

## Ketogenic diet in civilization diseases

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### Abstarct

The low-carbohydrate ketogenic diet (LCKD) is a high fat and low carbohydrate and low protein diet. It was found to be promising in controlling diabetes mellitus. (DM)., epilepsy, obesity, cardiovascular diseases. Ketogenic diet lowers blood sugar and insulin levels, and shifts the body's metabolism from carbs and towards fat and ketones. The primary goal of inducing ketosis is to help patients with rare metabolic disorders in a situation where pharmacological treatment was not effective.

### History

The beginnings of knowledge about the harmfulness of carbohydrates and cereals go back to the eighteenth century. In 1797 Scottish doctor John Rollo issued his notes regarding the treatment of a patient suffering from diabetes, who after switching to a diet based mainly on meat felt much better. In 1893, William Banting, an English funeral entrepreneur, described his own weight loss experiences and proposed a diet excluding bread, butter, milk, sugar and potatoes. In 1968, Polish dietitian physician Jan Kwaśniewski published the assumptions of an optimal diet (now called the Kwaśniewski diet), which recommends the consumption of large amounts fat and limitations of protein and carbohydrates. In 1972, the American cardiologist Robert Atkins published a book describing the low-carb diet.

The beginning of 1975 may be considered the beginning of the Paleo idea, when gastroenterologist Walter L. Voegtlin wrote the book *The Stone Age Diet*, in which he described successful trials of treating Leśniowski-Crohn disease, irritable bowel syndrome and colitis after presumed use diets of our ancestors. The term "paleo diet" itself was widespread in the book Lorena Cordaina published in 2002.<sup>1</sup>

## **Introduction**

The low-carbohydrate ketogenic diet (LCKD) is a high fat and low carbohydrate and low protein diet. It was found to be promising in controlling diabetes mellitus (DM), epilepsy, obesity and cardiovascular diseases.<sup>2</sup> DM is a serious condition which is increasing rapidly in the world. This disease is placed on the 6th place in the world to the frequency of deaths in the world - only in 2000, diabetes caused 5 million deaths.<sup>3</sup> The most important treatment in diabetes is a proper lifestyle, especially diet which allow maintain adequate level of glycemia. Ketogenic diet is promising therapy for patients with DM.

Low-carb diet character is low in supply carbohydrates, up to a maximum of 25% daily caloric demand. Extremely low-carbohydrate ketogenic diet, in which the supply of carbohydrates is below 10 % of daily consumption caloric demand or below 50 g per day.<sup>4</sup> The main source of energy in the body are carbohydrates. When they are missing, the body begins to look for another "fuel". These are fats, specifically ketones (so-called ketosis) formed in the process of fat breakdown.. After a few days of using a ketogenic diet, an euphoric state appears including great mood, cheerful, light. After 2-3 months everything goes by. Appearance loss, drowsiness and constipation appear, the smell of sweat, urine and breath changes, thirst increases.

## **Different Types of Ketogenic Diets**

There are several versions of the ketogenic diet, including<sup>5</sup>

- Standard ketogenic diet (SKD): This is a very low-carb, moderate-protein and high-fat diet. It typically contains 75% fat, 20% protein and only 5% carbs.
- Cyclical ketogenic diet (CKD): This diet based on periods of day without carbs and then day full in carbs, such as 4 ketogenic days followed by 2 high-carb days.
- Targeted ketogenic diet (TKD): Diet allows to add carbs around workouts.
- High-protein ketogenic diet: The ratio is often 60% fat, 35% protein and 5% carbs.

## **Indications**

The ketogenic diet has been used in the treatment of drug-resistant epilepsy in children and in some inborn errors of metabolism (eg congenital lack of glucose transporting protein GLUT-1). There are also other indications such as Rett syndrome, Draveta syndrome, epilepsy with myoclonic-asthmatic seizures (Doose syndrome), tuberous sclerosis. It also should be consider in autism, Alzheimer's disease, Parkinson's disease, Crohn's disease and other types of epilepsy or some encephalopathies.<sup>6,7</sup>

