KETOGENIK PARHEZ VA UNING QO'LLANILISHI

Shukurlayeva Mehriniso Xayrullo qizi - assistent
Sabirova Rixsi Abdukadirovna - t.f.d., professor
Tursunov Djahangir Xusanovich-t.f.n. dotsent
Xusanboyeva Mushtariy Dilmurod qizi
1-son davolash ishi fakulteti 2-kurs talabasi
Toshkent davlat tibbiyot universiteti (Toshkent, O‘zbekiston)

KETOGENIC DIET AND ITS USES

Shukurlayeva Mekhriniso Khayrullo qizi - assistant
Sabirova Rikhsi Abdukadirovna - DMSc., professor
Tursunov Djakhangir Khusanovich-CMSc., associate professor
Xusanboyeva Mushtariy Dilmurod qizi
2nd year student of the faculty of therapeutic work №1
Tashkent state medical university (Tashkent, Uzbekistan)

КЕТОГЕННАЯ ДИЕТА И ЕЁ ПРИМЕНЕНИЕ

Шукурлаева Мехринисо Хайрулло кизи - ассистент
Сабирова Рихси Абдукадировна - д.м.н., профессор
Турсунов Джахангир Хусанович-к.м.н., доцент
Хусанбоева Муштарий Дилмурод кизи
студентка 2 курса факультета лечебного дела №1
Ташкентский государственный медицинский университет
(Ташкент, Узбекистан)

Izoh. *Metabolik sindrom – bu qandli diabet, arterial gipertenziya, dislipidemiya va semizlik kabi bir necha xavf omillarining majmuasidan iborat bo‘lib, yurak-qon tomir kasalliklari va 2-tip diabet rivojlanish ehtimolini sezilarli darajada oshiradi. Ushbu sindrom dunyo bo‘yicha tobora keng tarqalmoqda va sog‘liqni saqlash tizimlari uchun katta muammo hisoblanadi. So‘nggi yillarda metabolik sindromni nazorat qilish va davolashda turmush tarzini o‘zgartirish, xususan, parhez usullari muhim ahamiyat kasb etmoqda. Shulardan biri ketogen dietadir. Katogenik dieta shu kabi jiddiy muommolarni oldini olishga, unga qarshi samarali kurashishga yordami ahamiyatlidir. Xususan yaqinda olib borilgan tajribalar keto dietaning saratonga ham ta'sir kuchi ijobiyligini aniqlashdi.*

Kalit so‘zlar: *metabolik sindrom, keto dieta, qandli diabet, yurak xastaliklari,*

saraton

Abstract. *Metabolic syndrome is a cluster of several risk factors, including diabetes, hypertension, dyslipidemia, and obesity, that significantly increases the risk of developing cardiovascular disease and type 2 diabetes. This syndrome is becoming increasingly common worldwide and is a major challenge for healthcare systems. In recent years, lifestyle changes, particularly dietary methods, have become increasingly important in controlling and treating metabolic syndrome. One of these is the ketogenic diet. The ketogenic diet is a significant help in preventing and effectively combating such serious problems. In particular, recent experiments have revealed that the keto diet also has a positive effect on cancer.*

Keywords*: metabolic syndrome, keto diet, diabetes, heart disease, cancer*

Аннотация. *Метаболический синдром представляет собой совокупность нескольких факторов риска, включая диабет, гипертонию, дислипидемию и ожирение, что значительно увеличивает риск развития сердечно-сосудистых заболеваний и диабета 2 типа. Этот синдром становится всё более распространённым во всём мире и представляет собой серьёзную проблему для систем здравоохранения. В последние годы изменение образа жизни, в частности, диетических методов, приобретает всё большее значение в контроле и лечении метаболического синдрома. Одним из таких факторов является кетогенная диета. Кетогенная диета оказывает существенное содействие в профилактике и эффективной борьбе с такими серьёзными проблемами. В частности, недавние эксперименты показали, что кето-диета также оказывает положительное влияние на онкологические заболевания.*

Ключевые слова: *метаболический синдром, кето-диета, диабет, сердечно-сосудистые заболевания, рак*

Metabolic syndrome is one of the problems that currently plagues many people around the world. Just as every disease has its own criteria, this disease also has several criteria. For example:

1- excess weight in the abdominal area.

2- Increased blood sugar (glucose) levels.

3- high blood pressure (hypertension).

