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Analysis of the effects of the ketogenic diet on diabetes

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Abstract. In recent years, there has been a notable rise in the occurrence and prevalence of both type 1 and type 2 diabetes worldwide. This increase can be attributed to the social and economic progress experienced by countries, leading to improved living standards for residents. Consequently, diabetes has emerged as a significant societal concern, posing a threat to global population health. As a result, governments and relevant authorities have directed their attention towards addressing this issue. Diabetes is a prevalent and often occurring condition that is typically managed with pharmacological interventions. However, prolonged drug treatment can lead to adverse effects on the body. In conjunction with adequate exercise and dietary modifications, these lifestyle interventions can offer significant assistance in the management of diabetes. This paper employs a comprehensive evaluation of existing literature to present a summary of the utilization of the ketogenic diet as an adjunctive therapy for diabetes. The objective is to examine the effects of the ketogenic diet on diabetes and offer a point of reference for future research endeavors.

Keywords: Ketogenic Diet, Diabetes, Positive Impact, Negative Effect.

1. Introduction

Diabetes mellitus is a chronic, systemic, and metabolic disorder resulting from the prolonged interaction of hereditary and environmental influences. In recent times, there has been a noticeable shift in the lifestyle and dietary patterns of individuals due to global social and economic advancements, as well as improvements in living standards. Consequently, there has been a steady rise in the prevalence of diabetes, posing significant health risks. Research reports indicate a gradual increase in the prevalence of diabetes, with projections suggesting that the global diabetic population is expected to reach 592 million by 2035 [1], and further increase to 629 million by 2045 [2].

The prevalence of diabetes among patients can mostly be attributed to prolonged adherence to unhealthy dietary patterns and insufficient understanding of diabetes management, resulting in dysregulation of blood glucose levels. The management of diabetes frequently involves pharmacological interventions and dietary regulation, both of which play crucial roles in the development and control of blood sugar levels. Diet regulation is considered a fundamental component of diabetes treatment, as it aids in the management of the condition, facilitates effective blood sugar control, and serves as a preventive measure against the onset and progression of diabetes-related complications [3]. Dietary management is a crucial intervention in the natural progression of diabetes throughout all stages [4]. As a non-pharmacological intervention, its primary mechanism involves assisting pancreatic islet β cells

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in restoring normal function by alleviating their burden. The regulation of blood sugar levels can be achieved by adhering to a diet that is high in sugar and fat [5].

Currently, a prevalent dietary intervention known as the ketogenic diet is utilized in the management of diabetes. However, new research has revealed both benefits and drawbacks associated with the use of the ketogenic diet for diabetes therapy. In this paper, the author intends to conduct a comprehensive analysis and evaluation of existing literature to examine the effects of a ketogenic diet on diabetes. The objective is to offer valuable insights that can potentially inform future approaches to diabetes therapy.

2. Diabetes

Diabetes mellitus is a metabolic disorder that is distinguished by elevated levels of glucose in the bloodstream. Hyperglycemia arises due to a malfunction in the secretion of insulin, reduced physiologic effects of insulin, or a combination of these factors. Prolonged hyperglycemia results in persistent harm and impairment of many organs, particularly the ocular, renal, cardiovascular, vascular, and neural systems. Pathogenic factors that contribute to the development of diabetes can be attributed to genetic and environmental influences. These factors are categorized into two main types: type 1 diabetes and type 2 diabetes. Clinical manifestations of type 1 diabetes primarily include excessive thirst, increased urine production, excessive hunger, and weight loss. On the other hand, type 2 diabetes is commonly characterized by fatigue and weakness, often accompanied by obesity prior to its onset. If left undiagnosed and untreated, individuals with type 2 diabetes may experience gradual weight loss. The diagnosis of diabetes is typically straightforward, involving the identification of certain blood glucose levels. A fasting blood glucose level equal to or exceeding 7.0 mmol/L, or a blood glucose level equal to or exceeding 11.1 mmol/L two hours after meals, might be indicative of diabetes and aid in its classification.

The onset of type 1 diabetes typically occurs at a young age, with the majority of individuals affected being under the age of 30. This form of diabetes is characterized by a sudden onset and presents symptoms such as excessive thirst (polydipsia), frequent urination (polyuria), noticeable weight loss, and changes in appetite. Elevated blood sugar levels are commonly observed, and many patients experience ketoacidosis as their initial symptom. Diagnostic tests often reveal low levels of serum insulin and C peptide. Additionally, the presence of antibodies such as ICA, IAA, or GAD antibodies may be detected. Consequently, treatment with oral medications alone is ineffective, and insulin therapy is necessary.