## **Diabetes**

Diabetes is characterized by changes in metabolism, high blood sugar and impaired insulin function. The form of diet can help in losing excess fat not only in type 2 diabetes but also in prediabetes and metabolic syndrome. In study by Yancy et al shows improvement of glycemia and reduction on medication in patients with type 2 diabetes on low carbohydrate ketogenic diet. What is more triglyceride decreased 42 %.<sup>8</sup> This form of diet have significant influence to low haemoglobin A1c and insulin sensitivity. In study Boden et al conducted in 10 obese patients with type 2 diabetes show mean 24 h plasma profiles and glucose levels

normalized, mean haemoglobin A1c decreased from 7,3 % to 6,8 % and what is the most important insulin sensitivity improved by 75 %. Moreover 35 % decreased in plasma triglyceride and 10 % decreased in cholesterol levels were observed. <sup>8</sup> In a study by Al-Khalifa et al investigate effect low carbohydrates ketogenic diet on diabetic rats. The results shows significant increase in body weight and maintaining blood glucose levels within the normal range. Around 95 % of patients on ketogenic were managed to eliminate or reduce diabetes medication, compared to 62% in the higher-carb group. <sup>7</sup>

### **Principles of ketogenic diet**

High fat intake while limiting the delivery of carbohydrates leads to blockage oxidation of fatty acids and formation of ketone bodies. The resulting compounds like acetone, beta-hydroxymate, methylglyoxal or acetoacetate may cause a number of changes in the body. They lead to the formation of ketoacidosis, protein glycation, oxidative stress, and interference in the mechanism of regulation of food intake or changes in the psychophysical condition<sup>1</sup>. There are a lot of ketogenic diets differing in the ratio of nutrients, the choice of fat type and the recommended calorie deficit. However, all have one common point - through drastic reduction of carbohydrates in meals should lead to increased production and accumulation of ketones in the body, i.e. ketosis. In a nutshell, after a few days of carbohydrate restriction (some experts believe this should be below 20g per day, according to the Ketose Food and Nutrition Institute can be prevented when consuming a minimum of 50g per day) glucose reserves are insufficient to fully oxidise fat. Ketone bodies are produced that reach the peripheral tissues. There they are used as a source of energy, thereby largely compensating for the deficit of glucose.<sup>9</sup>

### **Weight loss**

The ketogenic diet puts body into a ketosis, which ultimately allows to use fat for energy. Fat burning is the main benefit of ketosis that and it is an effective tool for weight loss. In addition, ketone bodies suppress the feeling of hunger. In study by Bonnie at all showed that patients in ketogenic diet lost 2.2 times more weight than those on a calorie-restricted low-fat diet. Triglyceride and HDL cholesterol levels also improved. Another study by Sumithran et al shows loss initial body weight in 13 % during 8 week ketogenic very-low-energy diet, also leptin and amylin were lower. <sup>3</sup> There are several studies indicates ketogenic diet lower blood sugar levels and improved insulin sensitivity. <sup>10 8</sup>

### **Ketogenic diet in epilepsy**

In a traditional ketogenic diet, consists of long chain saturated triglycerides in a 4: 1 - 3: 1 i.e. for 4 or 3 g of fat, 1 g of protein and total carbohydrates is used. Dietary fluids are limited to 60-665 ml / kg m.c./d. The diet begins in the hospital, under the supervision of a doctor and a dietitian, preceding its commencement with a 1-2-day hunger strike. Then gradually the amount of energy and nutrients given up increases to the values determined according to the diet. Further treatment takes place at home and usually lasts 2-3 years. During this time, diet rules should be strictly adhered to, as any deviation from the norm may favor epileptic seizures.

High supply of fats with a small amount of carbohydrates in the diet leads to changes in fat metabolism, as well as during fasting. From the fat, ketone bodies form in the liver: acetone, acetoacetate and beta-hydroxybutyric acid, which penetrate into the central nervous system and are a substitute for lack of glucose energy for neurons. In the patient's blood and urine, ketosis is observed, i.e. high concentration of ketone bodies. However, they are responsible for the anticonvulsant effect only indirectly. Suspected ketone bodies cause an increase in the activity of enzymes synthesizing  $\gamma$ -aminobutyric acid (otherwise GABA - acts as the main

neurotransmitter with inhibitory activity in the entire nervous system), which slows down the stimulation of neurons which activate the K<sub>2</sub>P potassium receptor and the sodium-potassium pump, which raises the seizure threshold. In addition, ketone bodies can protect nerve cells, including against damage from free radicals (limit oxidative stress).

