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PRACA POGLĄDOWA
REVIEW

Use of low-carbohydrate diets in patients with type 2 diabetes

Rozważania na temat stosowania diety niskowęglowodanowej u chorych na cukrzycę typu 2

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ABSTRACT

The treatment of type 2 diabetes should be supported with a proper diet paired with physical activity at every stage of therapy. Carbohydrates are key macronutrients with a direct effect on the level of postprandial glycaemia. For the past several decades, dietary intervention studies investigating and comparing the effects of limiting carbohydrate intake in favour of other macronutrients have been carried out. A low-carbohydrate diet has been and still is suggested by some experts as well as patient organizations as the most effective option that is associated with the smallest risk of side effects. The recommendations, however, have not been supported with evidence from high quality randomized control trials. The aim of this work is to review the published meta-analyses of randomized control trials, which compared the parameters relevant for the treatment of diabetes, including fasting plasma glucose, glycated haemoglobin, the lipid profile and weight loss. Currently, there is insufficient scientific evidence allowing a uniform recommendation to be made regarding the optimum amount of carbohydrates in the daily diet, hence the relevant recommendations should be tailored to each patient. In dietary interventions among type 2 diabetes, lowering the patient's diet energy content is of primary importance, as well as the quality of ingested macronutrients, especially carbohydrates and fats.

KEY WORDS

diet, type 2 diabetes, glycaemia, carbohydrate, clinical recommendation

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STRESZCZENIE

Leczenie cukrzycy typu 2 na każdym etapie powinno być wspomagane odpowiednią dietą połączoną z aktywnością fizyczną. Kluczowym makroskładnikiem diety, mającym bezpośredni wpływ na wzrost glikemii po posiłku, są węglowodany. Od kilkudziesięciu lat badane są efekty interwencji dietetycznych polegających na ograniczeniu procentowego udziału węglowodanów w diecie na rzecz innych makroskładników. Dieta niskowęglowodanowa była i nadal jest sugerowana przez niektórych ekspertów oraz środowiska pacjentów jako najskuteczniejsza i niosąca najmniejsze ryzyko skutków ubocznych. Sugestie te nie są jednak poparte dowodami pochodzącymi z wysokiej jakości randomizowanych kontrolowanych badań klinicznych. Praca stanowi przegląd publikowanych w ostatnich latach metaanaliz randomizowanych kontrolowanych badań porównujących parametry mające znaczenie dla leczenia cukrzycy: glikemię na czczo, hemoglobinę glikowaną, lipidogram oraz redukcję masy ciała. Obecnie brak wystarczających dowodów naukowych do zalecania jednej, optymalnej ilości węglowodanów w diecie, wobec czego zalecenia te powinny być indywidualizowane. Większą rolę w podejmowanych interwencjach dietetycznych u chorych na cukrzycę typu 2 mają obniżenie całkowitej wartości energetycznej diety oraz jakość dostarczanych makroskładników, szczególnie węglowodanów i tłuszczów.

SŁOWA KLUCZOWE

dieta, cukrzyca typu 2, glikemia, węglowodany, zalecenia kliniczne

INTRODUCTION

Type 2 diabetes mellitus is a chronic disease that requires interdisciplinary medical care. The Polish Diabetes Association defines the primary aim of diabetic treatment as maintaining metabolic control by achieving target values of glycaemia, blood tension, lipid profile and optimal weight to minimize the risk of complications [1]. At every stage of therapy, a proper diet combined with physical activity are key. Much more than transient dietary restrictions are necessary, as the modification of nutrition patterns must be permanent. According to the standards of the Polish, European and American Diabetes Associations, dietary recommendations for type 2 diabetes patients should be individual, depending on the patient's metabolic goals, and making adjustments for their eating preferences, economic status, age, health status and level of physical activity. As it is frequently necessary for the patient to lose weight, the diet energy content and its distribution among given meals throughout the day is of primary importance. At the same time, the quality of the ingested macronutrients is also essential [1,2,3,4,5].

Carbohydrates are key macronutrients, with a direct effect on the level of postprandial glycaemia. For the past several decades, dietary intervention studies investigating and comparing the effects of limiting carbohydrate intake in favour of other macronutrients (*low-carbohydrate diet* – LCD) have been carried out. At the same time, as type 2 diabetes is frequently accompanied by overweight or obesity, the outcomes of high-carbohydrate diets (HCD), limiting the ratio of ingested fats, have also been examined. This particularly concerns Asian populations where rice is the staple, but also populations where nutrition is based on "Western" eating patterns, largely relying on cereal and potatoes. These studies, depending on the time and place where they are conducted, the parameters relevant for the treatment of diabetes, including fasting plasma glucose (FPG), glycated haemoglobin (HbA1c), the lipid profile and weight loss are measured and compared.