Type 2 diabetes is prevalent among individuals in the middle-aged and senior population, with a notable association with obesity. This condition frequently coexists with hypertension, dyslipidemia, arteriosclerosis, and other related ailments. The development of this condition is characterized by a gradual and subtle progression, with the absence of noticeable symptoms during the initial phase or merely the presence of minor fatigue and thirst, without any apparent elevation in blood sugar levels. To definitively establish the diagnosis, it is necessary to do a glucose tolerance test. In the initial phases, serum insulin levels exhibit normal or heightened values, however in the latter stages, they tend to decrease.

3. Introduction to the ketogenic diet

The ketogenic diet (KD) is a dietary approach characterized by a high proportion of dietary fat, a reduced intake of protein, and a limited consumption of carbohydrates. During a state of simulated famine, there is a notable shift in the body's primary source of calories from carbs to fat. This shift leads to a large reduction in glucose levels, while the levels of ketone bodies (such as acetoacetic acid, β-hydroxybutyric acid, and acetone) and fatty acids increase. Due to the absence of essential enzymes for gluconeogenesis in extrahepatic tissues, peripheral tissues and the nervous system rely on the process of ketone oxidation for energy production. Hence, in situations where sugar utilization is limited, diverse organs, including the brain, rely on ketone bodies as the primary energy substrate for the body.

Currently, the ketogenic diet has undergone various modifications, with the classic ketogenic diet (CKD) being the predominant approach. The CKD entails consuming 80% to 90% of energy from fat,

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making it the prevailing choice in practice. The Atskin's diet restricts daily carbohydrate consumption to a range of 10 to 15 grams. The MCTKD mostly consists of medium-chain triglycerides (MCTs) such as caprylic acid and sunflower acid. The Low Glycemic Index (LGIT) diet necessitates the consumption of foods that possess a glycemic index value below 50. The distinguishing factor among the many forms of ketogenic diets lies in the variation of fat to non-fat ratio. Specifically, the classic ketogenic diet exhibits the highest proportion of fat, while adhering to stringent dietary guidelines. The modified Atkins diet demonstrates a near balance in its composition, resulting in improved patient compliance and tolerance. The consumption of a diet rich in medium-chain triglycerides (MCTs) has been found to result in a heightened synthesis of ketones. These ketones can serve as a direct source of energy for the brain, hence mitigating brain metabolic problems. However, it is important to note that this dietary approach may also lead to gastrointestinal symptoms such as vomiting, diarrhea, and spasticity. The low glycemic index diet is centered around the objective of maintaining stable blood sugar levels and permits the consumption of foods that possess a glycemic index value below 50 [6].

The KD induces a physiological state similar to "starvation mode" in the body. Following carbohydrate restriction, the body utilizes glycogen and fat as energy sources. The breakdown of fatty acids through the process of β-oxidation produces β-acetyl-CoA, which is subsequently converted into acetoacetic acid. This acid can be further reduced to β-hydroxybutyric acid and decarboxylated to produce acetone. Collectively, these compounds are referred to as ketone bodies, which serve as alternative fuel sources for the body [7]. Initially employed in clinical settings for the management of epilepsy, the utilization of the KD has progressively broadened across several illness domains as scientific investigations have advanced. These encompass type 2 diabetes, obesity, metabolic disorders including polycystic ovarian syndrome (PCOS), Alzheimer's disease, neoplasms, and others. The KD is characterized by its unique nutritional composition, which involves an increased intake of fats, reduced carbohydrates, and restricted micronutrients, dietary fiber, and other components. This dietary pattern may potentially lead to an imbalanced nutrient intake, resulting in various adverse reactions. However, the long-term treatment effects and associated adverse reactions of the KD remain unclear. This paper critically examines the advantages and disadvantages of ketogenic diets in the management of diabetes.