This diseaseIt affects 1 in 3 adults in the United States. Fasting was recognized as an effective treatment for many medical conditions as early as 500 BC. Fasting has continued into modern times, and in 1910, Guelpa and Marie proposed fasting as a treatment for epilepsy. In 1921, Woodyatt noted that fasting or a high-fat, low-carbohydrate diet provided two energy sources, acetone and β-hydroxybutyrate, produced by the liver in the absence of glucose, in individuals without significant medical conditions. A low-carb, high-fat diet was considered an alternative to fasting

or fasting, and was thought to have the same effect while continuing to nourish healthy cells. It is within this framework that the keto diet was developed. That is, using fat instead of carbohydrate energy (4).

How does the keto diet itself work?

The keto diet is a diet that significantly reduces carbohydrate intake and uses fat and protein instead, replacing glucose, the body's primary source of energy, with stored fat. Consuming less than 50 grams of carbohydrates per day significantly reduces insulin secretion, which puts the body into a catabolic state. During this process, glycogen stores are depleted, causing a number of metabolic changes, and the restriction of carbohydrates in body tissues plays an important role in the emergence of two new stages. These are: gluconeogenesis and ketogenesis (1).

During the diet to compensate for the reduced glucose energy, hormonal changes lead to an increase in fatty acids. They are metabolized to acetoacetate, which is then converted to β-hydroxybutyrate and acetone. The resulting ketone bodies accumulate in the body as the diet continues, providing alternative energy for the body. Experimental comparisons have shown that 100 grams of acetoacetate produces 9400 grams of ATP, 100 grams of β-hydroxybutyrate produces 10500 grams of ATP, and 100 grams of glucose produces only 8700 grams of ATP. This shows that even in the absence of ketone bodies, their energy provides the most efficient fuel for the body. In addition, ketone bodies reduce free radical damage and increase the body's antioxidant capacity. This makes an important contribution to the body's slow aging and maintaining health (1).

Russell Wilder was the first to use a ketogenic diet to treat epilepsy in 1921. Epilepsy is a condition characterized by excessive excitability and desynchronization of neurons, resulting from an imbalance between excitatory and inhibitory neurons in the brain. Ketone bodies themselves are thought to have anticonvulsant effects, reducing neuronal excitability, increasing their stability, and reducing the number of seizures.AIt stops neurons from firing by opening ion channels. It increases the activity of the inhibitory neurotransmitter GABA or reduces the effect of the excitatory neurotransmitter Glutamate. Through this process, it has been observed that the number of seizures in epileptic children is reduced (2).

Doctors at Great Ormond Street Hospital repeated this diet. They found that about half of the children who used it had a significant reduction in the number of seizures. Even the youngest children were seizure-free. They reported that the diet improved their cognitive, developmental, and learning abilities (3).

In addition, this diet is currently being used to treat and prevent serious diseases. In particular, a large study of cardiometabolic deaths in the United States in 2012 showed that about 45.4% of these deaths were confirmed to be related to heart disease, diabetes, and stroke (1). The keto diet is being tested against these diseases and has

achieved good results. This method is quite effective for the treatment of type 2 diabetes. The reason is that in type 2 diabetes, adipose tissue, muscle, and liver cells do not respond properly to insulin. This is due to the incorrect phosphorylation of insulin signaling proteins at the molecular level, which is mainly caused by excess fats (lipids) and inflammation. As a result, the GLUT4 transporters, which transport glucose into cells, do not work. The pancreas (beta cells), which initially worked hard to overcome insulin resistance, eventually become fatigued and damaged by glucose/lipid toxicity. As a result, they are unable to produce enough insulin to meet the body's needs.

These two problems combine to cause persistently high blood glucose levels. The keto diet, on the other hand, helps reduce glucose levels and help you lose excess fat. However, this method has been controversial due to its temporary nature.

Another of the diseases that cause many deaths on Earth is cardiovascular disease. Every year, an average of 17.9 million people die from it worldwide. These figures exceeded 19 million in 2020, which shows a significant increase of 18.7% compared to 2010. Although medicine has made various achievements, a 2006 publication predicted that 23.3 million deaths would be observed by 2030, and unfortunately, these estimates are increasingly approaching reality (5). Cardiovascular diseases include heart failure, cardiac arrhythmia, cardiomyopathy, congenital heart defects, rheumatic heart disease, and others. The main goal in preventing this is to control the diet. This idea was initially used when studying the effects of the keto diet on these diseases. A recent study revealed two key findings: first, that cardiac endothelial cells have the ability to oxidize ketone bodies, which in turn promotes cell proliferation, migration, and vascular growth; and second, that a ketogenic diet can increase endothelial cell proliferation and prevent the pathological process of vascular narrowing in a mouse model of cardiac hypertrophy (9). However, in 2021, it was reported that while weight loss may be possible, it does not reduce the amount of fat in the blood vessel wall, suggesting that this method cannot treat atherosclerosis in the heart. The effects are temporary, and therefore the Mediterranean diet is recommended. Researchers report that they have seen positive results in people who have been on a Mediterranean diet for a long time. However, the ketogenic diet does not meet the criteria for a healthy diet recommended by the European Society of Cardiology. Its effectiveness in long-term weight loss and metabolic changes is still under-evaluated, but the available evidence suggests that it is no better than current dietary standards for long-term effects. However, the keto diet is also being considered for overweight and diabetic people (7).