### **Diet for cancer**

Postprandial hyperglycemia, hence a high free concentration glucose in the blood after a meal, affects significantly on the growth and proliferation of cancer cells. It promotes the formation of many metabolic changes, such as the cellular and tissue levels of the body, including glycation of proteins, some lipid fractions, increase platelet reactivity, increasing the dynamics of oxidative stress. Chronic postprandial hyperglycemia, occurring in type 2 diabetes, it intensifies all these processes in the body. Co-occurring type 2 diabetes it also worsens the prognosis, especially for women with breast cancer. Permanent intake of meals that cause hyperglycaemia is associated with an increased risk of occurrence chronic diseases such as: obesity, diseases cardiovascular and type 2 diabetes. Diabetes type 2, characterized by chronic hyperglycaemia and in the initial phase of hyperinsulinemia, promotes glycation proteins, some lipid fractions, increased platelet reactivity, increasing the dynamics of stress oxidative, which may exacerbate the neoplastic processes in the body.<sup>7</sup>

### **The advantages of the ketogenic diet**

An undeniable advantage of this type of nutrition is the help in the treatment of specific cases of diseases in children, which is associated with a reduction in the amount necessary to receive medication. However, such treatment should only be carried out under the supervision of a physician. It does not take place without risk (eg delay of development). Ketone bodies also suppress the feeling of hunger, which is very important for people who are slimming. Although studies on the impact of ketogenic diet on satiety are not consistent, the last meta-analysis allows us to trust that this way of feeding prevents the growth of hunger even after calorie reduction and weight loss. The next step will be to set a minimum level of ketosis that will achieve this effect. The advantage of the ketogenic diet can also be quite good slimming effects, although it should be noted that the initial weight loss results in part from dehydration (cleansing from ketone bodies, loss of glycogen).<sup>11</sup>

### **Side effects**

A ketogenic diet, has its pros and cons. Ketone bodies burden the kidneys and liver. At the beginning of the ketogenic diet<sup>11</sup>, the nausea, constipation, fatigue, diarrhea, vomiting, abdominal pain may occur. It usually disappears after adapting. After prolonged use more energy is observed. Sometimes, shortage of vitamins, minerals, antioxidants, dietary fiber and protein may require additional supplementation. With a longer period of using ketogenic diet, the urolithiasis, hyperuricemia, cholelithiasis could be the main side effects. Renal stones are estimated in 5-8 % of children on ketogenic diet.<sup>9</sup> The danger associated with the accumulation of methylglyoxal and its by-products recognized as a risk factor for damage to blood vessels and tissues is also underlined.<sup>12</sup>

### **Conclusion**

The ketogenic diet could be a potent anti-epileptic therapy for patients suffering from diabetes mellitus. Some studies show the superiority of the ketogenic diet over a standard slimming diet when it comes to effects, especially for a short time. Supporters of ketosis will also cite research on its effectiveness in normalizing cardiovascular parameters. However, further detailed research is required.

## References

1. Morskiej A, Zespo G. Konsekwencja stosowania Nr 4. 2007:371-374.
2. Nielsen J V, Joensson EA. Nutrition & Metabolism bodyweight and glycemic control during 44 months follow-up. 2008;6:1-6. doi:10.1186/1743-7075-5-14.
3. Korzeniowska K, Jabłeczka A. Cukrzyca ( Część I ) Diabetes ( Part I ). 2008;(Część I):231-235.
4. Zieli M, Buczkowska-radli J. Wpływ diety niskowęglowodanowej na stan zdrowia człowieka The impact of a low-carbohydrate diet on human health. 2017;63(4):56-61.
5. Freeman JM, Kossoff EH, Hartman AL, Freeman JM, Kossoff EH, Hartman AL. The Ketogenic Diet : One Decade Later. 2014. doi:10.1542/peds.2006-2447.
6. Manuscript A. NIH Public Access. 2014;25(2):173-178. doi:10.1097/WCO.0b013e3283515e4a.Ketogenic.
7. Westman EC, Jr WSY, Mavropoulos JC, Marquart M, Mcduffie JR. Nutrition & Metabolism The effect of a low-carbohydrate , ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. 2008;9:1-9. doi:10.1186/1743-7075-5-36.
8. Jr WSY, Foy M, Chalecki AM, Vernon MC, Westman EC. Nutrition & Metabolism A low-carbohydrate , ketogenic diet to treat type 2 diabetes. 2005;7:1-7. doi:10.1186/1743-7075-2-34.
9. Vining EPG. Clinical efficacy of the ketogenic diet. 1999;37:181-190.
10. Talib H, Asfar AÆSK, Behbahani AÆAI, Al-zaid NS. Beneficial effects of ketogenic diet in obese diabetic subjects. 2007:249-256. doi:10.1007/s11010-007-9448-z.
11. Paoli A. Ketogenic Diet for Obesity : Friend or Foe ? 2014:2092-2107. doi:10.3390/ijerph110202092.
12. James W. The Ketogenic Diet : An Effective Medical. 2001:633-635.