Carbohydrates: definition, nutrition standards and clinical recommendations regarding carbohydrate dietary requirement

According to nutrition science, the definition of carbohydrates as the primary source of energy in the human diet covers all types of carbohydrates, regardless of their nutrition or physiological properties, including polyols and food components such as organic acids, polyphenols and lignin. The term "sugars" is used in reference to mono- and disaccharides present in foods (e.g. glucose, fructose, sucrose). In terms of metabolism, carbohydrates are classified as glycaemic (digested and absorbed in the small intestine) and non--indigestible, which in their unaltered form serve as a substrate for the growth of the bacterial flora of the large intestine (cellulose), or facilitate passage to the large intestine (carbohydrates that compose dietary fibre) [6]. Advances in food processing have led to the formation of new compounds which are considered functional fibre, including the technologically altered polysaccharide, known as resistant starch. It is not found in nature, yet at high temperature and low humidity, through the changes occurring in the structure of starch particles, it loses its gelatinizing ability, and becomes resistant to digestive enzymes. As such, it is classified as insoluble dietary fibre [7]. From the physiological point of view, dietary fibre is defined as the remnants of ingested plants that are resistant to digestive enzymes, and thus are not absorbed in the small intestine. In chemical terms, the structure of dietary fibre is heterogeneous, yet for the purpose of measuring its content in foods, it is assumed to be made up of carbohydrate polymers [8].

Fibre contains two fractions, which have distinct physiological properties and functions, namely soluble and insoluble. Insoluble fibre increases the speed of intestinal transit, decreasing the absorption of digestible (glycaemic) carbohydrates and improving insulin sensitivity. Soluble fibre increases the viscosity and volume of intestinal content, thus leading to slower gastric emptying and decreasing the absorption of macronutrients. This limits and slows down the postprandial rise of the blood plasma glucose level. As these processes are accompanied by increased bile production, high fibre intake lowers low-density lipoprotein (LDL) cholesterol and the total cholesterol level [9].

The body derives energy directly from the glucose supplied with ingested carbohydrates. The majority of cells in the body are able to produce energy from fatty acids when glucose deficiency occurs. Only the cells of the CNS, erythrocytes and other cells dependent on anaerobic glycolysis, require the availability of glucose. When prolonged glucose deficiency occurs due to a diet providing less than 50 g of glucose per day, adaptive mechanisms are activated, involving the use of ketone bodies produced in the liver from fatty acids, and subsequently, the acquisition of glucose from proteins and triglycerides [6].

Various factors affect the metabolism of carbohydrates, e.g. the microflora of the GI tract and thus the possibility of fermenting carbohydrates. This is the case with starch (a polysaccharide that accounts for 80% of carbohydrate intake in the average diet), which, depending on the source of its origin, degree of its modification during food processing, and the microflora present in the GI tract of the person consuming it may be broken down and absorbed (digestible starch), or not (resistant starch – RS) [6].

Apart from their obvious impact on glucose and insulin blood levels, carbohydrates control hunger and satiation mechanisms and the metabolism of lipids. By influencing the intestinal microflora, they are also important for the function of the intestinal epithelium, the control of immunomodulatory processes and the absorption of vitamins and mineral nutrients [6].

The recommended dietary allowance (RDA) for minimum carbohydrate intake must take into account the energy needs of the brain, requiring on average 100 g of glucose per day. The European Food Safety Authority (EFSA) recommends a total carbohydrate intake providing 45–60% of energy in the diet as appropriate for normal glucose tolerance and sensitivity in healthy individuals and patients with symptoms of metabolic syndrome. The Polish Nutrition Standards recommend carbohydrate intake at 130 g per day for children over 1 year old, adolescents and adults, 175 g for pregnant women, and 210 g for breastfeeding women (for the initial 6 months of breastfeeding). It has also been recommended that carbohydrate intake expressed as a percentage of the total energy content of food should account for 50–70%, including 10–20% from sugars (mono- and disaccharides), and not more than 10% from added sugars (used to sweeten or process foods) [6].