The ketogenic diet has also been tested against cancer. When studying the effect of keto bodies on cancer tumor cells, they found a cytotoxic effect on them. The mechanism is as follows: Glucose normally stimulates the β-cells of the pancreas to

release insulin, which allows glucose to enter the cells and provide energy. When consuming large amounts of carbohydrates and glucose, the pancreas produces more and more insulin, which increases the interaction between growth hormone receptors and growth hormone, which in turn promotes the production of insulin-like growth factor 1 (IGF-1) in the liver - a factor that promotes cell growth and proliferation, which can be harmful to cancer patients. Excessive production of Glut-1, Glut-3 is also found in many cancers. The keto diet significantly reduces glucose levels and prevents these processes. In addition, these diets slow cancer progression by inhibiting intracellular signaling pathways such as insulin/IGF and phosphoinositide 3-kinase (PI3K)/protein kinase B (Akt)/mammalian target of rapamycin (mTOR). Ketogenic diets increase adenosine monophosphate-activated protein kinase (AMPK), which inhibits aerobic glycolysis and suppresses tumor proliferation, invasion, and migration. Mouse models of metastatic cancer demonstrate that exogenous ketones themselves have direct cytotoxic effects on tumor viability. β-hydroxybutyrate can modify chromatin by binding to and thereby inhibiting histone deacetylase, ultimately blocking transcription and preventing cancer cell proliferation (4).

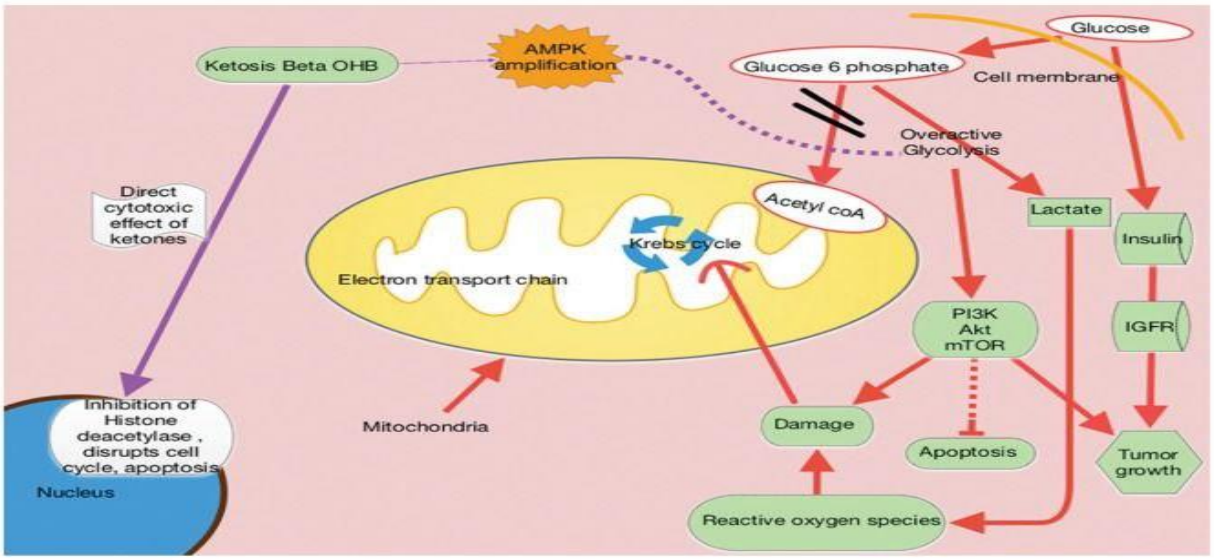


Figure 1.

One clinical trial involved breast cancer patients who followed a ketogenic diet for 12 week patients in the control diet group responded better to chemotherapy, including tumor reduction and downgrading, than those in the control diet group. However, its effect on metastatic progression—the leading cause of cancer-related death—remains unclear (4). In another study, in 1962, the New York City Department of Mental Hygiene published a paper on two women whose metastatic cancers disappeared after daily hypoglycemic insulin comas (brief and reversible). These patients were not amenable to conventional electroconvulsive therapy, and therefore medical psychotherapy. Not only did their psychotic and depressive symptoms disappear, but their cancer (cervical cancer and metastatic melanoma) was not detected within 2

months of treatment (8).

