucose and abnormalities in blood lipids are closely related, so it is important to control blood lipids while managing blood glucose. Lipids are a collective term for the fatty substances in the blood, consisting mainly of cholesterol and triglycerides. Cholesterol can be divided into LDL cholesterol (commonly known as "bad" cholesterol) and HDL cholesterol (commonly known as "good" cholesterol). HDL cholesterol has a protective effect on blood vessels, acting as a scavenger that transports excess cholesterol back to the liver for recycling. This process reduces excess cholesterol deposition in the blood vessels, preventing atherosclerosis. Conversely, excess LDL cholesterol gradually forms small plaques on the walls of blood vessels, leading to atherosclerosis. This condition makes blood vessels less elastic, narrows the vascular channels, obstructs blood flow, and can trigger myocardial ischemia, coronary heart disease, acute myocardial infarction, cerebral infarction, and other cardiovascular diseases.

Patients with type 2 diabetes often have dyslipidemia, and the relationship between blood glucose and blood lipids is very close. In diabetics with insulin resistance, once blood glucose levels rise, more insulin is needed to normalize blood glucose levels. However, excessive insulin stimulates fat synthesis, resulting in elevated blood lipids. These elevated lipids accumulate in adipose tissue and exacerbate obesity, further worsening insulin resistance and ultimately making it more difficult to control blood glucose [22].

5.2 Weight loss and regulation of energy metabolism

High carbohydrate intake requires high insulin doses, leading to significant variations in subcutaneous insulin absorption. Patients on intensive insulin regimens need multiple daily insulin injections, and repeated injections at the same site can cause adiposity. Insulin injected into hyperplastic adipose tissue increases absorption instability, complicating glycemic control in patients with endogenous insulin deficiency [23]. Conversely, a low-carb diet reduces glycemic variability, prolongs the percentage of time in range (TIR), and decreases the number of insulin injections and doses of insulin and oral hypoglycemic agents. A low-carb diet does not increase the risk of hypo-

glycemia and ketoacidosis in these patients.

Recently, the ketogenic diet (KD) has gained popularity as a dietary approach. Numerous studies show KD's hypoglycemic and weight-loss effects in diabetic and obese patients, reducing the dosage of insulin and oral medications, thereby regulating blood glucose levels and improving insulin resistance [24].

KD is a high-fat, low-carbohydrate diet supplemented with moderate protein and other nutrients. In the 1920s, KD was used to treat refractory pediatric epilepsy. Researcher found that KD induces ketone production, simulating starvation, which effectively inhibits epilepsy [25]. Further research revealed KD's neuroprotective and anti-inflammatory effects. With increasing obesity and diabetes rates, dietary intervention has become a hot topic. Low-fat diets can improve fat oxidative metabolism and promote weight loss [26]. Davidson et al. suggested that increased ketone bodies can prevent weight gain and obesity-induced cognitive impairment [27].

Recent studies show significant weight loss efficacy with KD, and over 90% of diabetic patients have concomitant obesity. Type 2 diabetes mellitus is closely associated with obesity. While the mechanisms of obesity and diabetes need further elucidation, ectopic fat accumulation may be a factor in metabolic syndrome [28]. Carbohydrate intake induces insulin secretion, reducing circulating concentrations of metabolic fuels by facilitating glucose uptake into tissue cells, inhibiting fatty acid release and ketone body synthesis in the liver, and promoting fat and glycogen deposition. High-carbohydrate diets, including refined starchy foods and sugars, tend to increase body weight by increasing hunger and slowing the metabolic rate. Dietary intervention is a simple, effective, cost-efficient approach for obese patients with type 2 diabetes. Evidence shows that LCKD is effective in reducing body weight and adiposity. Goss et al. [29] demonstrated that a very low-carbohydrate diet significantly reduced body weight, promoted the reduction of visceral and interstitial adipose tissue, and improved insulin sensitivity and reduced the risk of metabolic disease in the elderly. Conversely, excessive carbohydrate intake increases the risk of insulin resistance and may complicate early diabetic peripheral neuropathy [30]. Therefore, dietary choices significantly impact people with diabetes and obesity.

5.3 Regulation by natural products

A growing body of research confirms the link between gut flora and type II diabetes. Once in the body, flavonoids interact with gut microorganisms and directly influence their biological activity. Flavonoids, a class of secondary metabolites derived from 2-phenylchromenone as the parent compound, are widely distributed in vegetables, fruits, tea, and other sources, and play an important role in the amelioration and prevention of type II diabetes [31].

Over the past few decades, numerous in vitro, animal model, and clinical studies have shown that dietary flavonoids can improve type II diabetes. A meta-analysis of seven prospective cohort studies found that individuals with the highest intake of flavonoids had an 11% lower risk of developing type 2 diabetes compared to those with the lowest intake [31]. Additionally, it was concluded that flavan-3-ols significantly improved lipid metabolism, insulin resistance, and systemic inflammation in subjects [32].

In patients with type II diabetes mellitus, dysregulation of intestinal flora can lead to the development of insulin resistance. Numerous studies have confirmed that consuming foods rich in flavonoids, such as quercetin and apigenin, can improve intestinal flora disorders, reduce insulin resistance, and inhibit inflammation and oxidative stress [33]. This suggests that flavonoids may improve type II diabetes to some extent by regulating the structure of the gut flora [34].

6. Conclusion

High-fat, high-sugar diets have become the most common dietary pattern worldwide. Excessive intake of these components can lead to fat accumulation and obesity, which in turn can result in various metabolic diseases such as diabetes mellitus, cardiovascular disease, hyperlipidemia, hypertension, and other metabolic disorders. Obesity has become a global public health problem that poses a serious threat to human health. The effect of a high-sugar, high-fat diet on glucose-lipid metabolism plays an important role in the perception, uptake, and utilization of glucose in adipocytes and muscle cells through the activation of peroxisome proliferator-activated receptors.

Studies have shown that intestinal flora can effectively regulate the body's metabolism and energy balance, playing a crucial role in preventing the development of obesity. Intestinal flora is a large community of microorganisms residing in the host's intestinal tract, and its main function is to maintain the homeostasis of the body's internal environment. Low carbohydrate diet and ketogenic diet therapy focus on the intake of low-carbohydrate foods, which reduces the intake of total food calories and promotes fat metabolism. This helps to consume body fat and reduce body weight, while simultaneously improving insulin sensitivity, reducing insulin resistance, and lowering insulin levels. The intake of natural products in food, such as flavonoids, also effectively improves the symptoms of diabetes. In summary, a correct healthy diet and reasonable blood glucose control play an important role for diabetic

patients.

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