As for diabetics, the Polish Diabetes Association recommends that carbohydrate intake should account for approximately 45% of the total energy content from food. For individuals with a high level of daily physical activity, it may be increased to 60%, provided that the carbohydrates eaten are fibre-dense (25–50 g per day or 15–25 g per 1000 kcal) and have a low glycaemic index (GI). A lower energy content from carbohydrates (20–45%) may be temporarily recommended in patients with comorbidities preventing physical activity. The source of carbohydrates should be wholegrain cereal, especially those with a low glycaemic index (< 55 IG). The use of simple carbohydrates should be reduced to a minimum, with the daily fructose intake not exceeding 50 g. Other sweeteners may be used, however, sugar should not be replaced with fructose. Products containing soluble fibre (such as pectin or beta-glucans) are particularly recommended. Currently, no sufficient scientific evidence is available that would permit making a uniform recommendation concerning the optimal daily allowance of carbohydrates in the diet, hence all such recommendations should be tailored to the patient's needs [1].

Low-carbohydrate diet: risks and benefits

A low-carbohydrate diet is considered one that supplies ≤ 45% of energy from carbohydrates or ≤ 130 g carbohydrates per day [10]. This type of diet may improve the blood glucose level, glycated haemoglobin, and facilitate lower doses of anti-diabetic medications [11]. Short-term studies have shown its weight loss potential and beneficial impact on patients' lipid profile [12,13]. There have also been reports of negative LCD outcomes, manifested by an increased risk of vitamin and mineral deficiencies and an insufficient fibre intake. When used long term, this diet may be associated with very high levels of protein which, in turn, raises the risk of renal dysfunction and the appearance of irregularities in the water and electrolyte balance [14]. The use of a low-carbohydrate and high-protein diet carries the risk of nephropathy, which should be taken into account when dealing with patients already at risk of kidney failure due to diabetes.

Despite the improved lipid profile parameters, other markers of atherosclerosis may deteriorate due to its use. High methylglyoxal levels forming under ketogenic conditions are considered a risk factor for vascular and other tissue damage, and are largely responsible for diabetic complications and the impairment of insulin action [15,16].

Low/very low intakes of carbohydrate food sources may impact the overall diet quality and the long-term effects of such drastic diet changes remain at present unknown. There is no data supporting long-term efficacy, safety and health benefits of low-carbohydrate diets [17].

A study by the Australian authors of [13], published in 2015, compared the effects of a very-low-carbohydrate, high fat (58%, including < 10% of saturated fats, the remaining part from polyunsaturated fats) diet (LCD) with 28% energy from proteins with the effects of a high-carbohydrate diet (HCD) (53% of energy from carbohydrates, 17% from protein and 30% from saturated fats). This randomized control trial was conducted among a total of 115 obese patients with type 2 diabetes, aged 58 ± 7 years old, duration of diabetes: 6–8 years, BMI 34.6 ± 4.3 kg/m^2 and HbA1c: 7.3 ± 1.1%. The patient groups were block-matched for age, sex, BMI, HbA1c and anti-diabetic medication, with computer-generated assignments to either LCD or HCD in a 1:1 ratio (LCD n = 57, HCD n = 58), and the outcomes were evaluated at 24 and 52 weeks. The diet was combined with a supervised aerobic exercise activity programme (60 min; 3 d/wk). After 1 year, a total of 68% of patients completed the study (LCD n = 41, HCD n = 37). In both compared groups, similar outcomes were achieved in terms of weight loss (LCD mean -9.8 kg, HCD -10.1 kg; $p \geq 0.09$), reduction of blood pressure (LCD -7.1/-6.2 mm Hg, HCD -5.8/-6.4 mm Hg; $p \geq 0.3$), reduction of HbA1c in both groups by 1% ($p \geq 0.10$), lower fasting glucose (LCD -0.7 mmol/L vs HCD -1.5 mmol/L; $p \geq 0.10$) and lower LDL cholesterol (LCD -0.1 mmol/L vs HCD -0.2 mmol/L; $p = 0.8$). The LCH group achieved greater reductions in diabetes medication requirements, blood glucose stability (assessed by measuring the continuous overall net glycaemic action-1) and a slight increase in HDL cholesterol at a simultaneous reduction in the triglyceride level. Thus, both diet plans proved effective in terms of weight loss, HbA1c reduction and a decrease in the fasting glucose level, whilst a low-carbohydrate, high-unsaturated fat diet led to blood glucose stability, modified treatment (reduced medication doses) and an improved lipid profile.

