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**The influence of the ketogenic diet on the therapy of type 2 diabetes. A literature review**

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**ABSTRACT:**

**INTRODUCTION:** Diabetes mellitus type 2 (DM2) is a widespread and chronic disorder with high mortality and associated morbidity rates worldwide. DM2 individuals are more susceptible to developing heart disease, cardiovascular disease, diabetic neuropathy, and several other related complications, which are major causes of diabetes related death. New therapies and possibilities for the treatment of the diabetes are constantly being searched for, among which the ketogenic diet is increasingly becoming popular. There are studies being conducted all worldwide on the effects of this diet on the treatment of diabetes.

PURPOSE: The aim of the study is to present the current state of knowledge about the influence of the ketogenic diet on the therapy of type 2 diabetes.

**MATERIALS AND METHOD:** The available literature in PubMed was reviewed to write the article, using the keywords ,,ketogenic diet”, ,,diabetes mellitus”, ,,ketogenic diet diabetes”, ,,diabetes nutrition”.

**CONCLUSION:** A ketogenic diet has notable advantages on body weight and glycemic control, as well as on the enhancement of lipid profiles in overweight DM2 patients. This diet can decrease body weight, waist circumference, HbA1c, and triglycerides, and increase HDL levels. In addition, the ketogenic diet may have further benefits in improving body composition to attenuate the onset and progress of DM2 bz reducing body weight, lowering glycemic levels, and enhancing lipid profiles. More studies are needed in the future to support and even confirm the links between the ketogenic diet and patienst suffering from DM2.

**Keywords:** type 2 diabetes mellitus, ketogenic diet, diabetes mellitus, nutrition

1. **Introduction**

Diabetes mellitus type 2 (DM2) is a common and chronic disease with high rates of global mortality and morbidity due to its numerous related conditions. DM2 patients are more prone to cardiovascular disease, diabetic neuropathy, and various other associated complications, which are the leading reasons for diabetes-related mortality. Although drug treatment diet is an important intervention that is recommended for patients with DM2.(1,2,3,4)

Diabetes Mellitus Diabetes mellitus is a disease showing a dramatically increasing incidence. The global prevalence of diabetes has already reached more than 460 million people and is predicted to increase to 700 million by 2045. It is a long-term illness that occurs when the insulin-producing beta cells of the pancreas are destroyed. The characteristics of type 2 diabetes are an inability of the cells to respond to insulin, not a lack of the hormone. The condition typically evolves over a period of many years, as it is most commonly diagnosed adulthood. (5,6). The criteria for the diabetes mellitus diagnosis include

* fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L)
* random plasma glucose ≥ 200 mg/dL (11.1 mmol/L)
* 2-hour plasma glucose with a 75 g oral glucose tolerance test (OGTT) ≥ 200 mg/dL (11.1 mmol/L)
* glycated hemoglobin (HbA1c) ≥ 6.5% (48 mmol/mol).

The most precise and general definition of ketogenic diet is a diet that leads to an increase in the production of ketones (such as β-hydroxybutyrate, acetoacetate, and acetone) in the human body. The function is to mimic a state of starvation but without the negative effects of fasting. (7)

1. **The purpose of the study**

The aim of the study is to present the current state of knowledge about the role of the gut ketogenic diet on the therapy of type 2 diabetes mellitus.

1. **Materials and method**

The available articles were reviewed for their clinical relevance to the role of gut microbiota in patients with type 2 diabetes mellitus. The eligible English-language publications retrieved from the PubMed database were reviewed by using key words in different combinations: ,,ketogenic diet”, ,,diabetes mellitus”, ,,ketogenic diet diabetes”, ,,diabetes nutrition”.

1. **Description of knowledge**

**3.1. Ketogenic diet - definition**

In some diets the major energy source is glucose, the body in the ketogenic diet prefers ketone bodies. The body then enters a state of ketosis, which in turn offers numerous beneficial effects. This is a diet with a low content of carbohydrates, a high content of fat and a medium content of protein. It is likely that the vast majority of ketogenic diets involve limiting the intake of carbohydrates to a maximum of 50 g per day. In addition, the overall carbohydrate intake may be reduced to 30 g per day to help the body adapt to a more efficient use of ketone bodies. (18,19,20) Meanwhile, the proportion of fats rises, generally to 70-80%, and protein often accounts for about 20% of the energy content. In addition, the ratio of protein to fat can be more diverse and depends very much on the characteristics of the individual case. This kind of distribution of the macronutrients theoretically fits in most cases within the framework of the ketogenic diet, but it should be stressed that it is possible to use the least refined products. Among the foods most commonly found in such diets are eggs, meat and fish, vegetable oils, organ meats, vegetables without starch), avocado, olives, and nuts. (21,22,23,24)