Zuccoli and colleagues reported a case of glioblastoma that was successfully treated with oral temozolomide chemotherapy after the patient had started taking steroids. The patient had a radiographic response and good tumor control for approximately one year before the diet was discontinued. She was switched to chemotherapy, which included bevacizumab (an antivascular endothelial growth factor), but her disease progressed and she died. In addition, 2 pediatric female patients with astrocytoma experienced improved mood and decreased glucose uptake on PET-CT scans of tumor sites during an 8-week ketogenic diet. One of these patients continued the diet and remained disease-free for another 12 months. These early case reports provide compelling evidence for further research into the role of glucose metabolism in cancer treatment (4).

St. Joseph Hospital and Medical Center (Phoenix, AZ) is enrolling patients with newly diagnosed glioblastoma in a prospective phase 1/2 trial that includes KD followed by radiotherapy and concurrent temozolomide and chemotherapy. The primary endpoint is the number of patients with AEs, and secondary endpoints are overall survival, time to progression. The University of Iowa conducted 2 phase 1 studies in patients with prostate cancer and non-small cell lung cancer, including KD using Nutritia KetoCal 4:1 (Gaithersburg, MD). Their results showed promising news (4).

In conclusion, the keto diet is a group of diets that effectively support the body's needs by reducing the amount of carbohydrates, and it can be considered an effective method not only for diabetes but also for complex cancers. The ketogenic diet is considered one of the effective methods for treating metabolic syndrome. It helps improve insulin resistance, reduce weight, normalize dyslipidemia, and reduce arterial hypertension. However, its long-term use can cause some side effects. Therefore, it is advisable to use the KD under the supervision of a doctor and dietitian.

REFERENCES

1.Wajid Masood; Pavan Annamaraju; Muhammad Z. Khan Suheb; Kalyan R. Uppaluri.Last updated: 16 June 2023.[PubMed](2-5)

2.Department of Biosciences, COMSATS University Islamabad, Islamabad 45550, Pakistan

2 College of Applied Medical Sciences, Imam Abdulrahman bin Faisal University, Dammam 34212, Saudi Arabia

3 College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam 34212, Saudi Arabia

4 Department of General Medicine, Fauji Foundation Hospital, Rawalpindi 45000, Pakistan

5 National Institute of Genomics and Advanced Biotechnology (NIGAB), National Agricultural Research Center (NARC), Islamabad 44000, Pakistan

6 Neurology Center, King Fahad Specialist Hospital Dammam, Dammam 32253, Saudi Arabia [PubMed] (7-12)

3.Diet Department in collaboration with the Child and Family Data Group Last reviewed: November 2020(5)

4. Dr. Tan-Shalabi is a physician in the Department of Medicine, Division of Hematology and Oncology at the University of Pittsburgh Health System, and a clinical assistant professor at the University of Pittsburgh School of Medicine in Pennsylvania.

PMCID: PMC6375425 PMID: 30766299 [PubMed] (1-12)

5. Institute of Health Sciences, Faculty of Medicine and Health Sciences, Siedlce University of Natural Sciences and Humanities, 08-110 Siedlce, Poland;damian.dynka24@gmail.com (DD);katarzyna.kowalcze@uph.edu.pl (CC);anna.charuta@uph.edu.pl (AC) (2-3)[Pubmed]

6. 1Department of Medicine, Faculty of Medicine and Life Sciences, University of Barcelona, 08036 Barcelona, Spain;sara.castro@ub.edu (SC-B.);mariasipe4@gmail.com (MS-P.);restruch@clinic.cat (RE)

2Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), 08036 Barcelona, Spain; amruiz@clinic.cat

3Centro de Investigación Biomédica en Red, Fisiopatología de la Obesidad y la Nutrición (CIBEROBN), Instituto de Salud Carlos III, 28029 Madrid, Spain (6-8)

*Correspondence:rcasas1@clinic.cat; Tel.: +34-932275400; Fax: +34-932272907

PMCID: PMC7600579 PMID: 33003472

7.Department of Clinical Dietetics, Department of Bioanalytics, Medical University of Lublin, ul. Chodzki 7, 20-059, Lublin, Poland

Department of Cardiology, Cardinal Wyszynski Hospital, Lublin, Poland Online January 15, 2024, Written version January 19, 2024 .(4-5)

8-New Study Links the Keto Diet to Cancer Metastasis

News August 27, 2024 (3-4)

9.Institute of Health Sciences, Faculty of Medicine and Health Sciences, University of Natural Sciences and Humanities in Siedlce, 08-110 Siedlce, Poland; damian.dynka24@gmail.com (DD); katarzyna.kowalcze@uph.edu.pl (KK); anna.charuta@uph.edu.pl (AC) (8-12)