Due to its effectiveness, confirmed by multiple studies, a low-carbohydrate diet has been suggested by some experts [18] as well as patient organizations [19] as the optimal choice for the management of type 2 diabetes, one that is associated with the smallest risk of side effects. The recommendations, however, have not been backed with evidence from high quality randomized control trials (RCT), and the published studies tend to be short-term and vary in methodology (especially concerning the quantitative and qualitative content of the carbohydrates, fats and proteins used in the compared diets).

In 2016, the British *Diabetic Medicine* journal published a review of studies based on a predefined set of criteria, not finding any evidence that would support the superiority of LCD over HCD in the management of type 2 diabetes [20]. Out of 153 studies covered by 9 meta-analyses, only 12 studies met the inclusion criteria. The following inclusion criteria were applied: randomised control trials ≥ 4 weeks in patients aged > 18 years old with type 2 diabetes, a carbohydrate intake ≤ 45% of total daily energy intake per day, and a dietary intake assessment at the end of the study. No significant differences were found between the compared low- and high-carbohydrate diets in terms of glycaemia control and other metabolic markers. Weight loss due to LCD was greater in only one study. Based on this review which applied consistent criteria, it was determined that the total energy intake remains the primary dietary predictor of weight loss, regardless of the proportion of carbohydrate intake.

The latest available meta-analysis, published in early 2017, and serving as a basis for clinical recommendations for type 2 diabetes patients in Denmark, utilized the GRADE system (Grading of Recommendations Assessment, Development and Evaluation) [21]. It was geared towards identifying the impact of further restricting carbohydrate intake (< 45%) in a low-carbohydrate diet compared to the diet typically recommended to patients suffering from type 2 diabetes (45––60% of energy from carbohydrates). The primary endpoints in the analysis were: glycaemia control expressed as HbA1c rate and BMI after a minimum of 1-year of observation. Secondary end-points included HbA1c and BMI prior to the completion of a 1-year observation, as well as LDL cholesterol, quality of life and the rate of participants leaving the trial prior to its completion. Where BMI was not measured in a given trial, the patients' weight was used in the analysis.

Out of 692 randomized control trials, 12 were analyzed, covering a total of 1376 patients with type 2 diabetes (49% male and 51% female, mean age: 58 years old). The results of the meta-analysis have shown that low- and moderate-carbohydrate diets (LCD) compared with high-carbohydrate diets had the same effect on the patients' BMI and weight, both in short and long-term studies. A reduction in the waist girth, which represents visceral obesity (despite not being included in the inclusion criteria, it was evaluated in 6 of the studies covered by the meta-analysis), was found to be the same in both groups (LCD and HCD). The improvement in the HbA1c level after 1 year and longer was similar in both groups. The favourable effect on glycaemia increased with the reported reduction in carbohydrate intake. The largest reduction in the HbA1c level was achieved in two studies with the lowest daily carbohydrate intake, 57 and 58 g per day respectively [11,22]. Whether the dietary energy requirement was met through the supply of fats or proteins proved non-significant for the achieved outcome. The use of LCD facilitated a greater reduction in medication doses as compared with HCD at 3, 6 and 12 months [11,22,23,24,25,26,27]. One study found symptoms of hypoglycaemia in 3 participants following LCD [26].

The results of some studies covered by this meta-analysis suggest that the decreasing beneficial effect of LCD with time may be linked to the difficulties in adhering to the diet as well as the gradually changing intestinal microflora due to the decreased carbohydrate intake. The meta-analysis did not confirm any significant differences in the effect of the evaluated diets on LDL cholesterol [21]. The diets had a comparable effect on BMI and weight, both in short and long-term observation. The quality of life measured by means of the SF-36 survey showed a tendency for a worsening physical component score in the participants following LCD, whilst no differences were found as regards the mental component score. In the studies with a long-term observation period, the LCD groups had a larger drop-out rate. The rates differed significantly across studies, ranging from 2–60% in the LCD groups and from 2–46% in the HCD groups [21].