4. Effects of ketogenic diet on diabetes

4.1. Effects of ketogenic diet on type 1 diabetes

The assurance of KD's safety in managing type 1 diabetes remains uncertain, and its direct applicability to clinical dietary therapies is limited. Numerous studies indicate that a reduced consumption of carbohydrates has the potential to mitigate or avoid hyperinsulinemia in individuals diagnosed with type 1 diabetes, as it can effectively decrease the overall insulin requirements necessary for achieving optimal glycemic regulation. Furthermore, there exist investigations on the impact of low-carbohydrate diets (LCD) on the management of type 1 diabetes. Nevertheless, certain researchers have emphasized that interventions utilizing both LCD and ketogenic diets (KD) can provide beneficial therapeutic outcomes in terms of reducing HbA1c levels. It has been subsequently reported that adults with type 1 diabetes and kidney disease (KD) may exhibit HbA1c levels that are close to normal and experience minimal fluctuations in blood sugar levels when employing conventional glycemic management techniques. However, it is important to note that these individuals may face an elevated risk of dyslipidemia and hypoglycemia, which are crucial factors to consider in the treatment of hypoglycemic crises. Consequently, it is imperative to validate these findings through additional clinical trials.

Currently, while the existing literature both domestically and internationally has not definitively established the absolute safety of ketogenic diet (KD) for the treatment of patients with type 1 diabetes, its potential as a supplementary intervention is worthy of recognition. Therefore, it can be considered as a complementary approach alongside disease observation and KD intervention, with the precaution of preventing hypoglycemia, in order to reduce the required dosage of insulin in the treatment of type 1 diabetes [8].

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4.2. Effects of ketogenic diet on type 2 diabetes

Following a one-year period of KD intervention in individuals diagnosed with type 2 diabetes, there was a notable reduction in glycated hemoglobin (HbA1C) levels, decreasing from an initial value of 7.6% to 6.3%. Additionally, a significant proportion of patients, namely 94% of those who were previously using insulin, were able to quit their insulin therapy [9]. The advantageous impacts of a KD on individuals diagnosed with type 2 diabetes are primarily ascribed to its capacity for weight reduction. However, it is worth noting that KD exhibits superior glycemic control compared to a lower-fat diet, even when the weight loss benefits are identical. The KD has been found to have a direct impact on blood glucose levels, as it restricts the intake of carbohydrates and induces a state of physiological ketosis. This dietary approach has been shown to reduce fluctuations in blood glucose and decrease the production of insulin. Additionally, it has been seen that the KD enhances the expression of insulin receptors in tissues, hence treating conditions such as hyperinsulinemia and insulin resistance. Furthermore, the activation of AMPK and Nrf2, as well as SIRT1 and SIRT3 signaling pathways by ketone bodies, has been shown to effectively mitigate cellular oxidative stress, facilitate cellular repair mechanisms, enhance mitochondrial biogenesis, and suppress the production of inflammatory mediators [10]. A subsequent randomized crossover study has provided confirmation that the ketogenic diet possesses the ability to promptly stabilize blood glucose levels in individuals diagnosed with type 2 diabetes. Furthermore, this dietary approach has demonstrated the capacity to reduce fluctuations in blood glucose, leading to a significant improvement in glycemic control and fasting insulin levels. However, a study conducted in 2018 has revealed that the ketogenic diet may also give rise to adverse effects, including dizziness, exercise intolerance, fatigue, sleep disturbances, and constipation. According to the most recent data available up till 2020, it has been shown that a KD has a transient hypoglycemia effect and promotes weight loss in those diagnosed with type 2 diabetes. However, the long-term impact of this dietary intervention remains inconclusive.

From this perspective, the ketogenic diet exerts a notable influence on the management of type 2 diabetes. However, it should be noted that this intervention is mostly effective in the short-term, and the long-term effects of the ketogenic diet on glycemic control remain inconclusive. Consequently, additional study is important to ascertain the sustained benefits of the ketogenic diet in this context.

5. Conclusion

In conclusion, KD has shown promise as a complementary approach to drug therapy in the management of type 2 diabetes. While it may have a positive impact on short-term diabetes treatment, it is important to note that there is currently limited evidence regarding its long-term effects on blood glucose control. Therefore, additional high-quality prospective and clinical randomized trials are necessary to further assess the safety and efficacy of KD. Moreover, it is crucial to highlight that the safety of ketogenic interventions for type 1 diabetes and gestational diabetes remains uncertain, necessitating further research and experimentation in these areas. This paper aims to provide an objective review of the recent research advancements in the utilization of KD for the management of diabetes, both domestically and internationally. The objective is to offer improved guidance for clinical treatment and adjunctive therapy of diabetes, as well as to provide a scientific reference for the development of nutritional models for diabetic patients. Additionally, this paper aims to identify new directions and innovative ideas for future clinical research in this field.

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