**3.2. The Effect of the Ketogenic Diet on the Pharmacotherapy of Type 2 Diabetes**

The diabetes diagnosis is linked to an individualized treatment approach, which includes pharmacological therapy. The exceptionally large number of people with this condition indicates that it is a topic worthy of in-depth discussion. The available research suggests an important impact of the ketogenic diet on medication. They show, for example, a marked decrease in the body's need for insulin and doses of antidiabetic oral agents. The American Association of Clinical Endocrinology recommends patients on sodium-glucose cotransporter-2 (SGLT) inhibitor therapy to discontinue these drugs prior to initiating a ketogenic diet. This is due to the elevated risk of developing diabetic ketoacidosis. Patients treated with glucagon-like peptide-1 (GLP-1) receptor agonists during the ketogenic period should be closely supervised. As with SGLT2 inhibitors, this is associated with an enhanced potential for not only diabetic ketoacidosis associated with ketosis, but also hypoglycemic events. (25,26,27,28,29). No general contraindication has been identified for metformin, although it should be assessed on a case-by-case basis. In this specific dietary model, it is therefore conceivable that pharmacotherapy could be completely discontinued or at least reduced. This would help to minimize or avoid the possible side effects of medication, for at least some patients. Considering the high frequency of the condition, the percentage of individuals with the condition may be quite large. Continued observation and monitoring will make it possible to modify drug doses in such a manner as to avoid attacks of hypoglycemia, diabetic ketoacidosis and other associated complications of the disorder. Also relevant in the future, if a ketogenic diet is more frequently recommended in the management of diabetes. (30,31)

A large meta-analysis of randomized controlled trials showed that ketogenic diet was superior to low-fat diet in improving glycemic measures, body mass, and lipid profile, especially in patients with previously diagnosed diabetes who were also overweight. (32) In another meta-analysis, the effect of a ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with type 2 diabetes was investigated. It was shown that the ketogenic diet resulted in a mean decrease in glucose concentration of 1.29 mmol/L, a decrease in glycated hemoglobin (% HbA1c) of 1.07%, and a decrease in total cholesterol, LDL fraction, and triglyceride concentrations, while increasing HDL cholesterol levels. A significant decrease in body mass of 8.66 kg, a decrease in waist circumference of 9.17 cm, and a decrease in BMI of 3.13 kg/m2 were also noted. The study concluded that the ketogenic diet had a beneficial effect on glycemic and lipid profile control in type 2 diabetic patients, and also substantially reduced body mass. (33)

**3.3. A practical approach to ketogenic diet**

The ketogenic approach must always be followed under the direction of a nutritionist and physician. In addition, given the high fat and low carbohydrate nature of the diet, the base of products that can be used is limited. The amount of fluid in the diet is important. Particular care needs to be taken with the frequency of meals scheduled for a diabetic patient, due to fluctuations in blood glucose levels. The main intake of fluids during the day must be water, although tea or coffee may also be consumed. (34,35,36) In addition, patients must regularly monitor their blood glucose concentration and serum ketone bodies. During the early phases of a ketogenic diet, diabetic patients may need to restrict exercise to avoid possible hypoglycemic events. Individuals on prescription medications and insulin therapy must consult with their physician regarding diet and pharmacologic therapy. It may be necessary to decrease the dosage of medications or stop them altogether (e.g., insulin). It should be noted that returning to a high-carbohydrate diet can cause an increase in blood glucose levels. Returning to a high-carbohydrate diet must be done gradually and under the guidance of a physician. (37,38,39,40)

1. **Conclusion**

The findings of the present trial are encouraging, as the current data provide evidence for the beneficial effects of a ketogenic diet in the prevention and treatment of DM2. The possibility of reducing or even eliminating medication makes the subject even more exciting and requires further research. The positive benefits of the ketogenic diet in T2DM include the lowering and stability of serum glucose and insulin levels, the suppression of glycated hemoglobin levels, and the decrease of the HOMAR-IR indicator, insulin resistance, and body mass. With proper management of the patient's condition, a carefully managed diet does not pose a major risk. The occurrence of diabetic ketoacidosis or episodes of profound hypoglycemia is not common according to published studies, but should be considered and the patients monitored. In summary, the ketogenic diet may be beneficial in patients with DM2. The subject certainly requires further investigation and follow-up in clinical practice. The findings are sufficiently encouraging to make a contribution not only to the advancement of science, but also to a possible change in the recommendations for diabetic patients. This could lead to improved lives for many people around the world. (41,42)

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**Author contributions**

Conceptualization, A.M., H.S. ; Methodology, P.G. and A.M. ; Validation, P.B. and A.S. ; Formal Analysis, Z.M, M.D.; Investigation A.M; Resources, A.M. ; Data Curation, H.S. and A.M. ; Writing – Original, A.M. ; Writing – Review & Editing, A.M. and A.S. ; Visualization, P.B. and P.G. ; Supervision, A.S.; Project Administration, M.D.

**Conflicts of interest**

The authors have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

**Institutional Review Board Statement**

Not applicable.

**Informed Consent Statement**

Informed consent was obtained from all subjects involved in the study.

**Data availability**

The data have not been made public, but are kept with the authors, if necessary.

**Ethics approval**

Written informed consent for publication was obtained from the patient. We complied with the policy of the journal on ethical consent.

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