Macronutrient quality: the significance for metabolic parameters

One of the important trends in nutritional medicine is a shift in perspective, no longer perceiving a diet as a formula for normalizing macronutrient distribution. Even though digestible carbohydrates increase postprandial glycaemia, hyperinsulinemia, the triglyceride level and lower HDL cholesterol, many authors have been focused not on the amounts but the quality of the ingested carbohydrates and fats to minimize the risk of cardiovascular diseases [27]. In a meta-analysis of 13 randomized clinical trials lasting ≥ 18 months, covering a total of 605 type 2 diabetes patients, a beneficial impact of increased fibre intake on controlling glycaemia was demonstrated [28]. Diets that supplied 37.5–42.5 g of soluble fibre or were supplemented with 3.5–15 g of soluble fibre led to an absolute decrease in the HbA1c level of 0.55% (range: -0.96 to -0.13) and in FPG of 9.97 mg/dL (-18.16 to -1.78).

The results were achieved in patients following a diet of 2000 kcal/day. Another positive aspect of a fibre-rich diet is its good tolerance by patients. The high fibre content increases satiety and does not require portion size reduction. Observational studies and intervention trials studies on vegetarian and vegan diets in patients with type 2 diabetes have shown their benefits in terms of improving control of body weight and glycaemia and minimizing the risk for cardiovascular diseases, provided they are carefully planned and conformed to [29].

The glycaemic index (GI) of foods containing carbohydrates, and in a broader perspective, their glycaemic load (GL), which takes account of the GI of a food and the amount eaten, are concepts applied to manage postprandial glycaemia. Despite the improvements achieved in patients with type 2 diabetes in short-term studies, the long-term role and usefulness of low GL diets remain unclear [30]. It is important to bear in mind the limitations of this concept, resulting from the various, non-standardised methods of measuring the glycaemic index of given foods and their different properties depending on inter-individual variation, health status and sex of the patients suffering from type 2 diabetes [31].

A high-fibre diet may confer a beneficial effect on patients by prolonging the sense of satiety and reducing the energy density of food compared with a low-carbohydrate, high-fat diet. The energy density of fatty foods is over two times higher than that of carbohydrates and proteins. High-fat foods are tasty whilst having a relatively low satiating capacity. They have also been suggested to cause passive overconsumption known as hyperphagia [32]. Limiting the fat content of a diet without reducing the total energy intake may result in weight loss in an overweight persons [33].

Some studies have suggested that the increase in triglyceride level accompanying HCD is solely caused by simple sugars present in this type of diet and the quality of ingested fats, not carbohydrates as such [34,35]. The intake of fructose may play a special role in this mechanism, which, apart from natural sources, is largely supplied with refined sugar, syrups (which are commonly used by the food processing industry) and with sweetened drinks. Even though fructose is also a simple sugar, its metabolism essentially differs from the metabolism of glucose. It is absorbed from the GI tract to a lesser degree, and owing to a transport system independent from insulin, it is not utilized for fuel cells. As it is mostly metabolised in the liver, it replaces glucose in the production of glycogen. This may explain the increase in triglyceride levels (particularly at night), the stimulation of de novo lipogenesis, and the increase in visceral fat found in some studies in relation to fructose intake [36].

CONCLUSIONS

Numerous studies evaluating the usefulness of a low-carbohydrate diet to improve the primary metabolic parameters of type 2 diabetes and its impact on the risk of cardiovascular diseases have failed to arrive at unequivocal conclusions. A major problem of the clinical trials examining the efficiency of LCD are the discrepancies in the applied methodology and the resulting difficulties in formulating general conclusions. Currently, there is no sufficient scientific evidence allowing a uniform recommendation to be made as regards the optimum amount of carbohydrates in the daily diet, hence the relevant recommendations should be tailored to each patient [1].

For successful dietary interventions in type 2 diabetes, it is crucial to reduce the total energy value of daily food intake and improve the quality of the ingested macronutrients. The role of physical activity is also essential when attempting to achieve an improved energy balance and amelioration of metabolic anomalies, even though in overweight and obese individuals it may be limited by their overall fitness and the existing comorbidities. The dietary recommendations highlight the need to restrict the intake of simple and added sugars, as well as saturated fat, especially trans fatty acid isomers found in highly processed foods. A well-balanced diet providing the necessary vitamins and micronutrients is a must. It is also important to avoid smoking and limit alcohol intake. Dietary education should particularly emphasise the need for self-restraint and long-term modification of eating patterns. Implementing a lifestyle facilitating the management of diabetes is a long-term process, frequently requiring psychological counselling, one that is strongly correlated with the patient's level of awareness and their commitment to the entire treatment process [1].

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Author's contribution

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